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Contents

Editorial

Malaysia Collaborates with the New York Academy of Sciences to Develop an Innovation-Based Economy in Malaysia
Michel Wahome, Ellis Rubinstein

Review Article

Disorders of Sex Development:
Diagnostic Approaches and
Management Options—An Islamic
Perspective
Nasir AM AL JURAYYAN

Original Article

- In Silico Identification of Drug Targets for Antifertility from Natural Products by Differential Reaction Content Analysis of Metabolic Pathways Shriddha Shukla, Savita Dixit
- Spasmogenic Activity of the Seed of Terminalia chebula Retz in Rat Small Intestine: In Vivo and In Vitro Studies Seyyed Ali Mard, Ali Veisi, Mohammad Kazem Gharib Naseri, Peyman Mikaili
- Identification of Major and Minor
 Allergens of Black Tiger Prawn
 (Penaeus monodon) and King Prawn
 (Penaeus latisulcatus)

Syuhaidah Sahabudin, Rosmilah Misnan, Zailatul Hani Mohammad Yadzir, Jamaludin Mohamad, Noormalin Abdullah, Faizal Bakhtiar, Shahnaz Murad

The Relationship between Media
Use and Body Mass Index among
Secondary Students in Kuching South
City, Sarawak, Malaysia
Whye Lian Cheah, Ching Thon Chang, Saimon
Rosalia, Lai Dekun Charles, Sze Lin Yii, Pik
Hoong Tiong, Kim Pey Yeap

- A Comparison Study of Conjunctiva
 Disorders in Technical and
 Administrative Sawmill Workers in
 Nigeria
 Itiyafa Njinaka, Odarosa M Uhumwangho,
 Omolabake T Edema, Oseluese A Dawodu,
 Afekhide E Omoti
- The Socio-demographic and Clinical Factors Associated with Quality of Life among Patients with Haematological Cancer in a Large Government Hospital in Malaysia

 Das Priscilla, Awang Hamidin, Md Zain Azhar, Kon Noorjan, Md Said Salmiah, Khalid Bahariah
- Stress and Coping Strategies of Students in a Medical Faculty in Malaysia Sami Abdo Radman AL-Dubai, Redhwan Ahmed AL-Naggar, Mustafa Ahmed Alshagga, Krishna Gopal Rampal

Special Communication

Towards the Prevention and Management of Prostatic Diseases in Nigeria: A Framework
Chukwunonso ECC EJIKE

Case Report

- Wernicke's Encephalopathy in a Patient with Nasopharyngeal Carcinoma: Magnetic Resonance Imaging Findings Huong Ling Law, Suzet Tan, Rosleena Sedi
- A Case of Isolated Laryngeal
 Candidiasis Mimicking Laryngeal
 Carcinoma in an Immunocompetent
 Individual
 Arun R Nam Jagdish Charungent Maniple

Arun B Nair, Jagdish Chaturvedi, Manjula Battlahalli Venkatasubbareddy, Majorie Correa, Nandakumar Rajan, Anisha Sawkar

- An Unusual Case of Amoebic Liver
 Abscess Presenting with Hepatic
 Encephalopathy:
 A Case Report
 Anil Kumar Sarda, Rakesh Mittal
- A Case Report of Atypical Teratoid/ Rhabdoid Tumour in a 9-Year-Old Girl Kin Hup Chan, Mohammed Saffari Mohammed Haspani, Yew Chin Tan, Fauziah Kassim

Abstracts

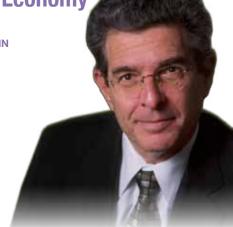
- Abstracts of Theses Approved for the MMed at the School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia
- Abstracts of Theses Approved for the MSc and PhD at the School of Health Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia
- Abstracts of Theses Approved for the MSc at the School of Dental Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia
- Abstracts of Theses Approved for the MSc at the Institute for Research in Molecular Medicine (INFORMM) Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia
- 183 Guideline for Authors
- 186 Authorship Agreement Form
- 187 Patient Consent Form
- Copyright Transfer Form
- 190 Subscription Form



Malaysia Collaborates with the New York Academy of Sciences to Develop an Innovation-Based Economy

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Abstract

If Malaysia is to become a high-income country by 2020, it will have to transform into a knowledge-based, innovation economy. This goal will be achieved by developing an atmosphere conducive to experimentation and entrepreneurship at home; while reaching out to partners across the globe. One of Malaysia's newest partnerships is with the New York Academy of Sciences. The Academy has expertise in innovation and higher education and a long history of promoting science, education, and science-based solutions through a global network of scientists, industry-leaders, and policy-makers. Malaysia's Prime Minister, Dato' Sri Mohd Najib Tun Abdul Razak, leveraged the Academy's network to convene a science, technology, and innovation advisory council. This council would provide practical guidance to establish Malaysia as an innovation-based economy. Three initial focus areas, namely palm-oil biomass utilisation, establishment of smart communities, and capacity building in science and engineering, were established to meet short-term and long-term targets.

Keywords: economic development, international cooperation, knowledge, Malaysia, science, technology, United States

On 17 May 2011 at the offices of the New York Academy of Science (NYAS) in Downtown Manhattan, the Prime Minister, Dato' Sri Mohd Najib Tun Abdul Razak, chaired the inaugural consultative meeting of the Global Science and Innovation Advisory Council (GSIAC). The council had been convened with the express purpose of catalysing international partnerships and providing practical advice on how to realise the goal of raising Malaysia's economic status to that of an industrialised nation, as articulated in Vision 2020 (1).

In order to accomplish this goal of graduating from a middle-income to a high-income economy, Malaysia will have to double its per capita income to USD15 000 in less than 9 years (2). The country's Vision 2020, as articulated in 1991 by the former Prime Minister, Tun Dr Mahathir Mohamad, as well as the more recent New Economic Model and the Tenth Malaysia Plan

identify science, technology, and innovation (STI) as critical to Malaysia's prosperity and increased global competitiveness. Malaysia's development strategies demonstrate an acknowledgement that global partnerships and a sophisticated knowledge of international markets are also fundamental to achieving industrialised nation status.

The Malaysian government has embarked on a strategic partnership with NYAS to help build the country's capacity in STI. It was after becoming familiar with the Academy's work in innovation and economic development for Mexico and Russia that the Prime Minister, Dato' Sri Mohd Najib Tun Abdul Razak, through the Office of the Science Advisor, expressed an interest in obtaining an international perspective on the fundamental components of STI-based development. In an article in the New Straits Times, Professor Emeritus Dato' Dr Zakri Abdul Hamid, the Science Advisor to the Prime Minister,

elaborated on the government's interest in the Academy. He explained that "the governmentacademia-corporate nexus that is the raison d'être of the NYAS makes it a natural choice to advise us on how to improve our approaches in achieving the New Economic Model, in particular the role of the private sector" (3). Furthermore, the Prime Minister had recognised parallels between his Global Movement of the Moderates initiative and the Academy's STI initiative for the Islamic world. In brief, NYAS, together with the United Nations Educational, Scientific and Cultural Organization (UNESCO), Islamic Educational, Scientific and Cultural Organization (ISESCO), and member countries of the Islamic Conference, is seeking to mentor young researchers at science and technology centres of excellence across the Islamic world.

The Prime Minister's interest in our Academy is emblematic of a yearning we increasingly encounter across academic, industry, and government sectors to establish multilateral partnerships to increase the impact of their strategic initiatives. The challenges and opportunities of our globalised world are so complex that only multi-stakeholder efforts are seen as robust enough to achieve our common objectives.

The Academy has a long history of fostering discussion and collaborative action by multiple actors. Established in 1817 as a scientific society, our membership has always been international and included prominent people from various walks of life—scientists from various disciplines, as well as business-leaders and policy-makers. Our programmes continue to evolve to reflect changing times, while serving our three mandates: to advance scientific research and knowledge, support scientific literacy, and promote the resolution of society's global challenges through science-based solutions. Our main tool is our ability to bring stakeholders together and create partnerships that bring about results in key areas. For example, in 1946, we held the first global conference on antibiotics. In 1983, we convened first global conference on immunodeficiency syndrome (AIDS), and in 2003, at the height of the severe acute respiratory syndrome crisis (SARS), we brought together, for the first time, experts in that area. In these cases, and others, we publish the proceedings of important scientific meetings and make them widely available. Some of our main dissemination channels include the journal, Annals of the New York Academy of Sciences, as well as our online e-Briefings.

GSIAC is the first product of Malaysia's strategic partnership with the Academy. Together with our Malaysian counterparts at the Malaysian Industry-Government Group for High Technology (MIGHT), we set about identifying experts in the Academy's network who were well-versed in innovation, entrepreneurship, and education. The GSIAC comprises 35 members: 10 from Malaysia and 25 international members from China, India, Russia, Japan, Korea, the Netherlands, the United Kingdom, and the United States of America. This accomplished group of experts was convened to distil the knowledge and expertise of its esteemed members into tangible and feasible projects that could step up Malaysia's performance in STI and translate that performance into economic growth.

Innovation-based economies are creative and dynamic. Since they continuously generate novel concepts and technologies, they avoid the obsolescence and stagnation faced by countries that rely on revenues from commodities or manufacturing. The 2020 target necessitates the timely development of the requisite ecosystem that will nurture a creative entrepreneurial innovationculture. A method to catalyse this process is connect to pre-existing knowledge centres around the world, thus, ensuring that Malaysia becomes a node in the global innovation network. Forming connections and strategic partnerships is duly part of Malaysia's STI strategy, and since it is part of the Academy's historic mandate, our alliance in fitting.

The product of Malaysia-NYAS collaborative efforts, including the 17 May GSIAC meeting, is the identification of three initial focus areas.

Palm oil

The palm oil industry is a sector in which Malaysia enjoys a significant comparative advantage. It follows that this is an area that offers opportunities for quick wins. Substituting palm oil in sectors that currently utilise petroleum-based products is one way to achieve the Prime Minister's Green Future objective. Palm Oil biomass can be diverted for use in energy generation as well as a raw material for the manufacture of various biochemicals.

Smart cities and smart villages

With billions of people expected to live in urban areas in coming decades, several countries are enganged transforming their urban centres into green, smart cities, where necessities like water, power, traffic, and communications are managed in a highly efficient way with sophisticated technological infrastructure.

Applying information technology to targeted municipal issues such as learning, health, and energy conservation will help Malaysia become a centre of excellence with distinct technical competencies that can then be exported to other emerging markets.

While a handful of smart cities are under creation elsewhere—mostly in highly-developed countries—Malaysia's Smart Village pilot project is a first in the region. The goal will be to apply information technology solutions to community challenges, where applicable.

Capacity building

In the long-term, Malaysia's success is likely to hinge on its ability to produce and retain a talented, skilled, and creative workforce, one that is particularly well grounded in science, engineering, and technical vocations. Recent reports by the World Bank revealed a general consensus among business people that Malaysia was falling behind in terms of producing a skilled and entrepreneurial workforce; furthermore, there has been a significant brain drain that is desiccating the talent pool (4).

The Academy's envisioned role includes taking stock of Malaysia's research and development assets, assisting the national government with creating and administering programs to promote mentoring and entrepreneurship, sharing best practices for post-secondary education reform, coordinating research strengths and education competencies among campuses, and creating university—industry research partnerships.

As 2020 fast approaches, Malaysia will have to step up its admirable economic achievements and double its economic growth in 9 years. Partnerships with global thought leaders could create a uniquely Malaysian innovation system that will serve as the engine for exponential economic growth. NYAS's intention has always been to ensure that science continues to be an instrument for prosperity and improvements in quality of life. Our continued interaction with Malaysia builds upon our long history of using science to create positive impact around the globe. We hope to contribute to Malaysia's fulfilment of Vision 2020 and sustaining that growth by building upon established strengths, creative problemsolving, and encouraging experimentation and entrepreneurship in its talents pool. Thereby, Malaysia can be an exemplar for emerging and developing economies around the world.

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Review Article

Disorders of Sex Development: Diagnostic Approaches and Management Options—An Islamic Perspective

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Abstract -

Ambiguous genitalia, currently defined as disorders of sex development (DSD), are not uncommon in the Muslim community. DSD constitute a complex, major social and medical emergency, as several forms of congenital adrenal hyperplasia can lead to significant salt loss, which may lead to shock if unrecognised and not appropriately treated. To ensure that the affected individual has a high quality of life (a successful outcome), medical practitioners must quickly and correctly assign the individual's gender and effectively assuage the family's concerns and anxieties. It is important to review and understand the embryology and physiology of sexual differentiation, and to understand the various aetiological causes of sexual ambiguity. In this review, the diagnostic approach and management of ambiguous genitalia is thoroughly discussed from an Islamic point of view.

Keywords: birth defects, case management, diagnosis, genitalia, Islam, sex development disorders

Introduction

Ambiguous genitalia, currently defined as disorders of sex development (DSD), constitute a complex, major social and medical emergency. Several forms of congenital adrenal hyperplasia can lead to significant salt loss, which, if unrecognised and not appropriately treated, may lead to shock. To ensure that the affected individual has a high quality of life (a successful outcome), medical practitioners must quickly and correctly assign the individual's gender and effectively assuage the family's concerns and anxieties (1-4). When approaching the treatment of any child diagnosed with sexual ambiguity, it is important to first review and understand the embryology and physiology of sexual differentiation. Although the basic developmental events have long been known, the genetic, biochemical, endocrine, and molecular mechanisms are complex and have only been partially elucidated (5-9).

The H–Y antigen, a minor male-specific histocompatibility antigen located on the long arm of the Y chromosome, was widely believed to be the primary testis-inducer. However, recent studies have implicated several genes on the short arm of the Y chromosome, including the gene known as sex-determining region Y (*SRY*), in the development of the testis and in the determination of male gender (10–12). The gene for the antimüllerian hormone (AMH) has been elucidated,

and a reliable assay for its measurement has been developed (13–15). The gene that codes for the androgen receptor has also been identified, furthering our understanding of complete and partial androgen-resistance syndromes (16). In addition, the genetic marker that results in 5- α -reductase deficiency has recently been identified (17), and this discovery extends our understanding of the actions of testosterone and dihydrotestosterone (DHT). Another important research project shows that the female pathway is not simply a default pathway and that several genes actively regulate female development (18).

The processes of sex determination and differentiation proceed in sequence, as shown in Figure 1. Genetically, sex is determined at fertilisation, by the contribution of a Y or an X chromosome from the sperm; this contribution determines the differentiation of the primordial gonads. Thus, the presence or absence of a Y chromosome, with its testis-determining factor, primarily determines the course of sexual differentiation. This differentiation is visible by the 4th week of gestation; the XY karyotype is normally associated with male differentiation, and the XX karyotype is normally associated with female development. Complete female sexual differentiation occurs in the absence of the male determinant, but female differentiation probably regulated by a specific genetic pathway that originates on the long arm of the X chromosome.

The presence of a single Y chromosome, even in the presence of more than one X chromosome. is sufficient to cause the development of a testis. Testicular differentiation to produce functional Leydig and Sertoli cells occurs by the 7th week of gestation and is a rapid phenomenon. This rapid differentiation contrasts with the slower development of the ovaries in the 20th week of gestation. At 7th week, the Sertoli cells are actively secreting AMH and Leydig cells are secreting testosterone, and this secretion is controlled by placental human chorionic gonadotrophin (hCG). Thereafter, the foetal pituitary gland controls testicular function in the 2nd and 3rd trimesters. Undifferentiated embryos possess 2 internal duct systems, müllerian (paramesonephric) ducts and wolffian (mesonephric) ducts, but the differentiation of the internal and external genitalia is essentially complete by the end of the 1st trimester. The presence of testosterone and AMH protects the genetically male foetus from inadvertent feminisation (4-19).

Locally secreted testosterone promotes the development of the ipsilateral wolffian duct into the epididymis, vas deferens, ejaculatory duct, and seminal vesicle. Testosterone production by 1 testis has no effect on the wolffian duct development on the opposite side. AMH produced by the Sertoli cells causes regression of the ipsilateral müllerian duct. Similar to the local control of the wolffian duct, müllerian duct regression is dependent

on the local secretion of AMH and unaffected by AMH secretion from the contralateral testis (4,20,21). Thus, differences in the secretion of testosterone or AMH by the 2 gonads can result in the presence of male internal ducts on 1 side and female structures on the other side. As male internal duct differentiation requires high local concentrations of testosterone, a virilised female with ovaries still has normal female internal structures (4,21). Exposure of female foetuses to androgen in early gestation, before 12th week, can lead to variable degrees of virilisation (Prader's classification), as shown in Table 1; however, labioscrotal fusion cannot be achieved after 12th week (21,22).

The lack of AMH, as well as insensitivity to AMH, is known to yield persistent müllerian duct syndrome. A recent study reports that males with a 46,XY karyotype can be characterised by the presence of Fallopian tubes and a uterus; the external genitalia of these XY individuals are male, and testicular function is otherwise normal (21).

Traditionally, the appearance of the external genitalia indicates the appropriate gender assignment. Male development depends on adequate testosterone secretion, peripheral metabolism of testosterone to dihydrotestosterone (DHT), and peripheral tissue response to androgens. Male external genitalia differentiate in response to DHT, which is formed in genital skin

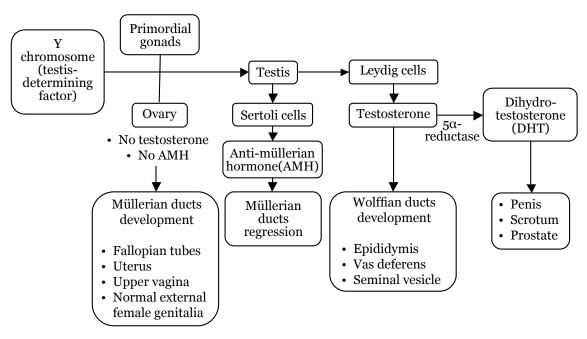


Figure 1: Simplified model for sexual differentiation and the development of internal and external genitalia.

Table 1: Degree of virilisation of the external genitalia according to Prader's classification (23)

Classification	Characteristics
Type 1 (P-1)	Clitoral hypertrophy
Type 2 (P-2)	Clitoral hypertrophy, urethral and vaginal orifices present, but very
	near
Type 3 (P-3)	Clitoral hypertrophy, single urogenital orifice, posterior fusion of the
	labia majora
Type 4 (P-4)	Penile clitoris, perioneoscrotal hypospadias, complete fusion of the
	labia majora
Type 5 (P-5)	Complete masculinisation (normal-looking male genitalia) but no
	palpable testes

and other sensitive structures by the metabolism of testosterone by the 5- α -reductase enzyme. The presence of DHT induces the elongation of the genital tubercle, fusion of the genital folds to form the penis, fusion of the labioscrotal folds to form the scrotum, and the formation of the prostate. The response of these structures to DHT requires the presence of a normal intracellular androgen receptor (16,17,23-30). The formation of the male external genitalia is complete by the end of the 1st trimester. After the 1st trimester, further development consists only of growth of the penis and the descent of the testes into the scrotum. Both of these developments depend on the levels of foetal pituitary gonadotrophin (31). In the normal female, the external genitalia do not differentiate into male-specific anatomy; the genital tubercle remains small and becomes the clitoris, and the genital and labioscrotal folds remain unfused to form the labia minora and labia majora, respectively (32).

Diagnostic approach and management

It is important to understand the physiology and embryology of sex-determination and sexual differentiation, but it is also essential to know the different causes of DSD; these causes are shown in Table 2 (1-4,33,37). Most patients are known to have either 46,XX DSD or 46,XY DSD conditions. In 46,XX DSD individuals (previously female-pseudohermaphrodites), normal ovaries and internal female organs are present; however, there are variable degrees of virilisation of the external genitalia among different individuals. Congenital adrenal hyperplasia, due to a deficiency in the 21α-hydroxylase enzyme or due to deficiencies in the 11β-hydroxylase and 3β-hydroxysteroid dehydrogenase enzymes, constitutes the majority of DSD

(Figure 2). Congenital adrenal hyperplasia is not an uncommon autosomal recessive condition; it is prevalent in the Arab population due to a high rate of consanguineous matings (38–41). Saedi-Wong et al. (41) reported a high prevalence of congenital adrenal hyperplasia (54.3%) among the Saudi Arabian population. However, 46,XY DSD individuals (previously known as male pseudohermaphrodites) develop normal testes but with incomplete virilisation(undermasculinised external male genitalia, as shown in Figures 3, 4, and 5) due to a variety of causes.

Only a small portion of patients have genital ambiguities extensive enough to make the determination of sex-of-rearing difficult. Ovotesticular DSD individuals (previously known as true hermaphrodites) are rare; both testicular and ovarian tissues are present in these individuals. The most common karyotypes in ovotesticular DSD cases is 46,XX, but karyotypes of 46,XY or 46,XX/46,XY can also lead to ovotesticular DSD. The appearance of the internal and external genitalia is variable in individuals with ovotesticular DSD, and the assignment of sex for ovodesticular DSD cases usually depends on the amount of functional testicular tissue. Other disorders of gonadal differentiation, such as pure or mixed-gonadal dysgenesia or testicular regression, should be considered potential causes of ambiguous genitalia, and the presence or absence of these gonadal disorders should be investigated at the time of diagnosis. The diagnosis of ambiguous genitalia can be made only by laparoscopy or by a combination of laparotomy and a histological examination of the gonads (4,42). Ambiguous genitalia in genetic males may be comprised of multiple malformation syndromes, such as Smith-Lemli-Opitz, Vater, and Meckel's syndromes (43,44).

Table 2: Major causes of disorders of sex development (DSD) according to karyotype

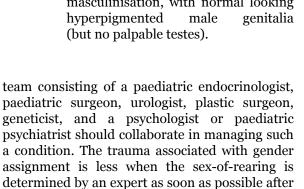
46,XX Karyotype	e	
46,XX DSD	Ovarian/adrenal tumours (mother-child) Exposure to exogenous medication (synthetic	 Enzyme deficiency 21α-hydroxylase 11β-hydroxylase 3β-hydroxysteroid dehydrogenase
	progestin preparation)	
Ovotesticular DSD	r Gerr r rr	
46,XY Karyotype	2	
46,XY DSD	testosterone	 Testicular differentiation pure gonadal dysgenesis absence of Leydig cells or luteinising hormone receptor testicular regression gonadotrophin hormone deficiency Enzyme deficiency in testosterone pathway 20,22-desmolase 17,20-lyase 3β-hydroxysteroid dehydrogenase 17α-ketoreductase
•	Lack of synthesis of dihydrotestosteroneEnd-organ-unresponsiveness (resistance)	 5α-reductase deficiency Partial Complete
Ovotesticular DSD		-
Multiple or local cor Mixed Karyotype	_	
Ovotesticular DSD 4		
Mixed gonadal dysg		

Thus, the presence of other morphogenic anomalies usually indicates a non-endocrine explanation for the abnormal appearance of the genitalia (4). Furthermore, local ano-rectal and uro-genital anomalies such as epispdius and bladder extrophy are known to be associated with external genital ambiguity (4,43–45).

The initial assessment of a DSD patient requires a detailed maternal and family history, as well as a careful physical examination for symptoms including hyperpigmentation and signs of salt-wasting; the initial assessment should also provide documentation of the existing external genitalia (1,3,4,33–37). Proper genital examination at birth and before declaring the sex of a child is always encouraged to prevent the trauma of sex reassignment later in life. Children with ambiguous genitalia should be transferred immediately to a facility where specialised physicians are available. A multidisciplinary



Figure 2: Ambiguous genitalia in a 46,XX patient known to have congenital adrenal hyperplasia due to 21α-hydroxylase deficiency. Note the complete masculinisation, with normal looking hyperpigmented male genitalia (but no palpable testes).



birth as opposed to the experience of a gender

re-assignment later in life.

The issue should be discussed clearly and openly, and parents need to understand immediately that their child's genitalia are abnormal but can be corrected by surgery, and that the sex-of-rearing will be either a male or female, but this decision requires reasonable time for investigation. The announcement of the baby's sex should be deferred until supportive data are available. The embryology of sexual differentiation should be reviewed at a level that allows the parents to understand the issue at hand. Also, parents should understand that virilisation is reflective of the magnitude of androgen stimulation during foetal development, and is not necessarily indicative of the most appropriate sex-of-rearing. Establishing the



Figure 3: Ambiguous genitalia in a 46,XY patient known to have congenital adrenal hyperplasia due to 3β-hydroxysteroid dehydrogenase deficiency. Note the pigmented, short, curved phallus, central urogenital slit, and separated labioscrotal testis.

genetic sex (karyotype) should be the first step, coupled with determining the anatomical status of the internal organs. Further specific hormonal investigations and therapeutic trials need to be undertaken to specify the cause of the anomaly and, hence, the appropriate therapy (3,4,33,46). A paediatric radiologist plays a significant role in elucidating the existing anatomy. Real-time pelvic ultrasonography (US) is not invasive, and this technique remains the modality of choice for such screening; however, US (Figures 6) performed in conjunction with genitography (Figure 7), which reveals further details of the vaginal structures, is far more informative than US alone (47). Magnetic resonance imaging (MRI) is helpful in cases where US and US/genitography examinations are inconclusive (48). Pelvic laparotomy or laparoscopy and gonadal biopsy are rarely needed.

The current Islamic recommendations put forward by the senior Ulama Council in Saudi Arabia as well as the experiences of local medical practitioners (3,4,46,49) yield a set of very useful general guidelines. These recommendations are translated as follows:



Figure 4: Ambiguous genitalia in a 46,XY patient known to have partial androgen insensitivity. Note the micropenis, urogenital sinus, and labioscrotal folds (the left fold contains a palpable gonad).



Figure 5: Ambiguous genitalia in a 46,XY patient known to have gonadotrophin hormone deficiency. Note the micropenis, underdeveloped scrotum, and bilateral undescended testes

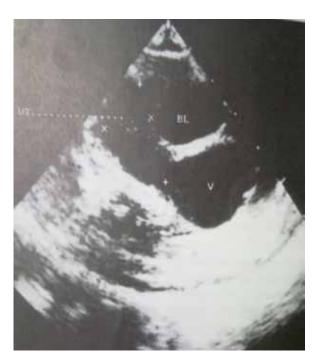


Figure 6: Ultrasound of the sagittal pelvis showing the bladder (BL) from an anterior view, uterus (UT) from a postero-superior view, and vagina (V) from a postero-inferior view.



Figure 7: A genitogram showing contrast material filling the bladder (BL), vagina (V), and uterus (arrow).

- A sex-change operation (i.e., converting someone with a completely developed gender to the opposite sex) is totally prohibited, and it is even considered criminal in accordance with the Holy Quran and the Prophet's sayings.
- 2) Those who have both male and female organs require further investigation, and if the evidence is more suggestive of a male gender, then it is permissible to treat the individual medically (by hormones or surgery) to eliminate his ambiguity and to raise him as a male. If the evidence is suggestive of a female gender, then it is permissible to treat her medically (by hormones or surgery) to eliminate her ambiguity and to raise her as a female.
- 3) Physicians must explain the results of medical investigations to the child's guardians and whether the evidence indicates that the child is male or female so that guardians are well-informed.

Therefore. genetically female children (46,XX karyotype) with normal ovaries and internal female organs (uterus, fallopian tubes, and upper vagina), but with some variable degree of virilisation of the external genitalia, should be raised as females; this decision is not only due to the ease of reconstruction of the female genitalia (50-52), but also due to the ability of these females to have high fertility rates and to bear children later in life (53). Any gender-reassignment surgery should generally be performed before 2 years of age, i.e., before the child develops gender-awareness. The techniques used for clitoral recession and vaginoplasty are continually improving. In contrast, a child with a sexual ambiguity and an XY chromosome creates a rather more difficult and challenging problem, not only for the child and his family but also for the medical caretaker. Although familial interactions with the young child during the first months of life are key factors in gender and sexual role-development, it is still difficult to predict the potential for penile growth in relation to future sexual function to determine if the male gender assignment will be satisfactory.

Also, it is important to understand that it is more difficult to reconstruct a penis than it is to create a vagina. The dominant role of the male gender in the Muslim community should not overrule Islamic Laws; these Laws should not be ignored, and they should be given prime consideration. There may exist a

bias concerning the influence of the karyotype, such as the perception that a child with a 46,XY genotypes should be raised as a male. Patients with complete end-organ unresponsiveness due to androgen receptor defects (referred to as androgen insensitivity syndrome or testicular feminisation) lack response to testosterone and, therefore, should be raised as females. It is advisable to remove the gonads at the time of diagnosis rather than wait until puberty, to avoid the adverse effects of testosterone on the neurons and to minimise the risk of the development of gonadoblastoma (4). The availability of oestrogen replacement therapy allows gender reassignment in such cases. However, the use of oestrogen replacement therapy was debated recently, and it was suggested that the removal of gonads should be deferred until puberty to allow for oestrogen formation, as carcinoma in situ is rare and the earliest reported case was at 14 years of age (37). On the other hand, in cases where genetic males demonstrate any appreciable response to exogenous stimulation, a testosterone treatment of short duration might indicate the degree of masculinisation achievable at puberty and facilitate the decision to raise such an individual as a male. In cases of 5- α -reductase deficiency, further virilisation occurs at puberty, along with the development of a male habitus. Many of these individuals will be fertile as adults; therefore, male gender is the appropriate choice for gender assignment, and surgical reconstruction should be performed at 18 months (2,4,21). In testicular regression syndrome, gonadotrophic hormone deficiency, and other defective testosteronesynthesis pathways, a male gender should be assigned, and the appropriate medical therapy should be given.

In individuals with ovotesticular DSD (46,XX, 46,XY, or 46,XX/46,XY karyotypes), pure gonadal dysgenesis (46,XX or 46,XY karyotypes), or mixed gonadal dysgenesis (45,X/45,XY), there can be different degrees of internal and external genital formation, depending on the amount of functioning testicular tissue. The sex-of-rearing should be female in most of these cases, and all testicular tissue must be removed at the time of diagnosis because of the risk of virilisation at puberty and the higher incidence of gonadal tumours (4).

In conclusion, appropriate genetic and psychosocial counselling should be made available to the family and when the patient is old enough to understand, all available information should be progressively disclosed.

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Original Article

In Silico Identification of Drug Targets for Antifertility from Natural Products by Differential Reaction Content Analysis of Metabolic Pathways

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Abstract -

Background: One of the major concerns of governments of developing and developed countries is to have a check on their population increase. Realising the importance of avoiding the harmful effects of synthetic compounds, scientists and researchers throughout the world are cooperating in efforts to design new and effective contraceptives from compounds of plant origin.

Methods: In this paper, we compared 11 plant species by analysing compounds showing antifertility properties with respect to the metabolic pathways involved. The Kyoto Encyclopedia of Genes and Genome pathway database was the source of metabolic pathway information. Protein sequences and classification numbers of unique enzymes exclusively present in certain species were identified using the Expert Protein Analysis System.

Results: Two enzymes, namely, L-aspartate dehydrogenase (EC no. 1.4.1.21) and transhexaprenyltranstransferase (EC no. 2.5.1.30), were identified as novel drug targets from the metabolic pathway analysis. Validation of the essential proteins identified through metabolic pathway comparison was done based on the literature information.

Conclusion: The *in silico* analysis resulted in identification of 2 enzymes that are predicted to be the targets for putative antifertility drug. These enzymes can further be modelled to obtain their 3-dimensional structures with the help of various protein structure modelling softwares.

Keywords: contraceptives, databases as topic, drug discovery, enzymes, metabolic pathways, natural products

Introduction

In the developing world, the population is projected to increase rapidly. By 2025, about threequarter of the 3.2 billion increase in the world's population is expected to take place in developing countries; the global increase is expected to double by 2050 to approximately 7.8-12 billion. China and India are the two most populous countries, with around half of the world's population living there (1,2). The rise in population can be a serious problem, as it has damaging economic and environmental consequences. The world's population has increased exponentially since the industrial revolution because of the modern technologies and medicines available. Thus, the population carrying capacity has increased. The planet is experiencing depletion of the world's net resources due to the requirement of food and other materials for sustenance. The increased use of fossil fuels presumably contribute to

global warming resulting in the melting of glaciers, the rising ocean levels, and the more frequent hurricanes. Due to the ever-increasing demands for food and palatable water from the population increase, deaths due to hunger and thirst will potentially be at higher numbers if the demands are not met. However, the lands are becoming infertile because of overcropping and urbanisation, considering that the constructions as well as the inflow of household wastes and industrial effluents increase the acidity of the soil (2). Population explosion is alarming; it results in the exploitation of natural resources and affects the economic growth of a country.

Population control is the practice of curtailing the population increase, usually by reducing birth rate. India was the first country with an official family planning programme, which commenced in the late 1950s and early 1960s, because the government could foresee the adverse effects of an increased population on economic growth

and living standards. A careful examination of history reveals that family planning has been practised since the dawn of literature. Initially, the family planning programme started with many contraceptive methods, but due to the side effects of most of the contraceptives such as oral steroidal contraceptive and abortifacient drugs, the use of these drugs has been prohibited due to their side effects such as myocardial infarction and breast cancer in females (3-5). Several very efficient synthetic drugs have been introduced in recent years, but despite their benefits, there are certain side effects that may result in severe disorders. Therefore, it has become necessary to synthesise contraceptive drugs of natural origin that are more effective, with negligible side effects and minimum cost.

The World Health Organization estimated that approximately 75% to 80% of the world's population uses natural products as a source of drugs, derived from either full plants or certain parts of plants, such as roots, stems, leaves, and flowers. Nowadays, due to growing health concerns, most people prefer natural alternatives to synthetic drugs, as they are cheaper and have fewer side effects (6–8). Since the ancient times, medicines obtained from various parts of plants, such as barks, leaves, and roots, provide efficient and long-lasting cure against several diseases, with negligible side effects. Some common examples are quinine, which is extracted from Chinchona oficinalis, ephedrine from Ephedra giardiana, and reserpine from Rauwolfia serpentine. Ancient Avurvedic and Unani literature reveals the use of plant species for fertility regulation. Several plant species with antifertility activity have been reported in the literature, such as Musa paradisiaca, Hibiscus rosa-sinensis, Beta vulgaris, Allium cepa, Carica papaya, Catharanthus roseus, and Populus trichocarpa (9-13). The knowledge of the mechanisms of action of most medicinal plants is scant and exploration of their use as therapeutic agents is limited; therefore, there is a need to implement newer techniques to determine their potential uses. With the advent of proteomics and genomics, this problem can be partially alleviated with these efficient methods for rapid identification of protein targets of herbal ingredients (14).

Several bioinformatics tools and software have been used to develop efficient methods for facilitating target identification, as the first step in drug discovery. Metabolic pathway analysis is one approach to identify the potential drug targets, as it involves the study of organism metabolism. The targets are evaluated using 2 criteria: essentiality and selectivity, that is, essential proteins that may effect the specific metabolic activity and are not synthesised inside human body, and thus have to be taken from outside source. These essential proteins selectively bind at their binding sites. Therefore, the essential proteins are identified by pathway analysis and can then be taken as novel drug targets (15). Due to a lack of information in databases, only a restricted number of drug targets have been identified.

The plants taken for the analysis are used in traditional medicines; however, there are many properties of these plants yet to be investigated. The present study involves 13 plant species: Allium cepa (onion), Beta vulgaris (sugar beet), Brassica napus (rape), Nicotiana tabbacum (tobacco), Populus trichocarpa (black cottonwood), Prunus persica (peach), Helianthus annuus (sunflower), Vitis vinifera (grapes), Glycine max (soybean), Hordeum vulgare (barley), Oryza sativa (rice), Triticum aestivum (wheat), and Zea mays (maize). Some of these plants have been experimentally tested for antifertility (9-13). The differential reaction content of the above plant species was analysed by comparing the metabolic pathways taken for in silico analysis.

Materials and Methods

Plant species taken for pathway comparison

Metabolic pathway analysis is a novel approach for identification of drug targets. In this study, metabolic pathway analysis is performed by identifying the unique metabolic reaction content in 13 plant species, out of which 8 species are assumed to have antifertility properties, based on the literature. Although these plant species are used as traditional medicines, some of them lack research evidence to support their antifertility properties.

These 13 plant species were divided into 2 groups. The first group include 8 plant species with antifertility properties (9–13): Allium cepa (onion), Beta vulgaris (sugar beet), Brassica napus (rape), Nicotiana tabbacum (tobacco), Populus trichocarpa (black cottonwood), Prunus persica (peach), Helianthus annuus (sunflower), and Vitis vinifera (grapes). The other group consist of 5 species assumed to be without antifertility properties: Glycine max (soybean), Hordeum vulgare (barley), Oryza sativa (rice), Triticum aestivum (wheat), and Zea mays (maize).

Metabolic pathways analysis

Twelve different metabolic pathways. alkaloid namely. alkaloid biosynthesis, biosynthesis II, androgen-oestrogen metabolism, biosynthesis, steroids caffeine metabolism, C-21 steroid hormone biosynthesis, fatty acid biosynthesis, flavonoid biosynthesis, nicotinate and nicotinamide biosynthesis, linoleic acid metabolism, sulphur metabolism, and tetracycline biosynthesis were analysed comparatively. These pathways were chosen from the Kyoto Encyclopedia of Genes and Genome (KEGG). Metabolic pathway comparison of these species provides facts regarding enzymes exclusively present in species that showed antifertility properties. Further mapping with human proteome was conducted using the Basic Local Alignment Search Tool (BLAST); the enzymes that are non-homologous to the human proteome were taken as novel drug targets. The information regarding the classification of enzymes was taken from various databases and web servers, namely, Braunschweig Enzyme Database (BRENDA), KEGG, and Expert Protein Analysis System (ExPASy).

Identification of essential proteins by metabolic pathway comparison

Each class and subclass of enzyme is described by its unique enzyme classification number (EC no.), which is designated by the International Union of Biochemistry and Molecular Biology according to the reaction catalysed. The KEGG pathway database was used as a source of metabolic pathway information. The Comparative Pathway Analyzer, an online web server tool (16), is referred for the comparative study. The differential pathway analysis of the selected species is performed, and their reaction content was visualised with the respective pathway in order to obtain enzymes showing antifertility properties. The enzymes uniquely present in plant species showing the antifertility property were identified.

Validation of essential enzymes by searching similarity against Database of Essential Genes

Protein sequences of unique enzymes (essential proteins) exclusively present in plants species were identified using ExPASy, a proteomics server of the Swiss Institute of Bioinformatics. The essential protein sequences were compared using BLAST against Database of Essential Genes for validating the essentiality of the proteins identified through metabolic pathway comparison.

Drug target identification: Mapping essential proteins on human proteome

The essential proteins were searched for similarity against human proteins. Mapping of the essential proteins identified was done against human proteome by a sequence similarity search using BLAST-Protein (BLAST-P). The e-value, $e = Kmn(e-\lambda s)$, which gives the number of entries required in the database for a match to happen by random chance, was set to default; all other parameters were also set to default values in order to predict probable drug targets.

Results

Comparisons of metabolic pathways of the 13 plant species led to the identification unique enzymes, which 2 may responsible for the antifertility property: trans-hexaprenyltranstransferase or heptaprenyl diphosphate synthase (EC no. 2.5.1.30), which is involved in the biosynthesis of steroids, and L-aspartate dehydrogenase (EC no. 1.4.1.21), which is involved in the biosynthesis of nicotinate and nicotinamide. The intermediate reactions in which these enzymes are involved in their corresponding pathways are as follows:

Trans-hexaprenyltranstransferase (EC no. 2.5.1.30)

Trans-hexaprenyltranstransferase is involved in the biosynthesis of steroids in onion. This enzyme catalyses the condensation reactions, resulting in the formation of all-trans-heptaprenyl diphosphate, isoprenoid sidechain of ubiquinone-7, and menaquinone-7. The enzyme adds 4 isopentenyl diphosphate molecules sequentially to farnesyl diphosphate with transstereochemistry.

Trans, trans-farnesyl diphosphate

- + 4 isopentenyl diphosphate
- ↔ All-trans-heptaprenyl diphosphate
- + 4 diphosphate

$$\mathbf{C_{_{15}H_{_{28}O_{_{7}P_{_{2}}}}} + 4C_{_{5}H_{_{12}O_{_{7}P_{_{2}}}} \\ \leftrightarrow \mathbf{C_{_{35}H_{_{60}O_{_{7}P_{_{2}}}}} + 4P_{_{2}H_{_{4}O_{_{7}}}} \\$$

Aspartate dehydrogenase (EC no. 1.4.1.21)

This enzyme is involved in the biosynthesis of nicotinate and nicotinamide in black cottonwood. The enzyme is strictly specific for L-aspartate as the substrate, and catalyses the first step in biosynthesis of NAD from aspartate. The enzyme has a higher affinity for NAD⁺ than NADP⁺.

L-aspartate + NADP⁺

↔ Iminoaspartate + NADPH + H⁺

$$\begin{aligned} &\mathbf{C_{4}H_{7}NO_{4}} + \mathbf{C_{21}H_{29}N_{7}O_{17}P_{3}} \\ &\leftrightarrow \mathbf{C_{4}H_{5}NO_{4}} + \mathbf{C_{21}H_{30}N_{7}O_{17}P_{3}} + \mathbf{H^{+}} \end{aligned}$$

Both plants have some antifertility properties, as observed in the ethanolic extract of onion (9) and the flavonoids of black cottonwood (13). Consequently, it can be predicted from the intermediate complexes formed by these enzymes in the biosynthesis of steroids, nicotinate, and nicotinamide that these enzymes have antifertility properties. The above 2 enzymes had no homologues in the human proteome, and therefore are putative drug targets.

Discussion

The inherent hazards of drugs of chemical origin has drawn attention to the search for better treatment options, such as drugs of natural origin with negligible side effects. Most contraceptive pills used today are potent steroidal ovulation inhibitors, but the constant use of steroidal pills can disturb the hormonal balance in the body. Synthetic drugs, being foreign to the human system, may induce foreign-body responses and cause damages, thus repressing and paralysing the functions of that particular organ or tissue. On the other hand, drugs of natural origin are more suitable and effective because they contain compounds, such as phytoproteins, flavonoids, and saponoids, that help to protect the body from harm. Furthermore, all synthetic drugs available up to now are modelled after the structures of natural compounds isolated from plants, and thus are related to plant drugs in several ways. Some drugs of natural origin have been proven effective against several fatal diseases, for example, the anticancer drugs Vincristine and Vinblastine obtained from the rosy periwinkle, Catharanthus roseus (17,18). Therefore, researchers are showing more interest on drugs derived from plants to obtain better results with negligible side effects compared with synthetic drugs. There are various types of pharmacological and physiological activities and substances of known structure in plants with demonstrated antifertility activity (19-21). In this paper, the differential reaction content of the 13 plant species was visualised using the Comparative Pathway Analyzer. Of these selected plants, only 2 (onion and black cottonwood) showed antifertility properties in identified enzymes. However, there may be many otheressential proteins that can be taken as putative drug targets. Due to restricted information in databases, we analysed only 2 essential enzymes: L-aspartate dehydrogenase (EC no. 1.4.1.21) and trans-hexaprenyltranstransferase (EC no. 2.5.1.30). These identified enzymes were not found in various plant databases, likely because the information available is limited. Based on the literature, onion and black cottonwood shows the antifertility properties (9,13), and thus these enzymes can be validated to be putative drug targets for antifertility regulation.

Conclusion

With the increased pace in technology, newer in silico methods of drug target identification are being evaluated frequently. Target identification is the first step of the drug discovery process, and the use of plants to derive drug candidates is desirable due to negligible side effects of these herbal drugs over synthetic drugs. Moreover, the approach used is also novel, as we used differential pathway analysis of metabolic pathways to visualise the differential reaction content of the various plant species. We identified 2 unique enzymes L-aspartate dehydrogenase (EC no. 1.4.1.21) and trans-hexaprenyltranstransferase (EC no. 2.5.1.30) showing antifertility properties from 2 different metabolic pathways, namely, nicotinate and nicotinamide metabolism and steroids biosynthesis. Due to restricted information in databases for different plant species, only a few drug candidates were traced from the plant species in the present study. These were validated based on information present in various databases and literature. The literature contains information on these plant species that indicates their terpenoids and flavonoids have antifertility properties. These enzymes were involved in the biosynthesis of steroids and the biosynthesis of nicotinate and nicotinamide; therefore, we can assume that these enzymes are potentially novel antifertility drug targets. In future, in vivo experiments can be performed using extracts of these plants to validate the results. The target obtained can be exploited for rational drug design, which includes ligand-based and structure-based drug designing approaches. Furthermore, we can design analogues by using or modelling the inhibitors for these enzymes.

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Authors' Contributions

Conception and design, collection, assembly, analysis, and interpretation of the data, drafting of the article: SS

Critical revision and final approval of the article, administrative, technical, or logistic support: SD

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Original Article

Spasmogenic Activity of the Seed of Terminalia chebula Retz in Rat Small Intestine: In Vivo and In Vitro Studies

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Abstract -

Background: Terminalia chebula Retz is traditionally used to relieve constipation. The current study was performed to investigate the pharmacological action of aqueous extract of Terminalia chebula seeds (ATC) in vitro and in vivo.

Methods: Terminal pieces of rat ileum were suspended in organ bath containing Tyrode solution. The ileum spontaneous motility frequency and contractility were recorded isotonically. To induce ileal contraction, carbachol and ATC were added to the organ bath. In addition, the effect of hexamethonium, indomethacin, atropine, and verapamil on the ATC-induced ileal contractions was also investigated. The effectiveness of ATC on relieving morphine-induced constipation was investigated in an in vivo study by measuring the faecal number, faecal water content, and intestinal transit ratio.

Results: ATC increased the frequency of ileum motility and tension of contraction dose-dependently (P < 0.05). Responses induced by ATC were inhibited by pre-treatment of the tissue with verapamil. The ATC activities were not affected by atropine, hexamethonium, and indomethacin. The faecal number and faecal water content were increased dose-dependently by ATC (P < 0.05).

Conclusion: The excitatory effects of ATC on ileal contractile frequency and tension are possibly mediated through Ca²⁺ channels activation. The results of the present study support the traditional usage of ATC for the treatment of constipation.

Keywords: calcium channels, qut, intestinal motility, morphine, plant extracts, rat, seed, Terminalia

Introduction

Terminalia chebula Retz. (Combretaceae) is commonly known as chebulic myrobalan. It grows throughout central Asia and some other parts of the world (1). Seeds of T. chebula is used in traditional medicine to treat kidney and urinary disorders (2) and can also be used as homeostatic, laxative, antitussive, diuretic, and cardiotonic remedy (3). The semi-ripe seed is considered as a purgative (4), and its gastroprotective effect against indomethacin-induced gastric ulceration has been reported (5). High performance liquid chromatography analysis revealed that T. chebula contains gallic acid, punicalagin, chebulic acid, ellagic acid, chebulagic acid, chebulinic acid, chebulanin, corilagin, neochebulinic acid, and 1,2,3,4,6-penta-O-galloyl-beta-D-glucose Antioxidant and hypocholesteromic properties of T. chebula have been scientifically demonstrated (7–9). Moreover, it is effective against several pathogens, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes* (10), and *Helicobacter pylori* (11). *T. chebula* also inhibits reverse transcriptase of human immunodeficiency virus-1 (12). It has been reported that *T. chebula* decreases the plasma glucose level both in normal and diabetic rats (11–13) and has cardioprotective effect against isoproterenol-induced myocardial injury in rats (14). In addition, *T. chebula* aqueous extract delays rat gastric emptying (15).

Morphine has been used to alleviate the chronic pain of cancer. However, a major side effect of morphine is constipation that often detracts from the patient's quality of life. Since *T. chebula* is used in traditional medicine in southern part of Iran to treat constipation, current work aimed to examine the excitatory effect of ATC on isolated ileum and its effect on morphine-induced constipation in rat.

Materials and Methods

Preparation of aqueous extract

The whole seed of *T. chebula* was purchased from a local market in Ahwaz, Iran, and was authenticated by Dr N Alemzadeh Ansari, Department of Horticultural, Faculty of Agriculture, Shahid Chamran University, Ahvaz, Iran. The voucher specimen (No. TCH-10-21) was deposited in the herbarium of Ahvaz Jundishapur University of Medical Sciences. The seeds (50 g) were crushed and soaked overnight in distilled water (500 mL) at room temperature. The mixture was filtered through a cheesecloth and centrifuged at 3500 rpm for 15 minutes. The supernatant was concentrated and lyophilised (yield: 13%) for preservation and stored at 4 °C until used.

Drugs

Carbachol (CCh), hexamethonium, atropine sulphate, indomethacin, verapamil, and charcoal were purchased from Sigma (USA), and morphine from Darou Pakhsh Company (Iran). All materials used for the preparation of Tyrode solution were purchased from Merck (Germany). Indomethacin was dissolved in Na₂CO₃ (100 mM) according to a published method (16). Other chemicals used were of the analytical grade available and dissolved in Tyrode solution.

Animals

Male adult Wistar rats (weighed 150–200 g) were prepared from the animal house of Ahvaz Jundishapur University of Medical Sciences. Animals were fed conventional diets and tap water ad libitum. Rats were maintained under standard conditions with temperature of 20–24 °C and 12 hours light/dark cycle. All animal experiments were carried out in accordance with Ahvaz Jundishapur University of Medical Sciences Ethical Committee Acts (PRC52).

In vitro study

Animals were deprived from food but not water 24 hours prior to experiments and killed by an overdose of diethyl ether. The ileum segment of intestine was dissected out and kept in oxygenated Tyrode solution; then, its surrounding mesenteries were dissected (17). Each segment (about 2 cm in length) was mounted under 1 g of resting tension in a 10 mL tissue chamber containing Tyrode solution, maintained at 37 °C and aerated with a mixture of oxygen and carbon dioxide (95% and 5%, respectively). The Tyrode solution composition was 136.90 mM NaCl, 2.68 mM KCl, 1.05 mM MgCl₂, 11.90 mM NaHCO₂,

0.42 mM NaH₂PO₄, 1.80 mM CaCl₂, and 5.55 mM glucose. An isotonic transducer (Bioscience, UK) coupled to Harvard Oscillograph (UK) was used for recording the ileum contractility.

30-minute equilibration period, CCh (1 µM) was applied to the tissue chamber, and the contractile response was assumed as control. In the first series of experiment, the effect of ATC on basal tone and frequency of spontaneous contractions of ileum were examined. Then, the effect of cumulative concentrations of ATC (0.01, 0.02, and 0.04 mg/mL) were recorded and responses were compared with CCh (1 µM). At the end of each experiment, response to CCh was retested to confirm the viability of tissue preparation. To study the mechanism of ATC spasmogenic activity, tissue was first incubated either with atropine (5 minutes, 1 μM), hexamethonium (5 minutes, 100 μM), or indomethacin (20 minutes, 1 µM) (18); then, ATC (0.04 mg/mL) was applied. The intervention of extracellular Ca²⁺ in the ATC-induced responses was evaluated by incubating the tissue with verapamil (5 minutes, 1 µM) or by recording responses in Ca2+-free Tyrode solution (18). Results were expressed as percentage of response induced by CCh. Contractile frequency was calculated as the numbers of contractile waves per minute. To confirm the Ca2+ agonist property of ATC, the tissue was allowed to stabilise in Ca2+-free Tyrode solution containing EDTA (0.1 mM) for 30 minutes in order to remove Ca⁺² from the tissue (17), and then contractions induced by cumulative concentrations of CaCl (0.45-2.25 mM) were recorded. The same experiments were repeated in the presence of ATC (0.04 mg/mL). All tested substances were applied in volume not exceeding 1% of the bath volume.

In vivo experiments

To test the effect of ATC on normal rats, animals were divided into control and 3 ATC-treated groups. Animals in control group received saline (1 mL/rat, p.o.) and the 3 treated groups received ATC at 62.5, 125, or 250 mg/kg, respectively (1 mL/rat, p.o.). This experiment was carried out within 3 consecutive days.

To examine the effect of ATC on morphine-induced constipation, animals were randomly assigned to control, negative control, and 3 ATC-treated groups of 7 rats each. Animals in control group, negative control, and the 3 ATC-treated groups received saline (1 mL/rat, p.o.), morphine (2 mg/kg, s.c.), and ATC (62.5, 125, or 250 mg/kg, p.o.), respectively. The animals in ATC-treated groups received ATC (p.o.) 4 hours

after the first trial of morphine administration. Morphine was injected subcutaneously, twice per day (19). All administrations were carried out for 3 consecutive days.

To carry out the aforementioned protocols, rats were housed in individual cages for 3 days. Every day at around 10 AM, faeces were collected from each cage. The number of the faeces pellets was counted, and weighed. Faeces of each rat were then lyophilised and weighed to determine faecal water content. The total number and water content of the faecal pellets were calculated as the average per 3 consecutive days for each rat.

Gastrointestinal transit ratio

Four groups of rats (7 in each) were fasted overnight. Control group received saline (1 mL/rat, p.o.) and 3 other groups received ATC at 62.5, 125, and 250 mg/kg, respectively (1 mL/rat, p.o.). After 90 minutes, all groups received 3% active charcoal suspension in saline (1 mL/rat, p.o.) as charcoal meal. One hour after the marker administration, the animals were sacrificed by an overdose of diethyl ether, and the small intestine from pylorus sphincter to ileocaecal sphincter was removed. The intestinal transit ratio was calculated by the percentage of the small intestine length in which the charcoal had travelled.

Statistical analysis

All values were expressed as the mean \pm SEM. The significant difference was tested by one-way ANOVA followed by Student's t test. Differences with P values of less than 0.05 were considered statistically significant.

Results

In vitro study

Effects of ATC on ileal spontaneous contraction

Ileum showed regular spontaneous phasic contractions, and ATC at 0.01, 0.02, and 0.04 mg/mL increased the contractile frequency and tension in a concentration-dependent manner (P < 0.01, Table 1). Figure 1 represents the actual recordings of CCh and cumulative concentrations of ATC on basal tone and ATC-induced ileal contractions, in which the maximal amplitude of the ATC-induced contraction was observed at 0.04 mg/mL, occurring at about 60% of the maximal response evoked by CCh (1 μ M).

Effect of hexamethonium, indomethacin, atropine, verapamil, and extracellular Ca²⁺ on ATC-induced contraction

The ATC-induced contractions were not inhibited by atropine (muscarinic receptor antagonist), hexamethonium (nicotinic receptor blocker), or indomethacin (cyclooxygenase inhibitor). In the Ca²⁺-free Tyrode solution, however, the spasmogenic effect of ATC was abolished. Verapamil (Ca²⁺ channel blocker) inhibited the ATC-induced contraction completely (Figure 2). Table 2 demonstrates the changes of frequency of spontaneous ileal contractile activity in these protocols.

Effect of ATC on $CaCl_2$ -induced ileal contractions in Ca^{2+} -free Tyrode solution

In Ca^{2+} -free Tyrode solution, ATC was unable to evoke ileal contraction. However, applying cumulative concentrations of $CaCl_2$ (0.45–2.25 mM) evoked ileal contraction in a concentration-dependent manner (P < 0.05). In the presence of ATC (0.04 mg/mL), the $CaCl_2$ -induced ileal contractions were potentiated (P < 0.05), as shown in Figure 3.

In vivo study

Effect of ATC on number of faecal pellets in the morphine treated and untreated rats

In morphine-untreated rat, ATC at doses of 125 and 250 mg/kg significantly increased the number of faecal pellets (P < 0.05, Figure 4). On the other hand, morphine decreased the number of faecal pellets significantly (P < 0.05), as shown in Figure 5. ATC at 625.5 mg/kg was unable to induce any change; however, ATC at 125 and 250 mg/kg significantly antagonised the morphine effect dose-dependently (P < 0.05), and the number of faecal pellets in these 2 groups were not different from control group, which received saline (Figure 5).

Effects of ATC on faecal water content

Table 3 shows that, in normal animals, the administration of ATC increased the faecal water content as compared with in the saline administration (P < 0.05). The mean percentage (SEM) of faecal water content in saline and ATC-treated (62.5, 125, and 250 mg/kg) groups were 30% (1.2), 31.2% (1.6), 36.2% (2.1), and 39.8% (2.5), respectively. As shown in Table 3, faecal water content in the ATC-treated groups (125 and 250 mg/kg) was significantly more than in the control group (P < 0.01 and P < 0.001, respectively).

Table 1: Effect of different concentrations of aqueous extract of *T. chebula* (ATC) on the contractile frequency and tension of rat ileum

		ATC (mg/mL)		
	0	0.01	0.02	0.04
Frequency (cycle/min)	7.25	7.36	10.00	15.54
	(0.25)	(0.31)	(o.85)**	(1.50)***
Tension (% of CCh response)	2.24	6.00	25.20	63.00
	(0.35)	$(1.42)^*$	(2.43) **	(4.12)**

Data are presented as mean (SEM). * P < 0.05, **P < 0.01, and ***P < 0.001 versus control (0 mg/mL). Abbreviation: CCh = carbachol.

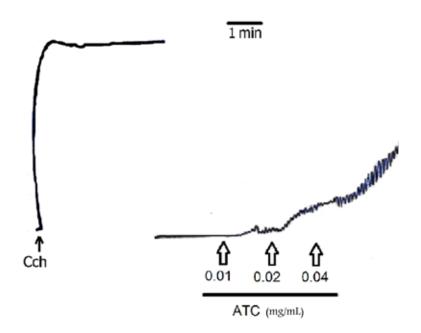


Figure 1: Representative tracing showing the contractions evoked by carbachol (CCh, 1 μm) and aqueous extract of *T. chebula* (ATC) to rat isolated ileum.

In the morphine-treated animals, although ATC increased the animals' faecal water content, the differences were not significant when compared with the animals that received morphine alone.

Effect of ATC on intestinal transit ratio

Figure 6 demonstrates that oral administration of ATC at doses of 125 mg/kg and 250 mg/kg has increased the intestinal transit ratio as compared with the saline group (P < 0.05 and P < 0.01, respectively).

Discussion

Our results showed that ATC increases the frequency of ileal contraction in a concentration-dependent manner. The excitatory effect of ATC on the contractile frequency of ileum was unaffected by pre-treatment with atropine, hexamethonium, and indomethacin. Furthermore, the ATC excitatory effect was dependent on extracellular Ca²⁺. In addition, ATC increased the intestinal transit ratio, number of faecal, pellets, and faecal water content.

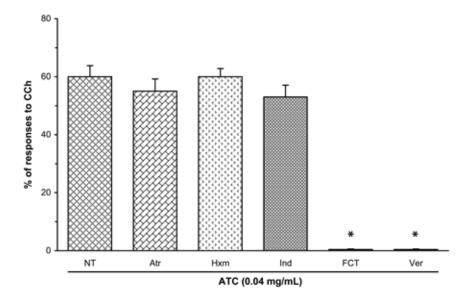


Figure 2: Spasmogenic effect of aqueous extract of *T. chebula* (ATC, 0.04 mg/mL) on rat ileum in normal Tyrode solution (NT) and after tissue incubation with atropine (Atr, 1 μM), hexamethonium (Hxm, 100 μM), indomethacin (Ind, 1 μM) and verapamil (Ver, 1 μM). ATC spasmogenic effect was also recorded in the Ca²⁺-free Tyrode solution (FCT). Data are presented as mean (SEM) percentage of responses induced by carbachol (CCh, 1 μM). **P* < 0.05 versus NT.

Table 2: Effect of aqueous extract of *T. chebula* (ATC, 0.04 mg/mL) on the contractile frequency of rat ileum after pre-treatment with antagonists

	ATC	Ind +	Hxm +	Atr +	Ver +
		ATC	ATC	ATC	ATC
Frequency (cycle/min)	15.54 (1.5)	15.1 (0.85)	15.8 (1.43)	14.24 (1.5)	0.00***

Data are presented as mean (SEM). ATC was applied without or after tissue incubation with indomethacin (Ind, 1 μ M), hexamethonium (Hxm, 100 μ M), atropine (Atr, 1 μ M), or verapamil (Ver, 1 μ M). ***P < 0.001 versus ATC alone.

In smooth muscle, there are several factors that increase the frequency of contraction, such as increased pacemaker activity and shortened action potential (20). The extracellular Ca2+ and Ca2+ influx are essential for excitability and contractility in smooth muscle cells. Intracellular Ca2+ elevation is the main regulating factor of smooth muscle tension (21); therefore, in Ca²⁺-free Tyrode solution, the contractile activity was appeared and augmented after adding cumulative concentrations of CaCl_a. However, in the presence of ATC (0.04 mg/mL), the stimulatory effect of Ca²⁺ was increased, indicating that ATC, in some way, has potentiated Ca²⁺ spasmogenic effect. To elucidate the mechanism of ATC activity, ileal preparations were incubated with atropine, hexamethonium, and indomethacin. It has been shown that prostaglandins (22) and acetylcholine at pre-ganglionic (23) and post-ganglionic levels (24) stimulate small intestine contractility. However, our results showed that ATC spasmogenic effect was unaffected by indomethacin, atropine, and hexamethonium, indicating that neither of these stimulatory pathways were involved in ATC activity. On the other hand, ATC was unable to induce ileal contraction in Ca2+-free Tyrode solution. The same results were obtained when ileal tissue was incubated with verapamil. Therefore, our results indicated that Ca²⁺ channels and Ca²⁺ influx were essential for inducing ileal contractions by ATC. The same conclusion could be obtained from the results of ileal frequency being affected by ATC alone or in the presence of applied antagonists and inhibitors.

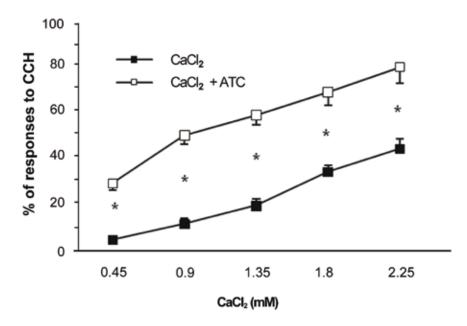


Figure 3: Spasmogenic effect of cumulative concentrations of CaCl₂ in rat ileum in the absence and presence of aqueous extract of *T. chebula* (ATC, 0.04 mg/mL). Data are presented as mean (SEM) percentage of responses induced by carbachol (CCh, 1 μM). **P* < 0.05 CaCl₂ versus CaCl₂ + ATC of the same concentration.

Table 3: Effect of aqueous extract of *T. chebula* (ATC) on the percentage of faecal water content (FWC) in normal and morphine-induced constipated rats

Groups	Dose (mg/kg)	FWC
Normal	Control (saline, 1 mL)	30.0 (1.2)
	ATC (62.5 mg/kg)	31.2 (1.6)
	ATC (125 mg/kg)	36.2 (2.1)**
	ATC (250 mg/kg)	39.8 (2.5)***
Constipated	Control (M)	28.0 (1.4)
	M + ATC (62.5 mg/kg)	29.0 (0.8)
	M + ATC (125 mg/kg)	30.0 (1.8)
	M + ATC (250 mg/kg)	30.8 (2.2)

Data are presented as mean (SEM) percentage. Constipation was induced by administration of morphine (M) at 2 mg/kg, twice per day. **P < 0.01, ***P < 0.001 versus control.

In the in vivo experiments, ATC increased the number of faecal pellets, indicating that ATC has augmented intestinal motility, which is also evidenced by the increase in water content of faecal pellets (Table 3). The same results were obtained from intestinal transit ratio, which was increased significantly by ATC. Our results are consistent with the report that aqueous extract of *T. chebula* increased the gastric emptying in rats (15).

It has been reported that morphine (as an opioid receptors agonist) decreases the rat faecal weight significantly (25) and abolishes the propulsive peristaltic waves in the intestine (26,27). The opiate also promotes water absorption in the intestine (28). In the present study, the total number of faecal pellets was significantly decreased by the morphine. Although ATC at 62.5 mg/kg was unable to prevent the effect of

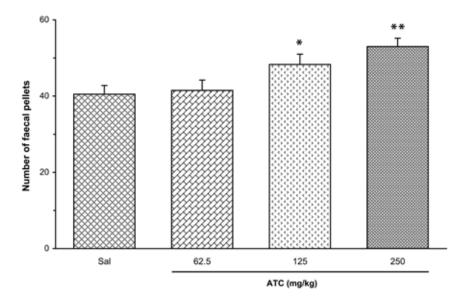


Figure 4: Effect of different doses of aqueous extract of *T. chebula* (ATC) on the number of faecal pellets in rat. Data are presented as mean (SEM). *P < 0.05 and **P < 0.01 versus control (Sal).

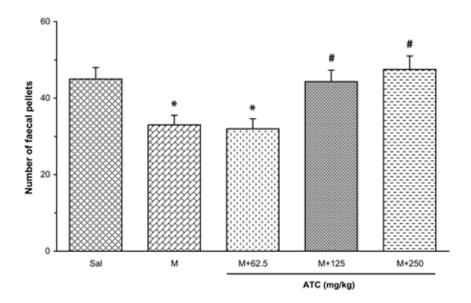


Figure 5: Number of faecal pellets in rats received saline (Sal), morphine (M) only, and morphine plus aqueous extract of T. chebula (ATC) at different doses. Morphine reduced the number of faecal pellets. ATC at higher doses (125 and 250 mg/kg) increased the number of pellets similar to that of the saline group. Data are presented as mean (SEM). *P < 0.05 versus saline, and *P < 0.05 versus morphine only.

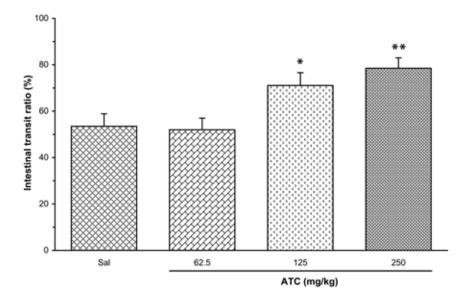


Figure 6: Effect of different doses of aqueous extract of *T. chebula* (ATC) on rat intestinal transit ratio. Data are presented as mean (SEM). $^*P < 0.05$ and $^{**}P < 0.01$ versus saline.

morphine, at higher doses (125 and 250 mg/kg), ATC antagonised the effect and these 2 groups had the similar number of faecal pellets as in the saline group. These results indicate the ability of ATC (at higher doses) to inhibit the morphine-induced constipation. However, the water content of the faecal pellets in groups co-treated with morphine and ATC did not show any significant differences.

Conclusion

Our study showed that aqueous extract of *T. chebula* seed improves constipation induced by morphine and increases the gastrointestinal transit ratio, which supports its traditional use in constipation. The in vitro study revealed that ATC activity was related to Ca²⁺ influx. More studies are necessary to elucidate the mechanism(s) of its action.

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Authors' Contributions

Conception and design, final approval of the article: SAM, MKGN

Obtaining of funding, analysis and interpretation of the data, drafting and critical revision of the article: SAM

Collection and assembly of the data: PM Administrative, technical, or logistic support: AV, PM

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Original Article

Identification of Major and Minor Allergens of Black Tiger Prawn (*Penaeus monodon*) and King Prawn (*Penaeus latisulcatus*)

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Abstract

Background: Prawns and shrimp are a frequent cause of seafood allergy mediated by IgE antibodies. Penaeus monodon and Penaeus latisulcatus, commonly known as black tiger prawn and king prawn, respectively, are among the most frequently consumed prawns in Malaysia. The aim of this study was to identify the IgE-binding proteins of these 2 prawn species.

Methods: Raw and boiled prawn extracts were prepared and then resolved by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE). IgE-immunoblotting was then performed using sera from patients with positive skin prick tests to the raw prawn extracts.

Results: SDS-PAGE analysis of the raw extracts of both prawn species revealed 23 protein bands; the boiled extracts yielded fewer protein bands. The bands in the range of 40 to 100 kDa were sensitive to heat and therefore were not found in the boiled extracts. Immunoblot of raw extracts of black tiger prawns and king prawns yielded 14 and 11 IgE-binding proteins, respectively, with molecular weights of between 15 and 200 kDa. Proteins at 36, 42, and 49 kDa were detected as the major allergens in both species of prawns. A protein of 75 kDa was also identified as a major allergen in black tiger prawns. Other potential allergens were also observed at various molecular masses.

Conclusion: Proteins of 36, 42, and 49 kDa were identified as the major allergens of both species of prawns. The 36 and 42 kDa proteins are hypothesised to be tropomyosin and arginine kinase, respectively. A high molecular weight protein of 75 kDa was found to be an additional major allergen in black tiger prawns.

Keywords: allergens, allergy and clinical immunology, hypersensitivity, Penaeus, immunoblotting, tropomyosin

Introduction

Prawns are classified in the phylum subphylum Crustacean, Arthropoda, Malacostraca, and order Decapods. The term "prawn" is commonly used to describe any large shrimp (1). According to Holthuis (2), prawns include approximately 33 genera with approximately 2500 species, of which less than 300 species are of economic interest throughout the world. More than 20 species of prawns are found in Malaysia, including the black tiger prawn, the king prawn, the white prawn, the sharp-rostrum prawn, and the yellow prawn (3). Local data has reported that more than 60 000 tonnes of marine prawns are landed annually, with the number increasing every year (3).

IgE-mediated hypersensitivity reactions have become important global health issues (4). In the United States alone, a recent survey reported that 1 in 50 Americans has a type of shellfish allergy, including allergy to prawns (5). Exposure to prawn allergens can occur through ingestion of prawn-containing meals, or by inhalation or skin contact while cooking or working (6,7). Sensitised individuals can develop urticaria, angio-oedema, asthma, or life-threatening anaphylactic reactions (8–10).

Over the last decade, various worldwide studies have identified tropomyosin as the major seafood allergen (9,11,12). Tropomyosin, a myofibrillar protein consisting of 2 subunits with molecular masses of 34–38 kDa, has been well-documented as the major cross-reactive allergen

of various species of prawns and shrimp, including brown shrimp (Pen a 1), black tiger shrimp (Pen m 1), and white leg pacific shrimp (Lit v 1) (13–15). Besides tropomyosin, a 40-kDa p known as arginine kinase has also been detected as an important minor allergen in black tiger shrimp (4,10). More recently, 2 new prawn allergens, sarcoplasmic calcium-binding protein and myosin light-chain, have also been characterised (1,16).

Penaeus monodon (black tiger prawn) and Penaeus latisulcatus (king prawn), 2 important aquaculture species in Asia, are commonly consumed in Malaysia. Both of these prawns are mainly caught in the coastal waters off the Indo-West Pacific, Southeast Asia, and South China Sea (3). There have not been any local studies characterising prawn allergens. Thus, the purpose of this study was to identify the major allergens of these 2 species of prawn among our local patients with prawn allergy.

Materials and Methods

Prawn extract preparation

Fresh black tiger prawns and king prawns were obtained from a prawn aquaculture pond in Selangor, Malaysia. Raw and boiled extracts were prepared following the procedure described by Daul et al. (9), with slight modifications. Briefly, the shell and meat of each species were blended in 1 M phosphate-buffered saline (pH 7.2) and extracted overnight at 4 °C under constant mixing. The homogenates were centrifuged at 14 000 rpm at 4 °C for 15 minutes. The supernatants were then sterile-filtered, lyophilised, and stored at -20 °C until use. For preparation of the boiled extracts, the homogenates of the prawns were boiled for 5 minutes before extraction, as described above. The protein concentration of each extract was determined using the Total Protein Kit (Sigma-Aldrich, UK) and bovine serum albumin as a standard.

SDS-PAGE of prawn extracts

Sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed as described by Nakano et al. (17), with some modifications. The samples of the extracts were heated at 97 °C for 4 minutes, and Precision Plus Protein Standards (Bio-Rad, USA) were used as protein markers. Protein bands were resolved by SDS-PAGE using 12% separating gels with 5% stacking gels using a Mini Protean 3 Apparatus (Bio-Rad, USA) at 120 mA for 45 minutes. The resulting protein bands were stained with Coomassie Brilliant Blue R-250 (Bio-Rad, USA)

and analysed using a densitometer instrument (Bio-Rad, USA).

Sera

Sera from patients with histories of prawn allergy and demonstrated positive skin prick tests to raw extracts of black tiger prawn (20 patients) and king prawn (22 patients) were used in this study. Skin prick tests were performed at the Allergy Clinic, Hospital Kuala Lumpur, by a medical officer. This study was approved by the Medical Research and Ethics Committee, Ministry of Health, Malaysia.

IgE-immunoblotting

IgE-immunoblotting experiments performed to determine the specific IgE-binding proteins in the raw extracts of black tiger prawn and king prawn. After electrophoresis, the resolved proteins were electrophoretically transferred onto nitrocellulose 0.45 µm membranes using the Mini Trans-Blot System (Bio-Rad, USA) at 100 V for 70 minutes. The membranes were stained with Ponceau S (Sigma-Aldrich, USA) and cut into 3-mm strips. The strips were washed with Tween-20 Tris-buffered saline (Bio-Rad, USA) and blocked with blocking buffer containing 5% non-fat milk in Tris-buffered saline for 2 hours. The blocked strips were incubated overnight with each individual patient's serum at 4 °C under constant mixing. The strips were incubated with biotinylated goat anti-human IgE (Kirkergaard and Perry Laboratories, UK) as a secondary antibody for 30 minutes, followed by incubation with streptavidin-conjugated alkaline phosphatase (Bio-Rad, USA) for 30 minutes. Detection of the antibody-bound complexes was conducted using the Alkaline Phosphatase Conjugate Substrate Kit (Bio-Rad, Immunoblotting results were analysed using a densitometer analyser (Bio-Rad, USA). Each plate or set of strips contained a blank (no serum) and a negative control (normal serum).

Results

SDS-PAGE of prawn extracts

SDS-PAGE gels of raw and boiled extracts of both prawn species are shown in Figure 1. Protein profile of raw extracts of both prawns revealed approximately 23 protein bands at various molecular weights between 15 and 200 kDa, whereas the boiled extracts of black tiger prawns and king prawns contained 18 and 16 protein bands, respectively. Several protein bands between 40 and 100 kDa were not detected

in the boiled extracts of both prawns. However, enhancement of the band at 18 kDa was found in both boiled extracts. A 36-kDa protein, which is likely to be tropomyosin, was detected in all extracts.

IgE-immunoblotting

As shown in Figure 1, immunoblotting of the raw black tiger prawn extracts identified 14 IgE-binding proteins at various molecular weights between 15 and 200 kDa, whereas immunoblotting of king prawn extracts identified 11 IgE-binding proteins ranging from 15 to 155 kDa. Four major IgE-binding components at the molecular masses of 36, 42, 49, and 75 kDa were detected in black tiger prawn extracts, whereas the king prawn extracts revealed 3 major IgE-binding proteins at 36, 42, and

49 kDa. Several potential minor allergens at 80 and 100 kDa have also been observed in both species of prawns. IgE-binding profiles of all sera tested are summarised in Figure 2. No binding was observed in the negative control and blank strips.

Discussion

Prawn allergy is a long-lasting and potentially life-threatening disorder (18). In Malaysia, large varieties of prawn and shrimp species are used for human consumption. Although seafood, especially prawns, has been reported to be one of the most frequent causes of allergic reactions among local patients (19), there have not been any reports on the characterisation of local prawn allergens.

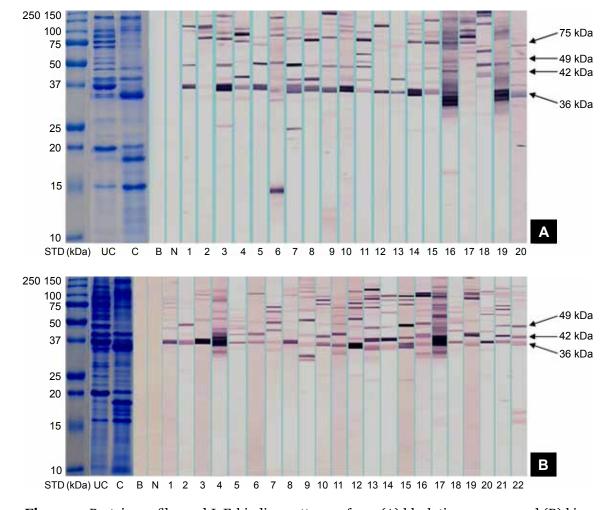
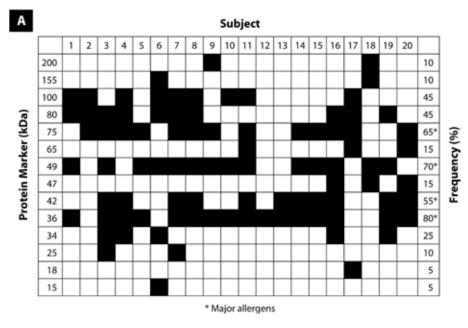


Figure 1: Protein profiles and IgE-binding patterns of raw (A) black tiger prawns and (B) king prawns. Lane STD consists of molecular weight markers (in kDa). Lanes UC and C contain protein profiles of raw and boiled extracts, respectively. Lanes B and N contain blank and negative controls, respectively. Lanes 1 to 22 contain the immunoblotting results of different serum samples.



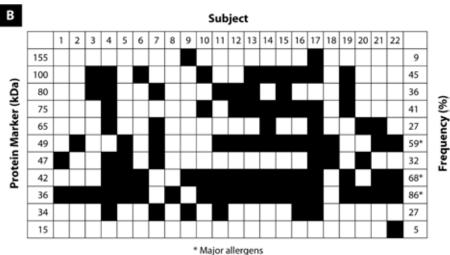


Figure 2: The frequency of specific IgE-binding of sera from patients with raw (A) black tiger prawn allergy and (B) king prawn allergy by immunoblotting analysis.

In our SDS-PAGE analysis, the raw extracts of black tiger prawns and king prawns revealed similar protein profiles. Most protein bands were located approximately 20, 36, and 50 to 100 kDa. Other researchers have also demonstrated similar findings (9,20,21). Very few studies have focused on the thermal effects on seafood protein (21,22). In our study, SDS-PAGE analysis of the boiled prawn extracts yielded fewer protein bands than raw prawn extracts due to denaturation of several protein bands in the range of 40 to 100 kDa. The reduction and loss of bands in the boiled extracts might be due to a loss of secondary and tertiary protein structures (20). Previous

studies have reported that at temperatures above 55 °C, proteins become unfolded and lose their secondary and tertiary structures while retaining their primary structure (20,23). In this study, bands at 18, 20, 36, and ~150 kDa were found to be heat-resistant, with enhanced intensity at the 18-kDa band with applied heat. This finding is similar to other studies that reported several heat-resistant proteins bands at 20, 36, and 70 kDa (20,24). The enhancement of the 18-kDa band might be due to various basic-charged proteins that became exposed due to unfolding, which might have resulted in increased interactions with the Coomassie blue dye molecules (23).

In our study, we detected several major IgE-binding proteins at 36, 42, 49, and 75 kDa in black tiger prawn extracts, and at 36, 42, and 49 kDa in king prawn extracts. We found that 80% and 86% of patients with black tiger prawn and king prawn allergy, respectively, exhibited IgE-binding proteins at 36 kDa. Tropomyosin, a 34 to 36 kDa heat-resistant protein, has been established as a major allergen in invertebrates, including prawn, crab, cockroach, and house dust mites (9,11,12,21). It is possible that our 36-kDa protein might be similar to the previously reported tropomyosin allergen from other prawn and shrimp species. Currently, tropomyosin is the most well-characterised prawn allergen, and its IgE-binding epitopes have been identified (14,25).

Besides tropomyosin, arginine kinase, with a molecular weight of 40 kDa, has also been reported as a crustacean allergen (10). Previous studies have identified a heat-sensitive prawn allergen from *Penaeus monodon*, Pem m 2, as arginine kinase (4,10). In this study, we hypothesise that our 42-kDa protein, which is present in 55% and 68% of our subjects allergic to black tiger prawn and king prawn, respectively, could be arginine kinase. Arginine kinase is a phosphagen kinase that plays a key role in energy metabolism in invertebrates (10). It has also been identified as a pan-allergen in other invertebrates, such as the moth, cockroach, and lobster (1).

Additional major allergens were also detected in our immunoblotting experiment. A protein at 49 kDa was identified as a major allergen in both prawn species, whereas a protein at 75 kDa was found to be a major allergen in only black tiger prawns. Although there have not been reports on the characterisation of these 2 allergens, other immunoblotting studies have identified these proteins as minor allergens (14,19,26). However, the detailed identification of these proteins has not yet been performed.

Conclusion

Our study identified proteins at the molecular masses of 36, 42, and 49 kDa as the major allergens of black tiger prawns and king prawns. Black tiger prawns contained an additional major allergen at 75 kDa. However, to confirm the results, further identification and characterisation of these major allergens should be done using immunological analyses of larger populations.

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Obtaining of funding: ZHMY
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Administrative, technical, or logistic support: ZHMY

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Original Article

The Relationship between Media Use and Body Mass Index among Secondary Students in Kuching South City, Sarawak, Malaysia

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Abstract -

Background: Overweight and obesity rates among adolescents have increased substantially over the years. This study aimed to determine the body mass index (BMI) of students and parents and the relationship among media use, BMI, socio-demographic profiles, and snacking behaviour during television watching of secondary school students in Kuching South City.

Methods: In accordance with the two-stage sampling method, a total of 316 adolescents aged 13–17 years from 7 secondary schools participated. Data were collected using questionnaire and anthropometric measurement. Independent *t* test, one-way ANOVA, Mann–Whitney U test, and chi-square test were performed.

Results: The mean BMI was 20.56 kg/m² (SD 4.33) for boys and 20.15 kg/m² (SD 3.91) for girls. No significant difference in terms of z score for BMI-for-age or socio-demographic factors was found. The mean duration of time devoted to media use was 4.69 hours (SD 2.93) on weekdays and 5.69 hours (SD 2.87) on weekends. Boys were found to spend more hours on media use than did the girls (t = 4.293, P < 0.01). Respondents were reported to consume more cereal compared with soft drinks and junk foods. Respondents whose fathers worked in the private sector devoted the fewest hours to media use, whereas those with self-employed fathers devoted the most time to media use. Respondents with mothers who were employed spent more time on media use than did respondents whose mothers were housewives (F = 4.067, P < 0.01). No significant difference was found between BMI and media time or snacking habits.

Conclusion: This finding indicated that media time has no effect on body weight, because respondents were found to have normal weight and to consume less unhealthy food.

Keywords: adolescent, behaviour, body mass index, public health, urban population

Introduction

Obesity affects adults, adolescents, and children (1,2). The World Health Organization (WHO) has indicated that at least 1.6 billion adults (age 15 years and above) are overweight (2). Globally, 400 million adults were obese and 20 million children under the age of 5 years were overweight in 2008. Around the world, children are increasingly vulnerable to overweight and obesity (3). The International Obesity Task Force

estimated that, in 2002, a total of 155 million school-age children (5–17 years) worldwide were overweight or obese. Approximately 30–45 million within that figure were classified as obese, which accounts for 2% to 3% of the world's children in this age group (3).

Adolescents who are overweight may begin to experience health consequences when they are young and run the risk of various weightrelated health problems later in life (4). Li et al. (5) have reported that respiratory function deficit has become a problem in obese adolescents, with a reduction of forced vital capacity and forced expiratory volume in 1 second. Furthermore, overweight adolescents have a significant risk of hypertension and lower limb joint disorders (6). Type 2 diabetes, previously considered as an adult disease, has increased dramatically in adolescents (7). Other health risks in obese individuals include heart disease, several types of cancers, sleep apnoea, and arthritis (7). However, the most immediate consequence of overweight, as perceived by children themselves, is social discrimination (7). Overweight children are at an increased risk of teasing and bullying, low selfesteem, and poor body image. Thus, childhood overweight has psychological and emotional consequences (8).

In Malaysia, the third National Health and Morbidity Survey, conducted in 2006, revealed that the national prevalence of underweight children was 13.2%, that the prevalence of normal-weight children was 81.4%, and that the prevalence of overweight children was 5.4%. In Sarawak, 13.5%, 80.3%, and 6.1% of the children were underweight, of normal weight, and overweight, respectively (9).

Many cross-sectional studies have identified a positive relationship between media use and children's weight status. Bradlee et al. (10) found that BMI was highest for children who watched the most television childhood and was lowest for those who watched the least television (mean BMI of 20.9 versus 18.6 kg/m² for those watching television for versus 1.75 hours/day, respectively). In particular, ownership and use of television are linked with the shift towards much greater inactivity (11) and snacking during television watching (12-14). As there was limited information on the relationship between media use and BMI among adolescents locally, this study was conducted to determine the BMI of students and parents; the association between media time, BMI and socio-demographic profiles; and snacking behaviour during television watching.

Subjects and Methods

Kuching is the most populated district in Sarawak, with an estimated population of 579 900 people, consisting of Chinese (220 400), Malays (207 000), Ibans (58 100), Indians and other ethnic groups (94 400). There are 38 secondary schools in Kuching district. In Kuching South City alone, there are 14 secondary schools with a total of 19 601 students. This

research was conducted among students aged 13–17 years in the secondary schools in Kuching South City.

This was a cross-sectional study using a two-stage sampling technique. One school was randomly selected from each of the 7 residential zones in Kuching South City; 1 of the schools was chosen for pilot study, and the remaining 6 schools were included in the main study. Within every school, 1 class was randomly selected from each of the forms (Form 1, 2, and 4); however, Form 3 and 5 students were excluded because they were involved in preparation for public examinations. The selected classes had 30-50 students per class. The minimum sample size was determined using the formula for single proportion (Epi Info version 3.3.2, Centers for Disease Control and Prevention, US). Based on the national overweight prevalence of 6.1% and sampling frame of 19 601, the minimum sample size to achieve results with a confidence rate of 95% or more was estimated to be approximately 346, with a non-response allowance of 10% and the precision of the prevalence of overweight selected as 2.5%. Ethical approval was obtained from the Ministry of Health and permission to conduct the study was granted by the Ministry of Education, Malaysia. Informed consent was obtained from respondents' parents prior to data collection.

dual-language (Malay and English), 3-section questionnaire was designed for this study. Section 1 included respondents' sociodemographic information such as age, race, gender, number of siblings, and parents' particulars. Section 2 consisted of 11 questions to determine the time devoted by respondents to media use, which included television viewing, computer playing, video games, and other electronic screen equipment. The questions in Section 2 were adapted from Saelens et al. (15) and Eisenmann et al. (16). As most studies found a relationship between snacking and television watching (12-14), Section 3, which contains 4 questions, was designed to investigate respondents' snacking habits while watching television. A series of discussions by experts in the same field verified the validity of the content. Items of the questionnaire were translated to the Malay language using the back-translation method. The questionnaire was piloted in one of the selected schools. Cronbach's alpha of the questionnaire in Section 2 was found to be 0.72.

All respondents were gathered in a designated room in the school during the co-curriculum session. The first, second, or third investigator

read the questionnaire to ensure the respondents responded to each item in the questionnaire. Height and weight were measured with the respondents in school uniforms and socks. Height was measured using a Seca body meter suspended upright against a straight wall. The respondents stood underneath the body meter, and the measuring beam was pulled down to rest on their heads. Height was recorded to the nearest tenth of a centimetre. Body weight was measured using a Seca digital weighing scale with an accuracy of 0.1 kg. For classification of overweight, z score for BMI-for-age were generated using AnthroPlus version 1.0.2 (WHO, Geneva, CH). A score of more than 2 standard deviations was classified as overweight.

Data were analysed using SPSS version 15 (SPSS Inc., Chicago, IL). Data were cleaned for outliers and checked for normality using box-plots and Kolmogorov–Smirnov and Shapiro–Wilkes statistics. Significant association between variables was determined using inferential statistics based on a *P* value of less than 0.5 (two-sided). Independent *t* test and one-way ANOVA were performed to compare the difference in means. If data were not normally distributed, Mann–Whitney U test was performed. Chi-square test was performed to determine the association between two categorical variables.

Results

A total of 316 out of 346 students participated in the study, yielding a response rate of 91.3%. There were similar numbers of boys (48.4%) and girls (51.6%), with a majority of respondents being Chinese (45.3%). Majority of the parents have educational level up to secondary schools. The majority of the respondents had fathers who worked in the private sector (50.9%), whereas their mothers were mostly housewives (52.8%). The mean self-reported total household income was RM3652.90 (SD 3740.60). Detailed background information is presented in Table 1.

The mean BMI for boys (20.56 kg/m², SD 4.33) was almost equal to the mean BMI for girls (20.15 kg/m², SD 3.91). However, the mean BMI of mothers (23.71 kg/m², SD 4.35) and fathers (24.83 kg/m², SD 3.82) differed slightly. Based on BMI-for-age z score, 8% of the respondents were found to be overweight (Table 1), with more overweight boys (64%) compared with girls (36%).

The association between BMI of respondents and socio-demographic factors is presented in Table 2. The findings revealed no significant difference in terms of BMI and socio-demographic factors. Fathers with diplomas and higher levels of education were found to have children with the highest mean BMI (21.62 kg/m², SD 3.96). In contrast, respondents' mothers with primary school educations were found to have children with the highest mean BMI (21.39 kg/m², SD 4.91).

Most of the respondents (39.6%) had 1 television set in the house, followed by 2 sets (37.0%), more than 3 sets (22.8%), and no television set in the house (0.6%). The mean number of television sets was 1.82 sets. Approximately 80.7% (n = 255) of the respondents reported having no television set in the bedroom. The Radio Televisyen Malaysia station was reported to be the major station (72.5%) available to the respondents, followed by the Astro station (46.5%), and the satellite stations (19.6%). The mean number of hours spent on media use was 4.69 hours on weekdays and 5.69 hours on weekends, with a total of 10.39 hours spent in this capacity in a given week.

As presented in Table 3, boys spent more hours on media use (11.66 hours, SD 5.64) than did girls (9.19 hours, SD 4.94) in a week. This difference was shown to be significant (P < 0.001). Respondents whose fathers worked in the private sector devoted the least amount of time to media use (9.88 hours, SD 5.49), whereas those who had self-employed fathers tended to spend the most hours in this manner (12.17 hours, SD 5.43). However, the difference was not significant. In terms of the mother's occupation, there was a significant difference in the hours of media use for respondents with mothers who were governmentemployed (11.64 hours, SD 5.47), those who worked for private companies (11.73 hours, SD 5.39), and those who were housewives (9.33 hours, SD 5.13). The parents' educational level did not show a significant difference in terms of the hours spent on media use by the child.

The respondents consumed mostly cereals (26.9%), compared with soft drinks (4.7%), fast food (7%), and junk food (11.7%), every day while viewing television. About 60% of the respondents did not consume food advertised on the television. A chi-square analysis was performed to determine the association between BMI-for-age and snacking habits (Table 4). The result revealed no significant association between different types of snacking habits and BMI-for-age. There was also no significant relationship between BMI and presence of television in the bedroom.

 Table 1: Background information of the respondents

Item	n		%
Gender			
Male	153		48.4
Famale	163		51.6
BMI-for-age			
Normal	291		92
High	25		8
Race			
Malay	115		36.4
Chinese	143		45.2
Others (including Iban and Bidayuh)	58		18.4
Father's educational level			
None	14		4.4
Primary	32		10.1
Secondary	187		59.2
Diploma & higher	83		26.3
Mother's educational level			
None	25		7.9
Primary	25		7.9
Secondary	202		63.9
Diploma & higher	64		20.3
Father's occupation			
Self-employed	21		6.6
Government sector	80		25.3
Private sector	161		51.0
Others	54		17.1
Mother's occupation			
Housewife	167		52.8
Self-employed	14		4.4
Government sector	54		17.1
Private sector	59		18.7
Others	22		7.0
Item	Me	an (SD)	Range
Monthly Income (RM)			
Total household	3653	(3740.6)	0-21 091
Father	2561	(2707.9)	0-20 000
Mother	1091	(1666.0)	0-10 000

Abbreviation: BMI = body mass index.

Table 2: Association between BMI of respondents and socio-demographic factors

Variable	BMI (kg/m²)	P value
Gender ^a		0.140
Male	20.56 (4.33)	
Famale	20.15 (3.91)	
Parents ^a		0.295
Father	24.83 (3.82)	
Mother	23.71 (4.35)	
Father's occupation ^b		0.953
Self-employed	20.83 (2.51)	
Government sector	20.27 (4.34)	
Private sector	20.35 (3.97)	
Other	20.27 (4.76)	
Mother's occupation ^b		0.893
Housewife	20.36 (4.16)	
Self-employed	20.30 (3.67)	
Government sector	19.89 (3.32)	
Private sector	20.55 (4.11)	
Other	20.83 (5.82)	
Father's educational level ^b		0.591
None	20.71 (5.57)	
Primary	20.39 (3.57)	
Secondary	20.11 (3.97)	
Diploma and above	21.62 (3.96)	
Mother's educational level ^b		0.557
None	20.61 (4.28)	
Primary	21.39 (4.91)	
Secondary	20.10 (3.86)	
Diploma and above	20.36 (3.94)	

Data were analysed using $^{\rm a}$ independent t test and $^{\rm b}$ one-way ANOVA and are expressed in mean (SD). Abbreviation: BMI = body mass index.

Discussion

Globally, the number of overweight adolescents is increasing at an alarming rate. The prevalence of overweight adolescents is as high as 21% to 30% in the United States (17). In Malaysia, the prevalence of overweight adolescents ranged from 16.7% to 35% (18,19). This study found that only 8% of the respondents were overweight, which is much lower than figures reported in other studies. This could be due to the voluntary participation of respondents in each randomly selected school and class. Parents with overweight children might not have consented to have their

children participate in this study.

Similar mean BMI for both genders was found in this study, which was in agreement with a study done by Norimah et al. (20) in 4 regions of Peninsular Malaysia, Sabah, and Sarawak (n = 9374), as well as another study conducted in Malaysia (18). This could be because adolescents in this study had similar dietary patterns in terms of quantity and quality of food intake, physical activities, and environmental factors. As adolescents have a more effective metabolism, their body weight is easily maintained if this metabolism is balanced by proper food intake and physical exercise (21).

Table 3: Association between media time, BMI and Socio-demographic profiles

Variable	Media ti	me (hours)	<i>P</i> value
Gender ^a			<0.001 ^d
Male	11.66	(5.64)	
Famale	9.19	(4.94)	
BMI-for-age ^b			0.729
Normal	10.364	(5.44)	
High	10.66	(5.34)	
Father's occupation ^c			0.245
Self-employed	12.17	(5.43)	
Government sector	10.76	(5.46)	
Private sector	9.88	(5.49)	
Other	10.65	(5.13)	
Mother's occupation ^c			<0.001 ^d
Housewife	9.33	(5.13)	
Self-employed	12.82	(5.85)	
Government sector	11.64	(5.47)	$0.047^{\rm e}$
Private sector	11.73	(5.39)	$0.026^{\rm e}$
Other	10.2	(5.94)	
Father's educational level ^c			0.591
None	10.14	(4.91)	
Primary	9.79	(5.59)	
Secondary	10.74	(5.76)	
Diploma and above	9.87	(4.65)	
Mother's educational level ^c			0.209
None	10.4	(4.25)	
Primary	8.3	(5.05)	
Secondary	10.45	(5.65)	
Diploma and above	11	(5.16)	

Data were analysed using a independent t test, b Mann–Whitney U test, and c one-way ANOVA, and are expressed in mean (SD). Differences with d P < 0.001 and c P < 0.05 are considered significant.

There was no significant association between BMI of respondents and their parents' occupational and educational level. Doustmohammadian et al. (21) also reported similar findings. However, fathers with a high school diploma or higher education tended to have children with higher mean BMI compared with those with lower educational levels. Rahman et al. (22) suggested that, because fathers are the main earners in most families, their level of education might play a role in providing more nutritious food for their children. Wang (23) suggested that those families with higher economic status would have better

access to meat and energy-dense food, which were more expensive, and they also tended to be more sedentary in their lifestyle. Thus, these factors might have contributed to higher BMI among the respondents in the present study.

However, mothers with only primary school-level educations were shown to have children with the highest mean BMI. Giuoglino and Carneiro (24) also found similar results. Mothers are usually responsible for shopping and cooking; therefore, their educational level may affect the food items purchased and the method of cooking (21). Mothers with only primary-school

Table 4: Association between BMI-for-age and snacking habits and presence of television in the bedroom

television in the bearoom					
	BMI-for-age				P value
	No	rmal	Н	igh	
Cereal					0.146
Everyday	77	(26.5)	8	(32.0)	
Occasionally	99	(34.0)	12	(48.0)	
Seldom	115	(39.5)	5	(20.0)	
Soft drink					0.06
Everyday	12	(4.1)	3	(12.0)	
Occasionally	164	(56.4)	9	(36.0)	
Seldom	115	(39.5)	13	(52.0)	
Fast food					0.212
Everyday	22	(7.5)	0	(0.0)	
Occasionally	157	(54.0)	9	(41.0)	
Seldom	112	(38.5)	13	(59.0)	
Junk food					0.294
Everyday	36	(12.4)	1	(4.0)	
Occasionally	162	(55.6)	13	(52.0)	
Seldom	93	(32.0)	11	(44.0)	
Presence of television in bedroom					0.289
Yes	54	(88.5)	7	(11.5)	
No	257	(92.9)	18	(7.1)	
D. 1 1 11 1			-		

Data were analysed using chi-square test and are expressed in number of respondents (percentage).

educations are most probably housewives. As housewives, they may have more time to devote to preparing meals for their children. In addition, they may lack knowledge regarding the factors that predispose individuals to high BMI as well as its consequences.

The mean number of television sets found in this study was 1.82, which was lower than that found by a study done in the United States, 2.86 (25). This difference could reflect the fact that American families are more affluent and earn better incomes and are thus able to afford more television sets. The difference could also be due to the fact that most Malaysians regard television as a basic necessity rather than a luxury. Approximately 80% of the respondents did not have a television set in their bedroom. This is in accordance with Malaysian culture, where the television set is commonly placed in the living room. Among respondents who had television sets in their bedrooms, a slightly greater percentage had higher BMI. The presence of a television in

the bedroom was found to be a stronger predictor of obesity than the amount of time spent watching television (26,27). This is because adolescents with a television in their bedroom were less involved in healthy activities, such as exercising, eating fruits or vegetables, and enjoying family meals, and they consumed larger quantities of sweetened beverages and fast food (17).

Respondents devoted approximately 10 hours of their time to media usage in a given week, with more time spent on media during the weekends. This finding is understandable because respondents would have more time for media use during the weekends, when they do not have to go to school. However, the time spent on media use was much lower than that of their American counterparts, who spent around 1 to 5 hours per day on media use (13,14). This was probably the reason for the low percentage (8%) of respondents who were found to be overweight in this study. Boys were shown to spend significantly more hours in a given week on media than did the girls.

This finding was in agreement with another study, where boys spent more time playing computer games (27). Study has shown that boys and girls may have different interests with regards to leisure time where boys spent more time playing video games, and girls spent more time in reading and doing homework (28). There was no significant association between the father's occupation and the respondent's television-viewing behaviour. Respondents who had fathers working in private and government sectors were reported to devote the least time to media use. This could be because these fathers have fixed working hours and hence, they might have more time to spend with their children by bringing them out rather than allowing them to stay in the house watching television during their leisure time. Meanwhile, respondents with fathers who were self-employed tended to devote the most time to media use. This might indicate that these fathers were too busy due to longer and irregular working hours; therefore, the respondents spent most of their leisure time at home watching television.

respondents' mother's occupation was found to be significantly associated with the respondents' television-viewing behaviour. Respondents with mothers who were governmentemployed or working for private companies spent more time on media use compared with respondents whose mothers were housewives did. Anderson et al. (29) stated that increased maternal employment would lead to a rise in the prevalence of overweight children. Due to constraints on the mother's time, children are left unsupervised (29); these children may engage in more sedentary activities after school (30). In addition, adolescents may be required to spend a great deal of time indoors rather than outdoors, perhaps due to safety concerns. As such, they spend their time watching television or playing video games rather than engaging in more active outdoor pursuits (29). However, mothers who are housewives may spend more time at home with their children. These mothers might also be able to ensure that their children spend their time engaging in academic activities rather than on media use.

This study found that a higher percentage of respondents consumed cereal as opposed to unhealthy foods, such as soft drinks, fast food, and junk food. This finding was different from findings in the United States, where soft drink consumption while watching television was higher (13).

More than half of the respondents (63%) did not consume food advertised on television. This might be associated with fewer television viewing hours; therefore, respondents had less exposure to food advertisements on television. When adolescents were exposed to more hours of television watching, there was also an increase in the consumption of advertised foods (14). Another factor that may result in less consumption of advertised food could be that families with higher education levels tend to be more health conscious (31).

There was no significant association between BMI and snacking habits. The majority of respondents with higher BMI reported that they seldom consumed soft drinks, fast food, or junk food; rather, they consumed more cereal. Cereal is known generally as a healthy food, and parents would tend to encourage their children to consume more, especially among those families with higher educational levels, who paid more attention to health considerations (31).

There were limitations in the study. Firstly, the possibility of having more respondents with normal BMI who consented to participate in this study could not be ruled out, which might have contributed to the low percentage of overweight observed. In addition, excluding the participation of students in Form 3 and Form 5 classes might limit the generalisability of the findings to the adolescents residing in Kuching South City. However, these preliminary findings are still valuable for future research related to media use and other contributing factors to overweight and obesity among adolescents in Malaysia.

Conclusion

Only 8% of the respondents were found to be overweight. The mean media time for respondents with normal and high BMI was almost equal. The mean media time per week was found to be much lower than that found in the United States. In addition, this study found that a smaller percentage of respondents had television sets in their bedrooms. The respondents also reported that, when watching television, they consumed cereal more frequently than other unhealthy foods. Thus, it can be concluded that the low percentage of overweight found in this study could be related to the respondents spending relatively less time on media use and consuming healthy food while watching television.

Original Article | Media use and body mass index

Authors' Contributions

Conception and design, critical revision of the article, administrative, technical, or logistic support: WLC, CTC, SR

Collection, assembly, analysis, and interpretation of the data, drafting of the article: WLC, CTC, LDC, SLY, PHT, KPY

Obtaining of funding, provision of study materials or patients, statistical expertise, final approval of the article: WLC, CTC

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Original Article

A Comparison Study of Conjunctiva Disorders in Technical and Administrative Sawmill Workers in Nigeria

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Abstract -

Background: Workers in the sawmilling industry are at risk of various ocular hazards as a direct result of the sawmilling processes. The aim of this study was to determine the pattern of conjunctival disorders between technical and administrative sawmill workers in Benin, Nigeria.

Methods: A cross-sectional study was performed on sawmill workers in Benin, Nigeria, between January and May 2009, with the aid of pre-tested questionnaires. Ocular examination was performed on all subjects. Data obtained were recorded and analysed using SPSS version 13.

Results: A total of 553 sawmill workers were studied, among whom 449 (81.2%) and 104 (18.8%) were technical and administrative workers, respectively. There were 496 (89.7%) males and 57 (10.3%) females. The age range was 15–80 years, with a mean of 38.9 years (SD 12.8). Pingueculum was found in 127 (23%) workers, among whom 122 (27.2%) were technical workers and 5 (4.8%) were administrative workers. Pterygium was present in 65 (11.8%) workers, among whom 64 (14.3%) were technical workers and 1 (1%) was an administrative worker. Seven (1.6%) technical workers used protective eyewear; 2 (0.4%) wore this protective eyewear regularly.

Conclusion: Technical sawmill workers are at risk of developing conjunctival disorders, which result from chronic ocular irritation. This can be prevented by the provision of protective eye devices in the workplace.

Keywords: air pollutants, conjunctival diseases, eye protective devices, occupational exposure, ophthalmology, pterygium

Introduction

A sawmill is a facility where logs of timber are cut into boards. The sawmilling process involves logging, which is the process of felling trees; this is followed by log bucking, which involves cutting them to length. The logs are then transported to the sawmills, where they are further processed (1,2). Removal of bark from a log, or debarking, is then done either mechanically or hydraulically. The processes involved in sawmilling put the workers at potential risk of health conditions such as asthma, dermatitis, and hearing defects (2–5). These workers are also at risk of various ocular disorders.

Debarking operations expose the workers to airborne soil as well as pathogenic fungi and bacteria that could be present on the wood. This could result in ocular infections, such as bacterial conjunctivitis, keratitis, and orbital cellulitis, if there is a penetrating injury. This could be both sight- and life-threatening. Cartwright et al. (6) reported that there was a high risk of infection following injuries from organic or vegetal foreign

bodies, such as wood. In the process of sawing wood, sawdust composed of fine particles of wood is released into the atmosphere. These particles are detrimental to ocular health, causing chronic ocular irritation, and can result in conditions such as pterygium and pingueculum (7). Exposure to wood dust during the sawmilling process may also cause exposure to the volatile components of wood, such as monoterpenes, aldehydes, and ketones. This could lead to both acute and chronic ocular irritations, with resultant chronic conjunctivitis. Sawmill workers usually have symptoms of tearing, redness, and itchiness of the eyes (2). Allergic conjunctivitis can be caused by naturally occurring chemicals, such as plicatic acid, which are present in some wood species. For example, the wood of western red cedar is known to cause ocular allergies, dermatitis, and bronchial symptoms because of its plicatic acid content (2).

Most of the tree species processed in Nigeria are highly allergenic (8). Ahman et al. (9) noted many woods contain chemicals that can irritate the eyes, nose, or throat. They also explained that some of these effects could be caused by

molds growing on the wood and not always by the wood dust itself. These mold spores become airborne when wood chips are moved, lumber is trimmed, or bark is stripped (2,9). Fungicides, such as azaconazole and chlorophenate, are sometimes applied to wood to prevent the growth of fungi if the logs will be stored for a long time before further processing (2). Treatment with insecticides and wood preservatives, such as pentachlorophenol and creosote, is sometimes used to protect the wood surface from mechanical wear or weathering (2). These fungicides as well as wood preservatives could result in chemical conjunctivitis upon accidental entry to the eye (2). These processes potentially put the sawmill worker at risk for ocular irritation, allergic reactions, ocular injury, and even severe ocular infections, which could result in blindness (2,7).

Nigeria is endowed with a good reserve of wood (8). Depending on the climate of the region and the size of the mill, sawing operations may be performed outdoors or indoors (2). In Nigeria, most of the sawmilling processes are performed outdoors. Workers in outdoor sawmills are at added risk of chronic exposure to ultraviolet radiation (290-400 nm), as are other outdoor workers (10). Thus, they are at risk of developing ocular disorders, such as pterygium, pingueculum, dry eyes, senile cataract, and age-related macular degeneration (11,12). Those in the tropics have a greater risk because of the hot, dry, sawdustfilled environment. Hence, it is necessary to protect the eyes by wearing large goggles with side shields. These workers are also at risk of bacterial and fungal ocular and orbital infections (6).

Certain types of occupational diseases are particular to various occupations, for example, miners' nystagmus and glass-blowers' cataract (13). Ocular hazards in industries are preventable if adequate precautionary measures are taken (14). The aim of this study is to compare the pattern of conjunctival disorders between technical and administrative sawmill workers in Nigeria and offer appropriate recommendations.

Subjects and Methods

A comparative cross-sectional study between technical and administrative sawmill workers was carried out in Benin, Nigeria, between January and May 2009. A list of all sawmills in Benin, Nigeria, and their various locations were obtained from the Forestry Division, State Ministry of Agriculture. The Ethics and Research Committee as well as the Health Department of the University of Benin Teaching Hospital, Nigeria, granted

approval to conduct this study. Informed consent was obtained from all participants.

Participants were the technical and administrative sawmill workers. Administrative workers were those involved in the payment of salaries, clerical work, and sales transactions. Technical workers included sawyers who fell trees, converters who transport the logs from the forest for processing, jack men who roll the logs from the field onto the various machines, machine operators, wood loaders who transfer the finished products for sale onto vehicles and sawdust packers who are involved in evacuating the sawdust generated, and clearing up bark.

Pre-tested questionnaires designed for the study were administered. Assessment of visual acuity (VA) for each eye was done using Snellen's chart, which was placed at a distance of 6 m outdoors. Aided and unaided VA was carried out where applicable. For individuals whose VA was less than 6/6, pinhole VA was done to exclude the presence of refractive errors. Near vision was assessed with the Roman tests. Further ocular examination was performed on site in improvised areas with some shade. All examinations were performed during the daytime by the first author. Anterior segment examination was done with a pen torch and a portable hand-held slit lamp bio-microscope (Scan Optics, EU).

A diagnosis of pterygium was made in the presence of a wedge-shaped fibrovascular subepithelial ingrowth of degenerative bulbar conjunctival tissue over the limbus onto the cornea. Allergic conjunctivitis was diagnosed in the presence of itching, redness, stringy mucoid discharge, or palpebral or limbal papillae on the conjunctiva. Bacterial conjunctivitis was diagnosed clinically in the presence of an acute onset of purulent discharge with conjunctival hyperaemia without a history of decreased vision (15).

Results

There were 62 registered sawmills of which 38 were operating during the period of the study. No randomisation was done; all of the workers were included in the study except those who declined. Out of 602 sawmill workers, 553 agreed to participate: 449 (93.3%) out of 481 technical workers and 104 (86.0%) out of 121 administrative sawmill workers. The response rate was 91.9%. Those who were unwilling to participate felt the study would interrupt and delay the completion of their tasks for the day. There were 496 (89.7%) males and 57 (10.3%) females, with a male to

female ratio of 8.7:1. The technical workers had a male to female ratio of 12.6:1, whereas for administrative workers, 3.3:1. All of the workers were Nigerians.

The age distribution of the sawmill workers is shown in Table 1. The age range was between 15 and 80 years, with a mean age of 38.9 years (SD 12.8). The mean age of the technical workers (38.2 years, SD 12.7) was significantly higher (P = 0.015) than the mean age of the administrative workers (41.6 years, SD 12.8).

The ocular symptoms in sawmill workers are presented in Table 2. Out of 378 sawmill workers who had ocular disorders, 235 (62.8%) workers complained of having symptoms; some had multiple symptoms. Symptoms such as tearing, itching, foreign body sensation, and photophobia were more common in the technical workers. The type and prevalence of conjunctival disorders seen in sawmill workers are shown in Table 3. Pingueculum was the most common disorder, present in 127 (23.0%) workers. Ninety-eight (25.3%) sawmill workers had multiple ocular problems.

The relationship between the nature of the work and the development of pterygium is presented in Table 4. There were 65 (11.8%) workers with pterygium, out of which 64 (11.6%) were technical sawmill workers and 1 (0.2%) was an administrative sawmill worker. A technical sawmill worker was more likely to develop pterygium than an administrative sawmill worker (odds ratio = 2.8, 95% CI = 0.9–4.8). A total of 127 (23.0%) workers had pingueculum, among whom 122 (22.1%) were technical sawmill workers, whereas 5 (0.9%) were administrative sawmill workers (Table 5). There was a significant relationship between the nature of the work and

the development of pingueculum. A technical sawmill worker was more likely to develop pingueculum than an administrative sawmill worker (odds ratio = 7.4, 95% CI = 2.9-18.6). Seven (1.6%) of the 449 technical sawmill workers used protective eyewear, whereas 442 (98.4%) did not. Only 2 (0.4%) workers used protective eyewear regularly; the other 5 (1.1%) did not.

Discussion

The response rate among technical workers was higher than that of the administrative workers. This may be due to the direct involvement of technical workers in the sawmilling process and the higher rate of exposure of their eyes to the ocular hazards of the profession, which made them more willing to have their eyes examined. Majority of the subjects are males, especially among the technical workers. This male predominance was also reported in a previous study (16); it is not surprising that more of them are involved in technical tasks because the profession necessitates manual labour, hence the need for more males (2).

Symptoms of ocular irritation, such as tearing, itching, foreign body sensation, and photophobia, were more common in the technical workers than in the administrative workers. A technical worker who was more exposed to the irritant effects of sawdust was more likely to present with the symptoms of ocular irritation.

The most common ocular disorders seen in this study were degenerative conjunctival disorders (pterygium and pingueculum), which were responsible for 34.8% of cases; 23.0% were secondary to pingueculum, whereas pterygium was responsible for 11.8% of cases. A similar

Table 1: Age di	stribution	of sawmill	workers
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Age		nical kers		Administrative workers		
	n	(%)	n	(%)	_	
11-20	29	6.5	5	4.8	0.015 ^a	
21-30	118	26.3	15	14.4		
31-40	120	26.7	30	28.8		
41-50	104	23.1	25	24.0		
51-60	52	11.6	24	23.1		
61-70	26	5.8	1	1.0		
71-80	0	0.0	4	3.9		

^a Student's t test, t (551) = 2.430.

Table 2: Multivariate analysis showing prevalence of ocular symptoms in sawmill workers

Symptom	Technical sawmill workers n = 449			Administrative sawmill workers n = 104				P value	
	Y	es	N	lo	7	Zes		No	
Tearing	74	(16.5)	375	(83.5)	7	(6.7)	97	(93.3)	0.009ª
Itching	35	(7.8)	414	(92.2)	5	(4.8)	99	(95.2)	0.400
Redness	25	(5.6)	424	(94.4)	6	(5.8)	98	(94.2)	0.963
Foreign body sensation	3	(0.7)	446	(99.3)	0	(0.0)	104	(100.0)	1.000
Eye pain/Eye aches	2	(0.4)	447	(99.6)	2	(1.9)	102	(98.1)	0.162
Discharge	13	(2.9)	436	(97.1)	3	(2.9)	101	(97.1)	1.000
Photophobia	6	(1.3)	443	(98.7)	0	(0.0)	104	(100.0)	0.599
Grittiness	7	(1.6)	442	(98.4)	2	(1.9)	102	(98.1)	0.679
Lid Swelling	0	(0.0)	449	(100.0)	1	(1.0)	103	(99.0)	0.100

Data are expressed in number of subjects (percentage). a Significant at 95% confidence level with Pearson's chi-square test.

Table 3: Multivariate analysis showing the relationship between conjunctival disorders and nature of work in sawmill workers

Disorder	Technical workers			Administrative workers		Total	
	n	(%)	n	(%)	n	(%)	
Pingueculum	122	(27.2)	5	(4.8)	127	(23.0)	<0.001 ^a
Pterygium	64	(14.3)	1	(1.0)	65	(11.8)	<0.001 ^a
Allergic conjunctivitis	44	(9.8)	7	(6.7)	51	(9.2)	0.330
Bacterial conjunctivitis	21	(4.7)	0	(0.0)	21	(3.8)	0.020 ^a

^a Significant at 95% confidence level with Pearson's chi-square test.

Table 4: Odds ratio analysis of pteryngium among workers

Nature of work	Pteryngium				Total	P value
	Pr	esent	Absent			
Technical workers	64	(14.3)	385	(85.7)	449	<0.001 ^a
Administrative workers	1	(1.0)	103	(99.0)	104	<0.005 ^b

Data are expressed in number of subjects (percentage). $^{\rm a}$ $\chi^{\rm a}$ (1) = 14.384. $^{\rm b}$ OR = 2.8, 95% CI 0.9–4.8. The Mantel-Haenszel common odds ratio estimate is not normally distributed under the common odds ratio of 1.00 assumption, owing to inadequate counts for sub-cell analysis, thereby showing a high level of imprecision. Hence, the natural log of the estimate was used.

Table 5: Odds ratio analysis of pingueculum among workers

Nature of work	Pingueculum				Total	P value
	Pre	esent	Absent			
Technical workers	122	(27.2)	327	(72.8)	449	<0.001 ^a
Administrative workers	5	(4.8)	99	(95.2)	104	

Data are expressed in number of subjects (percentage). $^{\rm a}$ OR = 7.4, 95% CI 2.9–18.6.

Table 6: Odds ratio analysis of allergic conjunctivitis among workers

Nature of work	Allergic co	Total	P value	
	Present	Absent		
Technical workers	44 (9.8)	405 (90.2)	449	0.333^a
Administrative workers	7 (6.7)	97 (93.3)	104	

Data are expressed in number of subjects (percentage). a OR = 1.5, 95% CI 0.7-3.4.

finding was reported by Omoti et al. (17) in other outdoor workers, with conjunctival disorders having the highest prevalence rate of 30.1%. Pingueculum and pterygium are ocular disorders associated with chronic exposure to ultraviolet radiation (10,18). Other risk factors identified include chronic ocular irritation, dust, windy conditions, and outdoor work (18). There were more cases of pingueculum than pterygium in this study.

The prevalence rates of pterygium in the general population in Nigeria varied from 4% to 9% (19,20). However, in a study that reviewed the risk factors for pterygium and pingueculum, it was reported that sawmill workers and welders have higher prevalence rates of pterygium (10). In the current study, there was a significant difference in the occurrence of both disorders depending on the nature of work, such that a technical worker was more likely to develop pterygium and pingueculum than an administrative worker was. The difference is likely due to the higher outdoor exposure to irritants among the technical workers as compared to the administrative workers.

Allergic conjunctivitis had a prevalence rate of 9.2% among all the workers studied. The prevalence rate was 9.8% and 6.7% in technical and administrative workers, respectively. This may be attributed to the higher exposure to sawdust among the technical workers. However, the difference was not significant. Previously, Omoti et al. (21) reported a high prevalence rate of 23.3% among the industrial workers they studied. This may have resulted from differences in the nature of irritants in these industries. Some wood species, such as Triplochiton scleroxylon and Nauclea diderrichii, milled in Nigeria are highly allergenic (22). The rubbing of the eyes during itching with hands that are likely not clean due to the working environment may have rendered the technical workers more prone to develop bacterial conjunctivitis.

Only 7 workers used protective eye devices in this study, yielding a compliance rate of 1.6%; 98.4% of the technical workers did not protect their eves while working. Some of the administrative workers occasionally assisted with minor technical work. Even when they did, none of them protected their eyes. This is similar to findings by Titiyal and Murthy (23) in India, where 96.4% of the workers studied did not use protective eye devices. This level of noncompliance may be attributed to the fact that the workers in this study are in a developing nation, in the North Indian town; thus, the level of compliance with eve safety precautions was low due to insufficient awareness of its usefulness or negligence on the part of the employers. Okoye et al. (16) in Enugu, Nigeria, reported an even lower level of compliance among the sawmill workers studied; none used protective eyewear. This may be due to the smaller sample size.

Conclusion

The most common conjunctival disorders among sawmill workers in Nigeria are pingueculum, pterygium, and allergic conjunctivitis. A technical worker is more likely to have a degenerative disorder (pingueculum or pterygium) than an administrative worker is. This may be due to poor compliance with safety eyewear. There is a need to educate sawmill workers on the necessity to comply with the use of protective eye devices. The government and legislative bodies should enforce laws on the use of protective eye devices and ensure that employers provide the appropriate safety equipment for their workers.

Authors' Contributions

Conception and design, analysis and interpretation of the data, drafting and final approval of the article, provision of study materials, statistical expertise: IN, OMU

Collection and assembly of the data: IN Critical revision of the article: IN, OMU, OTE, OAD, AEO

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Original Article

The Socio-Demographic and Clinical Factors Associated with Quality of Life among Patients with Haematological Cancer in a Large Government Hospital in Malaysia

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Abstract

Background: The paper examined the quality of life of haematological cancer patients according to their socio-demographic profiles and clinical diagnoses.

Methods: This cross-sectional study was conducted at the tertiary referral centre of Ampang Hospital, Kuala Lumpur, involving 105 patients. The European Organisation for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) questionnaire was used to measure their quality of life.

Results: The study involved patients diagnosed with all types of haematological cancer, including non-Hodgkin lymphoma (NHL), acute myelogenous leukaemia (AML), acute lymphoblastic leukaemia (ALL), Hodgkin lymphoma (HL), and multiple myeloma (MM), with a response rate of 83.3%. The patients with ALL, HL, without NHL, and without MM were younger than other patients. There were significant differences in quality of life scores in different socio-demographic groups and types of cancer diagnosis. The global quality of life of the female patients was much better than that of the male patients. Patients who were 40 years old or younger had a better global quality of life and physical functioning, as well as fewer symptoms of constipation, nausea, and vomiting. Employed patients were in less pain but showed greater impairments of cognitive function than did unemployed patients. Patients who earned a monthly wage of RM1000 or less had reduced physical function, more symptoms of pain, and more financial difficulties compared with patients who earned more. Patients with AML tended to have better physical functioning than did patients with MM, whose physical functioning was impaired. Comparatively, more symptoms of dyspnoea were found in ALL and HL patients than in other types of lymphoma. Compared with other patients, those with ALL had a greater loss of appetite, and other lymphoma patients had fewer symptoms of pain. Patients with NHL had impaired role functioning and more constipation compared with other patients. The results were all statistically significant (P < 0.05).

Conclusion: The quality of life of haematological cancer patients is affected by sociodemographic factors and clinical diagnoses. Efforts should be made to improve the overall quality of life of these patients.

Keywords: haematological malignancies, leukaemia, lymphoma, multiple myeloma, oncology, quality of life, socioeconomic factors

Introduction

Nearly 7.6 million deaths due to cancer occurred globally in 2008, and as many as 12.7 million estimated cases of newly diagnosed cancer were reported worldwide (1). In Malaysia, cancer is classified as a major health problem (2), with an estimated annual incidence of 30 000 cases (3). A total of 21 773 patients

from peninsular Malaysia were diagnosed with cancer (4).

Haematological cancers include leukaemia, lymphoma and myeloma (5). In peninsular Malaysia, lymphoma is 1 of the 10 most frequent cancers among all individuals (3.2%) and among women (2.4%). Lymphoma (4.2%) and leukaemia (3.6%) are among the top 10 most frequent among men (4).

Published studies (6,7) provide detailed descriptions of the quality of life among haematological cancer patients; however, these studies were primarily conducted in Western populations. The quality of life may vary according to the type of the haematological cancer diagnosis (7); thus, there is a need to examine the quality of life of Malaysian haematological cancer patients with respect to their clinical cancer diagnoses and socio-demographic factors. To the best of our knowledge, there are no studies on this topic in Malaysian haematological cancer patients.

The aim of the present study was to describe the quality of life scores of patients in a large Malaysian hospital and compare them by different socio-demographic factors and haematological cancer diagnoses: acute myelogenous leukaemia (AML), acute lymphoblastic leukaemia (ALL), Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), and multiple myeloma (MM).

Subjects and Methods

This cross-sectional study was performed at a tertiary referral centre for cancer at Ampang Hospital, Kuala Lumpur, Malaysia. The sampling population consisted of haematological cancer patients admitted to ward 7A (male ward) and 7B (female ward). Each ward had 28 beds, composing a total 56 beds available for study sampling. Approximately 1391 patients were admitted to the wards in 2009. Between January and October 2009, 710 male patients were admitted; 681 female patients were admitted between January and December 2009. The admitted patients were treated for various blood system diseases, such as haematological cancers. The study period was between May and December 2009. Consecutively admitted haematological cancer patients were included if they had a confirmed haematological cancer diagnosis; spoke English, Malay, Mandarin or Tamil; were at least 15 years old; and were in a conscious state and able to complete the questionnaire. The questionnaire was distributed after mutual consent for participation in the study was obtained from the patient. Clinical and socio-demographic profiles were retrieved from the patients' and the hospital's medical records. Approval for the study was obtained from the Ethical Committees, Ministry of Health, and the Faculty of Medicine and Health Sciences, University Putra Malaysia.

The European Organisation for Research and Treatment of Cancer Quality Of Life Questionnaire (EORTC QLQ-C30) is a diseasespecific questionnaire administered to cancer patients. The questionnaire, which evaluates the quality of life, has been validated in Malay (8), the national language of Malaysia. Studies showed that the Malay-version of the questionnaire was suitable for wordwide use by Malay-speaking patients (8). Questionnaires in other languages, namely English (9), Mandarin, and Tamil (10) were also used in this study.

The 30 questions in the questionnaire comprise 5 functional scales that measure physical, role, cognitive, emotional, and social functioning; 5 symptoms scales that measure fatigue, pain, and nausea or vomiting: 1 global health status scale; and a 6 single-item scale that measures dyspnoea, insomnia, appetite loss, constipation, diarrhoea, and financial difficulties. The questions were rated on a scale of 4 points: "Not at all", "A little", "Quite a bit", or "Very much". Global health status was rated on a 7-point numbered scale that ranged from "Very poor" to "Excellent" (11). Each scale was given its own total score that ranged 0-100 and was computed from the raw scores and transformed linearly by referring to the EORTC QLQ-C30 scoring manual. Higher scores represent better functioning and better global health status, except in the symptom and single-item scales, for which higher scores are indicative of more symptoms (11).

The SPSS version 17.0 (SPSS Inc., Chicago, IL) was used in the study. Non-parametric statistical tests such as the Mann–Whitney U test were used to compare 2 variables and to determine the level of significance using a one-tailed test (P < 0.05). The non-parametric tests were performed because the sample sizes for some groups were small (less than 30). The one-tailed test was used for statistical comparison of groups. The use of the one-tailed test is a study limitation, as the chance for a significant P value (less than 0.05) is greater with the one-tailed test.

Results

Of the 126 patients screened, 105 patients were included in the study (response rate of 83.3%). Exclusion occurred for the following reasons: 6 patients refused to give consent; 13 patients were diagnosed with non-cancerous haematological diseases; and 2 patients had language-barrier problems.

Of the patients, 52.4% were female. Diagnosed haematological cancers included NHL (23.8%), AML (22.9%), ALL (14.3%), HL (10.5%), MM (5.7%), other lymphoma (12.4%), other leukaemia (9.5%), and histiocytosis (1.0%). Ethnic groups included Malays (60.0%), Chinese

(24.8%), Indians (13.3%), and others (1.9%). The socio-demographic and clinical characteristics of respondents are shown in Table 1.

The mean age of the patients was 40.4 years (range 15–78 years). The mean age of male patients, 43.6 years, was significantly higher compared with the female patients, 37.5 years (t = 1.991, df = 103, P = 0.049). Table 2 shows the age comparison based on mean rank in different disease diagnoses. The mean rank age of ALL patients, 38.67 years, was lower compared with non-ALL patients, 55.39 years (P = 0.025). The HL patients were also younger compared with

other patients, at 26.00 years versus 56.16 years (P = 0.001). In contrast, the NHL and MM patients were older than the other patients, at 65.08 years versus 49.23 years (P = 0.012) and 81.83 years versus 51.25 years (P = 0.009), respectively.

Table 3 shows between-group differences in the quality of life mean rank score as a function of socio-demographic profiles among the haematological cancer patients. The global quality of life of female patients, mean rank score of 59.70, was significantly better compared with male patients, mean rank score of 45.63 (P = 0.009). In age counterparts, patients

Table 1: Socio-demographic and clinical characteristics of respondents

haracteristics n (%)			
Age			
≤40 years	53	(50.5)	
>40 years	52	(49.5)	
Gender			
Female	55	(52.4)	
Male	50	(47.6)	
Occupation status			
Working	35	(33.3)	
Not working	70	(66.7)	
Total monthly income household			
≤ RM1000	31	(44.3)	
> RM1000	39	(55.7)	
Haematological cancer diagnosis			
Acute myelogenous leukaemia	24	(22.9)	
Acute lymphoblastic leukaemia	15	(14.3)	
Hodgkin lymphoma	11	(10.5)	
Non-Hodgkin lymphoma	25	(23.8)	
Multiple myeloma	6	(5.7)	
Other leukaemias ^a	10	(9.5)	
Other lymphomas ^b	13	(12.4)	
Other ^c	1	(1.0)	
Cancer duration			
Less than 6 months	50	(47.6)	
6 months or more	55	(52.4)	

^a Other leukaemias include chronic lymphocytic leukaemia (1 case), chronic myelogenous leukaemia (2 cases), acute promyelocytic leukaemia (3 cases), hairy cell leukaemia (1 case), myelodisplastic syndromes-refractory anemia with excess blast towards leukaemia (1 case), myelodisplastic syndromes- chronic myelomonocytic leukemia towards chronic leukaemia (1 case), and unclassified leukaemia (1 case). ^b Other lymphomas include peripheral T cell lymphoma (1 case), natural killer T cell lymphoma (3 cases), central nervous system lymphoma (2 cases), intravascular lymphoma (1 case), follicular transform lymphoma (1 case), and unclassified lymphoma (5 cases). ^c The remaining 1 case was of histiocytosis.

40 years or younger had better global quality of life (P = 0.006) and physical functioning (P = 0.002)scores as well as fewer symptoms of constipation (P = 0.024), but more symptoms of nausea and vomiting (P = 0.031) compared with patients who were older than 40. In addition, male patients faced more financial difficulties compared with female patients (P = 0.041). Patients in employment experienced less pain (P < 0.001), but demonstrated reduced cognitive functioning (P = 0.018) compared with patients who were unemployed. Patients who earned RM1000 or less monthly had reduced physical functioning (P = 0.022), more symptoms of pain (P = 0.014), and more financial difficulties (P = 0.001) than did patients who earned more. Other variables, such as the duration of haematological cancer, did not significantly differ with the quality of life scores (data not shown).

Table 4 represents between-group differences in the quality of life mean rank score as a function of haematological cancer diagnosis. Patients with AML had better physical functioning scores (P = 0.001) compared with the others, whereas MM patients had lower physical functioning scores (P = 0.010). Patients with ALL had more symptoms of nausea and vomiting (P = 0.035), dyspnoea (P = 0.005), and appetite loss (P = 0.005) compared with other patients.

HL patients also had more symptoms of dyspnoea compared with other cancer patients (P = 0.020). In contrast, patients with the other types of lymphoma experienced less pain (P = 0.006) and had fewer symptoms of dyspnoea (P = 0.013) and insomnia (P = 0.032). The NHL patients had reduced role functioning (P = 0.009) and more constipation (P = 0.009) compared with the others.

Discussion

The present study examined the relationship between the quality of life and various sociodemographic as well as clinical factors. Female haematological cancer patients reported a much better global quality of life than did male patients. To the best of our knowledge, comparisons by gender of the global quality of life in patients with haematological cancer are difficult because there are no published articles investigating this factor. It is interesting to note that patients in employment experiences less pain compared with those who were unemployed. In addition, most of the patients with more symptoms of pain, reduced physical functioning and financial difficulties were among those who earned less than RM1000 per month. Male patients faced more financial difficulties than did female patients.

Table 2: Comparison of age based on mean rank in different disease diagnoses

Diagnosis		n	Mean Rank Age	Z	P value
AML	Yes	24	47.04	-1.091	0.138
	No	81	54.77		
ALL	Yes	15	38.67	-1.969	0.025^{a}
	No	90	55.39		
HL	Yes	11	26.00	-3.108	0.001^{b}
	No	94	56.16		
NHL	Yes	25	65.08	-2.272	0.012 ^a
	No	80	49.23		
MM	Yes	6	81.83	-2.388	0.009 ^b
	No	99	51.25		
Other leukaemias	Yes	10	57.10	-0.448	0.327
	No	95	52.57		
Other lymphomas	Yes	13	62.77	-1.236	0.109
	No	92	51.62		
Other	Yes	1	65.00	-0.396	0.346
	No	104	52.88		

 $^{^{\}rm a}$ P < 0.05 and $^{\rm b}$ P < 0.01 with Mann–Whitney U test.

Abbreviations: AML = acute myelogenous leukaemia, ALL = acute lymphoblastic leukaemia, HL = Hodgkin lymphoma, NHL = non-Hodgkin lymphoma, MM = multiple myeloma.

Table 3: Between-group differences in the quality of life mean rank score as a function of socio-demographic profiles

Factor		DL	PF	RF	EF	CF	SF	FA
Factor		<u> </u>		Kr		Cr_	Sr	- TA
Age	60	.420	61.730	E7 E80	E0 610	FF 700	F4 100	48 650
≤40 years >40 years		.420 .440	44.110	57.580 48.340	50.610 55.430	55.700 50.250	54.100 51.880	48.650 57.430
-		552	-2.976	-1.610	-0.815	-0.940	-0.382	-1.491
z P value		.006 ^b	$-2.9/0$ 0.002^{b}	0.054	0.208	0.174	0.352	0.068
Gender	0.	.000	0.002	0.034	0.200	0.1/4	0.332	0.000
Male	45.	.630	51.870	54.200	51.410	50.610	51.880	56.180
Female		700	54.030	51.910	54.450	55.170	54.020	50.110
Z		.396	-0.364	-0.399	-0.513	-0.786	-0.366	-1.029
<i>P</i> value		.009 ^b	0.358	0.345	0.304	0.216	0.358	0.152
Employment				0.10				
Unemployed	55.	550	52.260	55.640	54.150	57.310	54.210	50.900
Employed		.900	54.490	47.730	50.700	44.370	50.590	57.200
Z		230	-0.355	-1.299	-0.550	-2.105	-0.585	-1.008
P value		.110	0.362	0.097	0.291	0.018 ^a	0.280	0.157
Monthly salary								
> RM1000	35.	210	39.870	37.830	35.150	34.120	37.420	35.990
≤ RM1000	35.	870	30.000	32.560	35.940	37.240	33.080	34.890
Z	-0.	138	-2.023	-1.140	-0.160	-0.653	-0.908	-0.277
P value	0.	445	0.022^{a}	0.127	0.437	0.257	0.182	0.411
Factor	FI	NV	PA	DY	SL	AP	CO	DI
Age								
≤40 years	52.410	58.090	48.380	55.600	53.750	50.560	47.480	54.220
>40 years	53.610	47.810	57.710	50.350	52.230	55.490	58.630	51.760
Z	-0.210	-1.868	-1.619	-1.043	-0.279	-0.866	-1.981	-0.502
P value	0.417	0.031a	0.053	0.149	0.390	0.193	0.024ª	0.308
Gender								
Male	58.220	51.550	52.480	53.720	54.790	51.350	50.480	52.290
Female	48.250	54.680	53.470	52.350	51.370	54.500	55.290	53.650
Z	-1.740	-0.641	-0.172	-0.272	-0.625	-0.522	-0.854	-0.276
P value	0.041 ^a	0.261	0.432	0.393	0.266	0.291	0.197	0.391
Employment								
Unemployed	54.050	51.410	61.410	51.180	52.100	52.650	51.360	54.910
Employed	50.900	56.170	36.170	56.640	54.800	53.700	56.290	49.190
Z	-0.5190	-0.815	-4.127	-1.022	-0.466	-0.174	-0.826	-1.102
P value	0.302	0.208	0.000°	0.154	0.321	0.431	0.205	0.136
Monthly salary								
> RM1000	28.810	37.560	30.850	35.740	36.730	35.030	32.880	37.100
≤ RM1000	43.920	32.900	41.350	35.190	33.950	36.100	38.790	33.480
Z	-3.213	-1.035	-2,210	-0.130	-0.615	-0.228	-1.296	-0.917
P value	0.001 ^a	0.151	0.014 ^a	0.448	0.269	0.410	0.098	0.180
	0.001	0.101	0.014	0.440	0.209	0.410	0.090	0.100

 $^{^{}a}P < 0.05$, $^{b}P < 0.01$, and $^{c}P < 0.001$ with Mann–Whitney U test. Abbreviations: QOL = global quality of life, PF = physical functioning, RF = role functioning, EF = emotional functioning, CF = cognitive functioning, SF = social functioning, FA = fatigue, FI = financial difficulties, NV = nausea and vomiting, PA = pain, DY = dyspnoea, SL = insomnia, AP = appetite loss, CO = constipation, DI = diarrhoea.

Table 4: Between-group differences in the quality of life mean rank score as a function of haematological cancer diagnosis

Table 4. between-	group differen	nees in the q	danty of file fi	ican rank sco	ic as a functi	on or nacmati	ological called	i diagnosis
Diagnosis	QC)L	PF	RF	EF	CF	SF	FA
No-AML	50.3	380	47.990	51.520	53.960	53.710	55.010	52.260
AML	61.8	330	69.920	58.000	49.750	50.600	46.230	55.500
Z	-1.6	539	-3.111	-0.949	-0.598	-0.450	-1.262	-0.462
P value	0.0	051	0.001^{b}	0.172	0.275	0.327	0.104	0.322
No-MM	53.5	590	54.700	53.040	53.160	53.760	52.850	51.860
MM	43.2	250	25.000	52.42	50.420	40.420	55.420	71.830
Z	-0.8	818	-2.329	-0.050	-0.215	-1.069	-0.204	-1.574
P value	0.2	207	O.010 ^a	0.480	0.415	0.143	0.420	0.058
No-ALL	53.4	120	52.680	52.170	52.020	52.510	52.720	53.600
ALL	50.4	170	54.930	57.970	58.900	55.970	54.700	49.40
z	-0.3	353	-0.267	-0.707	-0.8140	-0.418	-0.238	-0.499
P value		362	0.395	0.240	0.208	0.338	0.406	0.309
No-HL	52.1		52.800	52.450	53.450	52.710	52.930	54.450
HL	60.4		54.730	57.730	49.180	55.500	53.590	40.590
z	-0.8		-0.200	-0.564	-0.442	-0.295	-0.069	-1.441
P value		194	0.421	0.287	0.330	0.384	0.473	0.075
No-other lymphoma	53.7			52.890	53.220	52.360		52.570
Lymphoma			54.420 42.960		53.220		53.520	56.040
• •	47.5			53.770		57.500	49.310	
Z Postler	-0.7		-1.275	-0.101	-0.196	-0.584	-0.475	-0.388
P value		242	0.101	0.460	0.423	0.280	0.318	0.349
No-NHL	53.8		55.040	56.830	52.130	52.750	52.390	53.320
NHL	50.2		46.480	40.760	55.800	53.800	54.940	51.980
Z	-0.5	534	-1.231	-2.385	-0.529	-0.154	-0.371	-0.194
P value		297	0.109	0.009 ^b	0.299	0.439	0.355	0.424
Diagnosis	NV	PA	DY	SL	AP	СО	DI	FI
No-AML	53.020	54.090	53.940	50.880	52.600	53.770	52.930	53.610
AML	52.940	49.330	49.810	60.170	54.330	50.400	53.250	50.940
z	-0.012	-0.692	-0.688	-1.430	-0.255	-0.504	-0.056	-0.393
P value	0.495	0.245	0.246	0.077	0.400	0.3070	0.478	0.3480
No-MM	54.080	52.590	53.060	53.420	53.400	53.060	52.440	52.980
MM	35.250	59.750	52.000	46.080	46.420	52.000	62.170	53.250
Z	-1.588	-0.576	-0.098	-0.624	-0.569	-0.088	-0.922	-0.022
P value	0.056	0.282	0.461	0.267	0.285	0.465	0.179	0.492
No-ALL	49.980	52.570	50.340	52.610	50.020	53.880	51.920	52.250
ALL	71.100	55.600	68.970	55.370	70.870	47.730	59.470	57.500
z	-2.685	-0.368	-2.586	-0.354	-2.561	-0.764	-1.078	-0.642
P value	0.035 ^a	0.357	0.005^{b}	0.362	0.005^{b}	0.223	0.141	0.261
No-HL	52.820	52.120	51.220	52.230	53.860	53.430	52.810	52.790
HL	54.550	60.550	68.230	59.550	45.640	49.320	54.590	54.770
z	-0.192	-0.895	-2.067	-0.820	-0.884	-0.448	-0.222	-0.212
P value	0.424	0.186	0.020 ^a	0.206	0.188	0.327	0.412	0.416
No-other lymphoma	52.860	55.760	55.130	54.900	53.730	53.400	53.020	52.770
Lymphoma	53.960	33.460	37.920	39.540	47.810	50.190	52.850	54.620
z	-0.131	-2.547	-2.249	-1.854	-0.685	-0.375	-0.024	-0.212
P value	0.448	0.006 ^b	0.013 ^a	0.032ª	0.247	0.354	0.491	0.416
No-NHL	54.790	50.570	55.040	53.510	52.900	49.280	53.430	52.700
NHL	54./90 47.280	60.780	46.460	51.360		64.920	51.640	53.960
					53.320			
Z Produc	-1.162	-1.508	-1.451	-0.336	-0.063	-2.369	-0.310	-0.188
P value	0.123	0.066	0.074	0.369	0.475	0.009 ^b	0.378	0.426

 $^{^{\}mathrm{a}}P$ < 0.05, $^{\mathrm{b}}P$ < 0.01, and $^{\mathrm{c}}P$ < 0.001 with Mann–Whitney U test.

Abbreviations: QOL = global quality of life, PF = physical functioning, RF = role functioning, EF = emotional functioning, CF = cognitive functioning, SF = social functioning, FA = fatigue, FI = financial difficulties, NV = nausea and vomiting, PA = pain, DY = dyspnoea, SL = insomnia, AP = appetite loss, CO = constipation, DI = diarrhoea, AML = acute myelogenous leukaemia, ALL = acute lymphoblastic leukaemia, HL = Hodgkin lymphoma, NHL = non-Hodgkin lymphoma, MM = multiple myeloma.

A possible explanation for this may be a previous finding that male cancer patients scored higher in working ability at 6 months after returning to work, but not at 12 or 18 months. Furthermore, haematological cancer patients were less able to work, leading to less overtime opportunity. The reduced ability to work was due in part to chemotherapy treatments (12).

Patients who were older than 40 years reported a reduced global quality of life and physical functioning scores and more symptoms of constipation, but fewer symptoms of nausea and vomiting compared with other patients. The ages of NHL and MM patients were significantly higher compared with other haematological cancer patients. Impaired role functioning and reduced physical functioning were found in NHL and MM patients, respectively. NHL patients also had symptoms of constipation. These findings support a recent study that reported older haematological cancer patients having a poor quality of life with more impaired physical and role functioning and more symptoms of constipation (7).

Overall, the patients with MM had the lowest mean rank score in physical functioning. This result corroborates the findings of Santos et al. (6), who reported that the physical functioning of MM patients was the most impaired compared with other haematological cancer patients. The AML patients in the current study had better physical functioning scores compared with the other patients. This result is consistent with that of a previous study and suggest that newly diagnosed AML patients have better physical functioning despite undergoing intensive chemotherapy treatment (13). The data indicate that different diagnoses of haematological cancer may have varied effects on the quality of life.

Patients diagnosed with ALL and HL had more symptoms of dyspnoea. This result is similar to that reported in a study of a mixed cancer population that included lymphoma patients (14). However, other types of lymphoma patients reported less pain, dyspnoea, and insomnia compared with other haematological cancer patients. The existence of insomnia in haematological cancer patients has been shown in a previous study (7). More symptoms of appetite loss and nausea and vomiting were noted in ALL patients compared with other patients. Symptoms such as appetite loss may have been caused by the active treatment regimens (7). Haematological cancer patients have more symptoms of pain (7). The present study found that lymphoma patients experienced significantly less pain compared with patients with other haematological cancers.

Current working ability, mental work ability, quality of life, fatigue, physical complaints, cognitive functioning, age, physical work load, work stress, gender, diagnosis, and treatment were all related to the time taken to return to work. Thus, the return to work was greatly influenced by the patients' mental and psychological factors. Interventions targeted at cancer patients should focus on their ability to return to work, particularly because no such targeted interventions presently exist (12).

These problems can be at least partly overcome by psychotherapy conducted by mental health professionals, verbally, interactively, or in combination. A variety of cognitive behavioural therapies, supportive psychotherapy, and problem-solving therapy may help to alleviate the problems faced by cancer patients (15). Clinicians may also play an important role in the detection of poor working ability among the patients to improve their quality of life (12).

The present study had several limitations. It applied a cross-sectional design; therefore, causal relationships cannot be determined. The EORTC-QOL is a self-rated questionnaire, and some parts of the questions were explained to the patients for clarification purposes. Responses depended on the patients' memory together with their emotional and physical state at the time of the study. These factors should be considered when interpreting the current results.

Conclusion

This study suggests that the quality of life of haematological cancer patients was affected by socio-demographic factors and clinical diagnoses. The study found that the youngest patients were in the ALL, HL, without NHL, and without MM groups. The younger patients (40 years or younger) had better global quality of life and physical functioning scores and fewer symptoms of constipation, but more symptoms of nausea and vomiting. The study also found that the female global quality of life was better than for the male patients. The MM patients had reduced physical functioning; the ALL patients had more symptoms of nausea and vomiting, dyspnoea and appetite loss; the HL patients had more dyspnoea symptoms; and the NHL patients had reduced role functioning and more constipation. Cost-effective psychotherapy combined with daily patient care are very important to reduce the burden of psychological distress and to improve the overall quality of life among patients with haematological cancers.

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Provision of study materials or patients, collection

and assembly of the data: DP, KB

Statistical expertise, analysis and interpretation

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Original Article

Stress and Coping Strategies of Students in a Medical Faculty in Malaysia

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Abstract -

Background: Stress may affect students' health and their academic performance. Coping strategies are specific efforts that individuals employ to manage stress. This study aimed to assess the perception of stress among medical students and their coping strategies.

Methods: A cross-sectional study was conducted among 376 medical and medical sciences undergraduates in Management and Science University in Malaysia. Stress was assessed by a global rating of stress. Sources of stress were assessed using a 17-item questionnaire. The validated Brief COPE inventory was used to assess coping strategies.

Results: The majority of respondents were females (64.4%), aged 21 years or older (63.0%), and were Malays (68.9%). Forty-six percent felt stress. The most common stressor was worries of the future (71.0%), followed by financial difficulties (68.6%). Significant predictors of stress were smoking (OR = 2.9 , 95% CI 1.3–6.8, P = 0.009), worries of the future (OR = 2.1 , 95% CI 1.3–3.4, P = 0.005), self-blame (OR = 1.3, 95% CI 1.1–1.5, P = 0.001), lack of emotional support (OR = 0.8, 95% CI 0.7–0.9, P = 0.017), and lack of acceptance (OR = 0.8, 95% CI 0.6–0.9, P = 0.010). Students used active coping, religious coping reframing, planning, and acceptance to cope with stress.

Conclusion: Stressors reported by the students were mainly financial and academic issues. Students adopted active coping strategies rather than avoidance. Students should receive consultation on how to manage and cope with stress.

Keywords: coping skills, Malaysia, medical school, social support, stress, students

Introduction

Medical students face different kinds of stressors in their studies and in life. Previous researchers have found high levels of stress among medical students (1,2). The overall prevalence of stress was 31.2% in 3 British universities (3), 41.9% in a Malaysian medical school (4), and 61.4% in a Thai medical school (5). According to Lazarus (6), stress is the result of an individual's perception that they do not have the resources to cope with a perceived situation from the past, present, and future. Stress occurs when an individual is confronted with a situation that is perceived as overwhelming and with which they cannot cope (7). Too much stress or chronic stress can affect mental and physical health and increase the risk of premature mortality (8). Adverse effects of stress

result from the interaction between stressors and individual perceptions of and reaction to these stressors. Musculoskeletal disorders, high blood pressure, disturbed metabolism (associated with the risk for type 2 diabetes mellitus), and cardiovascular problems may result from stress (8).

Medical students perceive themselves as being more likely to become ill than others (9). Deterioration in the health of students may affect learning ability and academic performance as well as goal achievement (10). In addition, stress also affects social relationships within and outside the university (10), thus impacting on mental health. In a Swedish study, 2.7% of students had made suicide attempts (2). Previous studies (11,12) identified some important academic and non-academic stressors among medical students. Academic stressors include excessive homework, unclear

assignments (11,12), lack of time management skills, uncomfortable classrooms, weekly tests and assignments, the pressure to earn good grades, and receiving a lower grade than expected (12). Non-academic stressors include social issues and financial problems (11). In Pakistan, the most common stressors among medical students were high parental expectations, frequency of examinations, vastness of academic curriculum, sleeping difficulties, performance in periodic examinations, and worries of the future (13).

Previous studies showed that coping plays a central role in adaptation to stressful life events (14). Coping strategies are the specific efforts, both behavioural and psychological, that individuals employ to master, tolerate, reduce, or minimise stressful events (15).

Coping strategies are classified into active and avoidant coping strategies (16). "Active coping strategies are either behavioural or psychological responses designed to change the nature of the stressor itself or how one thinks about it", while avoidant coping strategies "lead people into activities (such as alcohol use) or mental states (such as withdrawal) that keep them from directly addressing stressful events" (16). Active coping is considered a better way to deal with stress, while avoidant coping is considered as a psychological risk factor for adverse responses to stressful life events (17).

According to Carver (18), active coping strategies include "active coping", which means taking action or exerting efforts to remove or circumvent the stressor; "planning", thinking about how to confront the stressor and planning one's coping efforts; "acceptance", accepting the fact that the stressful event has occurred and is real; and "positive reframing", making the best of the situation by growing from it or seeing it in a more positive light. Avoidant strategies include "denial", defined as an attempt to reject the reality of the stressful event; "behavioural disengagement", giving up or withdrawing efforts from the attempt to attain the goal with which the stressor is interfering; "venting", an increased awareness of one's emotional distress and a concomitant tendency to ventilate or discharge those feelings; and "humour", making jokes about the stressor (18).

Approaches in coping with stress are influenced by ethnic, cultural, and socioeconomic characteristics. For example, symptoms of stress increase with decreasing social status (19), and females tend to use emotional and avoidant coping strategies more than males do (19). Studies from the United Kingdom (20,21)

have reported the use of alcohol, tobacco, and drugs as common coping strategies adopted by medical students. In a study in Pakistan (22), sports, music, hanging out with friends, sleeping, or going into isolation were employed in coping with stress. Students in Nepal (23) adopted active coping strategies (positive reframing, planning, acceptance, and active coping) rather than avoidant strategies (denial, alcohol/drug use, and behavioural disengagement). In a qualitative study of Malaysian students (24), common coping strategies adopted by students were regular exercise, praying, counselling, watching cartoons or comedies, practising meditation including yoga and tai chi, and listening to soft music.

Stress among students has not gained much attention in comparison to work-related stress (7). Only a few studies have assessed the perceptions of stress and coping strategies among medical students (25–27). This study aimed to assess the perceived sources of stress among medical students and coping strategies used to manage stress.

Subjects and Methods

A cross-sectional study was conducted on 376 medical and medical sciences students at the International Medical School, Management and Science University, during the middle of semester in 2009. A self-administrated paper questionnaire consisting of 4 parts was distributed to the students. Stress was assessed by a global rating of stress: "To what extent do you feel you are under stress?" rated from "Not at all" to "I have too much stress". Sources of stress were assessed by a 17-item questionnaire. Each item was rated on a 4-point Likert scale ranging from "Strongly disagree (score 1)" to "Strongly agree (score 4)". The stressors included in the questionnaire were derived by reviewing the literature and through discussion with a group of students. The internal consistency of this questionnaire as indicated by the Cronbach's alpha value was 0.80.

Coping strategies were assessed using the Brief COPE scale, which is an abbreviated version of the COPE Inventory (18). The Brief COPE is used to assess a broad range of coping behaviours among adults with or without clinical conditions (18). It consists of 28 items, and each item is rated on a 4-point Likert scale ranging from "I have not been doing this at all (score 1)" to "I have been doing this a lot (score 4)". The higher score indicates greater coping by the respondents. The items were scored to produce 14 dimensions, each reflecting the use of a coping strategy: active coping, planning, acceptance, denial, self-

distraction, use of substance, use of emotional support, use of instrumental support, behavioural disengagement, venting, positive reframing, humour, religion, and self-blame (18). It is a validated instrument in which the Cronbach's alpha values range 0.50–0.90, with only 3 coping strategies falling below 0.60.

The questionnaire also includes sociodemographic information. Written consent was obtained from the participants. Participation was voluntary, and students were assured that participation would be confidential and would not affect their academic progress. Approval was obtained from the ethics committee of the Management and Science University, Shah Alam, Malaysia.

Statistical analysis

Data analysis was performed using SPSS version 13 (SPSS Inc., Chicago, IL). After all data was entered into SPSS, they were reviewed for the accuracy of data entry. Perceived stress was dichotomised into 2 categories: "Not at all" and "A little bit" were considered "no perceived stress", and "I have too much stress" and "I have stress" were considered "perceived stress". To assess the association between perceived stress and the other variables, chi-square test was used. Student's t test for independent samples and one-way ANOVA were used to compare the mean values of coping strategies in relation to studied variables. P < 0.05 was considered statistically significant. All variables significantly associated with stress in bivariate analysis were entered into multivariate analysis. Multiple logistic regression analysis with backward stepwise technique was performed to obtain the most important predictors of stress.

Results

Socio-demographic characteristics

Of the 376 students, 242 (64.4%) were females, 237 (63.0%) were aged 21 years or more, 259 (68.9%) were Malays, and 359 (95.5%) were singles. The majority of students (275, 73.1%) were Muslims. Most students had monthly family income ranging RM2000–RM4000 (USD1 = RM3.3) (Table 1). Thirty-five students (9.3%) were smokers.

Perceived stress

There were 174 students (46.3%) who reported having some or too much stress, whereas 179 (47.6%) reported that they felt a little bit of stress. Only 23 students (6.1%) reported no stress (Table 2).

Among the socio-demographic factors, only smoking was significantly associated with perceived stress. The prevalence of stress among smokers (71.4%) was significantly higher (OR = 3.2, 95% CI 1.5–7.0, P = 0.002) than in non-smokers (43.7%).

Out of 17 sources of stress, 10 sources were significantly associated with perceived stress (P < 0.05). The prevalence of stress was higher among students who agreed that these factors were sources of stress for them (Table 3). Only sources of stress with significant associations were shown in the table.

There was a significant association between perceived stress and 5 of the 14 coping strategies (Table 4). Students who felt stressed used venting (5.0, P = 0.001), denial (4.5, P = 0.032), self-blame (5.0, P < 0.001), and disengagement (4.4, P = 0.004) more than non-stressed students did (4.5, 4.1, 4.3, and 3.9, respectively). However, non-stressed students used emotional support (5.9, P = 0.032) more than stressed students did (5.6). Non-significant associations were omitted from the table.

In the multiple logistic regression model (Table 5), the independent predictors of stress were smoking (OR = 2.9, 95% CI 1.3–6.8, P = 0.009), worries of the future (OR = 2.1, 95% CI 1.3–3.4, P = 0.005), self-blame (OR = 1.3, 95% CI 1.1–1.5, P = 0.001), lack of emotional support (OR = 0.8, 95% CI 0.7–0.9, P = 0.017), and lack of acceptance (OR = 0.8, 95% CI 0.7–0.9, P = 0.010). The total model accounted for 19% of the variance in perceived stress. The results of the analysis showed that the data did not violate the multicollinearity assumption (tolerance < 0.720).

Sources of stress among students

Sources of stress, ranked by the percentage of students who agreed that the items were sources of stress, are shown in Table 6. The most important sources of stress reported by students were worries of the future (71.0%), financial difficulties (68.6%), study in general (64.6%), hearing bad news (58.5%), and interpersonal conflict (54.3%). The least important source of stress was trouble with teachers (22.6%).

Coping strategies used by students

The students in this study used active coping strategies such as religious coping, with score (SD) of 6.2 (1.6); active coping, 6.2 (1.3); positive reframing, 6.1 (1.4); and acceptance, 6.0 (1.3); more than avoidant strategies such as denial, 4.3 (1.5); self-blame, 4.6 (1.6); and alcohol or substance use, 2.7 (1.4).

Table 1: Socio-demographic characteristics of participants

Variable		n	%
Age (years)	≤ 21	237	63.0
	> 21	139	37.0
Sex	Male	134	35.6
	Female	242	64.4
Marital status	Single	359	95.5
	Engaged	17	4.5
Ethnicity	Malay	259	68.9
	Indian	48	12.8
	Chinese	35	9.3
	Other	34	9.0
Religion	Muslim	275	73.1
	Hindu	41	10.9
	Christian	31	8.2
	Other	29	7.7
Monthly family	<2000	92	24.9
income (RM)	2000-4000	172	46.5
	>4000	106	28.6

Total number of participants = 376

Table 2: Perceived stress among students

Stress	n	%
Not at all	23	6.1
A little bit	179	47.6
I have stress	139	37.0
I have too much stress	35	9.3

Total number of participants = 376

Females used self-distraction, with score (SD) of 6.1 (1.4); religious coping, 6.3 (1.6); emotional support, 6.0 (1.4); instrumental support, 5.9 (1.4); and planning, 6.2 (1.3), more than males did, with scores (SD) of 5.7 (1.3), 6.0 (1.6), 5.4 (1.4), and 5.8 (1.5), respectively (P < 0.05). However, males were involved in alcohol or substance use, with score (SD) of 3.1 (1.6), more than females did, 2.5 (1.4), and this observation is statistically significant (P < 0.05). Older students (aged more than 21 years) used active coping, with score (SD) of 6.5 (1.2), reframing, 6.3 (1.3), and planning, 6.2 (1.2), more than younger students did, with scores of 6.0 (1.3), 6.0 (1.4), and 5.9 (1.3),

respectively, (P < 0.05). Smokers were more significantly involved (P < 0.05) in alcohol or substance use, with score (SD) of 3.4(1.7), than nonsmokers, 2.7 (1.4). Malay students used religious coping, with score (SD) of 6.5 (1.5), more than Chinese and Indian students did, with scores (SD) of 5.2 (1.6) and P = 0.001, and 5.6 (1.7) and P = 0.002, respectively. Muslims used religious coping, with score (SD) of 6.4 (1.5), more than Hindu students and those of other religious persuasions did, with scores (SD) of 5.6 (1.7) and P = 0.006, and 5.2 (1.7) and P < 0.001, respectively.

Table 3: Association between sources of stress and perceived stress

Source of stress	OR	95% CI	P value
Worries of the future	2.1	1.3-3.3	0.002
Financial difficulties	1.8	1.2-2.8	0.010
Study (in general)	1.6	1.1-2.5	0.023
Interpersonal conflicts	2.1	1.4-3.1	0.001
Family problems	1.7	1.2-2.6	0.008
Low self-esteem	2.2	1.5-3.4	<0.001
Conflict with roommate	2.0	1.3-3.0	0.001
Inability to find support from parents to solve problems	1.6	1.1-2.4	0.028
Living away from family	1.6	1.0-2.4	0.031
Change in eating habit	1.9	1.2-2.9	0.006

Data were analysed using chi-square test. For each item, the reference category was "Disagree". Only sources of stress with significant associations are shown. Total number of participants = 376.

Table 4: Coping strategies and their association with perceived stress

Coping strategy	Perceived stress	No perceived stress	P value
	Mean (SD)	Mean (SD)	
Emotional support	5.6 (1.3)	5.9 (1.4)	0.032
Venting	5.0 (1.4)	15.0 (1.3)	0.001
Denial	4.5 (1.5)	30.0 (1.4)	0.032
Self blame	5.0 (1.6)	25.0 (1.5)	< 0.001
Disengagement	4.4 (1.7)	24.0 (1.4)	0.004

Student's *t* test was used to compare mean coping strategies among students who had stress and who had not stress. Only coping strategies with significant association are shown. Total number of participants = 376.

Table 5: Multiple logistic regression analysis of predictors of perceived stress among medical students

<u> </u>	0		1	0	
Predictor		В	OR	95% CI	P value
Smoking	No		1.0		
	Yes	1.097	2.9	1.3-6.8	0.009
Worries of the future	Disagree		1.0		
	Agree	0.728	2.1	1.3-3.4	0.005
Interpersonal conflicts	Disagree		1.0		
	Agree	0.445	1.6	1.0-2.5	0.057
Roommate conflict	Disagree		1.0		
	Agree	0.446	1.6	1.0-2.5	0.056
Acceptance		-0.230	0.8	0.6-0.9	0.010
Emotional support		-0.213	0.8	0.7-0.9	0.017
Self blame		0.240	1.3	1.1-1.5	0.001

Total number of participants = 376.

Table 6: Sources of stress among students, ranked by number and percentage of students who agreed that the items were sources of stress

Source of stress	n	%
Worries of the future	267	71.0
Financial difficulties	258	68.6
Study (in general)	243	64.6
Hearing bad news	220	58.5
Interpersonal conflicts	204	54.3
Family problems	197	52.4
Low self-esteem	185	49.2
Trouble with friends	178	47.3
Trouble with boyfriend or girlfriend	174	46.3
Sleep disorders	170	45.2
Conflict with roommate	161	42.8
Inability to find support from parents to solve problems	153	40.8
Pressures related to finding a life partner	144	38.3
Trouble with parents (one or both)	141	37.5
Living away from your family	134	35.6
Change in eating habit	116	30.9
Trouble with teachers	85	22.6

Total number of participants = 376.

Discussion

This study found that the students used active coping strategies (active coping, religious coping, positive reframing, planning, and acceptance) more than avoidant strategies (denial, self-blame, and alcohol or substance use). However, we cannot ignore that some students are still using avoidant coping strategies, which are considered risk factors for adverse responses to stress. A previous study in Nepal (23) showed similar findings. Another qualitative study among medical students in Malaysia (24) found that most common ways to deal with stressful events were the active coping strategies; they did not report any undesirable coping strategies, such as drinking alcohol and smoking. This could be due to the use of focus group discussions, which might result in the students' hesitation to discuss culturally unacceptable behaviours in front of their peers and focus group leaders. In comparison with previous studies from the United Kingdom (20,21) that reported the use of alcohol, tobacco, and drugs as common coping strategies in medical students, it was encouraging to find in our study that alcohol or substance use was the least common coping strategy. This may be related to the students' religious beliefs, although under-reporting cannot be ruled out.

In this study, male students used active coping less, and alcohol or substance consumption more than female students did. This is in contrast to a previous study (23) in which male students used both active coping and alcohol or substance more than female students did.

In this study, older students used active coping, reframing, and planning more than younger students did. The reasons might be that older students have adapted to the college environment better, and that they have had a longer period of contact with mentors than younger students did.

One of the important findings in this study was the association of smoking with both coping strategies and perceived stress. Smokers used active coping strategies less than non-smokers, which might mean that smoking may affect a student's ability to cope positively with stress. Smokers also used alcohol or substance more than non-smokers did. The current cross-sectional

study cannot provide evidence for a causal relationship between smoking and drinking alcohol, although a previous prospective study among students by Morgen et al. (28) showed that smoking was associated with an increased risk of becoming a heavy drinker eight years later.

This study also showed that students who were smokers perceived greater stress than non-smokers did. Previous studies (29,30) showed that smokers have higher stress levels than non-smokers.

Worries of the future, financial difficulties, and academic life were the most common stressors among medical students in this study. This finding was similar to that of previous studies (13,24).

In this study, there was an association between perceived stress and coping strategies, which may mean that the way students cope with stress might affect their perception of stress. Therefore, teaching students to use desirable coping strategies may reduce stress. This study found a high prevalence of stress among students, at 46.3%, which was higher than that found in two previous Malaysian studies, at 41.9% (4) and 29.6% (31), but was lower than that among students at a medical college in Saudi Arabia, at 57.0% (32). However, these studies used different tools to measure stress.

Conclusion

A substantial number of medical students experience high amount of perceived stress, and the strategies stressed students used to cope with the pressure differ from that used by non-stressed students. Medical students were exposed to a variety of stressors during the course of their study. They used mainly active coping strategies rather than avoidant strategies. Males, smokers, and younger students used active coping strategies less than other students did. Smokers reported high stress and tended to use alcohol or substance more than non-smokers did.

Knowing the causes of stress among students and methods students use to deal with it will help lecturers, career-counselling centres, and university administrators monitor and control these factors in order to reduce stress experienced by students.

The findings of this study indicate a need for stress management programmes in all medical colleges. One approach is to eliminate, or at least reduce, the most commonly identified sources of stress among medical students. Another approach is to conduct workshops on stress and effective coping strategies through the academic years. The presence of counsellors among the faculty may help students overcome stressful conditions.

It is important to maintain a well-balanced academic environment for improved learning experience. A focus on students' needs and problems can help prevent the harmful effects of stress on heath and academic performance. Our results also emphasise the need for further study, particularly in the form of longitudinal follow-up.

Authors' Contributions

Conception and design, analysis and interpretation of the data, drafting of the article: SARA Collection and assembly of the data: MAA Critical revision of the article: RAA, KGR Administrative, technical, or logistic support: RAA, MAA

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Special **Communication**

Towards the Prevention and Management of Prostatic Diseases in Nigeria: A Framework

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Abstract -

The prevalence of prostatic diseases is reportedly high in Nigeria, and in some cases, it is comparable to figures from industrialised countries. However, to date, the research and policy responses in Nigeria are regrettably inadequate. The presence of "the double burden of diseases" and a limited appreciation of recent trends in prostatic diseases may be partly responsible for this situation. Given the frequently meagre healthcare budgetary allocations, it is pertinent to develop a properly thought-out plan for the prevention and management of prostatic diseases in Nigeria. A framework aimed at contributing to the development of such a plan is presented here. The development of a Central Prostatic Diseases Unit (CPDU) in the Federal Ministry of Health is advocated. The CPDU would be responsible for planning research and information dissemination programmes. Emphasis should be placed on targeting modifiable risk factors at the population level, proper surveillance to identify emerging trends, and research on both the operational dynamics and the efficacy of locally available herbs that could be useful in the management of prostatic diseases.

Keywords: disease management, health planning, Nigeria, prevention, prostatic diseases, public health

Introduction

The prostate gland is a walnut-shaped gland that ordinarily weighs approximately 26 g at the end of puberty. Androgens are the major factors required for the growth and development of the prostate (1). Prostatic fluid accounts for up to 30% of the volume of semen, and its production is the primary role of the prostate. Prostatic fluid constituents ensure the nourishment and proper motility of sperm. Currently, there is limited knowledge about all the secretory products of the prostate and how these products relate to reproduction and infertility (2). Three major disorders afflict the prostate gland: prostate cancer, benign prostatic hyperplasia, and prostatitis.

Prostate cancer is the most common noncutaneous cancer in men (3). It is thought to originate from the secretory epithelial cells that line the luminal surface of the ducts and acini of the prostate (4). The majority of cancers originate in the peripheral zone of the prostate, where prostate intraepithelial neoplasia is also found (4–6). The principal rate-limiting step in prostate cancer progression is thought to be the progression of histological cancer to tumours that are clinically evident (7). Benign prostatic hyperplasia (BPH) is an agerelated non-malignant enlargement of the prostate gland (8). It is a highly prevalent disease of older men and is the result of unregulated neoplastic growth of the prostate gland. In severe cases, BPH may lead to sepsis, irreversible bladder damage, renal failure, or even death (9). In humans, BPH originates as nodules in the glands and stroma of the transition zone. Massive enlargement and glandular proliferation occur within the nodules in men older than 70 years (10,11).

Prostatitis is a common debilitating urologic disease that is characterised by inflammation of the prostate gland. It has long been estimated that up to half of all men suffer from symptoms of prostatitis at some time in their lives (12). More recently, prostatitis has been reported to be the most common urologic diagnosis in men younger than 50 years old and the third most common urologic diagnosis in men older than 50 years old (13,14). The National Institutes of Health classification of prostatitis has four categories, designated I, II, III, and IV, representing acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis or chronic pelvic pain syndrome (inflammatory and non-inflammatory), and asymptomatic inflammatory prostatitis, respectively (15).

Studies have shown many developing countries that have long battled with largely communicable diseases are now also facing higher occurrence of chronic diseases (16). For example, in Nigeria, the prevalence of prostate cancer, BPH, and prostatitis are as high as figures reported in some industrialised nations (17-20). As much as 11% of all cancers in Nigeria are reported to be of the prostate (17), whereas as many as 25% and 12% of adult male Nigerians were reported to have BPH (19) and prostatitis (20), respectively. Mortality figures are not readily available from Nigeria, but they are presumably quite high. The need to address chronic diseases in the developing world, especially in sub-Saharan Africa and in Nigeria in particular, has therefore become evident (21). In countries that face this double burden of disease with meagre health care budgets, the goal should be the implementation of cost-effective prevention and management programmes for as many prevalent diseases as possible (22,23). Unfortunately, there is no clearcut programme for prostatic diseases.

Lifestyle risk factor modification is the most cost-effective approach to reducing the burden of chronic diseases. Cooper et al. (24) estimated that treating a chronic disease, such as hypertension, could cost approximately USD36 per person in sub-Saharan Africa, where the per capita health expenditure is less than USD30 (25) and poor patients pay more money for health services (26). This buttresses the advantage of prevention over management.

Although the prevalence of prostatic diseases has generated little or no attention among policy makers, the threat they pose to our health care system is quite enormous. Several studies have shown that prostatic diseases may be associated with conditions such as obesity, diabetes, insulin resistance, hypercholesterolemia, and hypertension (27–33), the prevalence of which are reportedly high in Nigeria (34,35). It is therefore important to develop a health policy framework that is geared towards the prevention and management of prostatic diseases in Nigeria.

The Framework

Premature morbidity and mortality reduction should be the centrepiece of any strategy that is aimed at the prevention and management of prostatic diseases, especially in resource poor countries, such as Nigeria. Such strategies should have clearly provided details that are not only relevant to the local needs of the communities but are also understandable to the individuals who will implement the strategies. In many sub-Saharan African countries, finely drafted policies have no impact if there is no political driving force to facilitate its implementation. Based on the above considerations, the following strategies are suggested.

Establishment of a Central Prostatic Diseases Unit in the Federal Ministry of Health

An established Central Prostatic Diseases Unit (CPDU) should be charged with providing guidance and leadership in the areas of research, information dissemination. health formulation (with respect to prostatic diseases) and appropriate legislation. Such a unit must have members drawn from relevant sectors of the economy-relevant government ministries, academia, health practitioners, educationists, society, National Assembly members, lawyers, et cetera-if it is to be successful and sustainable. The unit has to be funded directly by the government. International organisations and non-governmental organisations should also be lobbied to provide funding for the CPDU. Such a properly funded multi-sectorial unit would definitely highlight the prevention and management of prostatic diseases in our national discourse. Such a central unit proved effective for cardiovascular diseases in Mauritius (36) and will undoubtedly work for prostatic diseases in Nigeria.

A replication of the CPDU in all of the states of the federation would enhance the accessibility of the unit to grassroots organisations, thereby making programmes implementation easy. These state arms of the CPDU would be properly suited to perform activities, such as school health programmes and interventions, using participatory methods that target rural illiterate populations. Data collection at the grassroots level could be conducted at the state levels of the CPDU and transmitted to the central body for processing, interpretation, and utilisation. Therefore, proper information flow between the federal CPDU and the state CPDUs would enhance the timely and efficient bi-directional transmission of information (Figure 1).

The CPDU could also use the mass media, especially the radio, as they are known to be useful in targeting both urban and rural dwellers. Easy-to-remember jingles relaying relevant information on the programmes of the CPDU or information on health-related lifestyle modifications for the population could be produced and disseminated using the mass media. Telecommunication providers could be lobbied to send messages on

prostatic disease prevention and management to their subscribers using their short message services.

Modifiable risk factors linked to prostatic diseases include physical inactivity (37,38), alcohol consumption, and tobacco smoking Unfortunately, these factors (39-41).associated with urbanised lifestyles appear to be desirable markers of affluence and "breaking into a high social class" among the poor and middle-income segments of the society. Programmes targeted at correcting these erroneous concepts should be implemented and should focus on targeting the low and middleincome populations. Affluent urban dwellers are usually more inclined to change their lifestyles when presented with scientific evidence that shows its deleterious consequences. In addition, these individuals can often afford proper medical care if they develop a disease.

For such a programme to be successful and effective, it must have a component that addresses treatment and counselling to those who already have the aforementioned risk factors. Such a component could be located in existing tertiary health care facilities in all states of the federation and would build the confidence of the population in the programme and encourage participation. Health workers involved in the programme could be trained so that they are conscious of these modifiable risk factors among the high-risk groups (such as the urban dwellers, the elderly, and firstdegree relatives of known sufferers of prostatic diseases) irrespective of their place of residence and can identify the modifiable risk factors early. Individuals who belong to these high-risk groups should be encouraged to attend regular check-ups at designated facilities near their homes where basic tests and measurements can be completed, counselling can be provided, and medicines can be administered, while referrals would be directed to the tertiary health care facility nearest to their place of residence. Therefore, the activities of the CPDU will be integrated with existing three-tier health care infrastructure in the country.

Monitoring of emerging trends/risk factors and progress

Monitoring and evaluating emerging trends/ risk factors and assessing progress made in the fields is another important part of the programme. Researchers from academia or other facilities involved in prostatic disease research should be attached to centres that attend to high-risk individuals and the general population. Therefore, relevant data that could aid the understanding of the pathophysiological mechanisms, prevalence/dynamics, and correlates (especially in terms of emerging trends, such as local environmental factors, inflammatory cytokines, and microbial infections) of these disorders could be collected, analysed, and interpreted.

The researchers could also conduct further surveillance to assess the magnitude of prostatic diseases and the associated morbidity and mortality. Verbal autopsies, cohort studies, cross-sectional studies, and partnerships with other researchers working on other chronic diseases would be useful ways of gathering such information. With the necessary information, it would be possible to calculate aggregate mortality and morbidity figures, as well as the disability adjusted life-years and absolute risk of each of these diseases. Data from operational research could help assess the cost-effectiveness of intervention and management programmes and the barriers to their development.

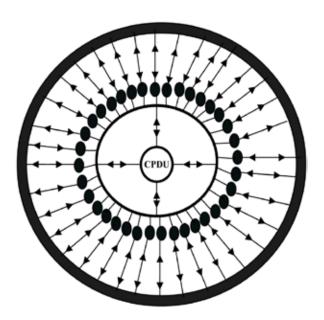


Figure 1: Diagram representing the suggested routes of information flow from the Central Prostatic Diseases Unit (CPDU) to the public and vice-versa. The dark circles represent the state versions of the CPDU, which are all linked to a common circle, whereas the outermost circle represents the population. The bi-directional arrows represent the vice-versa information flow from the CPDU to the state units and to the population.

Research on alternative treatment/management options

The use of locally available materials, mostly of plant origin, has recently gained recognition as alternatives to orthodox medicine. In fact, almost 90% of all medicines prescribed for BPH in Germany and Austria are phytotherapeutic agents (42). The biodiversity of plants found in Africa, which is arguably the richest in the world (43), coupled with the low purchasing power of Africans, especially with respect to orthodox drugs, make this type of research even more important. The research arm of the CPDU could coordinate the search for novel phytotherapeutics that could be useful in managing prostatic diseases.

Currently, extracts from plants, such as Serenoa repens (44), Urtica dioica (45), Pygeum africanum (46), Secale cereale (47), Curcubita pepo (48), Hypoxis rooperi (49), Piper cubeba (50), Bixa orellana (51), Cocos nucifera (52), and Telfairia occidentalis (53), are known to be potent botanicals in the management of prostatic diseases. It is reasonable to expect that many other locally available plants harbour phytochemicals that can be used to manage prostatic diseases. It is therefore imperative that these plants be assessed for possible therapeutic activity so that phytotherapeutics and nutraceuticals can be developed locally to aid the management of these debilitating conditions. Scientists could consult with practitioners of traditional medicine and operators of herbal homes to determine the herbs that they use to achieve certain results in their patients. For example, the herbs that are useful in the induction of urination in patients may contain agents that relax smooth muscles and, as such, can be useful in lowering prostatic muscle tone, a management goal in BPH.

Such research may have to include the isolation and characterisation of the active principles in the herbs and the determination of their specific mechanisms of action. Other factors, such as their interaction with other drugs and whether they act individually or in combination with other phytochemicals (synergism), will necessarily need to be determined. The results from such studies could lead to the development of novel therapies and possible blockbuster drugs.

Conclusion

Awareness on the prevalence and correlates of and risk factors for prostatic diseases need to be urgently increased in Nigeria. It is important to develop a framework that can be used to address these conditions, while not losing sight of the communicable diseases that blight the nation. The focus of such a framework should be on population-level interventions aimed at containing modifiable risk factors for prostatic diseases. Such interventions have been attempted for some other diseases in sub-Saharan Africa (36,54) and can be adapted for prostatic diseases in Nigeria. Clearly, to accomplish this task, a lot of funding would be required to conduct baseline studies and meaningful research, train personnel, disseminate vital information, and sustain the programme. Only a properly constituted and funded CPDU can effectively coordinate these responsibilities.

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Case Report

Wernicke's Encephalopathy in a Patient with Nasopharyngeal Carcinoma: Magnetic Resonance Imaging Findings

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Abstract -

We report a case of Wernicke's encephalopathy in a patient with nasopharyngeal carcinoma with a 3-month history of poor oral intake related to nausea and vomiting due to chemotherapy. The patient later developed deep coma while receiving in-patient therapy. Magnetic resonance imaging of the brain revealed typical findings of Wernicke's encephalopathy. The patient was treated with thiamine injections, which resulted in subsequent partial recovery of neurological function. This paper stresses the importance of magnetic resonance imaging for prompt diagnosis of Wernicke's encephalopathy.

Keywords: adult, male, magnetic resonance imaging, neurology, thiamine deficiency, Wernicke's encephalopathy

Introduction

Wernicke's encephalopathy (WE) is a neurological manifestation of thiamine deficiency. A history of alcohol abuse is present in 50% of patients with WE (1). In non-alcoholic patients, WE is due to malnutrition and malabsorption. WE is likely to be underdiagnosed and should be considered in patients with poor oral intake or nutrition, especially those with concurrent history of heavy alcohol intake (2). The most common presentation is altered consciousness ranging from disorientation to deep coma. The typical clinical triad of confusion, ataxia, and ophthalmoplegia is only present in 16%-38% of patients, making clinical diagnosis a challenge (1,3). Brain damage is related to osmotic injury and disruption of the blood-brain barrier at characteristic locations. This distribution gives rise to diagnostic findings on magnetic resonance imaging (MRI) of the brain. This case illustrates the importance of MRI in aiding the diagnosis of WE.

Case Report

The patient was a 41-year-old male with nasopharyngeal carcinoma who had completed radiotherapy (70 Gy/38 times) and 6 cycles of weekly cisplatin (30 mg/m², 60 mg) from

21 April to 10 June 2010. He was a social drinker and did not have any history of alcohol abuse. He presented to the oncology clinic complaining of a mouth ulcer, nausea, vomiting, and poor oral intake for 3 months since the commencement of therapy. Upon examination, the patient was orientated but was dehydrated and lethargic. His vital signs were stable, and the patient was afebrile. The patient's serum sodium level was 132 mmol/L, while the rest of the serum electrolytes and blood investigations were unremarkable.

The patient was admitted to the ward for hydration, antiemetic drug administration, and total parenteral nutrition. One week after admission, the patient was asymptomatic, but his serum sodium level was 111 mmol/L. Sodium replacement was commenced with slow bolus infusion of 3% normal saline given over 12 hours, followed by normal saline fluid maintenance. The serum sodium level was rechecked 24 hours later, and it was 126 mmol/L.

The patient began to experience diplopia and an unstable gait, which were attributed to hyponatraemia; therefore, sodium replacement was continued. The next day, he developed an episode of unresponsiveness but regained consciousness a few hours later. During this episode, a bolus of dextrose (50%) and mannitol each were given intravenously. His serum sodium level at this time was 129 mmol/L.

Subsequently, there was further deterioration of consciousness; the patient became deeply comatose after 2 days, with a Glasgow Coma Score (GCS) of 9. Computed tomography (CT) of the brain did not reveal any abnormality. A brain MRI was performed and showed symmetric hyperintensities in the medial thalami, periaqueductal grey, and mammillary bodies (Figure 1). Symmetric cortical hyperintensities at both frontal lobes were also present. These findings were consistent with WE.

There was a further reduction of the level of consciousness, with no response to pain stimuli and a GCS of 3. Pupillary reflexes were still present. Intubation was performed for airway protection. Intravenous thiamine replacement therapy was started immediately. There was a gradual improvement of the neurological function, and

the patient was able to demonstrate spontaneous eye opening and appropriate responses to pain stimuli after 1 week. His progress was complicated by aspiration pneumonia, which was treated with intravenous antibiotics and chest physiotherapy. A follow-up MRI of this patient 1 month later showed a reduction in the signal abnormalities seen previously (Figure 2), corresponding with the clinical improvement. Following this slight improvement, his condition remained the same with no further improvement.

Discussion

This case highlights the crucial role of brain MRI in the diagnosis of WE in non-alcoholic patients who can present in a variety of clinical settings. In the literature, non-alcoholic WE is

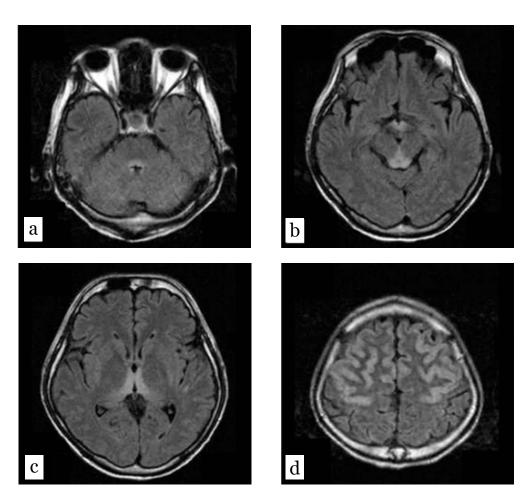


Figure 1: Magnetic resonance imaging of brain performed several days after acute neurological symptoms revealed bilateral symmetric T2 fluid-attenuated inversion recovery hyperintensities in a) the floor of the fourth ventricle, b) the periaqueductal grey and the mammillary bodies, c) the medial thalami, and d) the bifrontal lobes cortices. The patient was deeply comatose during this period.

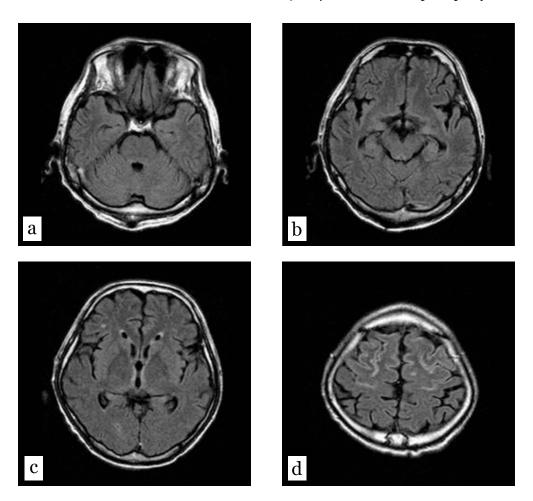


Figure 2: Magnetic resonance imaging of brain performed 1 month after the first imaging revealed a reduction and resolution of the high signal intensity on T2 fluid-attenuated inversion recovery in a) the floor of the fourth ventricle, b) the periaqueductal grey and the mammillary bodies, c) the medial thalami, and d) the bifrontal lobes cortices. There was a marked neurological improvement, with the patient being able to demonstrate spontaneous eye opening and appropriate responses to pain stimuli.

most likely to occur after prolonged therapeutic fasting, parenteral nutrition, intravenous infusion of glucose, and post-bariatric surgery (4,5). Less commonly, it is also reported in other varied circumstances, including hyperemesis gravidarum, chemotherapy, and incorrect feeding formula. In our patient, who was on chemotherapy with a poor oral intake due to poor appetite, mucositis predisposed him to the thiamine deficiency.

WE is an uncommon neurological disorder in the non-alcoholic population. Traditionally, WE is a clinical diagnosis in an alcoholic who presents with the triad of global confusion, ataxia, and ophthalmoplegia. Therefore, it is not surprising that in clinical practice, WE can be missed or underdiagnosed in non-alcoholic patients for a myriad of reasons from lack of awareness to its less typical course and other compounding factors. In this case, the co-existing hyponatraemia, underlying primary malignancy, and chemotherapy contributed to the difficulty in making a clinical diagnosis. Although the clinical triad of diplopia, unsteady gait, and confusion was present in this case, the diagnosis of WE was made only after a brain MRI showed the typical findings of WE. The administration of 50% dextrose during the initial episode of loss of consciousness in this patient may have precipitated the WE, because the patient subsequently went into a deep coma.

CT of the brain is not sufficiently sensitive to diagnose WE. The value of MRI is in the prompt diagnosis of acute WE to facilitate early treatment and to prevent irreversible brain damage (1,2). There is a recognisable pattern in WE, which, if present, is generally regarded as pathognomonic of WE. Findings on MRI include a typical distribution of high signal intensities on T2 and fluid-attenuated inversion recovery sequences at the medial thalami, head of the caudate nuclei, mammillary bodies, areas surrounding the aqueduct, third ventricle, and floor of the fourth ventricle. These changes are characteristically bilateral and symmetrical (1,2).

In addition to these typical lesions, our case also had bilateral and symmetrical lesions in the cortex of both frontoparietal regions. Cortical lesions surrounding the central sulcus are increasingly recognised as part of the WE spectrum. Other atypical findings that have been reported include the involvement of the dorsal medulla, red nuclei, and dentate nuclei (1,7). A lack of typical imaging features on an MRI does not exclude the diagnosis. In these cases, contrastenhanced MRI and diffusion weighted imaging may help to visualise early changes (8).

MRI is also helpful in predicting disease progression or prognosis (2). Cortical involvement is associated with deep coma and poorer prognosis, as was seen in our patient (2,6). Reduction in these signal abnormalities on follow-up imaging corresponds to clinical improvement, while progressive brain atrophy is associated with a poor neurological outcome (2). Follow-up MRI in this patient 1 month later showed a reduction of the signal abnormalities seen previously, corresponding with the clinical improvement.

Empirical treatment should be started as soon as WE is clinically suspected (3). Ocular symptoms will resolve within hours, with subsequent improvement of ataxia within days, and improvement of confusion within weeks after the start of treatment (3). We found that 67% of patients had full neurological recovery over a variable length of time, from 2 weeks to 1 year after thiamine therapy. Patients whose cases have been reported in the literature were administered 100 mg of thiamine intravenously or intramuscularly for 5 to 15 days after initial presentations (2).

Non-alcoholic WE is underdiagnosed. MRI facilitates early diagnosis by virtue of its typical findings. WE is a fatal but potentially treatable condition that can be resolved by thiamine administration. Prompt treatment administered prior to established brain damage ensures a

good outcome for patients. This case highlights the important practical role of MRI in aiding diagnosis as well as its prognostic value.

Authors' Contributions

Conception and design, critical revision and final approval of the article: ST

Provision of patient, collection and assembly of the data: RS

Analysis and interpretation of the data, drafting of the article: HLL

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Case Report

A Case of Isolated Laryngeal Candidiasis Mimicking Laryngeal Carcinoma in an Immunocompetent Individual

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Abstract -

Respiratory fungal infections are usually found in immunocompromised individuals who have received either long-term steroid therapy or broad-spectrum anti-microbial therapy or have a non-resolving underlying chronic disease. These infections are seen as a part of bronchopulmonary fungal infections, and their isolated and primary occurrence as laryngeal diseases is highly uncommon. Laryngeal fungal infections can also mimic various diseases, such as gastroesophageal reflux disease, granulomatous diseases, leukoplakia, and carcinoma, thereby misleading the treating team from correct diagnosis and management. It is therefore important to identify the lesion at the earliest point possible to avoid morbid or life-threatening consequences. We report a case of isolated laryngeal candidiasis in an immunocompetent Indian male with an unusual presentation mimicking laryngeal carcinoma. The clinical and histological features are highlighted with a review of relevant literature to demonstrate the possibility of such an isolated fungal lesion, even in an immunocompetent individual.

Keywords: candidiasis, clinical microbiology, diagnosis, immunocompetent, laryngeal diseases, mycoses

Introduction

Respiratory fungal infections are common occurrences; however, isolated fungal infections of the larynx are rare, accounting for approximately 40 reported cases in literature. Larynx can be involved primarily by inoculation of sputum, or secondarily to predisposing conditions. Isolated laryngeal candidiasis is infrequently recognised and poorly documented (1). It has been described in patients with predisposing factors, such as underlying chronic diseases, granulocytopenia, broad spectrum antimicrobial therapy, steroid administration, diabetes mellitus, and mechanical, chemical, or thermal injury to the mucosal barrier. Most cases are usually mild and typically show punctuate white patches on the laryngeal mucosa (2-4).

We report a case of isolated laryngeal candidiasis in an immunocompetent individual, with an unusual presentation mimicking laryngeal carcinoma, to highlight the clinical and histological features of this condition and provide a review of the relevant literatures.

Case Report

A 73-year-old, immunocompetent male patient presented to the Department Emergency Medicine of a tertiary referral centre in Bangalore, South India, with a 3-day history of fever, odynophagia, and respiratory distress. On examination, he was febrile with tender rightsided cervical lymphadenopathy. Haematological investigations showed elevated white blood cell count with predominance of neutrophils. Absolute neutrophilic count (5000 mm³), T4/CD4 count (900 mm3), immunoglobulin A (145 mg/dL), immunoglobulin G (1000 mg/dL), and immunoglobulin M (167 mg/dL) were in the normal range. Human immunodeficiency virus infection was ruled out by a negative ELISA. The lateral soft tissue neck X-ray showed a thumb sign suggestive of an acute supraglottitis.

An office endoscopy confirmed the presence of oedematous and congested epiglottis, arytenoids, and aryepiglottic folds, along with congested endolarynx and significant pooling of saliva. The patient was a non-smoker and hypertensive on regular treatment without any other comorbidities. A diagnosis of acute epiglottitis with laryngitis was made.

In view of respiratory distress, a single dose of 100 mg hydrocortisone was administered intravenously. He was admitted and treated conservatively with antibiotics for a week. Repeat video laryngoscopy showed an ulceroproliferative lesion involving the right aryepiglottic fold and arytenoids, extending to the medial wall of the right pyriform sinus with fixation of the right hemilarynx (Figure 1a). Contrast-enhanced computerised tomography (CT) of the neck showed a heterogeneously enhancing lesion measuring approximately 1.5×1.0 cm in the right true and false cords with preservation of the paraglottic fat strip and causing medialisation of the cord (Figure 2). The possibility of a malignancy was considered in correlation with the clinical presentation, and the provisional diagnosis was revised to carcinoma supraglottis T3NoMX. Direct laryngoscopy and biopsy of the lesion were carried out to rule out malignancy.

Histopathological examination revealed an acute inflammatory exudate covered by necrotic tissue containing multiple spores and yeast-like organisms with slender pseudohyphae suggestive of mucosal laryngeal candidiasis (Figure 3).

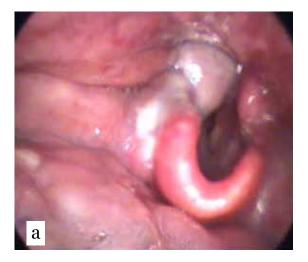
The patient was administered 200 mg of oral fluconazole once daily for 2 weeks. Video laryngoscopy after 1 week showed improvement in movements of the vocal cords on the affected

side. One week later, repeat video laryngoscopy revealed a normal endolarynx with bilaterally normal vocal cord movements and absence of the lesion (Figure 1b). Repeat CT scan also revealed a normal larynx. No sign of recurrence has been observed after 1 year of follow-up.

Discussion

Fungal infections of the larynx can cooccur with bronchopulmonary fungal infections. The condition is infrequently reported as an isolated and primary laryngeal disease (5,6). Candida and Aspergillus are possible causative agents (1). Laryngeal fungal infections can mimic laryngopharyngeal reflux (LPR) disease, granulomatous diseases, leukoplakia, and carcinoma (7). When the host immune mechanisms and the protective mucosal barrier are impaired, overgrowth can lead to infections of the larynx (8). In a 10-year retrospective analysis of 54 patients, inhaled steroids were the single most common predisposing factor, as seen in 89% of patients. Conditions such as LPR produce mucosal injury through retrograde acid transit via the oesophagus, while prolonged antibiotic therapy can reduce the bacterial burden at the larynx, thereby predisposing the patient to fungal laryngitis (7).

Clinical presentation of fungal laryngitis is variable and can include hoarseness, dysphagia, dysphonia, odynophagia, stridor, and respiratory distress (9). A high index of suspicion is necessary to make a diagnosis of isolated laryngeal candidiasis. *Candida albicans* usually causes superficial infections that are characterised by epithelial hyperplasia as a result of direct



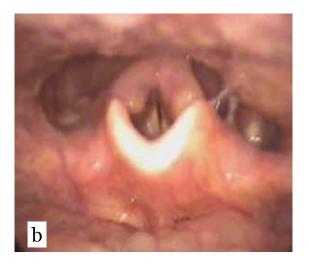


Figure 1: Images of 90° rigid optic videolaryngoscopy (a) before treatment and (b) after treatment.



Figure 2: Contrast-enhanced computerised tomography of the neck showing a heterogeneously enhancing lesion measuring approximately 1.5 × 1 cm in the right true and false cords with preservation of the paraglottic fat strip and causing medialisation of the cord on axial view.

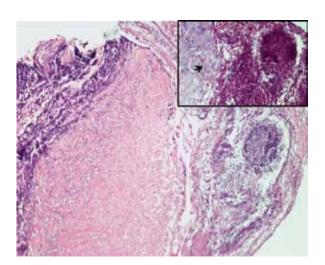


Figure 3: Haematoxylin and eosin staining (400× magnification) revealing acute inflammatory exudate covered by necrotic tissue containing multiple spores and yeast-like organisms with slender pseudohyphae suggestive of mucosal laryngeal candidiasis. Inset: Periodic acid-Schiff stain taken up by fungal colonies, showing fungal hyphae (arrow).

mucosal invasion. Most cases of muco-cutaneous candidiasis are superficial, but they can be invasive when they present with systemic manifestations of fever, chills, and malaise (9).

Video laryngoscopy typically reveals oedema, erythema, hyperkeratosis, adherent white plaques, shallow ulcerations, and white or grey pseudomembrane formations (9). Strobovideolaryngoscopy, although non-specific, provides important information on the integration of mucosal waves of the vocal cords. Diffuse mucosal oedema and erythema despite sufficient LPR therapy should prompt consideration of fungal laryngitis (7).

The role of biopsy is controversial, but it is justifiable if there is suspicion of a malignancy, as in this case, or of any other serious systemic disease, or if there is incomplete response to adequate therapy. The confirmation of a fungal infection can be derived from a histological evaluation. In borderline cases, laryngeal cultures and cytology can be obtained by bronchoscope brushings. Brush cytology has an advantage over biopsy in the diagnosis of mild cases because it is a less invasive procedure (8). However, the importance of laryngeal biopsy should not be underestimated, and it can be considered when a suspected fungal or bacterial infection is not responding to treatment. The possibility still remains that the patient might be suffering from a malignancy and an infection at the same time; a biopsy can help rule this out.

Treatment of laryngeal candidiasis has mainly been conservative, involving various anti-fungal drugs from intravenous amphotericin to oral flucanazole or ketoconazole to topical nystatin, based on the severity of the disease (10). The duration of treatment can vary from 10 to 30 days depending on the extent of clinical improvement. Regular videolaryngoscopy is advocated, as it not uncommon for the disease to recur (10).

Early recognition and treatment of this disease are important to prevent the spread of infection and systemic involvement. Misdiagnosis of the condition and inadequate treatment or premature biopsy can lead to impaired functioning of vocal cords and, on many occasions, a permanent disability. Sometimes an invasive infection can mask a concomitant underlying malignant lesion. Failing to perform a biopsy and performing tests for fungal diseases may allow the underlying malignancy to progress. Therefore, if a fungal pathology is ruled out, a biopsy must be considered next to rule out malignancy. Invasive laryngeal candidiasis has been traditionally linked to patients with immune deficiency. Our case

demonstrates the possibility of a fungal laryngeal lesion in an immunocompetent individual and the importance of considering it as a diagnosis prior to planning a biopsy to rule out malignancy.

Authors' Contributions

Drafting of the article: ABN, JC Critical revision of the article: MBV, MC, NR Final approval of the article: NR

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Case Report

An Unusual Case of Amoebic Liver Abscess Presenting with Hepatic Encephalopathy: A Case Report

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Abstract -

Amoebic liver abscess (ALA) with jaundice and encephalopathy is a rare occurrence and has been recognised and studied more frequently in recent years. We present a case of massive ALA presenting with jaundice, hepatic encephalopathy, and septicaemia that was treated successfully with percutaneous drainage of the abscess, right-sided chest tube insertion, and anti-amoebic therapy.

Keywords: amoebiasis, hepatic encephalopathy, hepatology, jaundice, liver abscess

Introduction

Amoebic liver abscess (ALA) is the most extra-intestinal manifestation Entamoeba histolytica infection. It has been reported that jaundice is uncommon and mild in liver abscess, and some even consider the presence of jaundice as a feature against the diagnosis of hepatic amoebiasis (1). The cause of jaundice in a case of ALA has been hypothesised to result from either hepatocellular dysfunction or intrahepatic biliary obstruction (2). The mortality of ALA with jaundice is reported to be high. It may cause general debility and sometimes even lead to hepatic encephalopathy and septicaemia, which are the leading causes of mortality in jaundiced patients (3).

Case Report

A 24-year-old male patient presented to the surgical emergency ward with history of high-grade fever with chills and rigors of 10-day duration, along with non-radiating pain in the right hypochondrium. There was history of falling from 10 feet high 5 days prior to the onset of fever. There was also a history of yellowish discolouration of the eyes for 5 days and disorientation for 1 day. On examination, he was febrile, with a pulse rate of 120 beats/minute, and was normotensive. He was drowsy, disoriented, and deeply jaundiced. On abdominal examination, his liver was enlarged, with a span of 20 cm, and there was intercostal tenderness over the lower spaces on the right side. There was no free fluid in the abdomen.

On chest examination, there was bilateral equal air entry. Upon investigation, haemoglobin was g/dL, with a total leukocyte count of 13 000 cells/mm3 (normal range is 4000-11 000 cells/mm³). Liver function tests revealed total serum bilirubin of 20 mg/dL, with direct bilirubin of 15 mg/dL, serum glutamic-oxaloacetic transaminase (SGOT) of 324 IU/L (normal level is less than 40 IU/L), serum glutamic-pyruvic transaminase (SGPT) of 340 IU/L (normal level is less than 40 IU/L), and alkaline phosphatase of 90 kAU/L (normal range is 3–13 kAU/L). The patient tested positive for amoebic serology by ELISA. A chest X-ray revealed that the right dome of the diaphragm was raised. Ultrasound showed a large hypoechoic lesion of 10 × 8 cm occupying the right lobe of the liver, suggestive of liver abscess; however, there were no ascites or pleural effusion. A computed tomographic scan showed a large mass in the right lobe of the liver with central hyperintense contents surrounded by a thick irregular hypointense rim (Figures 1 and 2). The patient was started on anti-amoebic therapy (ciprofloxacin and metronidazole), vitamin K, and intravenous fluids. His condition deteriorated over the next 24 hours, and signs of septicaemia persisted. He also developed altered sensorium. A 16F pigtail catheter was inserted into the abscess cavity under ultrasound guidance, and 100 mL of purulent fluid was drained. Subsequently, the patient developed dyspnoea, and on examination, there was dullness on the right side of the chest with the absence of breath sounds. Aspiration yielded purulent fluid, and a right-sided chest tube was inserted; 1000 mL purulent fluid was

drained. His respiration improved with the chest tube draining around 800 to 1000 mL over the initial few days. After 1 week of admission, he had profuse haematochesia. Because the bleeding profile parameters were within normal limits and in line with history of trauma, a possibility of haemobilia due to aneurysmal rupture in the abscess cavity was maintained, and an MR angiography was conducted. The MR scan revealed a large mass with central hyperintense contents surrounded by a thick irregular hypointense rim in the right lobe of the liver superiorly, but there was no evidence of aneurysm. The patient remained septicaemic for the next 4 to 5 days, but he improved slowly. The chest tube was removed on the 20th day of admission, and the drainage catheter in the abscess cavity was subsequently removed. The patient was discharged in good condition. Subsequent follow-up for 3 months and repeat ultrasound performed at the end of 3 months showed no residual abscess.

Discussion

Jaundice and encephalopathy are unusual manifestations of ALA. Most of the patients of ALA with jaundice either have multiple abscesses or a solitary large abscess compressing the biliary tract (4). In our patient, a solitary large abscess had presented with both jaundice and encephalopathy. In a series by Nigam et al. (5), cholestasis was seen in 29% of ALA cases, out of which 13% presented with hepatic encephalopathy. In a study by Vakil et al. (3), out of 58 patients with atypical presentations of ALA, 13 were found to have neurological manifestations. In a study by Kapoor et al. (6), all of the patients with neurological manifestations had multiple amoebic liver abscesses. Various hypotheses have been given for the cause of jaundice in ALA. The most accepted cause is hepatocellular dysfunction or intrahepatic biliary obstruction. Large ALA may compress the porta hepatis leading to stasis of the bile in the intrahepatic biliary radicals (7). In our case, alkaline phosphatase, serum bilirubin, SGOT, and SGPT were deranged, so both hepatocellular damage and biliary obstruction had occurred. Fifteen percent of patients may have multiple abscesses. They present with fever, toxaemia, deep jaundice, and encephalopathy (8). Toxaemia is suggestive of an additional bacterial infection leading to a more severe disease. E. coli and Klebsiella are the organisms commonly cultured. Changes in the classic electroencephalography (EEG) associated with hepatic encephalopathy are high-amplitude, low-frequency waves and



Figure 1: Computed tomography scan (coronal view) shows a large mass in the right lobe of the liver with central hyperintense contents surrounded by a thick irregular hypointense rim (arrow points to the centre of the abscess).

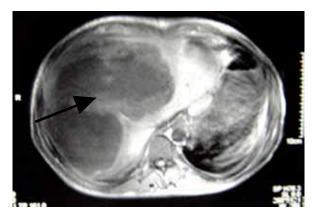


Figure 2: Computed tomography scan (axial view) of the abdomen shows a large mass with central hyperintense contents surrounded by a thick irregular hypointense rim in the superior right lobe of the liver (arrow points to the centre of the abscess).

triphasic waves (9). However, these findings are not specific for hepatic encephalopathy. Additionally, the changes in EEG are not typical enough to be useful in distinguishing hepatic encephalopathy from other conditions. Not many reports studying the changes in EEG in hepatic encephalopathy due to ALA are available in the literature.

Another unusual presentation in our case was that of haematochesia. Because there was history of trauma, the possibility of haemobilia was suspected. Causes of haemobilia include trauma, gallstones, inflammatory diseases, and vascular disorders. Though liver abscesses are known to rupture in biliary ducts, haemobillia has rarely been reported. There was therefore a dilemma regarding the cause of haematochesia in our case.

Though the treatment options vary from medical to open drainage, it is now universally accepted that aspiration and/or surgical drainage of ALA together with anti-amoebic therapy is effective (10). Our patient was managed successfully with anti-amoebic therapy and catheter drainage. Though there has been high mortality in ALA presenting with encephalopathy, our patient responded well to the treatment and was discharged in good condition.

Authors' Contributions

Conception and design, final approval of the article: AKS
Collection and assembly of data: RM
Analysis and interpretation of the data, drafting and critical revision of the article, administrative, technical, or logistic support: AKS, RM

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Case Report

A Case Report of Atypical Teratoid/Rhabdoid Tumour in a 9-Year-Old Girl

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Abstract -

Primary central nervous system atypical rhabdoid/teratoid tumour (ATRT) is a rare and highly malignant tumour that tends to occur in infancy and early childhood. The majority of tumours (approximately two-third) arise in the posterior fossa. The optimal treatment for ATRT remains unclear. Options of treatment include surgery, radiotherapy, and chemotherapy. Each of their role is still not clearly defined until now. The prognosis of the disease is generally unfavourable. This is a case report of ATRT in an atypical site in a 9-year-old girl.

Keywords: central nervous system neoplasms, child, oncology, recurrence, rhabdoid tumour, teratoma

Introduction

Atypical rhabdoid/teratoid tumour (ATRT) of the central nervous system (CNS) is a rare and malignant tumour that usually occurs in early childhood. This type of tumour was first described as a histological variant of Wilm's tumour that mainly occurs in infants and has a very poor prognosis. A CNS tumour of rhabdoid cells was first described in 1985, but its clinical and pathological features were not well defined until 1995–1996 (1).

The age at presentation is usually less than 2 years. However, it has also been reported to occur in older children and adults (2). Disseminated forms occur in 20% to 30% of cases. Patients with ATRT typically follow a dismal course, and the median time to death is only a few months after the diagnosis (3,4).

Radiological findings are non-specific (3,5). ATRT shares some morphological features with medulloblastoma and can also closely resemble choroid plexus papillomas (6). The histological hallmark of ATRT is the presence of rhabdoid cells; these cells have brightly eosinophilic cytoplasm, large and eccentrically placed nuclei, and a single prominent nucleolus each, with or without fibrillary globoid inclusions (6).

Because of its rarity and rapid course, there has been no consensus as to the optimal treatment of this tumour. However, surgery, radiation therapy, and chemotherapy may all play a role (7).

We report an unusual case of ATRT occurring in the temporal lobe of a 9-year-old girl.

Case Report

A previously healthy 9-year-old girl presented to our neurosurgical outpatient department with a 2-month history of progressive right hemiparesis. The onset was insidious and involved both the upper and lower limbs. There was no numbness or sensory loss. She experienced associated intermittent headaches that were worse in the morning but had no vomiting. There were no other neurological or systemic complaints.

On examination, the child was afebrile and had stable vital signs. She was alert, cooperative, and had intact higher mental functions. Her speech was normal, and her cranial nerves were intact. Her right upper and lower limbs were hypertonic compared with the left limbs and had grade 3 power. Reflexes were brisk with an extensor Babinski response on the right. Sensation was intact.

Magnetic resonance imaging (MRI) of her brain was done, but it was incomplete because of the patient's uncooperativeness. T1, T2, and fluid-attenuated inversion recovery sequences were obtained, but no contrast study was done. The results (Figure 1) showed a huge, lobulated intra-axial tumour occupying almost the whole left temporal lobe. It was mainly hypointense to grey matter on T1- and T2-weighted sequences. There were cystic components, as evidenced by areas of hyperintensity on T2-weighted images. It was large enough to cause effacement of the ipsilateral basal cisterns and a mild line shift of about 5 mm.

The patient underwent surgery to excise the tumour. During surgery, the tumour was found to be encapsulated, but it had diffusely infiltrated normal brain tissue in some areas. It was greyish, friable, and moderately vascular. The tumour was subtotally excised because of its infiltration of surrounding eloquent tissue. The patient recovered well post-operatively but her hemiparesis remained. On follow-up 1 month later, she had developed left 3rd cranial nerve palsy (Figure 2). Repeat computed tomography and MRI showed a recurrence of the tumour at the same location (Figures 2 and 3). Spinal

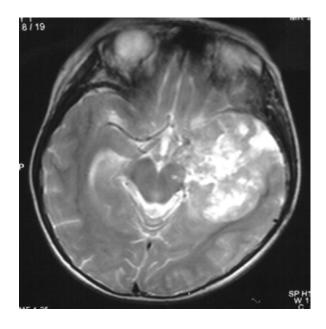


Figure 2: Post-operative T2 weighted magnetic resonance 1 month after surgery showed that the tumour had recurred to almost the same size of the previous tumour.

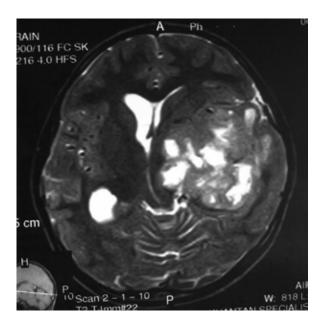


Figure 1: Pre-operative T2 weighted magnetic resonance image showing a large intraaxial tumour in the left temporal lobe, which was hypo- to isointense to the grey matter and had internal cystic components.

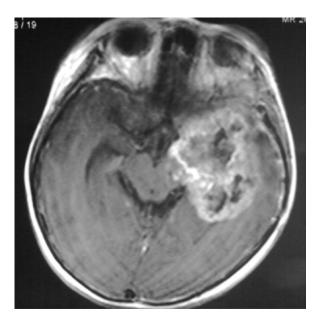


Figure Gadolinium-enhanced magnetic resonance image 1 month after surgery showed a nonhomogenously enhancing tumour with central areas of necrosis extending into the interpeduncular cisterns causing the third cranial nerve palsy.

dissemination could not be determined because a spinal MRI was not performed. However, there were no areas of leptomeningeal enhancement on the brain MRI to suggest cerebrospinal fluid (CSF) dissemination. Repeat surgery was performed and the patient was referred to the oncology team for radiation therapy.

Histological sections (Figure 4) showed a malignant tumour composed of cells arranged in a diffuse pattern interspersed in areas with dilated vascular channels and areas of necrosis. The tumour cells showed a mixture of primitive cells with scant cytoplasm, hyperchromatic nuclei, and epitheloid cells that are larger than normal. There were also rhabdoid cells with abundant eosinophilic cytoplasm and large vesicular nuclei containing nucleoli. There were some areas showing cords and strands of tumour cells with abundant chondromyxoid matrix. The mitotic activity was brisk.

Immunohistochemical staining (Figures 5 and 6) was positive for vimentin, glial fibrillary acidic protein (GFAP), and epithelial membrane antigen (EMA). Stains for synaptophysin, smooth muscle actin (SMA), and neurofilament were negative.

These features were consistent with a diagnosis of ATRT (World Health Organization grade IV). The patient was eventually lost during the follow-up period. A phone call to the patient's home revealed that the patient passed away at home 6 months after the onset of the disease.

Discussion

ATRT of the CNS are rare and present mainly in early childhood. They comprise 2%–3% of tumours in children under the age of 18 years and have a slight male predominance, with a male to female ratio of 1.6:1 (8). However, most patients who are diagnosed are younger than 3 years of age. The majority of these tumours (approximately two-third) occur in the posterior fossa (8,9). Other areas reported to be affected include the cerebral hemispheres, the pineal region, and the spine (10). Up to one-third of patients have CSF dissemination at diagnosis (4).

This is a case report of ATRT that occurred in a 9-year-old girl in the supratentorial region at the left temporal lobe. These tumours are highly aggressive and have malignant local infiltration, making total excision unfeasible if the tumour is in eloquent areas, as was the case for this patient. Prognosis is dismal, with a median survival of 6 months. Those with CSF dissemination have

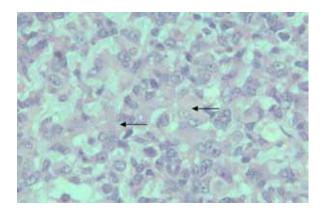


Figure 4: Haematoxylin and eosin stain of tumour tissue showing rhabdoid cells (arrows) with eccentrically placed vesicular nuclei and brightly eosinophilic cytoplasm. Some of the cells showed mitotic activity.

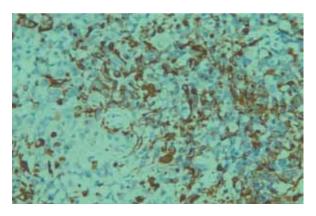


Figure 5: The tumour tissue stained positive for vimentin by immunohistochemistry.

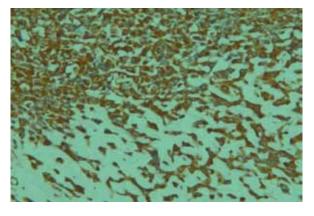


Figure 6: Tumour tissue stained positive for glial fibrillary acidic protein by immunohistochemistry.

been reported to survive only up to 2.5 months. This is especially true for children below 3 years of age. Moreover, children of this age group are more likely to have dissemination at diagnosis and have a faster rate of progression (4). In our case, the patient had already presented with a local recurrence and a new deficit just 1 month after subtotal excision. Dissemination at the time of recurrence could not be determined in this case because, even though brain MRI showed no area of leptomeningeal enhancement, no MRI of the spine was performed.

Histologically, the appearance of ATRT can vary, although the characteristic feature is the presence of rhabdoid cells (1,6). The cells have been described as medium to large cells with eccentrically placed nuclei and brightly eosinophilic cytoplasm equal to, or larger than, the size of the nucleus. The nuclei frequently contain prominent nucleoli (6). These features were present in this case. In addition, ATRT can have areas resembling medulloblastoma/ primitive neuroectodermal tumours, containing small, primitive looking neuronal cells with hyperchromatic nuclei and anaplasia (1). Rosette formation could also be seen (1). Our patient's tumour had this type of appearance. It is therefore important to have a differential diagnosis of ATRT in mind, especially in younger children.

On immunohistochemical staining, ATRT stain positive for vimentin, GFAP, EMA, cytokeratins, synaptophysin, chromogranin, and SMA (11). In our case, staining was positive for vimentin, GFAP, and EMA.

The optimal treatment for ATRT remains unclear. To date, the role of surgery for ATRT has not been well defined. While surgery is effective in reducing the mass, children who receive surgery without adjuvant therapy can die within a month (12). The role of the extent of surgery in different locations is also unclear. To achieve gross total resection, some authors have recommended aggressive surgical excision, including second surgery where feasible (4). Chemotherapy also has a part to play in treatment of this tumour, especially in children younger than 3 years of age, in whom radiation therapy needs to be delayed due to its deleterious effect on the developing CNS. Several different regimens have been tried, including baby Paediatric Oncology Group protocols, 8 drugs in 1 day, single-agent cyclophosphamide, and singleagent ifosphamide (4). However, the responses to these regimens are still not convincing, and some tumours have even been reported to progress during treatment. In addition, recurrent or

progressive ATRT appears to be chemoresistant in children younger than 3 years of age (4). The largest published series to date by the North American Atypical Teratoid/Rhabdoid Tumor Registry found long-term remission only in approximately 55% of patients with intensified chemotherapy (4). Gardner reported long-term survival with multi-drug chemotherapy, including high-dose methotrexate and myeloablative chemotherapy, after surgery in only 3 out of 7 patients. The disadvantages and side effects of chemotherapy include haematopoietic toxicity, sepsis, hepatic toxicity, and hearing loss (13).

As mentioned earlier, radiation therapy is usually delayed until the child reaches 3 years of age in order to avoid neurocognitive impairment. Tekauzt et al. (7) reported improved survival for children older than 3 who received combined radiation and chemotherapy. Chen et al. (5) and Tekautz et al. (7) also found that radiotherapy should be initiated in children older than 3 years of age soon after surgery and before chemotherapy. Bouvier et al. (2) reported a case of a 7-year-old with an ATRT in the left frontal lobe who had a 7-year event-free survival following treatment with gross total resection and external cranial radiotherapy. As children with ATRT may have leptomeningeal spread at diagnosis or recurrence (10), it may be desirable to administer craniospinal radiotherapy in addition to treatment of the primary tumour. In our case, spinal MRI needed to be performed first before proceeding to radiotherapy. Because the patient was an older child, she should have more favourable results from treatment compared with in children younger than 3 years of age.

This is an uncommon case of ATRT with typical histological features but presenting in an older child in the supratentorial compartment. This tumour is highly malignant and the optimal treatment is still unclear. Although older children with ATRT tend to have better outcomes than that of their younger counterparts', it has unfortunately carried fatal prognosis in this patient.

Authors' Contributions

Conception and design, collection, assembly, analysis, interpretation of the data, drafting and final approval of the article, administrative, technical, and logistic support: KHC

Provision of patient: FK

Critical revision of the article: YCT

Administrative, technical, or logistic support:

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Abstracts

Abstracts of Theses Approved for the MMed at the School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia

A RANDOMISED CONTROLLED TRIAL COMPARING THE EFFECTIVE DOSE OF METFORMIN IN THE TREATMENT OF ANOVULATION IN POLYCYSTIC OVARIAN SYNDROME. A COMPARISON BETWEEN METFORMIN 500 MG TDS AND METFORMIN SR 850 MG BD

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Introduction: Metformin had been used in the past 14 years for the treatment of polycystic ovarian syndrome in particular for menstrual regulation and ovulation induction. A number of reports have shown that metformin improved ovarian function. However, recent randomised clinical trials showed opposite findings. Nevertheless, while the debate continues, one factor has been overlooked: the dose and type of metformin preparation.

Objectives: The objective of the study was to evaluate the effectiveness of metformin SR 850 mg thrice daily (tds) in the treatment of anovulation in patients with polycystic ovarian syndrome in a randomised controlled study. The evaluation rate and the duration taken for ovulation in each treatment regime were assessed.

Methods: 40 patients were randomised: 20 received metformin SR 500 mg tds and another 20 received metformin SR 850 mg twice daily (bd). The patients were reviewed every 4 weeks; they were assessed for the presence of menstruation and side effects. Clinical examinations, which included measurement of weight, body mass index (BMI), waist-hip ratio (WHR), and Ferriman-Gallwey score, were performed. Blood investigations (follicular stimulating hormone, FSH; luteinising hormone, LH; testosterone; oestradiol; progesterone; and fasting lipid profile) were taken. Those who remained amenorrhoeic were required to continue with the same dose of metformin. If menses have not resume after an 8-weeks interval, bleeding will be induced medroxyprogesterone acetate. Success of treatment was considered in patients who had resumed their spontaneous normal menses and showed evidence of ovulation by a subsequent mid-luteal progesterone level of ≥ 30 nmol/L. Failure to resume menses after 24 weeks of starting treatment was considered as failure of treatment.

Results: Twenty patients received metformin SR 500 mg tds, and 17 patients received metformin SR 850 mg bd (3 patients from this group withdrew from

the study). There were significant reductions in weight and BMI in patients who were on metformin SR 500 mg tds (P = 0.024, and P = 0.37, respectively). There were also an improvement in features of hyperandrogenism in this group, a significant decrease in mean testosterone level (P = 0.046), and a significant improvement in the Ferriman-Gellway score (P = 0.009). Low-density lipoprotein level also showed significant reduction (P = 0.047). No significant differences were observed in the clinical and biochemical profiles of patients in the metformin SR 850 mg group. All the patients in the metformin 500 mg resumed normal menstruation compared to 14 patients (82.4%) in the metformin SR 850 mg group; this difference was not statistically significant (P = 0.139). Out of the 20 patients who menstruated in the metformin 500 mg group, 6 (30.0%) had ovulation compared with 2 patients (11.8%) in the metformin SR 850 mg group. The difference in the ovulation rate was not statistically significant (P = 0.157). There was no significant difference between the duration taken for ovulation. There were 2 conceptions during the study, all of whom belonged to the metformin 500 mg group.

Conclusion: The slow-release preparation of metformin was less superior to the immediate-release 500 mg tds regime for clinical and biochemical improvements in patients with polycystic ovarian syndrome. There were no significant differences in the ovulation rate and the restoration of normal menstruation between the 2 treatment groups.

Supervisor:

Associate Professor Dr Nik Mohamed Zaki Nik Mahmood

ATTENUATION OF HAEMODYNAMIC RESPONSE DURING INTUBATION WITH GLIDESCOPE® VIDEOLARYNGOSCOPE USING EITHER LIGNOCAINE OR MAGNESIUM: A RANDOMISED CLINICAL STUDY

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Introduction: Intubation with GlideScope videolaryngoscope (GSVL) has been associated with longer period of pressor response.

Objectives: This study aimed to look at haemodynamic parameters (systolic blood pressure, SBP; diastolic blood pressure, DBP; heart rate, HR; mean arterial pressure MAP) during laryngoscopy and intubation using GSVL with either lignocaine or magnesium used to attenuate the

pressor response.

Methods: The study involved 82 patients planned for general anaesthesia with endotracheal intubation. They were blinded and randomised into 2 groups: lignocaine (A) and magnesium (B). The agents were given at 1.5 mg/kg and 40 mg/kg to group A and B, respectively, and each drug was diluted into 20 mL syringe and given intravenously over 5 minutes before induction. Inductions were standardised with intravenous propofol 2 mg/kg, intravenous fentanyl 1 μ g/kg, and intravenous rocuronium 1 mg/kg. A single intubator with experience in GSVL performed the intubations. Haemodynamic parameters were collected at baseline, postinduction, at intubation, and 1, 3, 5, and 10 minutes postintubation. The interactions of haemodynamic parameters within and between groups were tested with repeated measure ANCOVA.

Result: There were significant interaction between time during intubation and estimated marginal mean of DBP, MAP, and HR in both groups (P < 0.05). The changes in estimated mean DBP and MAP were constantly less than baseline value post-induction and intubation. However, the rise in HR at 1 minute post-intubation in magnesium group was 11% above baseline and required 5 minutes to return to baseline (P < 0.05). The interaction in SBP was not significant (P > 0.05).

Conclusion: Magnesium at 40 mg/kg is less effective than lignocaine in attenuating pressor response to intubation with GSVL.

Supervisor: Professor Dr Kamarudin Jaalam Co-supervisor: Associate Professor Dr Wan Aasim Wan Adnan

STUDY OF COMPUTED TOMOGRAPHY PERFUSION IN TRAUMATIC CEREBRAL CONTUSION

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Introduction: Head injury is listed as the 5th principle cause of death in the Ministry of Health's hospitals, with a percentage of 6.07% of the total death. The prevalence rate of cerebral contusion was recorded as 15.0%. Non-enchanted computed tomography (NECT) of the brain is a sensitive primary diagnosis tool in the evaluation of patients with head injury.

Objective: The study aimed to determine perfusion status of pericontusional hypodensity area and correlation with clinical outcome.

Methods: Ten patients involved in motor vehicle accidents who fulfilled the inclusion and exclusion criteria were enrolled in this sturdy, which was conducted from July

2007 to November 2007. NECT scan of the brain was done on admission to confirm the presence of contusion, and followed by computed tomography perfusion (CTP). The data were analysed at the computed tomography workstation. Pericontusion areas were divided into 4 sections in relation to distance from the skull. Distance and size of contusion were measured from NECT scan. The regions of interest were drawn based on hypodensity and CTP colour map. Each parameters of perfusion were produced by the perfusion software and analysed. CTP results were categorised as normal, ischaemia, or infarct. Clinical outcome was evaluated using Glasgow Outcome Scale after 6 weeks post-trauma.

Results: Significant Spearman's correlations at the 0.5 level (2-tailed) were found between the distance of the contusion from the nearest skull vault and the perfusion status in the pericontusional hypodensity area, between the size of pericontusional hypodensity area with the perfusion status in the hypodensity area of that distance, and between the size of pericontusional hypodensity and the size of pericontusional hypodensity among each region of interest.

Conclusion: CTP is a useful and appropriate method is evaluating perfusion of pericontusional hypodensity area. However, no correlation was found between perfusion and clinical outcome in this study due to the small sample size. Ischaemia was present in all pericontusional hypodensity area. This suggests the importance of doing CTP in managing the traumatic.

Supervisor: Dr Win Mar @ Salmah Jalaluddin Co-supervisor: Dr Ab Rahman Izaini Ghani

CLINICAL EVALUATION OF 1-STEP QUALITATIVE
HEART-SPECIFIC FATTY ACID—BINDING
PROTEIN (H-FABP) TEST (CARDIODETRECT) AND
QUANTITATIVE CARDIAC TROPONIN T FOR THE
DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION
IN THE EMERGENCY DEPARTMENT

Dr Ahmad Suhailan Mohamed MMed (Emergency Medicine)

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Introduction: Coronary artery disease is a major cause of morbidity and mortality in most part of the world, including Malaysia. Patient presenting with chest pain to the emergency department (ED) poses a diagnostic challenge, especially those with atypical symptoms and non-diagnostic electrocardiogram. Cardiac biomarkers may be invaluable in establishing the diagnosis of acute myocardial infarction infarction (AMI) in the ED setting. A promising cardiac biomarker called heart-specific fatty acid binding protein (H-FABP) has been

shown to be released earlier than cardiac troponins into bloodstream and is specific for myocardial necrosis. A recent qualitative point-of-care test kit CardioDetect has been development to detect H-FABP in the circulation.

Objective: The first objective of the study was to assess the diagnostic indices of the CardioDetect assay and the quantitative cardiac troponin T test in diagnosing AMI in the ED, according to the onset time of chest pain. Secondly, to assess for improvements in the diagnostic indices of CardioDetect test if it is repeated 1 hour after an initial negative result. Thirdly, to assess for improvements in the diagnostic indices of CardioDetect assay when used in combination with cardiac troponin T test, and lastly, to assess the inter-observer variability in interpreting results of CardioDetect test in the ED.

Methods: This study was a prospective crosssectional study involving 80 eligible patients presenting with ischaemic-type chest pain who had symptoms within the last 36 hours. All patients were tested for H-FABP and troponin T at presentation to ED. The CardioDetect cut-off level for a positive detection of H-FABP was at 7 ng/mL. Quantitative troponin T was considered positive if its blood level exceeded 0.1 ng/mL. A repeated CardioDetect test was performed 1 hour after the initial negative result, and a repeated troponin T test was also performed 8-12 hours after an initial negative result. Based on pre-defined criteria, the attending physician made a final diagnosis and the patients were classified as having an AMI or non-AMI. The diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value, receiver operating curve) were analysed for CardioDetect and troponin T (individually and in combination), and also for the repeat CardioDetect test. Patients were categorised into 4 groups according to duration of chest pain. All diagnostic indices were determined for each test under consideration in all the 4 groups, at the following interval from the onset of chest pain: group 1 at 4 hours or less, group 2 at 4-12 hours, group 3 at 12-24 hours, group 4 after 24 hours. Data entry and analysis was performed using SPSS version 12.0 and Analyseit software.

Results: The CardioDetect test was more sensitive and had a higher negative predictive value than troponin T test during the first 12 hours of onset of chest pain. The repeat CardioDetect had better sensitivity and negative predictive value than the initial CardioDetect, especially in group 1. The sensitivity and negative predictive value of the combination test (CardioDetect and troponin T) was also superior to the each test performed individually, especially in group 1. The combination test, however, was inferior to the troponin T test in terms of diagnostic accuracy in almost all time frames except for the first 4 hours of chest pain onset. The agreement between the 2 observers in reading the CardioDetect test and the repeated CardioDetect test was reasonably good.

Conclusion: CardioDetect test is more sensitive and has a better negative predictive value than troponin T during the first 12 hours of AMI. It may be used to rule out myocardial infarction during the early phase of ischaemic chest pain.

Repeating the CardioDetect test 1 hour after an initial negative result does improve the diagnostic indices, especially during the first 4 hours after the onset of chest pain. The combination test of CardioDetect and troponin T should not be performed in all patients, but it may be useful in selected patients. Those who present with intermittent chest pain and are unsure or unable to recall the exact time of onset of chest pain may benefit from the combination test. The inter-observer agreement of CardioDetect test between the 2 observers was reasonably good. However, a comprehensive and continuous training should be incorporated to ensure accurate and proper interpretation of the CardioDetect test.

Supervisor:

Dr Nik Hisamuddin Nik Abdul Rahman

THE EVALUATION OF CLINICAL APPENDICITIS BY USING THREE DIFFERENT SCORING SYSTEMS AND THEIR ASSOCIATION WITH HISTOPATHOLOGY EXAMINATION IN ADULT SURGICAL PATIENTS: A PILOT STUDY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Previously published articles mentioned about the difficulty to make an accurate diagnosis of appendicitis. Because of this, in some centres, the rates of negative appendicectomy are still high. Many supporting tools have been introduced to help in the diagnosis, such as scoring system and radiological laparoscopic examination.

Methods: This study was conducted on 56 patients who have been admitted to adult surgical wards at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, from August 2007 to October 2007, for suspected appendicitis. All patients were assessed during the admission and 4 hours after, using 3 scoring systems: Alvarado Scoring System, Teicher-Landa Scoring System, and Christian Scoring System. The point from each individual scoring system were recorded and compared with results from the histopathology examinations. The score from this study were based on the previous study on the individual scoring systems. From the previous study on Alvarado Score by Chen et al. in Singapore, the score of 7 and above was considered as most likely appendicitis, score of 5 and 6 as probably appendicitis, and score of 4 and below as unlikely appendicitis. For the Teicher-Landa scoring system, score of -3 and above was most likely appendicitis, and the score of -4 and below was unlikely appendicitis. As for Christian scoring system, the score of 3 was the cut-off points to determine appendicitis. Since appendicitis is a progressive disease, the 4-hour score were used in the study.

Results: The results from the study showed that the scoring system is helpful as a diagnostic tool to support the clinical and histopathology findings of appendicitis. By using scoring systems, the percentage of true appendicitis cases was 91.1%. The association between each scoring system with the histopathology examination was determined. Both Alvarado and Christian systems showed significant associations, with P = 0.025 and P = 0.0017, respectively. On the other hand, the association between Teicher–Landa scoring system and histopathological findings was not significant. The sensitivity of the scores was also determined, Christian scoring system was found to be the most sensitive test among the 3 systems.

Supervisor:

Associate Professor Dr Mohamad Ziyadi Ghazali

THE EFFECTS OF RENAL DYSFUNCTION ON PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Chronic kidney disease (CKD) has been known to be a potent risk factor for cardiovascular-related death. It has been implicated in the adverse outcomes seen in patients after their coronary artery bypass grafting (CABG).

Objectives: The aim of this study was to evaluate the relationship between renal dysfunction and morbidity as well as mortality following CABG.

Methods: Records of 215 patients who underwent CABG between 1 January 2002 and 31 December 2005 at the Hospital Universiti Sains Malaysia, Kubang Kerian, were collected. These patients were divided into 2 groups according to their estimated glomerular filtration rate (GFR) using the Cockcroft–Gault formula. Estimated GFR of less than 60 mL/minute were grouped into the renal dysfunction, while GFR of more than 60 mL/minute were grouped as non-renal dysfunction. These retrospective data were analysed for its demographic and outcomes after the procedure, including the short- and long-term mortality rates.

Results: All 215 records representing 215 patients were successfully collected and analysed. Out of these patients, 117 (54.4%) had estimated GFR of less than 60 mL/minute and labelled as renal dysfunction group. This group of patient had a significantly lower body mass index, poorer pre-operative ejection fraction, and was older. There were also more incidences of diabetes mellitus and hypertension within this group (P = 0.005 and P = 0.031). Intra-operative data showed that the renal dysfunction group had shorter cross-clamp time (P = 0.018) and used up less cardioplegia (P = 0.004) during

the bypass. Post-operative data analysis showed that patients with renal dysfunction had more chance of developing acute renal failure (P < 0.001) and arrhythmia (P = 0.047). A total 10 patients died within 30 days and 15 patients died within 3 years of CABG; however, there was no significant difference noted between the 2 groups.

Conclusion: More than half of these patients were shown to have some degree of renal dysfunction before their CABG. This study supported the evidences that pre-operative renal dysfunction, even when subclinical, is associated with the adverse outcomes seen post-CABG, especially acute renal failure and arrhythmia. The relationship between renal dysfunction and post-operative mortality, however, had failed to be demonstrated in this study, as compared with many other studies before. This is most probably due to the small number of patients and total mortality seen.

Supervisor: Associate Professor Dr Mohamad Ziyadi Ghazali Co-supervisor: Dr Zulkarnain Hassan

THE ROLE OF PULSE WAVE VELOCITY AS A MARKER OF SEVERITY OF CORONARY ARTERY DISEASE (CAD) IN MALE PATIENTS IN A SINGLE CENTRE STUDY

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Introduction: Coronary artery disease (CAD) is one of the most common diseases in the world today, causing 6.9 million global deaths each year, and it is the leading cause of premature death in developed countries. There are many risk factors associated with increased risk of CAD, such as smoking, age, diabetes mellitus, hypercholesterolaemia, and hypertension. The benefits of early diagnosis and prevention of CAD have stimulated a search for reliable, non-invasive methods of detection. One of the non-invasive tests to diagnose CAD is the detection of arterial stiffness by measuring pulse wave velocity using the SphygmoCor machine. This technique is valid, reproducible, and widely applied.

Objectives: The aims of this study were to determine the role of pulse wave velocity as a marker of the severity of CAD, as well as to determine the association between pulse wave velocity with other cardiovascular risk factors.

Methods: A cross-sectional study involving 92 patients undergoing coronary angiography in ICL, Hospital Universiti Sains Malaysia, for the assessment of suspected coronary artery disease was carried out. Arterial stiffness was assessed through left carotid—right femoral pulse wave velocity using automated SphygmoCor® machine.

Results: The results of this study showed that pulse wave velocity was higher in patients with CAD than in those without CAD (11.13 ms⁻¹, SD 0.91, versus 8.14 ms⁻¹, SD 1.25; P < 0.001). When the severity of CAD was expressed as single-, two-, and multiple-vessel diseases, there was a significant association between the severity of CAD and pulse wave velocity (P < 0.05). The significant independent risk factors of CAD were age and total cholesterol (P < 0.05), whereas smoking, body mass index, systolic blood pressure, diastolic blood pressure, and diabetes mellitus were not significant (P > 0.05). Pulse wave velocity differed significantly with different categorical severities of CAD, even when their age and total cholesterol were controlled (P < 0.05).

Conclusion: Pulse wave velocity is an independent and complementary cardiovascular risk factor. Measuring aortic stiffness should serve as a marker of end organ damage regarding the arterial system, indicating an increased risk for cardiovascular complications, and helps to identify patients at high risk of CAD, who may benefit from more aggressive diagnostic and therapeutic strategies.

Supervisor: Dr Mohd Sapawi Mohamed Co-supervisor: Associate Professor Dr Zurkurnai Yusof

THE USE OF EARLY, MILD HYPOTHERMIA IN THE TREATMENT OF STABLE, SPONTANEOUS, SUPRATENTORIAL, INTRACEREBRAL HAEMORRHAGE

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Introduction: Haemorrhagic stroke or spontaneous intracerebral haemorrhage is a devastating condition that usually carries a poor prognosis, and the treatment options are limited. The use of therapeutic hypothermia in ischaemic stroke has been published with some encouraging, but not definite, results.

Objective: The study aimed to observe the effect of mild hypothermia in early post-haemorrhagic stroke patients with a stable condition, and to assessed stroke outcome score in 7, 30, and 90 days.

Methods: A prospective non-randomised study was performed involving a sample of confirmed haemorrhagic stroke patients presented at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. The patients were between the ages of 18 to 80 years. Patients with haemorrhagic stroke that was confirmed on CT scan and did not undergo any surgical intervention (including ventriculostomy) were offered to be recruited into the study; those who consented underwent

therapeutic hypothermia using an intravascular cooling catheter for 24 hours, followed by a period of slow rewarming, all conducted in an intensive care setting. Patients who did not consent to the procedure were given standard haemorrhagic stroke treatment and taken as control. All patients were assessed in 7, 30, and 90 days using National Institute of Health Stroke Scale and Modified Rankin Scale.

Results: A total of 24 patients were recruited. In the interventional arm, 6 patients were recruited; however, 2 of the patients died in the first week of the therapy. In the control arm, 18 patients were recruited; 3 died before the 90-day follow-up. There was statistically significant improvement of the Modified Rankin Scale score in the hypothermia group compared with the control group.

Conclusion: It can be concluded that the use of mild hypothermia is feasible and may be adjunctive to other treatment in the management of haemorrhagic stroke. However, due to the study limitation, we recommend a larger, multicentred trial to be done on early mild hypothermia treatment of haemorrhagic stroke.

Supervisor: Professor Dr Jafri Malin Abdullah

ROLE OF REPEAT HEAD COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF MILD TRAUMATIC BRAIN INJURY PATIENTS WITH A POSITIVE INITIAL HEAD CT

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Introduction: The advent of computed tomography (CT) has revolutionised the approach to mild traumatic brain injured (MTBI) patients. CT scan has now become standard practice in the initial management of MTBI patients. Those with a positive initial head CT not requiring surgical intervention will be warded for continuous neurological observation. As a routine, a repeat head CT is frequently ordered within 24 to 48 hours, even without any clinical neurological deterioration in the patient's condition. The logic of this practice is questionable, as convincing evidence is lacking. Indiscriminate ordering of radiological tests puts a strain on the healthcare system, especially in Malaysia where less than 30 government hospitals nationwide are equipped with CT scans.

Objective: The objective of this study was to evaluate the role of routine repeat head CT in providing useful information that leads to a neurosurgical intervention in MTBI patients.

Methods: This was a prospective observational study of MTBI patients admitted to the Neurosurgical Ward,

Hospital Sultanah Aminah, Johor Bahru, from 1 June 2008 to 30 September 2009. A total of 279 patients who met the inclusion criteria were included in the study. MTBI is defined as Glasgow Coma Scale (GCS) of 13, 14, or 15, with at least one of the followings: head trauma with loss of consciousness lasting less than 30 minutes, GCS of 13 or more, post-traumatic amnesia lasting less than 24 hours, any mental alteration at time of injury, and/or any transient or persistent neurological signs. A head CT was considered positive if there was a suspicion or clear evidence of an intracranial pathology. The result of the first head CT were obtained from the radiological report from this hospital's radiologist, or, when not available, from the attending neurosurgeon's interpretation as documented in the case notes. The patient's demographic data, initial neurological examination findings, and biochemical analyses were documented. Neurological status was also documented until discharge. The results of the repeat head CT scan were obtained from the radiological report from the hospital's radiologist or from the attending neurosurgeon's notes. These were categorised as improved, unchanged, or worsened. Any other additional neuroradiologic imaging or neurosurgical interventions were noted until discharge.

Results: Patients were divided into 2 groups: those with unchanged or improving repeat head CT (n = 217) and those with a worsened repeat head CT (n = 62). A total of 31 patients received urgent surgical intervention after the repeat head CT was done. In all cases, neurological deterioration preceded and prompted an urgent repeat head CT. When the 62 patients with the worsened repeat head CT were compared with the other 217 patients, they were found to have significant statistical correlation with older age of 65 years old or above (P < 0.001), lower GCS on admission (P = 0.003), associated symptoms of headache (P = 0.019), multiple lesion on initial head CT (P = 0.001), haemoglobin levels on admission (P = 0.009), longer hospital stay (P < 0.001), higher mortality rate (P = 0.001), higher risk to undergo surgical intervention (P < 0.001), and higher risk for neurological deterioration (P < 0.001). There was no significant difference on gender, ethnic groups, mechanism of injury, other associated symptoms on admission, types of intracranial injury on initial head CT, types of skull fracture sustained, and International Normalized Ratio levels. On applying multiple logistic regression, 3 factors were found to independently predict a worse repeat head CT: aged 65 years old or above, GCS of less than 15 (13 or 14), and multiple lesions on initial head CT.

Conclusion: The role of a repeat head CT in MTBI patients with a positive initial head CT had been evaluated in this study. Without a clinical neurological deterioration, a repeat head CT did not change the surgical outcome of patients. Patients with a GCS of 13–15 can be easily observed and assessed in the neurosurgical ward; therefore, it is unnecessary to order a repeat head CT in all MTBI patients. Due vigilance is warranted in those with risk factors for a worsening repeat head CT.

Supervisor: Dr Johari Siregar Adnan Co-supervisor: Dr Abdul Rahman Izaini Ghani

EFFECT OF EURYCOMA LONGIFOLIA JACK SUPPLEMENTATION ON RECREATIONAL ATHLETES' ENDURANCE RUNNING PERFORMANCE AND PHYSIOLOGICAL RESPONSES IN THE HEAT

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Objective: This study investigated the effects of Eurycoma longifolia Jack supplementation on recreational athletes' endurance running performance and physiological responses in the heat.

Methods: Nine healthy male recreational athletes (mean age of 23.3 years, SD 4.3; mean body weight of 69.2 kg, SD 9.6; mean VO₂max of 43.1 mL.kg-1.min-1, SD 6.6) were recruited for this study. In this double-blinded, placebocontrolled cross-over study, subjects completed 2 endurance running trials, performed on separate days, after either Eurycoma longifolia Jack (75 mg per capsule) or placebo supplementation. Two capsules per day of either Eurycoma longifolia Jack or placebo were taken for 7 days before and 1 hour prior to the experimental trial. On the trial day, after a 5-minute warm-up at 50% VO max, subjects were requested to run at 60% VO max for 60 minutes. This was immediately followed by a 20-minute time trial for determining endurance running performance. The experimental trials were carried out in the laboratory, where the temperature and relative humidity were kept at approximately 31 °C and 70%, respectively. Blood samples were taken before and after warm-up, and every 20 minutes time trial to determine haemoglobin concentration. At every 20 minutes during the trial, 3 mL.kg-1 body weight of cool water was given to the subjects.

Results: Study results showed that endurance running performance was not different statistically (P = 0.139) between Eurycoma longifolia Jack and placebo trials. Similarly, oxygen uptake, heart rate of perceived exertion, body weight changes, tympanic temperature, and haemoglobin concentration were not statistically different between trials.

Conclusion: A dosage of 150 mg per day of *Eurycoma longifolia* Jack for 7 days did not elicit beneficial effects on endurance running performance and physiological responses of recreational athletes in the heat.

Supervisor: Dr Chen Chee Keong Co-supervisor: Associate Professor Dr Mohamed Rusli Abdullah Dr Ooi Foong Kiew COMPARISON BETWEEN SERUM LACTATE LEVELS AND LEUKOCYTE COUNTS AS PREDICTORS OF MORTALITY IN EMERGENCY DEPARTMENT PATIENTS WITH SEPSIS-INDUCED HYPOTENSION AND SEPTIC SHOCK

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Introduction: Sepsis is a common problem precipitating admission to hospital, and it is the leading cause of death in Malaysia. In order to reduce the complications, early recognition, followed by rapid and accurate therapy, needs to be initiated. Recognising early stage of sepsis is difficult and challenging. Abnormal vital signs are late signs and do not correlate well with tissue hypoperfusion. Additional markers are sought to aid the early recognition, but little is known about risk-stratification biomarker in emergency department (ED) patient with sepsis. Leukocyte counts and lactate levels are possible candidates for use in the diagnosis of early stage sepsis. These measures are easily taken and evaluated in the emergency department.

Objective: In this study, we sought to determine whether serum lactate and leukocyte levels can be useful in predicting mortality in patients with sepsis-induced hypotension and septic shock.

Methods: This prospective cohort study was carried out in the ED of Hospital Universiti Sains Malaysia, a tertiary centre that received more than 50 000 patients in 2008. A total of 51 patients met enrolment criteria during the study period and 41 of them were included in the study. Inclusion criteria were patients 18 years old or above, diagnosed with either sepsis-induced hypotension or septic shock, and had investigated sepsis marker (blood lactate and leukocytes) measured. Other physiological variables were also measured in this study. Single reading of serum lactate and leukocyte counts taken before patients included in the study. The main outcome measure was 30-day mortality. Kaplan–Meier, Log-rank, and Cox's methods were used for statistical analysis using SPSS version 12.0.1.

Results: Out of the 41 patients, 61% were diagnosed to have sepsis-induced hypotension and 39% were diagnosed with septic shock. Twenty two (54%) deaths occurred within the 30 day follow up. Patient's mean distribution of age was 58.83, and most of the patients were in their 6th and 7th decades of life. The overall mean blood lactate level and leukocyte counts were 3.52 mmol/L (SD 2.29) and 11.37×10^9 cells/L (SD 6.38), respectively. A Cox Proportional Hazard Analysis revealed an increase in blood lactate levels in the ED was associated with an increased risk of death (B = 0.35, HR = 1.45, 95% CI 1.22, 1.73, P < 0.001). Leukocyte counts, however, do not show a significant association in predicting death in

patients with sepsis induced hypotension and septic shock (B = -0.44, HR = 0.957, 95% CI 0.882, 1.039, P = 0.295).

Conclusion: In this cohort of ED patients with sepsis-induced hypotension and septic shock, our results support blood lactate level as a promising risk stratification tool when compared with leukocytes counts. The multivariate analysis showed that for every increment of lactate value of 1 mmol, the hazards of dying are expected to increase by 1.5 times (P < 0.001). Multicentre validation needs to be done before widespread implementation.

Supervisor: Dr Nik Arif Nik Mohamed Co-supervisor: Dr Abu Yazid Md Noh

STUDY OF THE RELATIONSHIP OF VASCULAR PEDICLE WIDTH WITH CARDIOTHORACIC RATIO AND HAEMODYNAMIC DATA IN VENTILATED ICU PATIENTS

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Introduction: Intravascular volume assessment is one of the main concerns in managing critically ill ventilated patients. Invasive haemodynamic monitoring is commonly used to assess the intravascular volume status. Due to its invasiveness and other related serious complications such as bacteraemia, endocarditis, and thrombogenesis, the noninvasive diagnostic testing has gained increase importance. Chest radiograph is the readily available and most common tool used in managing critically ill ventilated patients. It is one of the invasive methods in the determination of the intravascular volume status. However, due to subjectivity on interpreting chest radiograph, on objective measurement like vascular pedicle width (VPW) is used to assess intravascular volume.

Objectives: The study aimed to determine the relationship of VPW with the haemodynamic data (weight and central venous pressure, CVP) and the cardiothoracic ratio (CTR) in ventilated patients using supine portable chest radiograph.

Methods: A cross-sectional study was done from May 2006 until December 2006, involving 140 adult ventilated patients in the intensive care unit (ICU) and the Neuroscience ICU, Hospital Universiti Sains Malaysia. The haemodynamic data (weight and CVP) was read within 1 hour after the VPW. The VPW and CTR were measured by researcher in separated occasion without clinical data related to patients available.

Results: Out of 140 subjects, 73 were males and 67 were females; 122 (87%) were Malays and 18 (13%) were Chinese.

The mean age was 46.6 years old, and the mean weight was 62.6 kg. The mean value for VPW was 64.3 mm, and the mean value for CTR and CVP was 0.5 and 13.0 mmHg, respectively. There was significant relationship between weight with VPW (P < 0.001), CVP with VPW (P < 0.001), and CTR with VPW (P < 0.001). However, using the multiple linear regression analysis, it is found that only CTR has a significant relationship with VPW as compare to weight and CVP. The VPW was found to be the only association seen with pulmonary oedema among the study population (P < 0.001, multiple logistic regression analysis); an increase of VPW measurement of 0.17 mm heightened the risk of a patient having pulmonary oedema by 1.2 times (P < 0.001).

Conclusion: There was statically significant correlation seen between the weight, CVP, and CTR with the VPW. The most significant correlation was seen between CTR with VPW. The patients had 1.2 time higher risk of having pulmonary oedema with every 0.17-mm increase in the VPW measurement. The mean value of VPW was noted to be smaller compared with in previous studies. This result suggests that the cut-off VPW measurement used to differentiate between high, low, or normal intravascular volume could be smaller in our population body habitus.

Supervisor: Dr Rohaizan Yunus Co-supervisor: Dr Rhendra Hardy Mohamad Zaini

COMPARISON OF 0.1% LEVOBUPIVACAINE + FENTANYL AND 0.1% ROPIVACAINE + FENTANYL INFUSION FOR LABOUR EPIDURAL ANALGAESIA

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Objectives: The purpose of this study was to compare analgaesic efficacies of 0.1 % levobupivacaine + 2 μ g/mL fentanyl and 0.1% ropivacaine + 2 μ g/mL fentanyl infusion for labour epidural analgaesia.

Methods: A randomised double-blinded prospective study was conducted, involving a total of 144 parturients ASA 1-2, singleton healthy pregnancy (36–42 weeks' gestation) with vertex presentation. Patients were randomly assigned to receive either 0.1% levobupivacaine + 2 μ g/mL fentanyl or 0.1% ropivacaine + 2 μ g/mL fentanyl. We measured pain score (using visual analogue scale, VAS), intensity of motor block (using Bromage score), haemodynamic parameters, and labour outcome between the two groups. Pre-block VAS score (0–100), VAS score after 5, 10, 15, 20, 25, and 30 minutes from time 0, and VAS at the time of request for additional analgaesia (end time) were recorded. During the first 30 minutes after the completion of epidural injection, the

systolic blood pressure, the highest sensory level to cold stimuli, and the maximum degree of motor block (based on a o to 3 of modified Bromage scale) were collected every 5 minutes. The duration of analgaesia was defined as the duration from time o to end time.

Results: There was no difference in the duration of analgaesia between the 2 groups. The degree of motor block was also indistinguishable. No difference in the serial systolic blood pressures was found.

Conclusion: As a conclusion, both 0.1% levobupivacaine + 2 μ g/mL fentanyl and 0.1% ropivacaine + 2 μ g/mL fentanyl can be used to induce epidural labour analgaesia effectively, without a difference in the duration of pain relief.

Supervisor: Dr Saedah Ali

ANTI-INFLAMMATORY AND ANTIOXIDANT EFFECTS OF TUALANG HONEY IN ALKALI CHEMICAL INJURY ON THE EYES OF RABBITS

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Introduction: Alkali chemical injury is one of the most devastating injuries to the eye. It results in permanent unilateral or bilateral visual impairment. Chemical eye injury is accompanied by an increase in the oxidative stress. Anti-inflammatory and antioxidant agents play a major role in the treatment of alkali chemical injuries.

Objectives: The objective of the study was to determine the anti-inflammatory (clinical and histopathological) and antioxidant effects (total antioxidant status and lipid peroxidation products) of Tualang honey versus conventional treatment in alkali chemical injury on the eyes of rabbits.

Methods: Alkali chemical injury was induced in the right cornea of 10 New Zealand white rabbits'. The rabbits were divided into 2 groups: group A was given conventional treatment and group B was treated with both topical and oral Tualang honey. Clinical features of the right eye were recorded at 12 hours, 24 hours, 72 hours, day 5, and day 7. The histopathological findings of the right corneas of all rabbits were also evaluated on day 7. The total antioxidant status and the level of lipid peroxidation products in the aqueous humour, vitreous humour, and serum at day 7 were estimated biochemically.

Results: There was no statistically significant difference in clinical inflammatory features (P > 0.05) between honeytreated and conventionally treated groups at different times of examination. There was also no significant difference in the total antioxidant status as well as the level of lipid peroxidation products in the aqueous humour (P = 0.117 and P = 0.382,

respectively), the vitreous humour (P = 0.917 and P = 0.248, respectively), and the serum (P = 0.917 and P = 0.332, respectively) between honey-treated and the conventionally treated groups.

Conclusion: Tualang honey has almost the equal effects when compared with the conventional treatment in treating alkali chemical injury on rabbit's eye. Future research with more number of rabbits and control group is warranted to explore the anti-inflammatory and antioxidant effects of Tualang honey.

Supervisor: Dr Zunaina Embong Co-supervisors: Associate Professor Dr Siti Amrah Sulaiman Associate Professor Dr KNS Sirajudeen Dr Venkatesh Naik

OUTCOME STUDY ON GLUCOSAMINE SULPHATE AS SYMPTOM-MODIFYING TREATMENT IN KNEE OSTEOARTHRITIS

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Introduction: Glucosamine sulphate is the sulphate derivative of the natural amino monosaccharide, glucosamine, a constituent of glycosaminologlycans in the cartilage matrix and synovial fluid. It is commonly used in osteoarthritis. Unfortunately, despite multiple controlled clinical trials of the use of glucosamine in osteoarthritis (mainly of the knee), controversy of efficacy related to the symptomatic improvement continues. Differences in results originate from the differences in the products, study designs, and study populations.

Objectives: The study aimed to evaluate the symptomatic outcome of patients treated with glucosamine sulphate in the management of knee osteoarthritis at Hospital Universiti Sains Malaysia, and the possible adverse effect of glucosamine treatment in the study population.

Methods: A cohort study was carried out from 1 December 2007 to 31 March 2008, involving 69 patients with knee osteoarthritis in the Orthopaedic Clinic of Hospital Universiti Sains Malaysia and Hospital Taiping. Out of the 69 patients, 34 (from Hospital Universiti Sains Malaysia) were prescribed glucosamine sulphate (1500 mg per day), whereas 35 (from Hospital Taiping) were selected as the control group. Rescue analgaesia was prescribed only when necessary. Socio-demographic characteristics of patients were documented. The primary outcome was measured using algofunctional Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire. The difference of the analgaesic usage was evaluated.

Result: The algofunctional KOOS and all sub scores (pain, other symptoms, quality of life, function in daily activities) except sport/recreation improved with time (P < 0.001) in the glucosamine group. In the between-group comparison, the glucosamine group showed improvement in pain, other symptoms, quality of life, and function in daily activities sub scores (P values ranged < 0.001-0.026). We found that 53% patients in glucosamine group consumed less analgaesic, but the difference was not statistically significant (P = 0.187). The adverse effects of glucosamine supplementation were minor, mostly in the form of mild gastrointestinal symptoms.

Conclusion: The results suggest that glucosamine supplementation can provide some degree of pain relief and improved function in patients with knee osteoarthritis. Usage of analgaesic may be reduced with glucosamine treatment. At a dosage of 1500 mg per day, the adverse incidence was minimal.

Supervisor: Dr Abdul Nawfar Sadagatullah

A PROSPECTIVE OBSERVATIONAL STUDY IN THE USE OF END-TIDAL CARBON DIOXIDE MONITORING IN PATIENTS WITH SHOCK IN THE EMERGENCY DEPARTMENT

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Introduction: Shock is the main presentation of many diseases presented to the emergency department (ED). Mortality remains high even with the advancing treatment and management of shock.

Objective: The study aimed to determine the usefulness of end tidal carbon dioxide (ETCO₂) monitoring in shock patients presenting to ED.

Methods: This was a prospective observational study in a tertiary ED involving 103 adults, with mean (SD) age of 54.07 years (17.58), who presented with shock. They were grouped according to different types of shock such as hypovolaemic, cardiogenic, septic, and others. Vital signs and ETCO₂ was measured on presentation and at 30-minute intervals for up to 120 minutes. Blood gases and serum lactate were obtained on arrival. The patient was managed according to standard protocols and treatment regimes. Patient survival up to hospital admission and at 30 days was recorded.

Results: Mean ETCO₂ for all patients on arrival was 29.07 mmHg (SD 7.39). Average ETCO₂ for patients in hypovolaemic, cardiogenic, and septic shock was 29.64 mmHg (SD 11.49), 28.60 mmHg (SD 9.87), and 27.81 mmHg (SD 7.39), respectively. ETCO₂ on arrival was

correlated with systolic and diastolic blood pressures, mean arterial pressure, pulse rate, respiratory rate, haemoglobin oxygen saturation (SpO_a), partial pressure of carbon dioxide in arterial blood (PaCO_a), bicarbonate, base excess, and lactate when analysed against all shock patients. Correlation with PaCO₂, base excess, bicarbonate, and serum lactate was seen in all shock groups when analysed separately. Only minimal ETCO₂ difference was seen among the various types of shock. Early ETCO2 measurement were found to be significantly lower in patients who did not survive to hospital admission (P = 0.005). Early measurement of diastolic blood pressure (P = 0.043), bicarbonate (P = 0.046), base excess (P = 0.038), and serum lactate (P = 0.007) also showed significantly difference. All patients who had ETCO, of 12 mmHg or less died in ED. However, normal ETCO, does not ensure patient's survival.

Conclusion: Monitoring ETCO₂ in the ED is a useful non-invasive way to gain additional information about the patient in shock. It is well-correlated with traditional shock markers such as systolic and diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate, SpO₂, PaCO₂, bicarbonate, base excess, and lactate.

Supervisor:

Associate Professor Dr Nik Hisamuddin Nik Abdul Rahman Co-supervisor:

Dr Tuan Hairulnizam Tuan Kamauzaman

MYOFASCIAL PAIN SYNDROME AMONG CHRONIC BACK PAIN PATIENTS: PREVALENCE, RISK FACTORS, AND OUTCOME

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Introduction: Myofascial pain syndrome is often overlooked in clinical settings owing to lack of awareness among clinicians. It is treatable but has received less attention as a major cause of pain and dysfunction among back pain patients. Thus, it is often under diagnosed and under treated.

Objective: The study aimed to determine the prevalence, the risk factors, and the outcome of patients with myofascial pain syndrome among chronic back pain patients.

Methods: A retrospective records review involving 126 patients attending Pain Management Unit for chronic back pain management between 1 January and 31 December 2008 was conducted.

Results: It was found that the prevalence of myofascial pain syndrome among chronic back pain sufferers was significantly high, with female gender as a significant risk factor. Secondary myofascial pain syndrome was observed in majority of the patients. Myofascial pain syndrome was found to be the main pain generator in more than half of all

secondary myofascial pain syndrome patients. The outcome of patients with this syndrome was favourable once proper diagnosis and expert management were provided.

Supervisor: Dr Nizar Abd Jalil

PERFORMANCE OF OSTEOPOROSIS SELF-ASSESSMENT TOOL FOR ASIAN (OSTA) FOR PRIMARY OSTEOPOROSIS IN POST-MENOPAUSAL MALAY WOMEN IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Osteoporosis, a major cause of morbidity and mortality in post-menopausal women, causes increase susceptibility to fragility fractures. Effective treatment for osteoporosis is now available. There is interest in identifying high-risk individuals to target therapeutic intervention. Dual energy X-ray absorptiometry (DEXA) is the gold-standard investigation in diagnosing osteoporosis. However, it is expensive and not widely available. The Osteoporosis Self-Assessment Tool for Asians (OSTA) had been developed to identify high-risk women; it is a simple test based on age and weight. OSTA can be used as a screening tool to identify high-risk patients who would benefit from bone mineral density measurement. OSTA score is calculated by subtracting age from weight and multiplying the difference by 0.2. It was develop based on data of 860 women from 8 Asian countries, including Malaysia. However, most of the respondents were Chinese (59%).

Objective: This prospective cross-sectional study aimed to evaluate the performance of OSTA among postmenopausal Malay women and to identify risk factors associated with osteoporosis.

Methods: 152 post-menopausal Malay women were sequentially recruited during the 1-year period. Data on demography and risk factors were collected. DEXA scan were performed on all respondents.

Results: In post-menopausal Malay women, OSTA score was able to predict patients at risk of osteoporosis based on bone mineral density measurements at the proximal femur. OSTA had a sensitivity of 87.5%, specificity of 95.8%, positive predictive value of 0.538, negative predictive value of 0.993, and area under the receiver operating characteristic curve of 0.895. Osteoporosis were associated with increased age, duration since menopause, as well as lower weight, height, body mass index, and OSTA score (P < 0.001). The prevalence of osteoporosis was 5.1%.

Conclusion: The use of OSTA in post-menopausal

Malay women is effective; the assessment has a high sensitivity and specificity. OSTA would enable prudent use of limited resources by avoiding excluding bone mineral density measurements in women with low risk of osteoporosis, and concentrating diagnostic and therapeutic modalities in high-risk women.

Supervisor: Dr Ahmad Sallehuddin Yaacob Co-supervisor: Dr Mohd Ezani Aziz

A RECORD REVIEW STUDY ON THE SUCCESSFULNESS OF RADIOIODINE ABLATION IN POST-OPERATIVE WELL-DIFFERENTIATED THYROID CARCINOMA PATIENTS USING 100 MCI OF ¹³¹I IN HUSM

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Introduction: Well-differentiated thyroid carcinoma is curable when discovered at an early stage. Post-operative radioiodine ablation is very useful. Its management, however, is often a challenge because there have been no prospective randomised trials and the optimal dose for successful single ablation is still a controversy. However, many published data showed a single high dose ablation had statistically significant results in the treatment of post-operative well-differentiated thyroid carcinoma.

Objectives: The objectives of this study were to determine the prevalence of success of single dose of radioiodine ablation using 100 mCi of ¹³¹I, to correlate successful ablation with other factors, and to determine the prevalence of patients who developed distant metastases after ablation therapy.

Methods: This record review study involved patients' records of over a period 10 years (1 January 1997 until 31 December 2007). A total of 214 samples that fulfilled the inclusion criteria were studied. The attached formal reported result of the first whole body scan and related associated factors were reviewed, and the required data were retrieved and studied by main researcher.

Result: The prevalence of successful ablation in our population was 54.2%, which is slightly lower than that reviewed in published data from other countries. The total thyroidectomy was found to be the only significant associated factor in this study. The prevalence of patients who developed metastases after initial ablation was 23.8%, with lymph node being the most common site of metastases.

Conclusion: In this study, we conclude that the present ablative dose of 100 mCi is effective in the treatment

of well-differentiated thyroid carcinoma remnants. We also found that only the type of thyroid surgery had a significant association with the outcome of radioiodine ablation.

Supervisor:

Associate Professor Dr Meera Mohaideen Abd Kareem

GASTROINTESTINAL STROMAL TUMOUR (GIST)— A CLINICOPATHOLOGICAL ANALYSIS OF CASES IN HUSM

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Introduction: Gastrointestinal stromal tumour (GIST) is a rare but the most common mesenchymal tumour in the gastrointestinal tract, and it arises from the interstitial cell of Cajal. The most important advance in the study of GIST is the discovery that the overwhelming majority of GIST are accompanied by activating mutations of *c-kit* (a gene belonging to the tyrosine kinase receptor family), which in turn leads to its detection at the immunohistochemical level with CD117. This has provided a very useful tool for the confirmation of the diagnosis of GIST. Another important marker, CD34, also plays a role in supporting the diagnosis of GIST.

Objective: The aim of this study was to evaluate the clinicopathological features of patients with GIST diagnosed in Hospital Universiti Sains Malaysia.

Methods: This is a cross-sectional study in which information obtained from patients who have been diagnosed with GIST in Hospital Universiti Sains Malaysia from October 1993 until October 2008. During this period, 37 patients were identified. Tissue blocks and stained slides were retrieved, and the case files were studied.

Results: Out of the 37 cases, only 28 with sufficient data for analysis were included. Only paraffin blocks from 18 cases were available for recut and staining, while in the remaining 10 cases, the histopathological data were based on the previous report and stained slides. In these 28 cases, 25 were Malays and 3 were Chinese; 13 were males and 15 were females. The mean age was 54.07 years. The most common clinical presentation was abdominal pain (10 cases), followed by upper gastrointestinal bleed and abdominal mass (7 cases each), altered bowel habit (3 cases), and intestinal obstruction (1 case). The primary site of the tumour was stomach (13 cases), followed by small intestine (8 cases), large intestine (6 cases), and 1 case with undetermined primary site. The tumour size varied from more than 100 mm (9 cases) to 51-100 mm (10 cases) and 20-50 mm (9 cases). The histopathological examination displayed spindle cell pattern in 27 cases and epithelioid pattern in 1 case. Immunohistochemical stain showed 25 out of 28 cases were positive for CD117. From the 25 CD117-positive cases, 16 showed co-expression of CD34 and 9 did not. In 3 cases, CD34 immunohistochemical stain was not done as paraffin blocks were exhausted. Staining for \$100 and \$MA (smooth muscle actin) were also done to see their differentiation into either neuronal, muscle or none of both. Neuronal differentiation only (positivity only for S100) was seen in 5 cases. Both neuronal and muscle differentiations (positive for both S100 and SMA) were seen in 2 cases, and 20 cases were negative of both. One case was positive for S100, but SMA staining was not done due to unavailable tissue block. Eleven cases had metastasis during presentation, while 3 cases had recurrence during follow-up after complete resection. Based on US National Institute of Health's guidelines, 82.1% of the patients are classified into the high risk group, 7.2% into the intermediate risk group, and 10.7% in the low risk group. Three patients died; 2 of them who presented with peritonitis died after laparotomy and biopsy within 3 days. Another patient had advanced disease with nodules in the liver and died after laparotomy and biopsy 37 days from the date of admission. 15 patients are still alive and are under follow-up. The remaining 10 cases were lost to follow -p.

Conclusion: The Hospital Universiti Sains Malaysia's experience of 28 cases of GIST shows that patients presented with a wide range of age and symptoms. The majority of the patients fall into the high-risk group, based on US National Institute of Health's guidelines. Most of the tumours were located in the stomach, and more than half of the tumours showed CD34 expression. Five cases showed neuronal differentiation only, and 20 cases did not show either neuronal or muscle differentiation. There was an association between CD34 expression and location of tumour. There was no association between CD34, tumour location, tumour size, and number of mitosis with metastasis and recurrence of the tumour.

Supervisor:

Associate Professor Dr Mutum Samarendra Singh

A COMPARATIVE STUDY OF TUALANG HONEY HYDROGEL WITH SAFECARE HYDROGEL DRESSING IN THE TREATMENT OF SPLIT-SKIN GRAFT DONOR SITES

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Introduction: An ideal wound dressing should have several key attributes: it should be able to protect the wound from infection, to control evaporative water loss and prevent dehydration, to control permeability of oxygen and carbon dioxide, to absorb wound exudate, and to enhance wound healing. Additionally, it should be composed of materials

that are non-toxic, non-immunogenic, flexible, durable, and comfortable when worn, pleasant in touch and painless in removal, with high elasticity but good mechanical strength. The healing properties of honey have recently gained recognition from the scientific community. Honey accelerates wound healing whether applied topically or administered systemically. Therapeutic effects of honey have been found in burn treatment; it promotes rapid healing of wounds with less scarring. Investigations have shown that honey is more effective than other natural and synthetic products in the management of burn wounds. In addition, honey is non-irritant, non-toxic, easily available, and inexpensive.

Objectives: The study was undertaken to compare the healing effects of 2 dressing materials on split skin graft donor sites.

Methods: This end-point blinded study was conducted from May 2008 to October 2009 in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, involving 70 patients who met the following criteria: aged 13-65 years, admitted for skin grafting procedure with donor sites restricted to only a single site, either the inner arm or thigh, and maximal length of the split skin graft donor wound of 25 cm (25 x 25 cm²). Immunocompromised patients, those with major systemic illness, those with an ASA score of III or more, and those who previously had a skin graft taken from the intended donor sites and donor site depths that are either too thin or too thick were excluded from the study. The patients were randomly allocated into 2 groups and assigned to a dressing regime of either Honey Hydrogel (n = 35) or Safecare Hydrogel (n = 35). The graft was harvested with a dermatome or Humby knife either under local, regional, or general anaesthesia aiming to take a medium thickness graft (0.012-0.018 mm), as judged by the appearance of the donor bed. Haemostasis of the donor site was achieved with topical Adrenaline (1:200 000). The wound was then cleaned with normal saline prior to application of the assigned dressing. An occlusive dressing technique using Hypafix® or Micropore® adhesive tape was employed for both the dressing materials. The patients were followed-up on post-operative day 10, 15, and 20. Donor site wound assessments and photodocumentation were performed at the time of dressing change.

Results: All the donor site wounds were healed by postoperative day 20. Combining the honey with hydrogel created a
wound-healing environment that appeared to meet the criteria
set forth above for ideal wound dressing. First, no signs of
bacterial infection were apparent during gross examination of
the wounds, suggesting that the materials effectively protected
the wound from bacterial infection. Second, the wounds were
moist and hydrated, demonstrating that evaporative water
loss and wound dehydration had been prevented. Third, the
honey component provided a pleasant odour, which was
noted as helpful in the overall healing process of the patient
and the caregivers. Fourth, the rate of healing was faster in
the Honey Hydrogel group, although all wounds eventually
healed. Finally, the acceleration of re-epithelialisation by
Honey Hydrogel indicated an enhancement of the overall

healing process.

Conclusion: We compared the wound healing rates and pain scale of the 2 dressings and found that wounds healed faster and with less pain in the Honey Hydrogel group. Honey, as a topical agent, does not adhere to the surface. In comparison to a plain hydrogel sheet, it promotes fast re-epithelialisation and decreases inflammatory reaction. In addition, Honey Hydrogel is cost effective because it shortens the duration of treatment. The honey may play a positive role in modulating wound healing when incorporated into the hydrogel matrix.

Supervisor: Professor Dr Ahmad Sukari Halim

DIAGNOSTIC VALUE OF PHYSICAL EXAMINATION IN CHILDREN WITH MILD HEAD INJURY IN COMPARISON WITH COMPUTED TOMOGRAPHIC FINDINGS

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Introduction: Mild head injury in children results in a large number of radiological evaluation and hospital admissions each year globally. Although some guidelines and proposals have been made in this area, there is still a great deal of controversy surrounding patients with a brief loss of consciousness (LOC) and Glasgow Coma Scale (GCS) scores of 13–15. Recent studies have indicated that avoiding head computed tomography (CT) scans in patients with LOC and a GCS score of 15 may be possible.

Objectives: The objective of this study was to determine the diagnostic value of physical examination for positive CT scan findings in children with mild head injury (GCS score 13–15) and with LOC or amnesia. From the result, the sensitivity, specificity, and predictive values of a normal physical examination after mild head injury and LOC were also analysed.

Methods: A retrospective medical-record review was conducted involving patients aged 1 to 12 years old who were evaluated for mild head injury with LOC or amnesia at the emergency department of Kuala Lumpur General Hospital between January 2007 and June 2009. Subjects who met the inclusion criteria were selected for the study, and the following data were recorded in a pro forma: age, gender, mechanism of injury, GCS on arrival, presenting symptoms, physical signs, head CT results, and further management of the subjects. The estimations of prevalence, sensitivity, specificity, positive predictive value, and negative predictive value were calculated, along with 95% confidence interval limits, using the Wilson score method. The agreement between physical examination

and brain CT in children with mild head injury and with LOC or amnesia was calculated using Kappa test.

Results: A total of 225 patients were included in the study; 63% of these patients were males, and 37% were females. Out of 44 patients (19.56%) with positive scan finding, 17 patients (7.56%) showed normal physical examination. Fifteen patients (6.7%) underwent neurosurgical intervention. For intracranial traumatic CT findings, sensitivity and specificity were 61.36% and 60.22%, respectively. The agreement between physical examination and CT scan was found to be K = 0.147 (P < 0.05, 95% CI 0.035 to 0.259).

Conclusion: The present study showed that physical examination was significantly associated with positive CT scan finding (P = 0.01). However, on further assessment of CT's predictive ability of a normal physical examination as well as the finding's unacceptably low sensitivity and specificity, a conclusion was made that intracranial pathology in children with minor head injury and having LOC or amnesia cannot be excluded based on physical examination alone. The K value calculated only showed a slight agreement between these 2 variables.

Supervisor: Dr Mohammed Saffari Mohammed Haspani

STANDARD PRECAUTIONS: KNOWLEDGE, ATTITUDE, AND PRACTICE AMONG HEALTHCARE PERSONNEL IN EMERGENCY DEPARTMENT, HOSPITALS IN KELANTAN

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Objectives: This study was done to determine the level of knowledge, attitude, and practice of standard precaution among various group of healthcare personnel in the emergency department of 4 selected hospitals in Kelantan, namely Hospital Universiti Sains Malaysia, Hospital Raja Perempuan Zainab II, Hospital Kuala Krai, and Hospital Tanah Merah. Validation of the questionnaire was done in March 2009.

Methods: A cross-sectional study was done for a period of 1 month, from 1 June 2009 until 30 June 2009, by using a self-reported questionnaire. The questionnaires were distributed to all healthcare personnel in 4 selected emergency departments/units. All healthcare personnel in emergency department at the time of data collection were included in the study, including those who were doing attachment or elective posting. The 5 groups of healthcare personnel were medical officers, assistant medical officers, staff nurses, assistant or community nurses, and health attendants.

Results: There were 199 healthcare personnel involved in this study. From this study, the level of good knowledge

was represented by 115 participants (57.8%), the level of good attitude was represented by 124 participants (62.3%), and the level of good practice was represented by 112 participants (56.3%). Comparison of mean knowledge, attitude, and practice level among various groups of healthcare personnel was done using Kruskal-Wallis test. Significant difference was observed between the groups of personnel for the mean comparison of knowledge and attitude (P < 0.001 each). Posthoc analysis for comparison of mean of knowledge revealed significant difference between medical officer and assistant medical officer (P < 0.001), medical officer and staff nurse (P < 0.001), medical officer and assistant nurse/community nurse (P < 0.001) and medical officer and health attendant (P < 0.001). Post-hoc analysis for comparison of mean of attitude score revealed significant difference between medical officer and health attendant (P < 0.001), assistant medical officer and staff nurse (P = 0.025), staff nurse and assistant nurse/community nurse (P = 0.010), and staff nurse and health attendant (P < 0.001). Simple linear regression test showed no significant association between the levels of knowledge (P = 0.225), attitude (P = 0.947), and practice (P = 0.681) with the frequency of needlestick injury. Independent t test showed there was no significant difference in level of knowledge (P = 0.061), attitude (P = 0.054), and practice (P = 0.731)among the healthcare personnel in emergency departments with emergency physicians and healthcare personnel in emergency departments/units without emergency physicians.

Conclusion: The level of good knowledge was only represented by 57.8% participants; good attitude, 62.3%; and good practice, 56.3%. The mean score differences among various categories of healthcare personnel were significant for the levels of knowledge and attitude, but not for the level of practice. There was no significant association between the levels of knowledge, attitude, and practice with frequency of needlestick injury. There was no significant difference in level of knowledge, attitude, and practice between healthcare personnel in emergency departments with emergency physicians and healthcare personnel in emergency departments/units without emergency physicians.

Supervisor:

Associate Professor Dr Nik Hisamuddin Nik Abdul Rahman Co-supervisor:

Dr Azriani Berahim @ Ab Rahman

ANTI-HEPATITIS A VIRUS SEROPREVALENCE AMONG CHRONIC VIRAL HEPATITIS B AND C LIVER DISEASE IN HUSM AND ITS ASSOCIATION WITH CPY3A4*18 POLYMORPHISM

Dr Fazlina Ahmad MMed (Internal Medicine)

Department of Medicine School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia Introduction: Vaccination against hepatitis A virus (HAV) is recommended in patients with chronic liver disease to prevent hepatic decompensation due to superinfection. CYP3A4 is the major cytochrome P450 in humans and its activity is reduced in chronic liver disease as well as hepatic cirrhosis. Detection of CYP3A4 polymorphism may predict detrimental effects on patients with chronic viral hepatitis with superimposed hepatitis A infection, due to reduced hepatic activity to eliminate drugs and harmful environmental toxin. Therefore, the need for vaccination is augmented.

Objectives: The aims of this study were to find out the seroprevalence of anti-HAV antibodies in patients with chronic viral hepatitis B and C liver disease and its association with CYP3A4 polymorphism as well as to justify the need for vaccination against hepatitis A in these patients.

Methods: A total of 120 patients attending the Gastroenterology Clinic, Hospital Universiti Sains Malaysia, from July until September 2009 were enrolled into this case control study. The diagnosis of chronic viral hepatitis B and C liver disease was based on presence of viral markers of more than 6 months, and the diagnosis of liver cirrhosis was based on clinical, biochemical, and radiological profiles. Patients' serum samples were tested for anti-HAV IgG using a commercially available kit, and blood samples were sent for CYP3A4 polymorphism analysis.

Results: The overall anti-HAV seroprevalence was 88.2%. The aetiology of chronic viral liver disease was hepatitis B in 96 patients (80.7%) and hepatitis C in 23 patients (19.3%). The mean age was 44.4 years (SD 14). Patients were categorised by decades of age: 24 patients (20.2%) were in the 21-30 age group, 22 patients (18.5%) were in the 31-40 age group, 31 patients (26.1%) were in the 41-50 age group, 23 patients (19.3%) were in the 51-60 age group, and 19 patients (16.0%) patients were more than 60 years of age. The seroprevalence according to age group was 66.7%, 95.5%, 93.5%, 91.3%, and 94.7%, respectively. There was marked increase of prevalence in age group after 30 years (P = 0.008). Seventeen patients were cirrhotics, and their anti-HAV seroprevalence was 100% compared with that of the noncirrhotic group, which was only 86.3% (P = 0.216). CYP3A4*18 polymorphism was detected in 3 patients with chronic viral liver disease, with the frequency of 2.5%. All patients with the CYP3A4*18 mutations were found to be heterozygous.

Conclusion: Our study demonstrated that the overall seroprevalence was 88.2% and age was the most important factor in determining anti-HAV positivity. Most patient aged more than 30 years are likely to have natural immunity towards hepatitis A. There was no significant association between CP3A4*18 mutation and anti-HAV serology. Since the prevalence of anti-HAV IgG is high, the hepatitis A vaccination may not be routinely required in this region especially in individual who are older than 30 years of age.

Supervisor: Dr Nor Aizat Che Hamzah Co-supervisor: Dr Nazri Mustaffa

A STUDY ON THE PREDICTORS OF GOOD TREATMENT RESPONSE IN METHADONE THERAPY IN HOSPITAL RAJA PEREMPUAN ZAINAB II

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Introduction: Methadone therapy is a part of a drug substitution programme, which is implemented to reduce the risk of contracting infectious disease through intravenous drug use. It is a national programme to prevent drug addicts from injecting heroine, by using oral intake of liquid methadone once a day as a substitute. However, there are participants of the programme who discontinued treatment due to various reasons. The dropout rates in foreign countries that conducted methadone programme were high, at an average of approximately 60%. There are many factors influencing patients' decision to continue the treatment, such as social factors, dosage of methadone, counselling sessions, and illness. It is important for us to identify the factors involved in order to aid patients in reviewing an effective treatment.

Objective: The aim of this study is to identify the factors predictive of a good treatment response to methadone therapy: whether socio-demographic factors (patients' background) such as older age and being married, higher dosage of methadone, and higher number of attendance in counselling session have influence in patients' response to methadone therapy. Good treatment response is defined as no positive urinalysis result of heroine within 6 months of enrolment into the methadone maintenance therapy programme, and retention in the programme for 6 month after the enrolment.

Methods: A cross-sectional study was performed to identify the factors that may predict a good treatment response in methadone therapy. Patients who were receiving anti-retroviral treatment and/or having mental illness were excluded from the study. Data on socio-demography, dosage of methadone, and counselling sessions were collected form medical records and patients' interview. The association between treatment response and the study parameters were assessed by applying chi-square and independent t test where applicable. Simple logistic regression was later performed to selected variables.

Result: Out of 150 patients, 82 (54.67%) had good treatment responses to methadone therapy, whereas 68 patients (45.33%) had poor responses, as shown by their positive urinalysis results or drop-out from treatment. It was found that there was an association between good treatment response and counselling session, but not with socio-demographic factors and methadone dosage. For every increase in counselling sessions, a patient has 1.190 times higher chance of having a good outcome (95% CI 1.049 to 1.349, P = 0.007)

Conclusion: Frequent attendance to counselling sessions was found to have an influence in the good treatment response to methadone therapy. Hence, counselling is an important component in patients undergoing methadone treatment. Socio-demographic factors and methadone dosage do not have any effect on the treatment response.

Supervisor: Dr Zahiruddin Othman Co-supervisor: Dr Mohd Nawan Hamzah Dr Mohd Ariff Mohd Nor

A RANDOMISED CONTROLLED TRIAL ON ADDITION OF VARIOUS DOSES OF INTRATHECAL PETHIDINE INTO HEAVY BUPIVACAINE IN THE PREVENTION OF INTRA-OPERATIVE SHIVERING IN PARTURIENTS UNDERGOING ELECTIVE CAESAREAN SECTION UNDER SPINAL ANAESTHESIA

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Introduction: Currently up to 65% of caesarean section (CS) has been performed under either spinal anaesthesia (SA) or combined spinal-epidural anaesthesia. Considering the frequent incidence of shivering associated with neuraxial blockade and its metabolic stress, prevention of this undesirable effect seems imperative.

Objectives: The aim of this study was to compare the addition of various doses of intrathecal (IT) pethidine into 0.5% heavy bupivacaine in the prevention of intra-operative shivering during elective CS under SA, as well as its associated adverse effects. A substudy on the incidence of hypothermia following SA in parturients and its relation with shivering was also explored.

Methods: A total of 64 subjects were recruited in this single-blinded, randomised controlled trial. All subjects received standard care during SA consisting of 10 mg of 0.5% heavy bupivacaine either alone (P_0 group, n = 21), with 5 mg of pethidine (P_{ϵ} group, n = 22) or with 10 mg of pethidine $(P_{10} \text{ group}, n = 21)$. Core temperature (tympanic membrane temperature), shivering score, blood pressure (BP), heart rate (HR), respiratory rate (RR) and oxygen saturation (SpO₂) were documented prior to SA and at different intervals after SA. Shivering scores of 2 or more were considered as shivering, and pethidine hydrochloride (0.5 mg/kg) was given intravenously as rescue treatment. Side effects were observed and treated accordingly. Differences in shivering scores were analysed with Kruskal-Wallis test or Mann-Whitney test. Comparison of the incidence of shivering and hypothermia and the relation between them were done with chi-square test. Differences in core temperatures, haemodynamic parameters and requirements of rescue therapy were analysed with ANOVA. Comparisons of adverse effects were done with chi-square test.

Results: Demographic data were comparable in all groups. Addition of IT pethidine was effective in the prevention of shivering without significant adverse effects. P10 group had lower incidence (2 out of 21 patients or 9.5%) and intensity of shivering compared with in the P_5 group (8 out of 22 patients or 36.4%), without any greater incidence of side effects. The incidence of hypothermia increased with time following SA, with as many as 100% of the studied subjects had shivering after 60 minutes; however, no significant differences were demonstrated among the 3 groups. Higher proportions of the hypothermic subjects experienced shivering, but this relationship only became statistically significant 20 minutes after the neuraxial block.

Conclusion: Addition of 10 mg of intrathecal pethidine is more effective in prevention of shivering without greater adverse effects in comparison with 5 mg of intrathecal pethidine. Hypothermia is common following SA. We suggest administration of 10 mg of pethidine intrathecally as an adjunct to prevent shivering, in addition to temperature monitoring and active thermal management to keep patients normothermic during CS under SA.

Supervisor: Dr Mahamarowi Omar Co-supervisor: Associate Professor Dr Saedah Ali

HONEY AS A MEAN OF GRANULATION TISSUE PROMOTER IN PATIENTS WITH DIABETIC FOOT ULCERS: A RANDOMISED CONTROLLED TRIAL

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Introduction: The increase of prevalence of diabetes mellitus in Malaysia and the profound complication of diabetic foot ulcers diabetic foot ulcers have been a huge burden to the patients and the health institutions. More recently, a resurgence of interest and an increasing number of case reports on the use of honey on diabetic foot ulcers reflect a growing awareness and a need for cost-effective therapies.

Objectives: Given honey's great potential as an alternative in wound dressing, this double-blinded randomised controlled study was designed to investigate the wound-healing property and the granulation tissue—promoting effect of honey, between the Malaysian tualang honey with the well-established "medical grade" manuka honey, in the management of patients with diabetic foot ulcers.

Methods: Thirty-four patients with Wagner stage II or

III diabetic foot ulcers were enrolled in the study. They were randomised into 2 groups of 17 patients each and treated with either manuka honey or tualang honey on a daily basis. Wound healing was assessed by measuring the granulation surface area using tracing technique. The primary outcome measure was checked in each group after 7 days.

Results: There was no significant difference (P = 0.687) between manuka honey and tualang honey groups in terms of mean percentage of granulation tissue surface area after 1 week of dressing in diabetic foot ulcers (manuka group, 60.7%; tualang group, 57.0%). All variables in both groups (age, wound size, HbA_{1c}, haemoglobin level, serum albumin level, absolute lymphocyte count, and ankle-brachial systolic pressure index) were comparable, and the differences were not statistically significant in the influence towards the primary outcome.

Conclusion: Tualang honey induced granulation and exhibited beneficial action in wound healing that was comparable to manuka honey. This result suggests that tualang honey could potentially be used as an alternative therapeutic agent for diabetic foot ulcers.

Supervisor: Dr Abdul Nawfar Sadagatullah Co-supervisor: Dr Mohammad Paiman

EFFECTIVENESS OF DESFURANE WITH
DEXAMETHASONE COMPARED TO TCI PROPOFOL
IN POST-OPERATIVE NAUSEA AND VOMITING IN
PATIENTS UNDERGOING OTORHINOLARYNGOLOGY
SURGERY

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Objective: The study was conducted to compare the prevalence of post-operative nausea and vomiting between 2 anaesthetic techniques: desflurane with dexamethasone and target controlled infusion (TCI) propofol.

Methods: In this prospective study, 80 ASA I and II patients aged between 18 and 52 years and undergoing elective otorhinolaryngology surgery were randomised into 2 groups. Groups 1 received desflurane and dexamethasone, whereas group 2 received TCI propofol. Haemodynamic parameters (systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate) were recorded at baseline. Patients were subsequently induced and paralysed with intravenous atracurium (0.5 mg/kg), and the patients were then intubated. Maintenance of anaesthesia was continued with desflurane and dexamethasone for group 1 and total intravenous anaesthesia using TCI propofol for group 2. Dosage of desflurane and

propofol were adjusted to maintain clinically adequate depth of anaesthesia with electroencephalogram bispectral index of 40–60. Once patients were extubated, they were monitored in recovery room. Haemodynamic parameters were again recorded.

Results: The number of patients who had postoperative nausea were less in group 1 (14 patients, 17.5%) compared with group 2 (31 patients, 38.8%). Combination of desflurane and dexamethasone is a good alternative technique to be used in otorhinolaryngology surgery. The usage of antiemetic rescue drug was also less in group 1 compared with group 2.

Supervisor: Dr Gnandev Phutane

NON-INVASIVE VENTILATION IN ADULT POPULATION IN INTENSIVE CARE UNIT, HOSPITAL UNIVERSITI SAINS MALAYSIA: A RETROSPECTIVE STUDY

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Objectives: The aims of this study were to review the practice of non-invasive ventilation (NIV) application in adult patients admitted in General Intensive Care Unit (ICU), Hospital Universiti Sains Malaysia (HUSM), and to investigate factors that contributed to its success and failure.

Methods: A retrospective study was done to review the NIV practice in HUSM. We defined the characteristics of adult patients (18 years old and above) admitted in ICU from 1 January until 31 December 2008 who had been put on NIV in any course of their stay in ICU. Data were collected from each patient's medical record, including the patient's ICU chart. Parameters taken were demographic data, diagnosis, patient's co-morbidity, simple acute physiology score (SAPS II), length of ICU stay, and patient's condition when discharged from ICU (survived or did not survive). The SAPS II was generated from the first 24 hours of patient's ICU admission. At the time when the NIV were being applied, specific data such as arterial blood gas analysis (ABG) values, status of organ failure, and type of supports that patients received (such as inotropes, vasopressors, and haemodialysis) were recorded. Subsequent evaluation on the NIV setting and the ABG were conducted at the following intervals: 1, 6, 12, and 24 hours after NIV application. If there was no ABG taken during those specific hours, the previous or next ABG within 2 hours duration was taken; if there was none, it was recorded as missing data. The duration of NIV (in hours) and the outcome of each patient were documented. Any deleterious events that happened during the course of NIV and the action taken by the attending

doctors were also recorded. The attending doctors' note was reviewed for the patients who had failed NIV and needed intubation or re-intubation. Descriptive analysis was used to describe the patients' characteristics. Relevant data were analysed using the appropriate non-parametric tests.

Results: We categorised 54 patients into de novo respiratory failure (de novo), acute on chronic respiratory failure (AOC), or acute cardiogenic pulmonary oedema (ACPO). The proportion of de novo was high (74.1%) when the other groups were low (14.8% for AOC and 11.1% for ACPO). Among the 3 groups, there were no significant differences in survival rates (77.5%, 87.5%, and 83.3% in de novo, AOC, and ACPO, respectively). ICU stay was significantly longer in de novo groups, at 11.5 days (SD 8.04), compared with 4.9 days (SD 1.46) in AOC and 6.8 days (SD 5.19) in ACPO (P = 0.029). When we looked further at patients in de novo group who were diagnosed with pneumonia, the mortality and the NIV failure rate were significantly higher than in the non-pneumonia patients (mortality rate of 50% versus 10.7%, P = 0.004, and NIV failure rate of 66.7% versus 39.3%, P = 0.017). In addition, when patients failed NIV and need intubation or re-intubation, the ICU stay would be doubled (15.1 days, SD 8.5, versus 7.5 days, SD 5.83). The overall mortality rate didn't deviate from the predicted mortality rate calculated from the SAPS II, and it was clearly shown that there was a significant difference in SAPS II between the survivors and non-survivors (35.7, SD 13.39, versus 46.1, SD 15.63; P = 0.036). However, there is no correlation between SAPS II and NIV failure rate.

Conclusion: In our ICU, most patients treated with NIV were de novo respiratory failure. There were no significant differences in mortality and NIV failure rates among different groups of respiratory failure, although ICU stay was clearly longer in de novo group. ICU stay would also be longer in those who failed NIV and needed intubation or re-intubation. SAPS II accurately predicted mortality rate but not NIV failure rate. Pneumonia patients in de novo group had significantly higher mortality rate as well as NIV failure rate compared with non-pneumonia patients. Indeed, among all of the analysed variables, pneumonia was the only one that had strong association with NIV failure. We concluded that our NIV practice results were not consistent with some reports in other clinical trials, except that pneumonia was a contributing factor for NIV failure and that those who failed NIV would have longer ICU stay. Nevertheless, we emphasised that differences might exist between controlled clinical trials and real clinical practice such as this retrospective study. From this retrospective study alone, it was not possible to determine whether our NIV practice had complied with the best standard practices. The NIV utilisation was low and it was expected that, had the medical officers been more confident, more patients should have been treated with NIV. The implementation of immediate NIV and alternate NIV were considered as good practices, but the high proportion of de novo, including pneumonia patients treated with NIV, suggested that the MOs might not be aware about the results from the previous

studies, which encouraged careful selection for that kind of patients. The presence of patients who died while on NIV would also speculate that intubation should have been taken earlier. The absence of NIV guidelines in our institution might leave improper decisions to be widely opened, and the status as a teaching hospital might become a disadvantage as new medical officers with less experience would come and those experienced ones would go. Therefore, we believed that the availability of standard protocol and proper training were essential for future improvement in NIV application in our institution.

Supervisor: Dr Rhendra Hardy Mohamad Zaini Co-supervisor: Professor Dr Nik Abdullah Nik Mohamad

DRUG COMPLIANCE AMONG EPILEPSY PATIENTS ATTENDING HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN

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Objective: The study was conducted to examine the percentage of drug non-compliance among epilepsy patients and its associated factors.

Methods: This cross sectional study the completion of a questionnaire by 297 epilepsy patients attending the Neurology Clinic, Hospital Universiti Sains Malaysia, from January 2008 until November 2008. The questionnaire consisted of the followings: compliance assessment, which contained 10 items, and psychological questionnaire, which contained 39 items. Patients were also given a form on demographic and clinical characteristics data to be filled out.

Result: Percentage of drug non-compliance was 52.2%, and the factors that contribute to non-compliance were the duration of epilepsy, patients' understanding of their illness, and medication barriers. Medication barriers that were significantly related with drug compliance include the complexity of the drug regime as well as the cost and physical properties of the meditation. There were no associations between drug compliance and socio-demography, patient satisfaction with health care, and other psychosocial factor: motivation, attitude, communication, and perception of disease severity.

Conclusion: Poor drug compliance was high in epilepsy patients. Factors associated with drug compliance include duration of epilepsy, patients' understanding of illness, complexity of the drug regime, and the cost and physical properties of the meditation. Assessment of drug compliance should be a routine part in managing epilepsy patients.

Re-organisation of factors that contribute to non-compliance will help the health care provider in planning an intervention programme to improve drug compliance, and consequently reduce the cost of managing epilepsy patients.

Supervisor: Dr Juwita Saaban Co-supervisor: Dr Adibah Hanim Ismail

FACTORS INFLUENCING LATE BOOKING AMONG ANTENATAL MOTHERS IN KOTA BHARU, KELANTAN

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Introduction: Antenatal care is a branch of preventive medicine dealing with prevention and early detection of pregnancy disorders. First antenatal visit after 12 weeks period of amenorrhoea is defined as late booking.

Objectives: The aimed of this study were to determine the factors influencing late antenatal booking and mothers' understanding of first booking, late booking, and its complications among antenatal mothers in Kota Bharu, Kelantan.

Methods: A cross sectional study was carried out from April 2008 to May 2008 involving 497 antenatal mothers who attended 11 health clinics in Kota Bharu. Systematic sampling method was applied, and consented respondents were interviewed using a revalidated questionnaire. The questionnaire consisted of socio-demographics data, obstetric and gynaecological data, health care factors, and socio-cultural factors. The study adopted the definition of late booking as the first antenatal visit after 12 weeks of amenorrhoea as used by Ministry of Health (2002).

Results: There were 250 of late booking mothers (50.3%), and 247 of early booking mothers (49.7%) involved in this study. The mean age of antenatal mothers in the late and early booking groups were 30.9 years (SD 6.6) and 28.7 years (SD 6.0) respectively. Respondents were predominantly Malays (98.0%), and all of them were married. Multivariable analysis revealed antenatal mothers with higher parity (OR = 106, 95% CI = 2.40, 5.91), those who had unplanned pregnancy (OR = 1.7, 95% CI = 1.10, 2.34), lower household income (OR = 1.7, 95% CI = 1.03, 1.18), and those who were not aware of the recommendation on early booking by the Ministry of Health (OR = 1.7, 95% CI = 1.14, 2.47) were more likely to come late for booking. Factors contributing to late antenatal booking were lack of awareness regarding Ministry of Health's recommendation on early booking, problems in arranging childcare for their children, influence from respondent's mother against early booking, longer waiting time, and lack of knowledge regarding appropriate time for first booking as well as maternal and foetal complications of late antenatal booking.

Conclusion: Recommendation on early booking should be given more priority in the health care programmes at all levels. Mass awareness programmes, particularly among women of reproductive age group, should be planned, targeting the identified risk factors for late booking, especially for multi grada and for antenatal check-up. The health staff should also give detailed counselling regarding the adverse outcome to the mother and foetus among late-booking antenatal mothers in order to prevent them from coming late for booking in the next pregnancy.

Supervisor: Dr Mohamed Hashim Mohd Hassan Co-supervisor: Dr Zaharah Sulaiman

THE EFFECTS OF TWO RELAXATION TECHNIQUES ON PSYCHOMOTOR, PSYCHOLOGICAL, AND PHYSIOLOGICAL VARIABLES FOLLOWING REPEATED SUB-MAXIMAL INTENSITY EXERCISE AMONG SCHOOL ATHLETES

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Objective: The present study was undertaken with an objective to investigate the effects of two relaxation techniques on selected psychomotor (choice reaction time), psychological (rating of perceived exertion, RPE) and physiological (heart rate; oxygen consumption, VO₂) variables following repeated sub-maximal intensity exercise.

Methods: The study involved 24 physically active young males with the mean age of 14.1 years (SD 1.3), height 157.3 cm (SD 6.1), weight 45.6 kg (SD 7.2), VO₂max 45.7 mL.kg⁻¹.min⁻¹ (SD 4.2), and maximum heart rate 205.9 beats per minute (SD 1.3). They were randomly divided into 1 of the 3 groups: autogenic relaxation (AGR), progressive muscle relaxation (PMR) and control. AGR and PMR groups were tested in 2 experimental sessions, prior to and after the relaxation training. However, the control group performed all experimental procedures except the relaxation training. Each experimental session consisted of 4 trials, where the participants had to cycle at 60% VO max for 10 minutes followed by 90% Vo max for 2 minutes in each trial. Then, a 3-minute rest interval was given, where choice reaction time (CRT) was tested. RPE, heart rate, and VO max were recorded at the end of each trial.

Results: The results of two-way repeated measure ANOVA revealed a non-significant interactions between

the groups across the experimental trials in all selected parameters (P > 0.05). However, results of the main effect revealed a significant difference for experimental sessions for RPE and $\mathrm{VO_2max}$ (P > 0.05). Pair wise comparison analysis revealed significant reductions, from pre- to post-intervention sessions, in RPE value for PMR group and in $\mathrm{VO_2max}$ value for AGR and control groups (P < 0.05 in each).

Conclusion: This study concludes that both relaxation techniques do not differ in terms of choice reaction time, RPE, VO₂max, and heart rate following repeated sub-maximal intensity exercise. However, when analysed separately, PMR appears to reduce RPE while AGR appears to reduce VO₂.

Supervisor: Dr Hairul Anuar Hashim Co-supervisor: Associate Professor Asok Kumar Ghosh

A RANDOMISED CONTROLLED TRIAL ON THE EFFECTIVENESS OF COMBINATION TRAMADOL/PARACETAMOL AND COMBINATION CODEINE PHOSPHATE/PARACETAMOL AS EARLY ANALGAESIA AT TRIAGE COUNTER FOR MODERATE PAIN IN EMERGENCY DEPARTMENT, HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Pain is a common symptom patient presenting to the emergency department. For more than a decade, we have identified that pain is undertreated in emergency medicine. Pain score assessment and analgaesia at triage counter is new and need further research, because effective pain management at triage counter is paramount in improving service delivery.

Objectives: The objective of this study is to compare the effectiveness of tramadol/paracetamol and codeine phosphate/paracetamol as early analgaesics at triage counter for acute traumatic moderate pain.

Methods: The study was conducted from April to September 2008 in Emergency Department, Hospital Universiti Sains Malaysia. Patients who fulfilled the inclusion criteria were selected for the study. Patients were randomised into Panadeine group or Ultracet group on the randomisation plan. Paramedics in charged are the assistants and, at the same time, the observers. Patients were given an analgaesic (Panadeine or Ultracet), and pain score using numerical rating scale and vital signs were taken at 0 minute, 30 minutes, and 60 minutes. If patients were still having pain after 60 minutes, rescue analgaesic would be given. A questionnaire was before each patient left the Emergency Department.

Results: 40 patients were enrolled; 72.5% (n = 29) were males, and 27.5% (n = 11) were females. All patients were Malays. The mean age was 29.6 years old. The patients were distributed equally (20 patients in each group) to receive either Ultracet or Panadeine. Mean pain scores via numerical rating scale on arrival were 5.95 (SD 0.88) in Panadeine group and 5.65 (SD 0.93) in Ultracet. Mean pain scores after 60 minutes were 3.40 (SD 1.75) for Panadeine group and 3.25 (SD 1.58) for Ultracet group. There was statistical significance in the pain score reduction in both Panadeine and Ultracet groups (P < 0.05). However, there was no significant difference in the pain score reduction between two groups (P > 0.05). The percentage of patients who achieved pain score reduction of 1 or more after 30 minutes was 77.5% (n = 31), and 92.5% (n = 37) patients achieved pain score reduction of 1 or more after 60 minutes. There was statistical association between patient's satisfaction and pain management (P < 0.05).

Conclusion: Panadeine and Ultracet are equally effective as early analgaesia at triage counter for acute traumatic moderate pain.

Supervisor: Dr Rashidi Ahmad

THE INFLUENCE OF TUALANG HONEY IN TENSILE STRENGTH AND MICROSCOPIC ASPECT (FIBROBLAST AND EPITHELISATION) OF LAPAROTOMY WOUND HEALING IN MALNOURISHED RABBITS

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Introduction: Based on published reports that honey accelerates wound healing, an investigation on its role in laparotomy wound healing, in terms of tensile strength and microscopic aspects (fibroblast and epithelialisation) on malnourished rabbits was carried out.

Methods: Forty-six female New Zealand white rabbits at the age of 6 weeks, weighing approximately 2–3 kg, were inflicted with a 4-cm infraumbilical laparotomy wound on their abdomen. They were divided into 3 groups: a malnourished group treated with topical and oral use of honey as well as malnourished and well-nourished groups treated with topical and oral used of normal saline. Wound dressing was done every day, and any changes over the wound were documented.

Results: The mechanical strength and histopathological examination were more favourable towards the malnourished group treated with topical and oral used of Tualang honey. At day 7 and day 14, the malnourished group treated with Tualang honey displayed a better tensile strength result compared with malnourished and well-nourished groups treated with normal

saline did (P < 0.05). For histopathological examination, both epithelial and fibroblast counts were also favourable towards the malnourished group treated with Tualang honey. At day 7 and day 14, the epithelial and fibroblast count were better in the malnourished group treated with Tualang honey compared with malnourished and well-nourished groups treated with normal saline (P < 0.05), except for the epithelial count at day 14 in comparison with well-nourished group treated with normal saline (P > 0.05).

Conclusion: Our study suggest that oral and topical Tualang honey enhances the laparotomy wound healing in malnourished rabbits by increasing the numbers of fibroblast and epithelial cells, which lead to increased wound strength.

Supervisor:
Dr Syed Hassan Syed Abd Aziz
Co-supervisors:
Dr Zulkarnain Hassan
Associate Professor Dr Siti Amrah Sulaiman
Associate Professor Dr Mutum Samarendra Singh
Dr Rumaizi Shaari

NASALANCE SCORE ANALYSIS AMONG MALAY POPULATION WITH NON SYNDROMIC CLEFT PALATE (WITH OR WITHOUT CLEFT LIP) IN HOSPITAL KUALA LUMPUR

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Introduction: The goal of cleft palate surgery is to establish a fully functioning velopharyngeal system with the least interference to the maxillofacial growth. An intact system will facilitate feeding, reduce the occurrence of upper respiratory tract infections, as well as improves otologic health and normal resonance balance. Post-palatoplasty speech therapy is commenced early in childhood to enhance vocabulary development and communication skills.

Objective: The study aimed to determine the speech outcome of primary palatoplasty and the association of hypernasality with cleft palate confounding factors.

Methods: This is a cross-sectional study of nonsyndromic cleft palate (with or without cleft lip) patients treated at Hospital Kuala Lumpur. The speech of 40 normal Malay subjects and 40 cleft lip/palate patients were assessed for hypernasality using Nasometer II 6400.

Results: The overall normal oral phoneme produced by Malay-speaking individuals demonstrated scores of between 3% and 5% higher than English-speaking individuals. The normal oral passage nasalance score obtained for Malay Language is 12% (SD 4). The cleft oral passage nasalance score for Malay language is 29% (SD 16). The comparison is statistically significant (P < 0.05). For post-palatoplasty cleft

patients who attended speech therapy, the mean nasalance score of the oral passage was 27% (SD 16); for patient who did not receive speech therapy, the mean was 32% (SD 17). The comparison was not statistically significant (P < 0.05). Further analysis of nasalance difference between genders, age groups, cleft sub types, and techniques of primary palatoplasty did not show any statistical significance. However, the mean scores of bilateral cleft lip and palate is demonstrated to be 10% to 15% higher than other cleft sub types.

Conclusion: Nasalance score was found to be useful adjunct to measure speech outcome objectively.

Supervisor: Dr Wan Azman Wan Sulaiman

NON-CORONARY LESIONS DETECTED ON MULTI-DETECTOR ROW CARDIAC COMPUTED TOMOGRAPHY IN PATIENTS WITH ATYPICAL CHEST PAIN

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Objective: The study aimed to report the prevalence of non-coronary lesions detected on cardiac multi-detector computed tomography (MDCT) angiography in patients with atypical chest pain. The prevalence of atypical symptoms for the study group and the association between the detected non coronary lesions and atypical symptoms were also reported.

Methods: A total of 123 patients underwent cardiac MDCT in Adventist Hospital, Penang, from May 2005 until November 2009. The MDCT images were reviewed by 2 radiologists, who were blinded to the clinical findings, in 4 different CT windows, and non-coronary lesions were observed and recorded. The presenting symptoms were also noted for all those patients.

Results: Non-coronary lesions were found in 91 patients (73.9%). Of these extra-coronary lesions, 5 (4.1%) were significant and required further follow-up and evaluation, while the rest were not significant and can be considered benign findings with no need for further evaluation. Lung lesions were seen in 81 patients (65.8%), cardiac abnormalities in 1 patient (0.8%), vascular abnormalities in 24 patients (19.5%), mediastinal lymph nodes in 33 patients (26.8%), esophageal abnormalities in 1 patients (0.8%), liver abnormalities in 49 patients (39.8%), splenic lesions in 11 patients (8.9%), bone abnormalities in 5 patients (4.1%), and other abnormalities in 7 patients (5.7%). In the study group, 33 patients (26.8%) were scanned due to pain in the arms, epigastrium, shoulder, or the neck, and the rest of the patients were scanned for screening. Of the 33 patients, 5 (4.1%) had lung bulla, 5 (4.1%) had interstitial lung changes, 11 (8.9%) had hepatomegaly, and 4 (3.3%) had other findings.

Conclusion: Our study supports several other studies that highlighted the importance of careful reviewing of the non-cardiac structures that was scanned with the heart and coronary arteries as part of cardiac MDCT angiography, preferably by a radiologist or trained cardiologist. Any significant non-coronary lesions must be reported and followed-up if necessary under clear and specific guidelines. Non-significant coronary lesions need no follow-up and should not require further investigations that may put more psychological and economic burdens on the patients.

Supervisor: Dr Rohaizan Yunus Co-supervisor: Professor Dr Ibrahim Lutfi Shuaib

NOSOCOMIAL INFECTION IN INTENSIVE CARE UNIT: A RETROSPECTIVE ANALYSIS

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Introduction: Intensive care unit (ICU)—acquired infection rates are 5–10 times higher than hospital-acquired infection rates in general ward patients. Knowledge in the use of antibiotics in ICU is important to ensure an optimal clinical outcome, to control the emergence of resistance among pathogenic microorganisms, as well as to reduce cost.

Objective: The aim of this retrospective study was to determine the current status of ICU infection in Hospital Universiti Sains Malaysia.

Methods: A retrospective review of nosocomial infection (NI) in Hospital Universiti Sains Malaysia was performed in a 1-year period, from April 2008 until March 2009. NI is defined according to the Centers for Disease Control and Prevention's guideline. The overall NI rate, the incidence density rate of NI, patients' demography, length of ICU stays, duration on devices, type of NI, the Simplified Acute Physiology Score (SAPS) II score, and the patient's outcome were determined. The organisms and antimicrobial susceptibility profiles were further investigated.

Results: Out of 795 patients admitted to ICU, 60 patients were identified with nosocomial infections. The overall NI rate was 7.5 per 100 patients, with incidence density rate of 91 per 1000 days. The mean length of stays was 17.13 days (SD 10.11). The percentages of patients with diabetes mellitus and hypertension were almost similar to patients with no co-morbidities (33.3%, 36.7%, and 31.7%, respectively). The mean SAPS II score was 41.82 (SD 16.5). The percentage of patients who survived was 56.7%, whereas 6.7% was re-admitted to the ICU. The main type of NI were bacteraemia

and pneumonia (38.3%), with mostly gram-negative bacteria isolated (59.6%). The main isolated organism was *Acinetobacter* sp. (24.5%) from tracheal aspirates. The initial treatment was monotherapy, mainly by meropenem (29.8%); the drugs least used were the cephalosporins. Four main organisms that developed resistance to the treatment were *Acinetobacter* sp. (28.6%), *Klebsiella* sp. (14.3%), methicillinresistant *Staphylococcus aureus* (14.3%), and *Escherichia coli* (7.1%). There were no specific resistant to any group of antibiotics. Five cases of multidrug-resistant *Acinetobacter* sp. were isolated (35.7%). In addition, 3 cases of extended-spectrum beta-lactamase-producing *Klebsiella* sp. and *E. coli* were isolated (21.4%).

Conclusion: Gram-negative organisms remain as the main pathogens in ICU infection, especially *Acinetobacter* sp., which potentially could lead to the emergence of multidrugresistant species. A future local prospective study would facilitate the surveillance of ICU infection.

Supervisor: Associate Professor Dr Saedah Ali Co-supervisor: Associate Professor Dr Wan Aasim Wan Adnan

RADIATION DOSE REDUCTION IN ADULT ABDOMEN AND PELVIS CT SCAN

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Introduction: Computed tomography (CT) scan is an extremely valuable tool, as it yields a lot in information regarding the internal human anatomy. With future advances in scanner technology, the number of the CT examination will likely continue to rise. CT of the abdomen and that of the pelvis have the highest effective dose. Thus, it is important to minimise the dose by adjusting scanning parameter. Major technical factors that influence radiation dose from CT scan include tube voltage, tube current, scanning time, pitch, slice thickness, and scanning volume. In this study, only the tube current (mA) was adjusted to as minimum as possible, while the other factors were kept constant.

Objective: The study was performed to determine whether a lower radiation dose could be used in adult abdomen and pelvis CT scan without affecting the diagnostic accuracy of the images.

Methods: This was a randomised cross-sectional prospective trial. Age, gender, and abdominal dimension were recorded from 82 adult patients who underwent contrasted abdomen and pelvis CT scan from April 2008 until October 2008; 41 patients underwent CT at 240 mA (control group), and 41 patients at 180 mA (trial group: 25% dose reduction).

The anatomic details, images quality, and the degree of confidence in reaching in diagnosis were graded as a scale of 1 (unsatisfactory) to 4 (excellent).

Results: The difference in perceived images quality between control and trial group was not statistically significant (P = 0.14). There is no significant difference in image quality score in patients with less than 34.5 cm and those with 34.5 cm or more of transverse abdominal diameter (P = 0.20). There is also no significant difference in image quality score in patient with cross-sectional abdominal area of less than 800 cm and those with 800 cm or more (P = 0.72)

Conclusion: The study proves that 25% dose reduction can be achieved in adult abdomen and pelvis CT scan, if performed at 180 mA, without deterioration of diagnostic image quality.

Supervisor: Dr Noreen Norfaraheen Lee Abdullah Co-supervisor: Associate Professor Dr Wan Ahmad Kamil Wan Abdullah

PREVALENCE OF ANAL INCONTINENCE IN PATIENTS WITH PELVIC ORGAN PROLAPSE AND ITS EFFECTS ON LIFESTYLE IMPACT OF THESE PATIENTS IN HOSPITAL IPOH

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Introduction: Anal incontinence is defined as the voluntary loss of the control of intestinal contents, covering from slight traces of stool in the underwear during the loss of wind to marked episodes of uncontrolled evacuation of soft or hand faeces. The causes for this humiliating symptoms can be multiple and complex. In women, the most frequent aetiological factor is injury to the pelvic floor structures due to childbirth. Medical practitioners often do not realise that anal incontinence can be prevented and treated. Quality of life of these women can be significantly improved after the appropriate diagnostic tests and subsequent individual therapy.

Objectives: This study aimed to observe the prevalence of anal incontinence in gynaecology patients with uterovaginal prolapse and how anal incontinence affects the quality of life these women. The study was conducted among women presenting for investigation of genital prolapse, to identify any variables important in the cause of anal incontinence, with particular focus on obstetric, medical, and surgical factors, and to establish whether there is an association between anal incontinence and genital prolapse.

Methods: A cross-sectional descriptive analysis was conducted on 270 women at the age of 40–60 years old attending Gynaecology Clinic, Hospital Ipoh, Perak, from September 2006 until September 2007. Anal incontinence and lifestyle impact was measured using self-administered validated questionnaire. The questionnaire consists of demographic data, an anal incontinence scoring system, and questionnaire on lifestyle impact of incontinence in these women. The prevalence of anal incontinence was calculated, and both univariate and multivariate analyses were performed. For univariate analysis, the chi-square test and independent t test were used to assess the association between the various demographic factors and anal incontinence with the severity of pelvic organ prolapse. Statistical significance was set at the 95%; P value of less than 0.05 was considered statistically significant. In multivariable analysis, multiple logistic regression analysis was used to identify the independent factors influencing the risk perception on anal incontinence.

Results: The prevalence of anal incontinence in women with genital prolapse and urinary incontinence was 33% and 24.1%, respectively, which was consistent with the other studies. The outcomes for age, parity, body mass index (BMI), spontaneous vaginal delivery, and baby's weight were significant as expected. The mean age of patients with anal incontinence was 54.6 years (P = 0.001). A BMI of 28.7 (P < 0.001) and parity of more than 5 (P = 0.012) were found to be significant factors. Menopausal participant and those with history of chronic constipation showed significant results (P = 0.008 and P < 0.001, respectively). Participants who had undergone vacuum delivery or had history of an extended tear had significant association with anal incontinence (P = 0.005and P < 0.001, respectively). Participants who had more caesarean section had reduced incidence of anal incontinence; this results was significant (P < 0.001). Participants with second degree pelvic organ prolapse had significant result of 2.4 (P < 0.001). Baby's weight of 3.4 kg had significant results (P = 0.003). An unexpected finding was that forceps delivery was not significantly related to genital prolapse. In types of anal incontinence, 3% participants had solid incontinence (P = < 0.001), 22.3% had liquid incontinence (P < 0.001), and 28.9% had gas incontinence (P < 0.001); the score of sometimes and always were added. A moderate lifestyle impact was significantly associated with second degree pelvic organ prolapse and anal incontinence (P = 0.004)

Conclusion: In the study, prevalence of anal incontinence observed among the woman with pelvic organ prolapse was significant. Therefore, all women undergoing urogynaecologic assessment for urinary incontinence or genital prolapse at their local setting should be routinely questioned about anal incontinence and other anorectal symptoms. This vital information should be assessed during routine gynaecological examination so that these patients can be offered anal sphincter repair at same sitting as pelvic floor reconstruction. Childbirth remains the major contributory factor for the development of either anal or urinary incontinence or genital prolapse. This is associated with functional and anatomical alterations in the muscles, nerves, and connective tissue of the pelvic floor. We conclude

that increasing age, obesity, menopause, second degree pelvic organ prolapse, vacuum delivery, larger baby's birth weight, history of constipation, urinary incontinence, and extended perineal tear during childbirth subjected women to a higher risk of anal incontinence. Women who had caesarean section were relatively free from this humiliating and uncomfortable problem. Anal incontinence also has a significant lifestyle impact on these patients, disabling them from carrying out daily activities, religious worships, and travelling.

Supervisor: Associate Professor Dr Nik Hazlina Nik Hussain Co-supervisor: Dr Zaharah Sulaiman

KNOWLEDGE, ATTITUDE, AND PRACTICE
OF MANAGEMENT IN OBESITY AND
ANTHROPOMETRIC CHANGES AMONG
PSYCHIATRIC PATIENTS ATTENDING A WEIGHT
MANAGEMENT BEHAVIOURAL PROGRAM IN HUSM

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Introduction: Weight gain has long been recognised and commonly encountered problem in psychiatric practice. The high prevalence of overweight and obesity in schizophrenia and bipolar disorder patients becomes a main concern worldwide because of the increasing awareness of its potential health consequences. Various intervention programmes have been designed to curb the worrying epidemics. Weight management via behavioural intervention has been one of the preferred ways in managing the problems because of its encouraging outcome and zero side effect compared with pharmacological approach. To date, weight change has been the main measure of the programme. None has looked into the change in knowledge, attitude, and practice of management in obesity after attending the program.

Objectives: The aim of this study was to compare the mean score of the knowledge, attitude, and practice (KAP) of management in obesity and the anthropometric changes (weight, waist and hip circumferences) before and after attending the weight management programme.

Methods: The interventional study consisted of 3 phases. First phase was the development of a new KAP questionnaire in relation to weight management and behavioural modification of overweight individuals. Second phase was pre-intervention evaluation, and followed by the intervention program, which is the weight management behavioural modification programme. Third phase was the evaluation of the effectiveness of the program by comparing the mean differences of the KAP scores, weight, as well as

waist and hip circumference of the participants.

Results: The KAP was found to have satisfactory validity and reliability and was used as a tool in assessing the effectiveness of the program. The changes were -1.22 (SD 29.43), - 3.55 (SD 35.35), and -0.97 (SD 13.02), respectively; however, no significant change was observed in the mean scores of KAP at the end of the program. The weight reduction was not significant, but the mean waist circumference change of 2.2 cm (SD 4.57) was statistically significant. Interestingly, the change in practice score was significant in those who attended more than 50% of the educational sessions, but not the exercise sessions. Bipolar disorders patients were found to have significant change in practice domain compared with the schizophrenia patients. Patients on atypical antipsychotics were found to have lesser weight reduction compared with those on conventional antipsychotics.

Conclusion: The educational sessions play an important role in modifying patients' practice of healthy living. The participants showed improvement in practice towards healthy living and eating when they attended adequate numbers of educational sessions, and this was not influenced by the frequencies of the exercise sessions. Though there was no significant weight reduction, the mean waist circumference reduction was significant and was a worthwhile outcome, as it reduces their risk of having metabolic syndromes.

Supervisor: Dr Asrenee Abdul Razak Co-supervisor: Dr Zarina Zainan Abidin

A STUDY OF CONTINUOUS MONITORING OF ENDOTRACHEAL TUBE CUFF PRESSURE USING AN ELECTRONIC DEVICE IN CRITICAL CARE SETTING

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Introduction: The endotracheal tube (ETT) cuff pressure measurement is not a routine practice in many critical care units.

Objective: The main purpose of this study is to determine the accuracy and the relationship of electronic measurement of ETT cuff pressure by continuous method, using aneroid manometer method as the control, and the usefulness of the continuous method toward reducing endotracheal tube-related complications in intensive care setting.

Methods: A total of 56 ICU patients intubated with ETT with cuff were recruited. A preliminary study was also conducted to determine the safety and stability of

this electronic device. The precision of reading of ETT cuff pressure were compared with manual aneroid manometer and the variability of cuff pressure changes were also assessed apart from ETT cuff related complications. The complications that we looked for were the prevalence of ventilator-associated pneumonia (VAP), post-extubation stridor, sore throat, and ETT dislodgement.

Results: We found that there was a significant correlation between the readings by aneroid manometer with that of electronic measurement device (mean of 44.16 mmHg versus 44.22 mmHg, P < 0.001). The prevalence of VAP, sore throat, and ETT dislodgement were 1.8%, 3.6%, and 3.6%, respectively. No patient was noticed to have post-extubation stridor.

Conclusion: The readings recorded by the electronic device for ETT cuff measurement was comparable with aneroid manometer, and the use of the electronic device could potentially reduce ETT cuff-related complications.

Supervisor: Associate Professor Dr Wan Aasim Wan Adnan

DYNAMIC EVALUATION OF UPPER AIRWAY IN OBSTRUCTIVE SLEEP APNEA SYNDROME USING FLEXIBLE NASOPHARYNGOLAGARYNGOSCOPE

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Objectives: This study was conducted to identify level of upper airway obstruction in patients with obstructive sleep apnea syndrome (OSAS), and to determine the relationship between the severity of upper airway obstruction and confounding factors such as gender, ethnicity, apneahypopnea index, body mass index (BMI), and neck circumference.

Methods: This descriptive cross-sectional study patients attending OSAS Clinic, Department Otorhinolaryngology-Head and Neck Surgery, Hospital Universiti Sains Malaysia, was conducted from July 2007 to June 2008. Patients with apnoea-hypopnea index of more than 5 and fulfilled all set criteria were recruited in the study. Consent to participate in the study were taken after the patients had been given thorough explanation and they understood the purposes, importance, and benefits of this study. The assessment of risk and hypersomnolence was done using Berlin's questionnaire and Epworth Sleepiness Scale, and followed by otorhinolaryngological examination. Flexible nasopharyngolaryngoscopy was performed in seated, erect, and supine position. Retropalatal and retroglossal regions were continuously recorded during quiet breathing and Muller manoeuvre in both positions. Captured images were measured using computerised image processor, and narrowing rate was calculated. Level of each site was classified based on Fujita classification and severity of obstruction using Sher scoring system for Muller's manoeuvre.

Result: A total of 59 patients participated in this study, and most of them were categorised into the severe group (29 patients, 49.2%), followed by the moderate group (16 patients, 27.1%) and the mild group (14 patients, 23.7%). Based on Fujita classification, 29 patients (49.1%) had type 1 (retropalatal) obstruction, 23 (39.0%) had type 2 (retropalatal and retroglossal) obstruction, and 7 (11.9%) had type 3 (retroglossal) obstruction. Using Sher scoring system for Miller's manoeuvre, sub-categorised into severe obstruction (51%-100% collapse) and less severe obstruction (0%-49% collapse) for statistical analysis, we found that retropalatal region in supine position was effected the most, with 50 patients (84.7%) in the severe obstruction group. This is followed by retropalatal region in erect position, with 35 patients (59.3%) in the severe obstruction group. In the majority of patients, retroglossal region in erect position and retropalatal region in supine position fell into the less severe obstruction group. We also found that obesity, high Mallampati score, age, male gender, Malay ethnicity, and high apnoea-hypopnoea index were significant risk factors that contribute to the severity of upper airway obstruction in patients with OSAS.

Conclusion: We concluded that nasopharyngolaryngoscopy with Muller's manoeuvre is reliable, easy, and minimally invasive, and it can be done as an office procedure in evaluating multilevel obstruction of the upper airway. It can provide dynamic information regarding morphology and physiology of upper airway obstruction in patient with OSAS. Retropalatal region was more affected compared with retroglossal region in either erect or supine position. However, when we compared retroglossal region in erect and in supine position, the latter has more contributing factors towards the obstruction severity.

Supervisor: Dr Baharudin Abdullah Co-supervisor: Dr Suzina Sheikh Abdul Hamid

A STUDY ON PATIENTS UNDERGOING CORONARY ANGIOGRAM IN HUSM CARDIOLOGY UNIT: RELATIONSHIP OF AN ANKLE BRACHIAL PRESSURE INDEX (ABI) WITH SEVERITY OF CORONARY ANGIOGRAPHY FINDINGS

Dr Khairul Azmi Ibrahim MMed (Internal Medicine)

Department of Medicine School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia Introduction: Several large population-based longitudinal studies had shown that a low ankle brachial pressure index (ABI) is an indicator of future cardiovascular events and mortality. Presently, there is only limited study done to investigate the relationship of ABI with the severity of coronary heart disease (CHD) based on coronary angiogram in our local population.

Objectives: The objective of this study was to determine the association between low ABI (defined as ABI < 0.9) with presence of angiographically documented CHD in patients who underwent coronary angiogram in Hospital Universiti Sains Malaysia, Kelantan. This study would also compare the mean difference of ABI for different severity of coronary angiographic findings and correlate the ABI values obtained in the study. We also aimed to determine the usefulness of low ABI in predicting angiographically documented CHD in local population.

Methods: In this study, 120 patients who were referred for coronary angiogram for first time were examined. Their ABI was obtained before they underwent coronary angiogram. Association of low ABI with angiographically proven CHD was examined using chi-square and Fischer exact tests. The difference in mean ABI values between different groups of CHD severity was analysed using ANOVA, and the correlation between ABI values and the severity of angiographic findings was examined. The sensitivity, specificity, and predictive value of low ABI for angiographically documented CHD were also calculated.

Results: The mean age of the subjects was 55.8 years (SD 9.7). Of the 120 subjects recruited, 43 (35.8%) had no significant coronary obstruction, 20 (16.7%) had 1-vessel disease, 27 (22.5%) had 2-vessel disease, 27 (22.5%) had 3-vessel disease, and 3 (2.5%) had left main stem disease. Low ABI was observed in 7 (16%) of the subjects with no significant coronary obstruction and 21 (27%) of the subjects with no significant coronary obstruction. There was no significant association between low ABI and the presence of angiographically documented CHD (P = 0.187). However, mean ABI value in subjects with 2-vessel disease (0.857, SD 0.193) and 3-vessel/LMS disease (0.849, SD 0.203) were significantly lower compared with subjects with no significant obstruction (1.059, SD 0.122), with P < 0.001each, and compared with subjects with 1-vessel disease (1.021, SD 0.171), with P = 0.017 and 0.008, respectively. There was a significant but weak inverse correlation between the ABI values and the severity of coronary angiographic findings (P < 0.001, Pearson's correlation coefficient = -0.48). The low ABI was not sensitive (27%) but have high specificity (84%) for angiographically proven CHD. The positive predictive value of low ABI was 75% and the negative predictive value was 39% for angiographically proven CHD.

Conclusion: Low ABI was not associated with the presence of angiographically documented CHD in our study population. However, mean ABI values for patients with multivessel/LMS disease were significantly lower compared

with patients with no significant obstruction or single vessel disease, and were below the normal range. The ABI examination may be used as an adjunct tool to predict the severity of CHD. Low ABI was not sensitive, but specific for angiographically documented CHD.

Supervisor: Dr Mohd Sapawi Mohamad

SINGLE-PEDICLE SUPERFICIAL INFERIOR EPIGASTRIC ARTERY FLAP VERSUS BIPEDICLE SUPERFICIAL INFERIOR EPIGASTRIC ARTERY AND SUPER EXTERNAL PUDENDAL ARTERY FLAP: THE FLAP PERFUSION AND VIABILITY STUDY IN THE RABBIT MODEL

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Introduction: Among the abdominal flaps, the superficial inferior epigastric artery (SIEA) flap is recognised as the least invasive technique with minimal donor site morbidity. The SIEA flap is usually raised as hemi-abdominal flap. The perfusion and viability of the SIEA flap extending above the umbilicus require further exploration with the rabbit paramedian SIEA flap model.

Objectives: The present study was undertaken to determine the vascular anatomy of the rabbit ventral abdomen, to develop a rabbit SIEA flap model, and to compare the flap perfusion and viability between the single and bipedicle flaps. The vascular anatomy was dissected for direct observation and documentation.

Methods: Twelve bilateral 12 \times 5 cm symmetrical paramedian flaps were raised on the ventral abdomen of 6 male New Zealand white rabbits. The right flaps were based on single pedicle of SIEA whereas the left flaps were based on bipedicle of SIEA and superficial external pudendal artery (SEPA). The perfusion of flaps was objectively determined with laser Doppler flowmetry (LDF), and the flap viability was assessed with two-dimensional planimetry over 14-day duration post-operatively.

Results: The SIEA was the dominant vascular supply of the rabbit ventral abdomen. It was joined by the SEPA just proximal to the inguinal fat pad. There was no significant size muscular perforating vessel from the rectus abdominis or lateral abdominal muscles for establishing a perforator flap model. The LDF of the bipedicle SIEA/SEPA flap were marginally superior to single pedicle SIEA flap in overall mean (67.8 perfusion units, SD 10.3, versus 59.2 perfusion units, SD 10.3) and over time from post-operative day 1 to day 14, but the differences were not statistically significant (P > 0.05). The overall mean LDF reading at the centre of flap was higher

than at the distal flap (66.3 perfusion units, SD 7.4, versus 60.7 perfusion units, SD 7.4), but the difference was not statistically different (P = 0.561). The mean flap viability of the bipedicle SIEA or SEPA flap was better than the single pedicle SIEA flap (99.6, SD 6.6%, versus 90.6, SD 6.6%), but the finding was not statistically significant (P = 0.361). The LDF measurements on post-operative day 1 and 3 moderately correlated with the outcome of flap viability on day 7 and 14 (P < 0.05).

Conclusion: The paramedian rabbit SIEA flap model can be an analogue of the human SIEA hemi-abdominal flap that extends above the umbilicus. The single pedicle SIEA could achieve satisfactory perfusion and viability for both the ipsilateral vascular territories of the SIEA and lateral thoracic artery. There was no significant difference of flap perfusion and viability between single and bipedicle SIEA flaps.

Supervisor: Professor Dr Ahmad Sukari Halim Co-supervisor: Dr Rumaizid Shaari

IN VIVO EVALUATION OF THE ANGIOGENIC AND ANTIMICROBIAL PROPERTIES OF TUALANG HONEY USING A FULL-THICKNESS BURN WOUNDS IN ANIMAL MODEL IN COMPARISON TO HYDROFIBRE

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Introduction: Tangential excision and skin grafting are inevitable in managing full-thickness burns. Wound bed preparations prior to surgery are necessary in order to prevent wound infection and promote wound healing. Honey can be used to treat burn wounds. However, not all types of honey have the same properties.

Objectives: The study was conducted to evaluate the effect on the wound contraction, the antimicrobial properties, and the histopathological aspects of the Tualang honey in full-thickness burn wounds in a rat model, in comparison with Aquacel dressings.

Methods: Thirty-six female Sprague Dawley rats were randomly divided into 3 groups. Under anaesthesia, 3 full-thickness burn wounds were created on the dorsum of the rats. The full-thickness burn wounds were inoculated with a specific organism (10^4), namely *Pseudomonas aeruginosa* (n=12), *Klebsiella pneumoniae* (n=12), or *Acinetobacter baumannii* (n=12). The 3 burn wounds were dressed with Tualang honey, plain Aquacel, or Aquacel Ag. Swab samples were obtained every 3 days (day 3, 6, 9, 12, 15, 18, and 21) for microbiological analyses. Clinical assessments were performed. At day 7, 14, and 21 days of burn, tissue samples were sectioned and histopathological examination was performed.

Results: There was a rapid 32.26% reduction in wound size by day 6 (P = 0.008) in the Tualang honey-treated wounds, and 49.27% by day 15 (P = 0.005). The wounds were smaller by day 18 (P < 0.032). Tualang honey-treated rats demonstrated a reduction in bacterial growth in P. aeruginosa-inoculated inoculated wounds (P = 0.005). However, Aquacel Ag-treated and plain Aquacel-treated wounds are superior to honeytreated wounds in A. baumannii inoculation (P = 0.035). Neutrophil count was reduced in honey-treated wound on day 7 in both A. baumannii- and K. pneumoniae-inoculated wounds (P < 0.05) and, similarly, on day 14 in P. aeruginosainoculated wounds (P = 0.003). Granulation thickness on day 14 of honey treated wound was 50.42 µm compared with Aquacel-treated wound, 24.87 µm, in P. aeruginosa group (P = 0.045). On day 21, in K. pneumoniae group, there was complete epidermis coverage of the wound (P = 0.002) and increased thickness of granulation tissue (P = 0.001) in honey-treated group. In histological analysis of new capillary formation, there was no statistical significance between all dressings.

Conclusion: This experiment shows the positive effect of Tualang honey as a topical dressing for full-thickness burn wounds in an animal model. Tualang honey has better results with regard to the eradication of *P. aeruginosa*. It also promotes burn wound healing process on wound inoculated with *P. aeruginosa* or *K. pneumoniae*.

Supervisor: Professor Dr Ahmad Sukari Halim Co-supervisors: Dr Kirnpal Kaur B Singh Dr Md Salzihan Salleh

THE COMPARISON OF EFFECTIVENESS BETWEEN
THE USE OF RINGER'S LACTATE AND NORMAL
SALINE FOR FLUID THERAPY IN HYPEREMESIS
GRAVIDARUM IN HOSPITAL UNIVERSITI SAINS
MALAYSIA

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Introduction: The aims of treatment of hyperemesis gravidarum are to stop vomiting and correction of dehydration, starvation, as well as electrolytes imbalance. Various kinds of fluid have been suggested as fluid therapy, but none was proven superior to the others. Being isotonic, both normal saline and Ringer's Lactate have long been used to correct dehydration state in patients with hyperemesis gravidarum. However, there was a fear that the lactate component in Ringer's lactate solution may delay the clearance of urine ketones as well as worsen the starvation state of the patients. This study was

performed to evaluate the effectiveness of Ringer's lactate and normal saline as fluid therapy in hyperemesis gravidarum.

Objectives: The study aimed to compare the effectiveness of Ringer's lactate and normal saline to correct dehydration and starvation state in hyperemesis gravidarum, by comparing the amount of fluid required to correct dehydration, clear urine ketones, and correct the electrolytes imbalance, as well as the duration taken for urine ketone clearance, level of serum lactate, and duration of hospital stay.

Methods: This is a single-blinded prospective controlled trial conducted in HUSM over 6 months. Patients who fulfilled the inclusion and exclusion criteria were randomised to receive 6 pints per day of either Ringer's lactate or normal saline infusion for their treatment. Laboratory investigations such as haematocrit level, blood urea, serum electrolytes, serum lactate, urine specific gravity, and urine ketones were done on admission and repeated every 12 hours until all values become normal in order to assess their response to each treatment. The data was collected and analysed using SPSS version 12.0.

Results: In total, 100 patients were recruited; 50 patients received Ringer's lactate and 50 patients received normal saline. The mean maternal age was 25.29 years (SD 5.34). The mean gravidity was 2.02 (SD 1.39), mean gestational age was 10.64 weeks (SD 3.67), and mean body mass index was 25.75 kg/m^2 (SD 2.08). The mean duration for urine ketone clearance were 46.56 hours (SD 10.18) for normal saline group and 46.56 hours (SD 11.01) for Ringer's lactate group (P = 1.00). Most patients required a total of 12 pints to clear urine ketone. All patients had normal value of serum lactate on admission. Patients who received Ringer's lactate did not show any rise in lactate level (P = 0.28). The mean amount of fluid received to correct dehydration was 11.73 pints (SD 2.83). Most patients needed 48 hours for their haematocrit level to be corrected. Statistically, there was no difference for normal saline group and Ringer's lactate group in the correction of haematocrit level (P = 0.21). Most patients had their urine specific gravity normalised at 48 hours. There was no significant difference between normal saline group and Ringer's lactate group for the normalisation of urine specific gravity. The mean amount of fluid required for potassium ion correction were 8.88 pints (SD 2.63) for normal saline group and 8.34 pints (SD 2.44) for Ringer's lactate group (P = 0.29). The mean duration of hospital stay for normal saline group was 2.12 days (SD 0.66), and for Ringer's Lactate group, 2.20 days (SD 0.42); the difference was also not statistically significant (P = 0.48).

Conclusion: Ringer's lactate was noted to be as effective as normal saline in correcting dehydration and starvation state in patients with hyperemesis gravidarum. The lactate component in Ringer's lactate did not delay the urine ketone clearance or worsen the starvation state of the patients.

Supervisor: Dr Adibah Ibrahim

THE VISUAL INSPECTION AND MICROBIOLOGICAL ASSESSMENT OF THE ENVIRONMENTAL SAMPLES FROM RESTAURANTS REGISTERED UNDER THE DISTRICT HEALTH OFFICE, KOTA BHARU

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Introduction: Lack of proper hygiene practice in restaurants can lead to a high prevalence of food-borne diseases. Food safety control and monitoring activities for restaurants include routine visual inspection and microbiological sampling. A simple method of assessment such as visual inspection helps in early implementation of corrective action, but its relationship with microbiological assessment has not been not widely studied.

Objective: The objective of this study was to determine the relationship between routine visual inspection results and microbiological studies of environmental samples from selected restaurants registered under the District Health Office, Kota Bharu.

Methods: This was a cross-sectional study of 285 randomly selected restaurants from the registry in District Health Office, Kota Bharu. The parameters from the Food Premise Evaluation form, KMM3P1, produced by the Ministry of Health, were selected for the restaurants' inspection, and 3M Quick Swabs were used for environmental swab samplings. The swabs were analysed at Food Safety and Quality Laboratory in Peringat, Kota Bharu, for total plate coliform and *E. coli* counts.

Results: The mean visual inspection scores of food handlers and the food storage/preparation area were significantly lower compared with the mean score of the equipment/utensils (P < 0.001). The mean total plate counts was significantly higher (P = 0.03) in swab of refrigerators compared with swab of plates. The mean coliform counts was significantly higher (P = 0.001) in swabs of plates compared to swab refrigerators. Wearing improper shoes (OR 2.21, 95% CI 1.06–4.63, P = 0.035) and violation of $E.\ coli$ counts for food handlers' hands (OR 2.07, 95% CI 1.00-4.27, P = 0.049) were significantly associated with violation in total plate count for refrigerators. Wearing improper shoes (OR 4.19, 95% CI 1.43-12.28, P = 0.009) was significantly associated with violation in coliform count for refrigerators. Unsuitable area of food preparation (OR 3.31, 95% CI 1.29-8.44, P = 0.012), wearing improper shoes (OR 9.55, 95% CI 1.21-75.55, P = 0.033), and using water from other source than Air Kelantan Sendirian Berhad (OR 2.96, 95% CI 1.04-8.43, P = 0.042) were significantly associated with violation in E. coli counts for refrigerators. Violation of E. coli counts for food handlers' hands (OR 2.35, 95% CI 1.10-5.06, P = 0.028) was significantly associated with violation in total plate counts for eating plates. Improper food holding method (OR 3.62, 95%CI, 1.26–10.39, P = 0.017) and violation of $E.\ coli$ counts for food handlers' hands (OR 3.75, 95% CI 1.36, 10.36, P = 0.011) were significantly associated with violation in $E.\ coli$ counts for eating plates.

Conclusion: The violations of microbiological counts in refrigerators were associated with the following factors: food handlers, food storage and preparation areas, source of water, and violation of *E. coli* counts for food handlers' hands. The violations of microbiological counts on eating plates were associated with food holding methods and violation of *E. coli* counts for food handlers' hands.

Supervisor: Dr Zaliha Ismail Co-supervisor: Dr Nor Azwany Yaacob

AUGMENTATION INDEX IN SPONTANEOUS INTRACEREBRAL HAEMORRHAGE AND ITS RELATIONSHIP WITH OUTCOME

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Introduction: Intracerebral haemorrhage was the most disabling and least treatable form of stroke. The risk factors for intracerebral haemorrhage were old age, hypertension, diabetes mellitus, hypercholesterolaemia, smoking, and high alcohol intake, which were also associated with arterial stiffness. Augmentation index was one of the surrogate markers for arterial stiffness.

Objective: The aim of the study was to determine the association between high augmentation index and 3-month outcome and mortality in intracerebral haemorrhage.

Methods: Patients with spontaneous supratentorial intracerebral haemorrhage admitted to the Hospital Universiti Sains Malaysia from May 2006 until May 2008 were recruited in the study. All patients were followed-up for 3 months. The following data were collected for all patients in a computerised database: demographic parameters (age and sex), clinical parameters (modifiable risk factors for intracerebral haemorrhage, admission Glasgow Coma Scale score, height, weigh, body mass index, systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, bilateral internal carotid blood flow, and augmentation index), laboratory parameters (total white cell count, haemoglobin level, platelet count, random blood sugar, serum sodium, potassium, urea, creatinine, international normalised ratio, activated partial thromboplastin time, serum total cholesterol, low density lipoprotein, high density lipoprotein, and triglyceride), radiological parameters (chest X-ray findings and brain CT scan findings), in-hospital treatment (conservative or surgical treatment), type of surgical treatment (craniotomy or external ventricular drainage), 3-month outcome (Modified Rankin Scale score) and mortality. All data were entered into SPSS version 12 and logistic regression analysis was carried out among significant variables to identify independent predictors of 3-month poor outcome and mortality.

Result: This prospective study involved 60 patients with spontaneous intracerebral haemorrhage. Out of the total, 24 patients (40%) had 3-month good outcome (Modified Rankin Scale 0-4), and 36 patients (60%) had poor outcome (Modified Rankin Scale 5-6). Out of the 36 poor outcome patients, 12 (33.3%) had high augmentation index. At 3-month follow-up, 38 patients (63%) survived, and 22 patients (37%) passed away in 3-month post-ictus; 10 (45.5%) of these 22 patients had high augmentation index. Independent predictors of 3-month poor outcome were Glasgow Coma Scale score (OR = 0.7, 95% CI 0.450 to 0.971, P = 0.035), total white cell count (OR = 1.2, 95% CI 1.028 to 1.453, P = 0.023), and haematoma volume (OR = 1.1, 95% CI 1.024 to 1.204, P = 0.011). The significant predictors for 3-month intracerebral haemorrhage mortality were high augmentation index (OR = 8.6, 95% CI 1.794 to 40.940, P = 0.007), and midline shift (OR = 7.5, 95% CI 1.809 to 31.004, P = 0.005).

Conclusion: Glasgow Coma Scale score, total white cell count, and haematoma volume were the most important predictors for 3-month outcome. The significant predictors for 3-month intracerebral haemorrhage mortality in this study were high augmentation index and midline shift.

Supervisor: Professor Dr Jafri Malin Abdullah '

SEVERE TRAUMATIC BRAIN INJURY: OUTCOME IN PATIENTS WITH DIFFUSE AXONAL INJURY MANAGED CONSERVATIVELY IN HOSPITAL SULTANAH AMINAH, JOHOR BAHRU—AN OBSERVATIONAL STUDY

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Introduction: Severe traumatic brain injury has been one of the major causes of death in Malaysia. There has been limited numbers of intensive care facilities to cater for the escalating numbers of severe traumatic brain injury patients. Due to certain limitations, not all patients in this group had been managed strictly according to the recommendation of the Brain Trauma Foundation, especially those who did not warrant any neurosurgical intervention such as a craniotomy.

Objective: The study aimed to compare the outcome of the severe traumatic brain injury with diffuse brain injury and without surgical lesion treated with different treatment

modalities, namely ICP-CPP targeted, ventilation, and intubation groups. We also aimed to assess the usefulness of routine serial head computed tomography (CT) scan in severe traumatic brain injury without surgical lesion, and to determine the hazards risk of severe traumatic brain injury patients with diffuse brain injury without surgical lesion.

Methods: This was a prospective observational study involving severe traumatic brain injury patients admitted with diffuse brain injury without surgical lesion, as defined by Marshall Classification of Diffuse Brain Injury, to the Neurosurgical Intensive Care Unit, Hospital Sultanah Aminah, Johor Bahru. The study was conducted between 1 December 2006 and 31 May 2008, with a total of 72 patients recruited from 1 December 2006 until 30 November 2007. The followup was done at the 3rd and 6th month after the date of discharge of the recruited patients. All recruited patients, both sexes included, were with severe traumatic brain injury and admission Glasgow Scale of 8 or less, had sustained blunt head injury without surgical or mass lesion, and were admitted via direct admission or transferred from another hospital within 24 hours post-trauma. Surgical or mass lesion was defined as any mixed-density lesion of more than 25 cc, as defined by Marshall CT Classification. The following patients were excluded from the study: patients with polytrauma that caused unstable haemodynamic status requiring immediate non-head surgical intervention and post-operative ventilation support, those with severe underlying medical disorders (such as major organ failure and endocrinological or haematological disorders), those suspected of drug or alcohol intoxication, those who were mentally subnormal, those with history of chronic epilepsy before the event of head trauma, those who arrived with unilateral or bilateral fixed and dilated pupils believed to be due to on-going herniation, those clinically showing absence of brain stem reflexes, those with no improvement after resuscitation or failed resuscitation upon admission, those with a known history of hemiparesis, and those with any condition that lowered their functional status score. Data were analysed using SPSS version 12.0.1. Means and standard deviations were calculated for continuous variables, and frequency and percentages for categorical variables. Pearson's chi-square test was used for categorical data between 2 groups (good and poor outcomes); however, if the expected frequency of less than five were more than 20% of the cells, Fisher's exact test was applied. Chi-square was applied to assess association between binary dependent variables and 3 treatment variables. One-way ANOVA was applied for numerical variables of 3 treatment variables after normality checking when the assumptions were met. Median and interquartile rage were calculated for numerical variable if it was not normally distributed and Kruskal-Wallis Test was applied. Multiple Mann-Whitney tests were performed and interpreted if the P value was significant, set at less than 0.05. The prognostic factors of diffuse brain injury without surgical lesion among severe traumatic brain injury patients were determined using Cox Proportional Hazards Regression Model. For Multiple Cox Proportional Hazards Regression

Model, forward stepwise was applied. Log-minus-log plot, hazards function plot, and partial residuals were applied to check the model assumption.

Results: Twenty-two patients with severe traumatic brain injury without surgical lesion treated were studied. The age of patients ranged 8.0-64.8 years, with a median of 34.1 years, a mean of 34.2 years, and a standard deviation of 14.7 years. The majority of patients were males (61 patients, 84.7%), and the remaining were females (11 patients, 15.3%). From a total of 72 patients admitted for diffuse brain injuries without any surgical lesion, 41 (56.2%) were treated with intubation for airway protection and given oxygen via oxyvent device with continuous oxygen saturation monitoring. A total of 16 patients were treated with ventilation support ICP-CPP guided cerebral resuscitation. Eleven patients (15.3%) died during hospitalisation. Out of remaining 61 patients, only 49 patients (80.3%) were followed-up during the 3rd month (with 3 death), and 45 out of 58 patients (77.6%) were followedup during the 6th month (with no death). On the 3rd month follow-up, 7 (15.2%) were still severely disabled, 4 (8.7%) were moderately disabled, and 29 (63.0%) had good recovery. On the 6th month follow-up, only 1 patient remained severe disabled, while the rest of 44 patients (97.8%) improved, with either moderate or good recovery. Outcome was worse in the ICP-CPP targeted group with median (IQR) Glasgow Outcome Scale (GOS) of 2.00 (2) compared with intubation group (P = 0.001). This difference was also seen during 3rd month follow-up but it was between intubation group and ventilation group (P = 0.012) with lower median GOS in ventilation group. On 6th month follow-up, the intubation group has a better median GOS compared with ICP-CPP targeted group and ventilation group, with statistically significant P < 0.001and P = 0.004, respectively. Routine CT scans were done and our findings showed that 42 patients (80.8%) did not show any progression. None of patients whose repeat head CT showed progression without clinical deterioration was given any intervention. The analysis demonstrated that the following factors were significantly associated with outcome at 6th month follow-up: best motor response on admission (P = 0.012) and Glasgow Coma Score (GCS) on admission (P = 0.009). There was statistically significant increase in the hazards of dying in the ICP-CPP targeted management group compared with the intubation group (P = 0.008).

Conclusion: In diffuse brain injury without surgical or significant mass lesion, the severity of the brain injury may not be as bad as compared with those with associated surgical lesion such as intracerebral haemorrhage and acute subdural haemorrhage. This is concluded based on the finding of lower hospital mortality rate (15.3%) in this subgroup of patients with severe head injury compared with in most studies that included those with surgical lesion, where the mortality rate ranged 20.7%–37.8%. These findings may be influenced by a high number of patients with diffuse injury type I and II, who were not associated with increased intracranial pressure compared with in type III and IV injuries. In terms of recommendation for the management of brain injury without

surgical lesion, the devastating outcome of patients treated with the best-recommended plan shown in this study may alert us if we have done more than what is required. However, the poor outcome seen in this group of patients may resulted from the primary brain injury itself, as most of the patients were with more depressed level of consciousness on admission and more severe diffuse brain injury as seen in CT imaging. Based on study, to the author proposed a more conservative management, which may be suitable for a subgroup of patients with minimal CT findings of type I and II diffuse injury, better admission GCS ranging 6–8, and normal motor response to be treated with the best available facilities as recommended by the Brain Trauma Foundation.

Supervisor: Dr Mohammed Saffari Mohammed Haspani

DIEGO BLOOD GROUP (Dia ANTIGEN): ITS PREVALENCE AND ROLE AS A RISK FACTOR FOR NEONATAL JAUNDICE IN BABIES BORN IN HUSM

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Introduction: Neonatal jaundice is a major health problem in Malaysia; however, its pathogenesis and risk factors are not completely understood.

Objectives: The objectives of this study were to evaluate the importance of some potentially important risk factors of Diego blood group (Di^a) and the frequency of incompatibility for this blood group in a Malay population in Kelantan. The results were related to the clinical picture in the baby and to other risk factors for neonatal jaundice.

Methods: This cross-sectional study was performed in the labour room, operation theatre, neonatal intensive care unit, and the nursery of Hospital Universiti Sains Malaysia from February 2008 until August 2009. Two groups of babies were included in the study. The non-jaundiced group consisted of term Malay newborns delivered at the hospital and screened for risk factors of jaundice, including Diego blood group. They were reassessed at day 7 of life to ensure they did not develop jaundice, and data about breast feeding practice, weight loss, and their bowel habits were collected. The second group was the jaundiced group consisting of term Malay newborns admitted at the hospital within 7 days of life because of jaundice. They were also screened for risk of jaundice, including Diego blood group. The recorded risk factors were subjected to statistical analysis for comparison between the groups.

Results: The prevalence of Diego blood group was 3.5% in the term Malay newborns. Diego blood group incompatibility occurred more in the jaundice group than in the non-jaundice group; however, the difference was not

statistically significant. Out of the 8 babies in the jaundiced group with Diego blood group incompatibility, 4 had severe and early onset jaundice with a high reticulocyte count, suggesting that Diego incompatibility may play a role in the pathogenesis of the neonatal jaundice in these babies. A multivariate analysis of other risk factors for neonatal jaundice showed that the followings were significantly associated with neonatal jaundice: mode of delivery, breast feeding practice, bowel output, and haemoglobin level.

Conclusion: The prevalence of Diego blood group (Di^a) in a Malay population in Hospital Universiti Sains Malaysia was low (3.5%) compared with in other Asian populations. About half of the babies in the jaundiced group with Di^a incompatibility showed signs of haemolysis.

Supervisor: Dr Noraida Ramli

THE EFFECTS OF TUALANG HONEY ON POST-MENOPAUSAL WOMEN

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Introduction: Results of recent trial have shown some negative effects of hormone replacement therapy on postmenopausal women. Therefore, there has been a move towards using alternative medicine as a treatment for menopausal problems, and honey is one of the alternatives.

Objectives: The study aimed to investigate the effects of Tualang honey on the safety profiles, cardiovascular risk factors, changes in hormones, and bone density in postmenopausal women.

Methods: A randomised, controlled trial comparing the effects of Tualang honey 20 g/day for a 4-month intervention period among healthy post-menopausal Malay women aged 45–60 years old was conducted. The primary outcome measures were to evaluate changes from baseline on the safety profiles, cardiovascular risk factors, hormonal profiles, and bone loss in Tualang honey treatment as compared with hormone replacement therapy (HRT). Paired t test was used to analyse the difference between the outcome at baseline and 4 months of intervention in both groups. Analysis of covariance (ANCOVA) was performed to evaluate the difference between groups at the study end-point with baseline scores as co-variates.

Results: The subjects were divided into 2 groups: 40 and 39 women with no statistical difference in socio-demography, anthropometry, and duration of menopause were randomly assigned to Tualang honey and HRT groups, respectively. There was no difference in the bone densitometry at the end of the 4 month in both groups. There were also no significant

changes in safety parameters seen in the haematological profile, liver enzymes, and renal function in the 2 randomised groups. However, there was a significant increase in the total cholesterol, LDL-C, and FBS in the honey-treated group compared from baseline. There was improvement of FSH, LH, and oestradiol levels in the HRT group. There were 35.4% of participants who reported per vaginal bleeding; all of them were from the HRT group.

Conclusion: Daily intake of honey at 20 mg/day for 4 month was found to be safe to use and have the same effect on bone densitometry as compared to hormone replacement therapy. However, consumption of honey for 4 months was associated with an increase in the cholesterol and fasting blood sugar level.

Supervisor: Associate Professor Dr Nik Hazlina Nik Hussain Co-supervisor: Associate Professor Dr Saiful Bahari Ismail

A SURVEY OF MALAYSIAN EMERGENCY PERSONNEL ON FAMILY PRESENCE DURING RESUSCITATION

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Introduction: The practice of family presence (FP) during resuscitation is gaining a foothold in Western countries but still largely not encouraged by Asian healthcare personnel (HCP).

Objective: This study aims to provide a Malaysian data on HCPs opinions of FP.

Methods: A non-probability survey was conducted in emergency departments (ED) of 4 hospitals. A questionnaire was designed based on previous similar surveys conducted in Singapore. It was edited by 2 emergency physicians, and a pre-test was conducted in HUSM to validate the reliability of the questionnaire. All HCP in the 4 hospitals were included in this study, which was conducted from October until December 2009.

Results: A total of 273 responses were obtained, of which one-third were from doctors, and the rest, paramedics. The mean age was 32 years, and there were equal number of male and female participants. The HCP had worked an average of 7.5 years, with 5.1 years in the ED. It was found that 27% of doctors were more agreeable to FP compared with paramedics did (P = 0.001). However, 54% of doctors and 32.4% of paramedics agreed that relatives had a right for FP, and 57.6% of doctors, compares with 67.6% of paramedics, would like to be present during their own relative's resuscitation. Among the reasons for not allowing FP were that it would be a traumatic

experience to the family or a breach of the patient's privacy, or that it may result in medico-legal issues, interference to the resuscitation process, overcrowding, increase in HCP's stress, or prolonged resuscitation efforts. The identified advantages of FP were that it assures the family everything had been done, facilitates mourning, strengthens family bond, and allows the final rites to be performed. Logistic regression of variant showed that the odds of a doctor agreeing to FP was 2.86 that of a paramedic's (P = 0.002).

Conclusion: It was found that Malaysian emergency HCP generally do not agree to FP. Surveys of the public may help to assess their opinions and whether it contradicts the HCP's opinions.

Supervisor: Associate Professor Dr Rashidi Ahmad Co-supervisor: Dr Chew Keng Sheng

HEARING LOSS IN MALAYSIAN MILITARY PILOTS: A STUDY OF PREVALENCE AND RISK FACTORS

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Introduction: Military pilots are exposed to high-level aircraft noise, which is considered to be one of the factors of noise-induced hearing loss.

Objective: The study was conducted to determine the prevalence and risk factors of hearing loss among military pilots in Malaysia.

Methods: This was a descriptive cross-sectional study. The sources of population were from Malaysian military pilots. The data was collected as a sample of convenience during the pilot's annual medical check-up at Institute of Aviation Medicine, Kuala Lumpur, from January until June 2008. All consented pilots underwent an interview involving questionnaire completion, ear examination, and hearing assessment with pure tone audiometry (PTA) and distortion product otoacoustic emission (DPOAE).

Results: A total number of 127 military pilots were included in this study. All of them were male with age range of 22–48 years old; most of them were in the age group 30 to 39 years old. The majority of the pilots (89%) were from Royal Malaysia Air Force. The means of total hours and years of flight was 1599.94 hours and 10.16 years, respectively. In this study, the prevalence of hearing loss was 23.6%, with 25 dB as the cutting point of normal hearing. All pilots with hearing impairment had mild hearing loss only. The frequencies most affected in this study were 4 kHz and 6 kHz. The prevalence of hearing impairment was higher in older age group of pilots. Helicopter pilots had worse audiogram as compared to transport and fighter pilots, especially in high-frequency

sound. There was a significant association of hearing loss with age, smoking, total hours, and years of flight. There were significant associations between DPOAE and hearing status, as well as failed DPOAE and sensorineural hearing loss, at frequency of 4 kHz and 6 kHz (*P* < 0.05).

Conclusion: Results from this study showed that military pilots were exposed to the risk of acquiring noise-induced hearing loss. Additional measures and intervention from the Ministry of Defence and Royal Malaysian Air Force in the hearing conservation program is needed to minimise or prevent military pilot from developing noise-induced hearing loss.

Supervisor: Professor Dr Dinsuhaimi Sidek Co-supervisor: Dr Rosdan Salim

COMPARISON OF DIGITISED AND CONVENTIONAL MAMMOGRAM IN EVALUATION OF BREAST MASS AND CALCIFICATION

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Introduction: Conventional mammography, or screen-film mammography, has been the standard method for breast cancer screening and in making a clinical diagnosis. It is proven to have a high sensitivity and specificity for the detection of breast cancer. The specificity ranged from 90% to 98%, and the sensitivities ranged from 83% to 95%. Screenfilm mammography can be converted to a digital image, which is referred to as a digitised mammogram. In its digital format, the image can be manipulated in a variety of ways to improve the detection of any breast lesions. However, the primary restriction in digital images is its lower spatial resolution that might be an obstacle for the detection and characterisation of microcalcifications.

Objective: The study aimed to determine whether digitised mammogram is accurately diagnostic as the conventional mammography in detecting breast mass and calcification.

Methods: The study was carried out in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, for 3 years, from January 2004 until December 2006. A total of 178 samples were obtained, which included 65 samples without any breast mass or calcification, 44 samples with breast mass, 45 samples with breast calcification, and 24 samples with both breast mass and calcification. A single sample was considered as 1 breast with 2 mammography standard views. The original screen-film mammograms were digitised using Diagnostic PRO Advantage digitiser. Both conventional and digitised images were interpreted by 2 observes for the presence of any

breast mass and clarification. Two weeks elapsed between the review of 2 mammogram images to reduce the effect of learning and memory. A 5-scale Breast Imaging-Reporting and Data System category (BI-RADS 1-5) was used to categorise the finding. Agreements were analysed using Kappa analysis.

Results: Kappa agreement between conventional and digitised mammogram images in detecting breast mass was 0.869 for observer 1 and 0.855 for observer 2. However, Kappa agreement between conventional and digitised mammogram images in detecting breast calcification was 0.494 for observer 1 and 0.358 for observer 2. Kappa agreement between observers in detecting breast mass digitised mammogram was 0.673 compared with 0.706 on conventional mammogram. Agreement for BI-RADS categories in digitised mammogram was analyses using Roc curve. For observer 1, area under curve was 0.843; for observer 2, 0.697.

Conclusion: Digitised mammography images have a nearly perfect Kappa agreement in detecting breast mass. In detection of breast calcification, the Kappa agreement was low. The Kappa agreement between observers in detecting breast mass and calcification using digitised mammogram was lower compared with conventional mammogram. This was mainly due to small digitisation matrix that made visualisation of microcalcification impossible. However, this study did not reflect the accuracy of digitised mammogram in differentiating benign from malignant breast mass or calcification.

Supervisor: Dr Mohd Ezane Aziz Co-supervisor: Dr Nik Munirah Nik Mahdi

EXPLORATION OF REAL-TIME PCR AS A NEW DIAGNOSTIC METHOD OF FRAGILE X SYNDROME

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Introduction: Fragile X syndrome (FXS) is the most common form of inherited mental retardation in males caused by FMR1 gene abnormality that is associated with CGG repeats expansion and hypermethylation status of its promoter. Methylated alleles usually lead to transcriptional inhibition and, consequently, loss of fragile X mental retardation protein (FMRP) production. Chemical modification of cytosine to uracil by sodium bisulfite treatment has provided an additional method for the laboratory diagnosis of FXS, thus avoiding the use of the laborious Southern blot analysis, which is the gold standard test for FXS diagnosis.

Objective: The study was done to explore a rapid, easy, reliable, and inexpensive method for FXS diagnosis that can replace the laborious, time consuming, and expensive

Southern blot method.

Methods: Genomic DNA was extracted from peripheral blood of 45 clinically diagnosed FXS patients. Samples were treated with sodium bisulfite followed by amplification using real-time multiplex methylation specific PCR (RT-M-MSPCR) with XIST gene as an internal control, followed by melting curve analysis.

Results: Our results showed that all control samples with known methylation status were correctly diagnosed using RT-M-MSPCR. For method validation purpose, the methylation status of other 45 male patients sample were also successfully diagnosed using our RT-M-MSPCR method and were in concordance with the results of the Southern blot. Thirty-nine samples had unmethylated alleles, 4 samples had fully methylated alleles, and 2 samples have both methylated and unmethylated alleles, implying a diagnosis of mosaicism. The developed method was confirmed to be specific as the melting temperature of both methylated and unmethylated FMR1 promoter was found to be varied in only a small range of melting temperature differences of 84.91 °C (SD 0.41) and 90.57 °C (SD 0.34) for methylated and unmethylated promoters, respectively. The methylation percentage of the mosaic patients were successfully calculated, with a detection ability of as low as 5% methylation percentage. However, due to random inactivation, female methylation status cannot be identified, thus premutation and full mutation females cannot be differentiated from normal females. Having said that, male patients are more commonly diagnosed with FXS, thus this is not a major limitation for FXS screening.

Conclusion: Our results showed that RT-M-MSPCR is a reliable, inexpensive method that has 100% equal sensitivity as well as specificity compared to Southern blot. This newly developed method is also very convenient in screening large number of male FXS patients, as it is non-time consuming and easy to perform, especially when there is a low quantity of samples (final concentration of genomic DNA) that need to be sensitively and accurately determined.

Supervisor: Dr Zilfalil Alwi Co-supervisors: Dr Salmi Abdul Razak Professor Dr Ravindran Ankathil

EFFECTS OF *GARCINIA MANGOSTANA* LINN. ON WOUND HEALING IN EXPERIMENTAL WOUND MODELS IN RATS: A PRELIMINARY STUDY

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Introduction: Wound healing is a very complex interplay between the overlapping phases, involving many cell

types, mediators, and growth factors. The amount of knowledge and understanding concerning the wound healing process and dressing practices has expanded and changed overtime. Its management is often costly; therefore, researchers are exploring alternative solution from natural sources that are useful in wound healing. *Garcinia mangostana* Linn., or mangosteen, has never been scientifically studied for its wound healing potential. However, there are numerous *in vivo* and *in vitro* studies that pointed to the medicinal properties of *Garcinia mangostana* L.

Objectives: This study aimed to explore and relate the medicinal properties of *Garcinia mangostana* L. to wound healing in an animal wound model. The main objective of this study is to evaluate the effect of *Garcinia mangostana* L. on specific wound healing properties in rats, namely wound contraction, period of epithelisation, and breaking strength. A semi-quantitative histological examination was also performed.

Methods: The wound contraction and epithelisation were studied in an excision wound model, which comprised of 10 rats in the treatment group and 10 non-treated rats as the control group. The wound breaking strength was studied in the incision wound model, which comprised of 6 rats in each group. A semi-quantitative histological examination was then performed for both excision and incision wound models.

Results: This study demonstrated a significant increase in wound contraction at post-operative day 1 and day 5 in wounds treated with *Garcinia mangostana* L. extract (P < 0.001 and P < 0.005, respectively). It was also found that the wound breaking strength was significantly higher in the treatment group (P < 0.04). Unfortunately, semi-quantitative histological analysis did not show any significant difference in inflammation, angiogenesis, and fibroblast proliferation.

Conclusion: Garcinia mangostana L. showed evidence of wound healing promotion. However, the exact mechanism is still vague, requiring further in vitro and in vivo studies before a clinical study could be performed.

Supervisor: Dr Wan Azman Wan Sulaiman Co-supervisor: Dr Shah Jumaat Mohd Yusof Dr Venkatesh R Naik

ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN MALAYSIA MILITARY HOSPITAL

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Introduction: The anterior crucioate ligament (ACL) is probably the most commonly injured ligament of the

knee. Sports and army physical training in the Armed Forces account for a significant number of ACL injury and lost of duty time. Therefore, they give an impact on the military readiness. ACL tear frequently occurs; however, people are expecting early return to normal daily activity, especially the military training, duties, and sports. For the Malaysian Armed Forces, ACL reconstruction is only practiced in 94 Hospital Angkatan Tentera, Terandak, Melaka, and 96 Hospital Angkatan Tentera, Lumut, Perak, because of the availability of facilities. The injury is due to military training, sports activities, or accidents. This study observed the cause of the injury and the outcome of ACL reconstruction in terms of the improvement in the military health grading (PULHEEMS).

Objectives: The study aimed to analyse demographic data of military personnel who underwent ACL reconstruction surgery in military hospitals, as well as to determine the main cause of ACL injury, among military personnel, that needs reconstruction. Another objective in our study is to observe the early outcome post-surgery in terms of the improvement in the military health grading and presence of instability symptoms.

Methods: The study is a retrospective observational study that was conducted in 2 military hospitals in Malaysia. The study period was from 1 August 2006 until 31 July 2007. We selected military personnel who underwent ACL revision surgery and those who had the injury before joining the military service. When assessing the outcome of the study, those who had associated injuries such as multiple ligamentum injuries, meniscus injuries, control injuries, or fractures around the knee were excluded. We gathered the patients' information from their medical records, as well as demographic data, such as military health grading before and after the surgery. The causes of ACL injury, the operative finding, and the type of surgical procedures performed were recorded in the assessment form. The assessment for the post-operative military health grading (PULHEEMS) was done by the respective military surgeons after the patients had completed their post-operative rehabilitation. The patients were called and interviewed to assess the symptom of instability during walking, running, and jumping, according to the severity of the instability symptoms they experienced.

Results: There were 111 cases of ACL reconstruction included in the study. The mean age is 31.71 years, with the highest number of cases from the Junior/Other Rank group. Most patients were operated within 18 months after injury. The most common graft and type of reconstruction was patella tendon autograft (54%), followed by double bundle hamstring autograft (26%), and single bundle hamstring autograft (20%). The percentage of isolated ACL injury compare with associated ACL injury is 64% to 36%, respectively. Causes of ACL injury were sports in 81%, military training in 14%, and other causes in 5% of cases. The mean follow-up until the patients were discharge from hospital was 9.21 months. Following reconstruction and rehabilitation, 97.1% of these patients were upgraded back to military grade FE. Patients with patella tendon autograft had better stability compare with those with hamstring autograft (P = 0.01). However, there were no significant different (P = 0.18) in terms of symptoms of instability between patients with single bundle hamstring autograft and double bundle hamstring autograft.

Conclusion: The majority of patients who undergone ACL reconstruction were from Junior/Other Rank group. The main cause of injury was sport-related activity. The surgery and post-operative rehabilitation helped them return to their normal military health grading. The symptoms of post-operative instability were better in patients in bone patella tendon group. There was no difference between single and double bundle hamstring groups.

Supervisor: Dr Tengku Muzaffar Tengku Shihabudin

VALUE OF SHOCK INDEX IN RISK STRATIFICATION OF ILLNESS SEVERITY AMONG PATIENTS IN EMERGENCY DEPARTMENT

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Introduction: Risk stratification of patient is very important, starting at the time the patient arrive in the emergency department. Wide range of patient's presentation can sometimes appear normal; the patient's vital signs may be normal, but they actually deteriorate in time. We should not overlook this group of patients, as the mortality rate may increase.

Objectives: The study aimed to develop range of Shock Index value to risk-stratify patients into three groups: low risk, intermediate risk, and high risk.

Methods: This study was done in Hospital Universiti Sains Malaysia and Hospital Kuala Lumpur from June 2008 until November 2008. Patients older than 18 years who came to the emergency department of the 2 hospitals and met the inclusion and exclusion criteria were enrolled. The first vital signs of each patient were recorded by single reviewer, and the standard care of management was proceeded with. Afterwards, the patient's disposition was recorded by the same reviewer. Significant variables were initially identified; based on these variables, the range of Shock Index values were developed using receiver operating characteristic (ROC) curve. A minimum value was identified, while the maximum value of 0.9, which had been extensively validated, was applied.

Result: A total of 48 patients were enrolled in this study. The significant parameters were systolic blood pressure (P < 0.001), diastolic blood pressure (P = 0.006), heart rate (P < 0.001), and respiratory rate (P = 0.004). Heart rate was the variable with the most significant area under the curve in ROC curve were 0.844. From there, minimum value of Shock Index obtained was 0.74 (sensitivity 80%, specificity 74%)

Conclusion: The range of Shock Index values are less than 0.74 for low risk group, 0.75–0.9 for intermediate risk group, and more than 0.9 for high risk group.

Supervisor:

Dr Nik Hisamuddin Nik Abdul Rahman

A COMPARISON BETWEEN METOCLOPRAMIDE AND PROMETHAZINE PLUS PYRIDOXINE IN THE MANAGEMENT OF HYPEREMESIS GRAVIDARUM: A RANDOMISED CONTROLLED TRIAL

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Introduction: Hyperemesis gravidarum is a debilitating condition, involving the general health and psychological aspects of the patients as well as creating financial burden to the family. An effective treatment will be beneficial in reducing these stressful conditions. The mainstay treatment for hyperemesis gravidarum is to stop the bouts of vomiting, rehydration, and correcting the starvation state of the patients. A lot of antiemetics have been widely used as the first-line treatment. However, their efficacy has never been compared, thus the aim of this study.

Objective: This study was performed to compare the efficacy of metoclopramide with the combination of promethazine and pyridoxine as antiemetics in patients with hyperemesis gravidarum. The efficacy of either regime was measured by the mean pregnancy-unique quantification of emesis and nausea (PUQE) score achieved after treatment, the duration taken to clear the ketones in the urine, the duration of hospital stay, as well as the side effects encountered.

Methods: Patients admitted to Ward 1 Utara of Hospital Universiti Sains Malaysia with hyperemesis gravidarum were randomised to receive either metoclopramide 10 mg 3 times a day or combination of promethazine 25 mg 3 times a day with pyridoxine 20mg 3 times a day. The degree of vomiting was assessed by using the PUQE score at 12, 24, 36, 48, 60, and 72 hours after administration of each regime. Ketone in the urine was quantified daily. The duration of hospital stay as well as the side effects encountered were compared.

Results: A total of 60 patients were recruited with 30 patients in each regime. There was no difference in the PUQE score of patients receiving metoclopramide with those receiving combination of promethazine and pyridoxine after 72 hours of drug administration (5.4, SD 1.4, versus 5.3, SD 1.6, respectively; P > 0.05). The duration taken for urine ketone clearance also did not significantly differ (2.03 days, SD 0.61, for metoclopramide group versus 2.26 days, SD 0.63, for the combination group; P = 0.15). Both groups of patients have mean hospital stay of approximately 3 days. More than

half of the patients in the combination group were sedated after the drug administration.

Conclusion: Both regimes have similar efficacy as antiemetics in patients with hyperemesis gravidarum and may be used as the first-line antiemetics in such cases.

Supervisor: Associate Professor Dr Adibah Ibrahim

THE RISK FACTORS OF EXTERNAL VENTRICULAR DRAINAGE-RELATED INFECTION IN HOSPITAL KUALA LUMPUR

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Introduction: External ventricular drainage (EVD) has been widely used for the purpose of cerebrospinal fluid (CSF) diversion in the treatment of hydrocephalus caused by various aetiology in neurosurgical centres, including Hospital Kuala Lumpur. The usage of this system has widened to the extent of providing diagnostic and therapeutic tools in cases of intracranial pressure of head trauma patients or in cases of intraventricular administration of thrombolytic agent or antibiotic therapy in certain condition. However, the main limitation of this procedure is the risk of infection.

Objectives: The study aimed to determine the incidence and the risk factors associated with EVD-related infection.

Methods: This prospective observational study has been conducted in Hospital Kuala Lumpur from December 2006 until December 2008, involving patients who were subjected for EVD for various reasons. A total of 87 patients were sampled following strict inclusion and exclusion criteria. All patients were followed-up during the hospital stay and noted for presence of infection, and related data including the aetiology that required for the EVD insertion, the length of the EVD from the burr hole to the skin exit site, the duration of catheterisation, the venue of the procedure, the organism causing infection, as well as the basic biodata of the patients were recorded. EVD-related infection is defined as positive culture and Gram stain with the presence of other supportive finding including pleocytosis, a decrease in the CSF glucose level (less than 205 mmol/L), or an increase in the CSF protein level (more than 0.4 g/L). The time of infection is recorded as the time sample was obtained.

Result: EVD-related infection in Hospital Kuala Lumpur was 32.2% (95% CI 23.3–42.57). There is a slight female predominance in the cases of infected EVD, and the majority of the cases were aetiologically related, that is, hemorrhagic in nature (60.9%), but these findings were statistically not significant. This study clearly demonstrated

that tunnelling of the catheter for more than 5 cm, from under the scalp to the exit site of the skin, significantly carried a lower risk of infection (6.9%) than tunnelling of 5 cm or less (OR = 0.18, 95% CI 0.08–0.46, P < 0.001). The majority of the cases (19 out of 28) with EVD-related infection were among the samples with more than 10 days of catheterisation (OR = 0.33, 95% CI 0.17–0.65, P < 0.001). Gram-negative bacteria were the predominant organisms in EVD-related infections (53.6%). The location where the procedure was conducted, surgeon's status, and the aetiological disease required for the EVD insertion were not significantly related to the duration of catheterisation.

Conclusion: The role of ventriculostomy technique and management of the EVD system in neurosurgical unit for various pathological diseases in relation to the risk of infection have been studied. As a result, both tunnelling techniques in extended fashion of more than 5 cm and exchange of the catheter after period of 10 days should be implemented as a standard protocol in order to reduce the risk of EVD-related infection.

Supervisor: Dr Mohammed Saffari Mohammed Haspani

A PILOT RANDOMISED CLINICAL TRIAL COMPARING INTRAMUSCULAR PROCHLORPERAZINE WITH PROMETHAZINE FOR ACUTE VERTIGO IN EMERGENCY DEPARTMENT

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Introduction: Dizziness is the third most common presenting complaint in emergency department (ED). Vertigo represents a subset of dizziness and is defined as an illusion of movement, usually rotational, of patients or their surrounding. Patients with vertigo have imbalance which leads to loss of function, fall, and injuries. Thus evaluation and treatment of vertigo is paramount. The objective of this study is to compare the effectiveness of prochlorperazine and promethazine for acute vertigo in the ED.

Methods: The study was conducted from April 2008 until August 2009 in the ED, Hospital Universiti Sains Malaysia. Patients who fulfilled the inclusion criteria were selected for the study and were equally randomised into prochlorperazine or promethazine group based on the randomisation plan. They were given an anti-vertigo drug, prochlorperazine or promethazine, and vertigo score (using visual analogue score) and blood pressure while lying and standing were taken at baseline (0 hour), 1 hour, and 2 hours. The researcher completed the questionnaire before patients left the ED.

Results: A total of 32 patients were enrolled in this study: 78.5% (n = 25) were females and 21.9% (n = 7) were males. The mean age was 51.5 years old. The mean vertigo score while ambulating on arrival is 8.44 (SD 1.75) in prochlorperazine group and 8.81 (SD 1.78) in promethazine group. Mean vertigo score after 2 hours was 3.12 (SD 2.09) for prochlorperazine group and 4.94 (SD 2.43) for promethazine group. There was statistical significant reduction in VAS score for both prochlorperazine and promethazine groups (P < 0.05); however, there was no significant reduction with respect to comparison between the 2 groups (P > 0.05). Although more patients in prochlorperazine group were ready to go home after 2 hours of admission (75.0%, n = 12), the difference was not significant. Patients receiving prochlorperazine had relative risk of 1.80 (95% CI 0.97 to 3.35) times more likely to develop orthostatic hypotension than among those taking promethazine. However, the relative risk was not statistically significant.

Conclusion: Prochlorperazine and promethazine are equally effective as anti-vertigo drugs in treating acute vertigo in ED.

Supervisor:

Associate Professor Dr Nik Hisamuddin Nik Abdul Rahman Co-supervisor:

Associate Professor Dr Rosdan Salim

A SURVEY ON KNOWLEDGE, ATTITUDE,
AND CONFIDENCE LEVEL OF ADULT
CARDIOPULMONARY RESUSCITATION (CPR)
AMONG JUNIOR DOCTORS IN HOSPITAL
UNIVERSITI SAINS MALAYSIA (HUSM) AND
HOSPITAL RAJA PEREMPUAN ZAINAB II (HRPZII)

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Introduction: In hospitals, junior doctors are often the first to initiate resuscitation attempts. Therefore, it is important that they have adequate knowledge, positive attitude, and good confidence level in managing cardiac arrests according to the current guidelines for resuscitation. Previous studies have shown poor levels of resuscitation training and knowledge among junior doctors. In addition, their self-reported clinical skills in managing emergency situation are low, highly variable, and do not increase during their first year after graduation. However, it remains to be proven whether these results of researches, mainly from other countries, are applicable to our local population. There is currently a lack of CPR research, especially among junior doctors in Malaysia.

Objectives: The aims of this study were to determine the level of knowledge, attitude, and confidence of junior doctors in Hospital Universiti Sains Malaysia (HUSM) and Hospital Raja Perempuan Zainab II (HRPZII) and to describe the factors that influence these levels. This study was also aimed to serve as a starting point to create a database in which additional data can be deposited by other centres in the nation.

Methods: This is cross-sectional study using convenient sample. A questionnaire was design based on AHA Guidelines 2005 and review relevant literature. It was edited by 2 emergency physicians, and pre-test was conducted in HUSM to validate and test the reliability of the questionnaire. All junior doctors in HUSM and HRPZII were included in this study, which was conducted from October until December 2008. Questionnaires were circulated with the help of representatives from each hospital; the data collection was done anonymously, with no time limit. The questionnaires were then collected and coded according to the hospital and checked to confirm that the doctors had trained for 3 years and less. Statistical analysis was used using software SPSS version 12.0.1

Results: A total of 70 junior doctors were analysed. Average age was 26.9 years, and 68.6% had been in practice for less than 1 year. Out of the 70 doctors, 68.6% had received basic resuscitation training during internship; 33% had the training in the previous 1 year. Only 11.4% had advanced training in resuscitation, and 50% of doctors had attended cardiac arrest cases. However, 60% of the doctors never performed defibrillation. The mean knowledge score was 68%. The differences between subjects' variables and knowledge score were statistically not significant. The attitude score was 64.4%. The majority of the doctors disagree that their internship training was adequate (71.4%) and that agree all junior doctors should have advance cardiac life support (ACLS) training (94.3%). The confidence score was 28%. Most of the doctors were not confident to be a team leader (85.7%), to perform intubation (65.7%) or defibrillation (78.6%), to administer amiodarone (82.9%), and to insert central venous line (74.3%) during resuscitation. Factors that improved a doctor's confidence in resuscitation were ACLS training, work experience of more than 1 year, and completion of rotation in 6 departments.

Conclusion: The resuscitation knowledge was average, and most doctors have positive attitude on resuscitation. However, self-reported confidence was poor among junior doctors. We suggest mandatory attainment of basic life support training during undergraduate and ACLS during internship, increased exposure of real resuscitation situations to improve undergraduate training, and regular practical or skill course 6 monthly.

Supervisor: Dr Abu Yazid Md Noh Co-supervisor: Dr Chew Keng Sheng

EFFECTS OF SOY PROTEIN SUPPLEMENTATION ON HIGH INTENSITY CYCLING PERFORMANCE IN HOT AND HUMID ENVIRONMENT

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Objective: The purpose of the present study was to investigate the effect of soy protein isolate supplementation during high intensity cycling exercise on subsequent time trial performance in comparison with a placebo. The subjects were 13 male trained cyclists from Kelantan, Malaysia, with mean age, weight, height, and VO₂max of 15.9 years (SD 1.4), 55.3 kg (SD 8.0), 164.6 cm (SD 7.7), and 58.2 mL.kg⁻¹.min⁻¹ (SD 3.7), respectively. The study was designed as randomised, double blind, placebo-controlled crossover comprising of 60-minute exercise on a cycle ergometer at 60% VO₂max, followed by a 15-minute time trial. Subjects ingested soy protein or placebo before and every 20 minutes during steady state cycling at 60% VO₂max in hot (31.1 °C, SD 0.2) and humid (69.7%, SD 2.3) environment.

Result: The work output during the 15-minute time trial for soy protein and placebo supplementations were 172.7 kJ (SD 26.1) and 169.01 kJ (SD 19.0), respectively. A paired t distribution test revealed that soy protein supplementation did not improve the time trial performance in the heat, evaluated based on the total work output. Two-way repeated measure ANOVA (meal × time) followed by a simple effect analysis revealed that soy protein supplementation (meal) had no effect on any of the hormonal and metabolic variables (plasma insulin, plasma glucose, plasma free fatty acid, plasma lactate, and plasma ammonia) during exercise in the heat, as compared to the placebo. Plasma insulin was significantly lower than the resting value during soy treatment at 45 and 60 minutes (P < 0.05), and it also decreased significantly at 60 minutes in the placebo group (P < 0.05). Plasma glucose was elevated in soy supplementation (P < 0.05) after 15-minute time trial. Plasma free fatty acid increased significantly after 15 minutes of state cycling for both soy and placebo supplementations. Plasma lactate and ammonia significantly increased after 15-minute time trial for soy and placebo treatments (P < 0.05) because of the high intensity exercise.

Conclusion: From the present study, it was concluded that soy protein isolate supplementation during steady state exercise at 60% VO₂max did not improve the work output in a 15-minute time trial cycling performance in the heat.

Supervisor: Associate Professor Dr Ashok Kumar Ghosh Co-supervisor: Dr Amit Bandyopadhyay A COMPARATIVE STUDY OF THE EFFECTS OF TUALANG HONEY ON HEALING OF TRAUMATIC FINGER TIP INJURY IN COMPARISON WITH PARAFFIN GAUZE DRESSING: A PILOT STUDY

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Introduction: Fingertip injuries are commonly seen in emergency departments. Regular paraffin gauze dressing (PGD) is a common mode of treatment for this type of injury. However, it is associated with long period of healing process, pain during frequent change of dressing, and hypersensitivity of the healed fingertip.

Objective: This study was conducted to determine the potential of tualang honey dressing (THD) in producing better outcome compared with PGD in treating fingertip injuries.

Patients & Methods: Twenty-two patients with fingertip injuries were recruited and randomised into PGD and THD groups. The fingertip wounds were debrided under local anaesthesia and dressed with the respective method. Dressings were changed every other day in the first week and, subsequently, weekly until the wound healed. The severity of pain during change of dressing and the duration for the wound to heal were noted. After at least 3 months post-injury, the healed fingertip was assessed for two-point discrimination, hypersensitivity, cutaneous sensibility, and sensation to temperature.

Results: The average duration for the fingertip to heal was 3.3 weeks and 3.4 weeks for THD and PGD groups, respectively. The average severity of pain during change of dressing using the visual analogue score was 4.1 and 3.8 in THD and PGD groups, respectively. The two-point discrimination test was normal in all fingers. Cutaneous sensibility using Semmes-Weinstein monofilament test showed normal sensibility in 2 PGD patients, diminished light touch in 13 patients (10 in THD group, 3 in PGD group), and diminished protective sensation in 7 patients (2 in THD group, 5 in PGD group). Hypersensitivity was found to be absent in 6 patients (3 in THD group, 3 in PGD group), mild in 15 patients (9 in THD group, 6 in PGD group), and severe in 1 patient from PGD group. Sensation to temperature was intact in 18 patients (10 of THD group, 8 of PFD group), impaired in 3 patients (1 of THD group, 2 of PFD group), and absent in 1 patient from THD group. There was no significant difference between THD and PGD group in terms of duration of wound healing (P = 0.546), pain during change of dressing (P = 0.712), hypersensitivity (P = 0.074), two-point discrimination, cutaneous sensibility (P = 0.455), and sensation to temperature.

Conclusion: This study showed that THD is comparatively as effective as PGD in treating fingertip injuries.

Supervisor: Associate Professor Dr Mohd Iskandar Mohd Amin Co-supervisor: Dr Mohammad Paiman

PROVISION OF FIRST AID REQUIREMENTS IN SECONDARY SCHOOLS, KAP, AND RISK PERCEPTION TOWARDS SAFETY AND HEALTH AMONG SCHOOL HEALTH TEACHERS IN KOTA BHARU, KELANTAN

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Introduction: First aid requirements in the workplace include the provision of first aid facilities, services, and personnel required for early treatment.

Objectives: The aim of this study was to determine the current first aid requirements and the level of knowledge, attitude, and practice (KAP), as well as the risk perception towards safety and health among secondary school health teachers in Kota Bharu, Kelantan.

Methods: A cross-sectional study was conducted to collect information regarding occupational safety and health (OSH) status and KAP of first aid requirements, as well as risk perception towards safety and health in schools. A community intervention study was done involving two groups: intervention and control. All 38 secondary schools and 105 school health teachers in Kota Bharu consented to participate in this study. Checklist of OSH status consists of school background, first aid box, first aid room, first aid services, and first aider. School health teachers were asked using self-administered questionnaire consisting of knowledge about first aid services, knowledge about first aider, attitude and practice pertaining to first aid requirement, as well as risk perception towards safety and health at school, outside school, and magnitude and severity of risk at school.

Results: The majority of schools were daily schools (63.2%), with mean (SD) of age of school of 33.8 (20.0). The median (interquartile range) number of school health teachers in every school were 2.5 (4.0), and 60.5% of the schools do not have first aider. The majority of the schools have safety and health organisation (92.1%). Checklist scores for first aid box in terms of location was 41.3%; identification, 92.0%; contents, 30.2%; relevant information, 11.8%; training, 11.0%; and person in-charge, 57.0%. Thirty-six secondary schools (94.7%) have first aid rooms. Approximately 18.4% of secondary schools have mechanism for the management of injury or disease, and 68.4% had documentation on injury or disease. In addition, 36.8% of schools had trained their first aiders, and 71.4% of the courses were certified. Majority of the respondents were Malays (90%), and females (70%). The mean

(SD) of respondents' age was 41.7 years (7.05) and working experience was 16.24 years (7.12). Mean (SD) scores on knowledge about first aid services was 21.67 (2.87), knowledge about first aider, 31.69 (3.28), and attitude, 11.83 (3.16), which were relatively satisfactory, but poor in median (IQR) practice, 2.00 (3.00). The highest risk areas identified in risk perception at school were injury consequence of fire (58.1%), explosion (53.3%), and fall of objects (48.6%). The highest influence to the magnitude and severity of risk at schools was giving a bad consequence to future community (56.2%), followed by news published by newspapers and mass media (51.4%). After the intervention program were conducted, there were significant higher mean scores in both knowledge about first aid services (P < 0.001) and knowledge about first aider (P < 0.001).

Conclusion: The status of OSH in secondary schools Kota Bharu, Kelantan, pertaining to provision of first aid requirements was unsatisfactory. The proposed method of teaching of first aid requirements has been developed to train the teachers. Sustainability of intervention activities can be achieved if the recurrent intervention program is considered and implemented in the school health-planning programme.

Supervisor:

Associate Professor Tengku Mohammad Ariff Raja Hussin Co-supervisor: Dr Sarimah Abdullah

ACUTE POST-OPERATIVE ANALGAESIA AFTER CRANIOTOMY: THE ANALGAESIC AND OPIOD SPARING EFFECTS OF INTRAVENOUS PARECOXIB

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Introduction: Acute post-craniotomy pain was previously reported to be between moderate to severe. Parecoxib is the only available intravenous COX II inhibitor that has great potential to treat acute post-craniotomy pain. Its prescription can avoid the side effects of opiod as well as avoid potential conventional non-steroidal anti-inflammatory drugs side effect of post-operative haematoma.

Objective: The main aim of this study was to determine analgaesic efficacy and opiod-sparing effect of Parecoxib for acute pain post-craniotomy.

Methods: This was a prospective, double-blinded, randomised controlled trial involving 60 post-elective craniotomy patients. Patients were divided into 2 groups in which 1 group received parecoxib and patient-controlled analgaesia (PCA) morphine (n=30) and the other group received PCA morphine (n=30). In the first group, intravenous parecoxib 40 mg was given 2 hours prior to extubation, and another dose was given after 12 hours. The other group was given intravenous normal saline at same

intervals. PCA morphine was prepared as rescue analgaesia. Their pain intensity was assessed by visual analogue scale (VAS) at specific interval post-operatively for 24 hours. Total morphine consumption over 24 hours, opiod side effects, and post-operative haematoma were also recorded.

Results: There was significant different between the parecoxib and morphine groups in VAS at 2, 4, 16, and 24 hours post-extubation. Mean VAS at 2 hours was 2.2 (SD 0.85) in the parecoxib group and 5.0 (SD 0.94) in the morphine group (P < 0.001). At 4 hours, mean VAS was 2.0 (SD 0.66) for the parecoxib group and 3.3 (SD 1.2) for the morphine group (P < 0.001). VAS at 8 and 12 hours were not significantly different (P > 0.05). At 16 hours, the mean VAS for the parecoxib group was 1.1 (SD 0.30) and 1.4 (SD 0.49) for the morphine group (P < 0.05). The mean VAS at 24 hours was 1.0 (SD 0.32) in the parecoxib group and 1.4 (SD 0.49) in the morphine group (P < 0.001). The total morphine consumption was significantly reduced in the parecoxib group, in which the total consumption was 4.8 mg (SD 2.68) compared with 9.0 mg (SD 2.03) in the morphine group (P < 0.001). The reduction in the morphine consumption was 46.6%, indicating an opiod-sparing effect of parecoxib. There was no significant different in opiod side effects and post-operative haematoma.

Conclusion: Parecoxib provided better analgaesia and delivered opiod-sparing effect in post-craniotomy patients.

Supervisor: Dr Wan Mohd Nazaruddin Wan Hassan Co-supervisor: Dr Mahamarowi Omar

A STUDY ON DYSLIPIDAEMIA IN PATIENTS WITH END-STAGE RENAL DISEASE ON DIALYSIS IN TWO REFERRAL HOSPITALS IN KOTA BHARU, KELANTAN

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Introduction: The mortality due to cardiovascular disease in dialysis patients is substantially higher than in the general population. Dyslipidaemic factors obviously contribute to the high cardiovascular risk in dialysis patients but are often an underestimated problem.

Objectives: The study was conducted to determine and compare the prevalence of dyslipidaemia among end-stage renal disease (ESRD) patients on dialysis in two referral hospitals in Kota Bharu who were treated either by haemodialysis (HD) or continuous ambulatory peritoneal dialysis (CAPD), and to determine the factors associated with dyslipidaemia.

Methods: A cross-sectional study was conducted among ESRD patients from Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II who had been on dialysis,

either HD or CAPD, for at least 3 months. The number of study subjects was 146: 87 patients (59.6%) were undergoing HD, and 59 patients (40.4%), CAPD. The medical records were reviewed to collect appropriate data. After an overnight fasting of 8 to 12 hours, 5 mL of blood was withdrawn, pre-dialysis from HD patients or during clinic visit from CAPD patients, to determine the lipid profile. Univariable analysis using simple logistic regression was applied to determine factors associated with dyslipidaemia. Multivariable analysis using multiple logistic regression was applied to further determine the association between dialysis modality and body mass index (BMI) status with dyslipidaemia.

Results: The age of our subjects ranged from 11 to 74 years old, with mean (SD) of 45.7 (15.4). Male predominance was observed 81 (55.5%), and Malay subjects composed the largest ethnic group. The majority of the subjects, 127 (86.9%), were non-obese, with mean (SD) BMI of 22.7 kg/m² (4.25). Diabetes mellitus was the most common aetiology of ESRD among our subjects, accounting for 78 cases (53.4%). With regards to the type of dialysis, the majority of the patients were receiving treatment by HD, 87 (59.6%), compared with CAPD, 59 (40.4%). The median (IQR) duration of dialysis treatment was 36 months (60.0). Seventy-one patients (48.7%) were receiving lipid-lowering therapy: 42 (71.2%) from the CAPD group and 29 (33.3%) from the HD group. The prevalence of dyslipidaemia was profoundly high, at 76.7% (112 patients): 60 (53.6%) from the HD group and 52 (46.4%) from the CAPD group. The CAPD group was found to have higher mean (SD) for low-density lipoprotein cholesterol and median (IQR) for triglyceride compared with in the HD group: 3.07 (1.03) versus 2.00 (1.10), and 2.00 (1.10) versus 1.60 (0.91), respectively. Multivariable analysis showed CAPD had 3 times odds of being dyslipidaemic compared with HD group had (OR = 3.44, 95% CI 1.38-8.61, P = 0.008)

Conclusion: Dyslipidaemia is highly prevalent in our dialysis patients, and it is more often observed in CAPD-treated than in HD-treated patients. There were no significant association of dyslipidaemia noted with diabetes, obesity, duration of dialysis, and smoking status.

Supervisor:

Associate Professor Dr Kamaliah Mohd Daud

KNOWLEDGE, ATTITUDE, AND PRACTICE (KAP)
AND ASSOCIATED FACTORS FOR LEPTOSPIROSIS
AMONG TOWN SERVICE WORKERS IN KOTA
BHARU, KELANTAN

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Introduction: Leptospirosis is presumed to be the most widespread re-emerging zoonotic disease in the world. It

occurs in tropical, subtropical, and temperate zones.

Objective: This study was designed to estimate the seroprevalence, explore the knowledge, attitude, and practice (KAP), and determine the associated factors for seropositive leptospirosis among town service workers in Kota Bharu Municipal Council, Kelantan.

Methods: A cross-sectional study was conducted in May 2008 among 296 town service workers in Kota Bharu Municipal Council. All workers who fulfilled the inclusion and exclusion criteria were recruited in the study. Workers were interviewed using a validated questionnaire that consisted of sociodemographic, occupational, and environmental history, as well as KAP questions. Venous blood was taken from subjects at their workplace for microscopic agglutination test.

Results: All respondents were Malay males with the mean age of 42.1 years (SD 8.38). The mean duration of employment was 15.6 years (SD 8.62). The overall seroprevalence of leptospirosis was 24.7% (95% CI 19.7-29.6) and the predominant pathogenic serovar identified was Bataviae (12.3%). In KAP assessment, majority of workers had poor knowledge score (87.2%) and unsatisfactory practice score (64.5%), whereas for attitude, majority of workers had satisfactory attitude score (64.9%). The significant factors associated with seropositive leptospirosis were those who lived 200 m or less from the river (OR 2.24, 95% CI 1.20-4.16, P = 0.011), presence of rat in their houses (OR 3.48, 95%) CI 1.70-6.85, P = 0.001), and gardening activity (OR 2.21, 95% CI 1.22-3.98, P = 0.009). Workers who practised wearing boots while working (OR 0.36, 95% CI 0.20-0.64, P = 0.001) and washing hands with soap after work (OR 0.34, 95% CI 0.17-0.67, P = 0.005) had better protection from leptospirosis.

Conclusion: High seropositivity rate of leptospirosis indicates that the town service workers are in the occupational group with at risk for leptospiral infection. Workers' knowledge and practice were inadequate to protect them from leptospirosis infection. There were relationships between seropositive leptospirosis with occupational and environmental factors as well as recreational activities.

Supervisor: Dr Mohd Nazri Shafei Co-supervisor: Dr Nor Azwany Yaacob

SURVIVAL AND PROGNOSTIC FACTORS OF ADULT HUMAN IMMUNODEFICIENCY VIRUS (HIV) PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) FROM 2002 TO 2006

Mohd Sapuan Baharuddin MSc (Medical Statistics)

Department of Community Medicine School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia Introduction: The estimated number of person living with human immunodeficiency virus (HIV) around the world in 2007 was 33.2 million. It was estimated that 80 938 people have been infected with HIV in Malaysia, and 10 334 deaths were caused by AIDS from 1986 until December 2007. Needle sharing is the dominant mode of HIV transmission in Malaysia.

Objectives: The objectives of this study were to determine median survival time HIV patients and the 5-year survival of these patients, as well as to identify prognostic factors of HIV patients in Hospital Universiti Sains Malaysia.

Methods: The study design for this study was a retrospective record review. All patients diagnosed as HIV positive in Hospital Universiti Sains Malaysia during the study period, from 1 January 2002 until 31 December 2006 (5 years), were considered as potential subjects. A total of 107 patients fulfilled the selection criteria and were included in this study. Additional follow-up for this study was conducted within 12 months, from 1 January 2007 until 31 December 2007. Data of HIV patients were collected from medical record unit using data collection sheet. Patients' survival status was obtained from their medical record or through phone call enquiry. The process of data entry for this study was done using SPSS version 12.0.1. The data were transferred into STATA version 9.0 program using STAT Transfer software version 6.0. The statistical analysis were used in this study was Kaplan-Meier and Cox proportional hazard regression analysis.

Results: The overall median survival time and 5-year survival in this study were 6.23 months (95% CI 1.77–10.63) and 17.53% (95% CI 5.57–34.98), respectively. Prognostic factors that were found to be significant during simplex Cox regression analysis were co-infections, opportunistic infections, clinical stage, and clinic visit frequency. During multiple Cox regression analysis, prognostic factors such as clinical stage and clinic visit frequency were significant in this study. Final model in this study only had clinical stage as prognostic factor (adjusted HR = 2.40, 95%CI 1.42–4.01, P = 0.001).

Conclusion: Overall, median survival time in this study and survivorship among HIV/AIDS patients in Hospital Universiti Sains Malaysia was low. The 5-year survival in this study was affected by late diagnosis as HIV positive and the unavailability of the highly active anti-retroviral therapy (HAART) in the hospital. The prognostic factor that influenced the risk of death among HIV patients was clinical stage. The prognostic factors such as CD4 count, viral load, and HAART will be including in this final model in future in order to increase the strength of the model to predict survival of HIV patients in Hospital Universiti Sains Malaysia.

Supervisor: Dr Wan Mohd Zahiruddin Wan Mohammad Co-supervisor: Professor Dr Syed Hatim Noor

PREVALENCE AND SOURCES OF STRESS AMONG MEDICAL STUDENTS IN SCHOOL OF MEDICAL SCIENCES. UNIVERSITI SAINS MALAYSIA

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Introduction: The medical course has always been regarded as highly stressful. Excessive stress can cause physical and mental health problems. Persistent stress will impair students' academic achievement as well as personal and professional development. Early detection and prevention of this condition will help in reducing the negative impacts of stress on medical students.

Objectives: The study aimed to explore the nature of stress among medical students by determining the prevalence, sources, pattern, and determinant factors of stress. Is it hoped that understanding the nature of stress will help medical educators find ways to reduce and minimise the stress level of medical students during their study.

Methods: All medical students in the School of Medical Sciences, Universiti Sains Malaysia, were taken as subjects in this study. Data collection was done 2 months after the start of the 2008/2009 academic session. A validated questionnaire was used. Clearance was obtained from the School of Medical Sciences and the ethical committee prior to the start of the study. Data were analysed using Statistical Package for Social Sciences (SPSS) version 12.

Results: 761 students (72%) participated in this study. The prevalence of stress among medical students in the School of Medical Sciences, Universiti Sains Malaysia, was 29.6%. The top 10 stressors were academic-related. Prevalence of stress for the first-, second-, third-, and fifth-year students were 26.3%, 36.5%, 31.4%, and 21.9%, respectively. Year of study was the only significant determinant factor of stress among medical students (LR statistics = 527.18, P = 0.034).

Conclusion: The prevalence of stress among medical students in Universiti Sains Malaysia is high. Academic related problems were the major stressors among medical students. Year of study was the factor most significantly associated with medical students' stress level. There was bimodal pattern of stress level throughout the year of study, peaking at the second and fourth years of study.

Supervisor: Dr Ahmad Fuad Abdul Rahim Co-supervisor: Associate Professor Dr Mohd Jamil Yaacob COMPARING SEDATIVE EFFECTS OF EPIDURAL BUPIVACAINE WITH ROPIVACAINE ON BISPECTRAL INDEX DURING AWAKE PHASE AND GENERAL ANAESTHESIA

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Introduction: Combined epidural/general anaesthesia technique has widely been used in major abdominal, lower limbs, and thoracic surgeries. Epidural anaesthesia has been shown to produce sedative effect and to reduce the requirements of volatile and intravenous anaesthetic agents.

Objectives: The aim of this study was to evaluate the sedative effect of epidural anaesthesia, bupivacaine and ropivacaine, on the bispectral index (BIS) during awake and general anaesthesia.

Methods: A prospective, randomised double-blinded clinical trial was conducted on 54 patients planned for elective abdominal or lower limbs surgery under combined epidural and general anaesthesia. This was done in a time frame of 12 months at the operation theatre of Hospital Universiti Sains Malaysia after the approval of the Research and Ethics Committee, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan. The patients were randomly allocated to 2 groups receiving either 10 mL of 0.5% epidural ropivacaine (group R) or the same volume of 0.5% bupivacaine (group B). The BIS measurements during awake phase were performed at 5, 10, 12, 14, 16, 20, and 25 minutes after the epidural injection. General anaesthesia was then induced with fentanyl, propofol, and rocuronium and maintained with 2.0% sevoflurane. From approximately 10 minutes after tracheal intubation, the BIS measurements were made at every 1-minute interval for 10 minutes. Amount of sevoflurane administrated was adjusted to maintain the bispectral index scale between 40 and 60.

Results: There were no significant differences in demographic data among the groups. There was statistically significant mean difference in the BIS values between epidural bupivacaine (group B) and epidural ropivacaine (group R) during awake phase. However, the BIS value during general anaesthesia was not significantly different between 2 groups. This study also demonstrated that the requirement of sevoflurane was not statistically significant different between 2 groups.

Conclusion: Mean BIS values during awake phase was significantly lower in epidural ropivacaine compared with in epidural bupivacaine. However, the mean BIS values during general anaesthesia phase between 2 groups were not significantly difference. The requirement of sevoflurane concentration between 2 groups during general anaesthesia was also not significantly different.

Supervisor: Dr Gnandev Phutane

THE ASSOCIATION BETWEEN OBSTRUCTIVE SLEEP APNEA SYNDROME AND EPILEPSY: THE PREVALENCE AND PREDICTORS OF SLEEPINESS

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Introduction: Epilepsy and obstructive sleep apnea syndrome (OSAS) are both associated with abnormal brain activity and frequently co-exist. Epilepsy patients were found to be drowsier when compared with the general population using the Epworth Sleepiness Scale (ESS).

Objectives: The aim was to study OSAS in epilepsy patients, as well as the prevalence of obstructive sleep apnea and the predictors of sleepiness among epileptics.

Methods: This was a prospective cross-sectional study in Hospital Universiti Sains Malaysia on patients already diagnosed and treated with epilepsy. The study was conducted from November 2008 to April 2010. The consented participants who fulfilled the set criteria were interviewed using questionnaire regarding demographic data, symptoms of obstructive sleep apnea, and ESS, followed by a full ear, nose, and throat examination and an overnight polysomnography (PSG).

Results: Five of 60 participants (8.3%) were diagnosed with OSAS, and 4 of them were males. OSAS was mild in 1 patient, moderate in 2 patients, and severe in the other 2 patients. Age, neck circumference, ESS score, and BMI were significantly associated with OSAS (P < 0.05). Epilepsy-related risks (type of seizures, duration and type of antiepileptic drug) have no significant association with OSAS.

Conclusion: The prevalence of OSAS among epilepsy patients is 8.3%. The use of Malay version of ESS is appropriate and effective in screening patients for OSAS. Future role of PSG as part of assessment in high-risk epileptics is recommended.

Supervisor:

Associate Professor Dr Baharudin Abdullah Co- supervisor: Associate Professor Dr Suzina Sheikh Ab Hamid Associate Professor Dr John Tharakan

A STUDY ON VISUAL ACUITY AND VISUAL SKILLS AMONG PRESUMED SLOW LEARNERS IN PRIMARY SCHOOL IN KOTA BHARU, KELANTAN

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Introduction: The issues of slow learner have become a matter of increasing personal and public concern. Inability to read and write is a major obstacle to learning and may have social and economic implications. Those students who experience learning difficulties may also experience a treatable visual difficulty in addition to their primary learning difficulties.

Objectives: The aims of this study were to determine the visual acuity and the level of visual skills (near point of convergence, convergence and divergence break and recovery, accommodative amplitude, accommodative facility, and saccadic tracking skills) among presumed slow learners in primary schools in Kota Bharu, Kelantan. We also studied the possible association between the level of visual acuity and the level of visual skills.

Methods: A school-based cross-sectional study was carried out from January 2009 to April 2010. Multistages sampling was performed on all primary schools in Kota Bharu. Ocular examinations were carried out in all selected students. Visual acuity and visual skills were measured in 1010 students (average age of 9.5 years) in 20 primary schools. Participating students had been identified by their school teachers as presumed slow learners.

Results: The majority of the students (96.5%) had good visual acuity in both eyes; there were only 4.5% with visual impairment. The main cause for poor visual acuity was due to refractive errors. There were 7.8%, 3.3%, and 2.0% of the students with bilateral myopia, astigmatism, and hypermetropia, respectively. Most of them were undiagnosed and untreated before. Divergence skills and saccadic tracking skills were the most affected visual skills in this study population. Near point of convergence, convergence skills, accommodative amplitude, and accommodative facility were still good. There was statistically significant association between the level of visual acuity and the level of convergence break and accommodative facility.

Conclusion: The results showed that the majority of the presumed slow learner students had poor visual skills but less numbers of students with visual impairment. There were statistically significant association between the level of visual acuity and the level of visual skills.

Supervisor: Associate Professor Dr Shatriah Ismail Co-supervisor: Dr Adil Hussein

A STUDY ON THE PREVALENCE OF HEARING IMPAIRMENT AND ITS ASSOCIATED FACTORS AMONG ARMY PERSONNEL IN KELANTAN

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Objective: This study was conducted to determine the prevalence of hearing impairment and associated factors among army personnel in Kelantan.

Methods: This is cross-sectional study that had been conducted among army personnel in Kem Desa Pahlawan, Kelantan, from July until November 2007. Two major groups were involved: high-noise-exposure military occupational specialties (infantry and artillery) and low-noise-exposure military occupational service (transport unit and workshop). Each participant was subjected to otoscopic examination and hearing tests, namely Distortion Product Otoacoustic Emission (DPOAE) screening tool and pure tone audiometric (PTA)

Result: A total of 320 army personnel were recruited. The prevalence of hearing impairment among army personnel was 36.3%. There was significant difference in the percentage of hearing impairment between the high-noise-exposure and low-noise-exposure groups (42.5% and 30.0%, respectively). Statistical analysis showed significant correlations between hearing impairment with age and duration of service. Majority of the army personnel suffered from sensorineural hearing loss, specifically noise-induced hearing loss.

Conclusion: There was high prevalence rate of hearing impairment among army personnel. While loud noise is recognised as a hazard, initiatives are required to increase the use of effective preventative measures. Hearing conservation programmes are beneficial, and its implementation should be considered by the Ministry of Defence.

Supervisor: Professor Dr Dinsuhaimi Sidek Co-supervisor: Dr Hazama Mohamad

FACTORS AFFECTING EXCLUSIVE BREASTFEEDING AMONG NURSES IN BACHOK KELANTAN: A QUALITATIVE STUDY

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Department of Public Health School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia **Introduction:** Breastfeeding is important to provide good nutrition to infants up to 6 months of age. Despite the benefits of exclusive breastfeeding, the prevalence of exclusive breastfeeding practice is still low in Malaysia. Many nurses, even though they have the breastfeeding knowledge, cannot practice exclusive breastfeeding successfully.

Objective: This study aimed to explore and compare the factors influencing the breastfeeding experience among nurses who practice exclusive and non-exclusive breastfeeding in Bachok, Kelantan.

Methods: Six nurses were conveniently selected: 3 from exclusive and another 3 from non-exclusive breastfeeding groups. The nurses were interviewed regarding their experiences in breastfeeding practice.

Results: Five themes that influence breastfeeding practice among nurses in Bachok, Kelantan, were derived from the interviews. First is husband's, family members', and peers' support; second, delivery experiences; third, workplace condition and employer's support; fourth, determination of breastfeeding and reproductive role of a woman; and lastly, appreciation of the benefits of breastfeeding and initiation of breastfeeding.

Conclusion: Nurses who were successful at exclusive breastfeeding experienced positive factors that support them to continue breastfeeding, unlike the non-exclusive respondents who had factors that limit their breastfeeding practice.

Supervisor: Dr Zaharah Sulaiman Co-supervisor: Dr Tengku Alina Tengku Ismail

A RANDOMISED CROSS-OVER CONTROLLED TRIAL
OF COMBINED SODIUM AND ULTRAFILTRATION
PROFILING IN PATIENTS ON CHRONIC
HAEMODIALYSIS: THE EFFECT ON INTRADIALYTIC
HAEMODYNAMIC PROFILE

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Introduction: Haemodialysis-induced hypotension is one of the most serious complications in renal replacement therapy. The main cause of intradialytic hypotension is hypovolaemia due to an imbalance between the amount of fluid removed and the refilling capacity of the intravascular compartment. The proposed interventions such as sodium and ultrafilration profiling can be use to make dialysis treatment more effective and comfortable for patients. However, the effectiveness of profiled haemodialysis has not been fully evaluated in local set-up.

Objectives: The study was conducted to determine the incidence of intradialytic hypotension in different haemodialysis settings, and to determine the relative blood volume changes during haemodialysis process between conventional and profiling settings.

Methods: This was a randomised control study involving end stage renal failure patients with haemodialysis treatment at haemodalysis units, Hospital Sultanah Nur Zahirah from May until June 2008. The study was based on 2 different haemodialysis settings, conventional (constant sodium and ultrafiltration haemodialysis) and profiling (combination sodium and ultrafiltration profiling haemodialysis), crossover designed with repeated measures of haemodynamic parameters. The study protocol was reviewed and approved by the Universiti Sains Malaysia Ethics and Research Committee.

Results: Originally, 95 patients participated in the study; however, 6 patients were excluded because of the dropped in haemoglobin level (below 10 g/dL) and unwillingness to continue. Data collected from 89 patients were analysed, and 356 haemodialysis sessions were evaluated (178 conventional setting, 178 profiling setting). The incidence of intradialytic hypotension was significantly lower in profiling setting, 32%, compared with in conventional setting, 48% (P = 0.03). The pattern of relative blood volume was significantly different (P < 0.001) between conventional and profiling haemodialysis settings.

Conclusion: This study showed that the incidence of intradialytic hypotension was significantly lower in the profiled setting haemodialysis. The pattern of relative blood volume with this combination profiled setting was more stable at late dialysis time. We concluded that this combination profiled setting is suitable for patient with intradialytic hypotension occurring at late dialysis time.

Supervisor: Associate Professor Dr Zainal Darus

INTRARENAL RESISTIVE INDEX (RI) IN TYPE
2 DIABETES MELLITUS: CORRELATION WITH
CREATININE CLEARANCE AND ASSOCIATION WITH
URINARY ALBUMIN EXCRETION

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Introduction: Diabetic nephropathy is a common cause of native kidney dysfunction, and it is the most common cause of end-stage renal disease worldwide. Currently, sonographic imaging does not have an important role in the diagnosis of diabetic nephropathy or in the follow-up of

possible cases. Several studies showed associations between changes in the intrarenal arterial waveform and intrinsic as well as extrinsic renal disorders. Resistive index (RI) is suggested as a useful parameter in quantifying the intrarenal blood flow. Renal Doppler sonography has been shown to be useful in detecting and predicting subsequent renal status in various renal disorders, including in diabetic patients.

Objective: The study aimed to evaluate the potential relationship between the intrarenal Doppler parameter and renal function in type 2 diabetes mellitus.

Methods: A cross-sectional study was conducted from October 2007 until October 2008. All type 2 diabetes mellitus patients from Hospital Raja Perempuan Zainab II, KKKB, and district hospital who were referred for ultrasound and fulfilled the set criteria were subjected to renal Doppler sonography. The procedure was performed at Radiology Department, Hospital Raja Perempuan Zainab II, by single operator, using 3.75 MHz curvilinear transducer (Toshiba SSA-550, Nemio 20). Patients' weight, blood pressure, urinary albumin excretion (UAE) rate, and serum creatinine level were noted. Creatinine clearance was calculated using Cockcroft—Gault formula. The subjects were then divided into 3 groups (normal, microalbuminuria, and overt albuminuria) according to their UAE rate.

Results: A total of 91 type 2 diabetic patients were included in the study; 85 were Malays and 6 were Chinese, with 49 males and 42 females. Only 2 Doppler parameters, RI and pulsatility index (PI), were shown to be associated with UAE rate. Other Doppler parameters (peak systolic velocity, end diastolic velocity, and AT) showed no significant difference among the groups. The mean values of RI according to UAE rate was 0.67 (SD 0.05) for normal, 0.72 (SD 0.08) for microalbuminuria, and 0.76 (SD 0.06) for overt albuminuria. There were significant differences between normal and overt albuminuria groups (P < 0.001), and between normal and mircoalbuminuria groups (P = 0.033). For PI, the mean values were 1.15 (SD 0.16) for normal, 1.34 (SD 0.30) for microalbuminuria, and 1.48 (SD 0.27) for overt. There were significant differences between normal and overt albuminuria groups (P < 0.001), and between normal and microalbuminuria groups (P = 0.038). This study also found significant correlation between creatinine clearance and RI (r = 0.559, P < 0.001).

Conclusion: Significant differences were observed in RI and PI values among type 2 diabetic patients according to their UAE rate: between normal and overt albuminuria groups, and between normal and microalbuminuria groups. There was significant negative correlation between calculated creatinine clearance and RI.

Supervisor: Dr Rohaizan Yunus Co-supervisor: Dr Md Ariff Abas

KNOWLEDGE, ATTITUDE AND PRACTICE (KAP) OF RISKY SEXUAL BEHAVIOUR AND ITS ASSOCIATED FACTORS AMONG ADOLESCENTS AND YOUNG **ADULTS IN KOTA BHARU**

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Introduction: Adolescents' risky sexual behaviour has become an increasingly significant social and health concern because of the risk of contracting sexually transmitted diseases, including human immunodeficiency virus, and the negative social consequences of teenage pregnancies and of transgressing the Asian religious and cultural norms.

Objectives: The study was conducted to develop a new and validated self-administered questionnaire in order to assess the knowledge, attitude, and practice (KAP) of risky sexual behaviour and its associated factors. This study was also aimed to determine the prevalence of such behaviour among adolescents and young adults in Kota Bharu.

Methods: The study was conducted in 2 phases. Phase 1 was a qualitative study where in-depth interviews with 10 respondents selected from a shelter for troubled female adolescents were carried out to explore in detail the factors associated with risky sexual behaviour. One-to-one interviews were done, and their responses were recorded and transcribed. The qualitative data were analysed manually to find the common themes and recurring meanings. In Phase 2, a cross-sectional study was done involving 210 respondents who were selected using systematic random sampling from 3 private institutions of higher learning, which were randomly selected in the district of Kota Bharu. The data was collected using a validated self-administered questionnaire, which was developed based on the data from Phase 1, literature review, and expert opinions, to assess the KAP of risky sexual behaviour and its associated factors.

Results: The new KAP questionnaire showed good internal consistency with Cronbach's alpha of 0.986, 0.982, and 0.824 for knowledge, attitude, and practice domain, respectively, and the construct validity analysis revealed that each sub domain has factor loading ranging from 0.39 to 0.93 with Eigen values of more than 1. The study population was predominantly Malay (99.0%), and all were Muslims. 14 (6.7%) out of 210 respondents had premarital sex, which qualified them to be categorised as having risky sexual behaviour; 13 (92.9%) were males. In the KAP segment, 111 (52.9%) have good knowledge (scored ≥ 75%) of risky sexual behaviour, while 137 (65.2%) showed liberal attitude (scored < 75%), and 108 (51.4%) demonstrated liberal practice (scored > 25%). The significant factors associated with good knowledge were older age (adjusted OR = 1.54, 95% CI 1.18-2.02, P = 0.002) and having a father who received at least secondary school education (adjusted OR = 2.74, 95% CI 1.34-5.60, P = 0.006).

However, respondents who were renting were less likely to have good knowledge (adjusted OR = 0.23, 95% CI 0.11-0.57, P = 0.000). The significant factors associated with liberal practice were older age (adjusted OR = 1.34, 95% CI 1.02-1.75, P = 0.036) and male gender (adjusted OR = 7.01, 95% CI 3.76–13.10, P = 0.000). As for the associated factors for attitude, males were less likely to have conservative attitude. The significant associated factors for risky sexual behaviour were male gender (adjusted OR = 39.46, 95% CI 3.52-442.52, P = 0.003) and being easily influenced by boyfriend or girlfriend (adjusted OR = 31.44, 95% CI 6.41-154.35, P = 0.000). On the other hand, having a father who received at least secondary school education (adjusted OR = 0.17, 95% CI 0.26-0.53, P = 0.005) is a protective factor against risky sexual behaviour.

Conclusion: The new KAP questionnaire is a valid and reliable instrument to assess knowledge, attitude, and practice of risky sexual behaviour. This study revealed that the prevalence of risky sexual behaviour among adolescents and young adults aged 17-21 years old is lower compared with in the majority of previous studies in this country. More than half of the students have good knowledge about risky sexual behaviour and demonstrated liberal (more tolerant or open-minded) attitude and practice towards it. Risky sexual behaviour was significantly associated with male gender and being easily influenced by boyfriend or girlfriend, while having a better educated father is protective against it.

Supervisor: Associate Professor Dr Mohd Jamil Yaacob Co-supervisor: Dr Zaharah Sulaiman

COMPARISON OF DIFFERENT DOSES OF RECTAL **DICLOFENAC AS ADJUVANT TO INTRATHECAL BUPIVACAINE MORPHINE ANAESTHESIA FOR** CAESAREAN SECTION

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Introduction: Spinal anaesthesia with anaesthetic and opiod is a well-accepted technique. Pain from post-caesarean section that is related to somatic component from the wound itself is treatable with spinal anaesthesia. However, the visceral pain component from the uterus may be more difficult to treat and need further medication, for example, with non-steroidal anti-inflammatory drugs (NSAID). These drugs are effective in relieving pain related to menstrual cramping, and as a result, there has been some interest in the use of NSAID to treat the visceral component of pain after delivery. A Study (Dahl et al, 2002) has shown that 2 doses of 100 mg rectal diclofenac are opiod sparing and have good analgaesic properties.

Objectives: We studied the effectiveness of a single dose of rectal diclofenac, at different concentrations, in relieving 24 hours of post-operative visceral pain, to help improve the medication compliance and reduce staff workload.

Methods: After ethical committee approval, prospective randomised study was conducted on 72 parturients, aged 18–40 years, who had undergone elective or emergency caesarean section under intrathecal bupivacaine—morphine anaesthesia using 9.5 mg (0.5% hyperbaric) bupivacaine and 0.1 mg (0.1 mL) morphine. The subjects were divided into 2 groups: at the end of operation, group I received 1.0 mg/kg rectal diclofenac sodium and group II received 1.5 mg/kg rectal diclofenac sodium. The visual analogue scale at 4, 12, and 24 hours post-operation, the duration until first rescue analgaesia was given, and the side effects were recorded.

Results: There was no statistically significant difference in the pain score at 4, 12, and 24 hours. One parturient from group I requires rescue medication at 18 hours post-operation. There was no side effect noted.

Conclusion: Single dose of 1.0 mg/kg rectal diclofenac sodium as an adjuvant to intrathecal bupivacaine morphine anaesthesia for caesarean section is comparable to 1.5mg/kg dosage and required no rescue medication. Single dose of 1.0 mg/kg rectal diclofenac sodium can be suggested as an alternative to multiple doses administration of drug.

Supervisor: Dr Gnandev Phutane Co-supervisor: Dr Aisai Abdul Rahman

A STUDY ON FACTORS AFFECTING THE CORONARY ANGIOGRAPHIC FINDINGS AMONG POSITIVE EXERCISE STRESS TEST (TREADMILL) IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Coronary artery disease (CAD) is the common cause of death worldwide, and treatment strategies for this disease are continually evolving. Treadmill exercise stress test (ETT) is one of the common non-invasive diagnostic methods used to detect CAD.

Objectives: The purpose of this study was to determine the prevalence and factors affecting the coronary angiographic findings among the positive ETT patients. A total of 196 patients with positive ETT from 2003 to 2009 who subsequently underwent coronary angiography were

analysed retrospectively.

Methods: The socio-demographic variables, risk factors for CAD, co-morbidities, clinical and biochemical profiles, baseline electrocardiogram (ECG), echocardiography, ETT parameters, and angiographic findings were evaluated and analysed from the patients' folders. The result was analysed using SPSS 12.0 software.

Results: The results were divided into true positive and false positive based on coronary angiography. The prevalence of true positive results was 59.2%. The factors affecting the angiographic findings among positive ETT patients are male gender (P < 0.001), age (P = 0.012), hypertension (P = 0.04), smoking (P < 0.001), blood pressure baseline (particularly diastolic BP), high density lipoprotein cholesterol (P = 0.002), and triglyceride level (P = 0.010). ETT parameters that were significantly associated with the angiographic findings were failure to achieve 85% of target heart rate (P < 0.001), angina during ETT (P = 0.006), inferolateral lead involvement during exercise, MET lower than 6.5, and ST-segment depression more than 2 mm during exercise. Strongly positive ETT result also determined the true positive outcome. However, the ECG leads involved during ETT was not associated with the specific coronary artery involvement.

Conclusion: This study proves that the ETT is still an important investigation that can detect significant CAD.

Supervisor: Associate Professor Dr Zurkurnai Yusof Co-supervisor: Dr Ng Seng Loong

BONE DENSITY CHANGES FOLLOWING TREATMENT WITH ALENDRONATE IN PATIENTS WITH LOW BONE DENSITY USING DUAL ENERGY X-RAY ABSORPTIOMETRY

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Introduction: Osteoporosis is an important disease that has increased in its occurrence. It is more common in elderly female. Risk factors of osteoporosis include increasing age, female, as well as smoking. As the incidence of osteoporosis is increasing, with more younger population affected, and since the costs of managing osteoporotic fracture has risen, it is important to get an accurate diagnosis and to identify people at risk of getting osteoporotic fracture. Alendronate is a widely used drug to treat osteoporosis worldwide. Although this drug has been in the market since 30 years ago, only recently its efficacy has been tested. Since osteoporosis varies in its environmental factors, there is need to evaluate patients' response to alendronate.

Objectives: The study aimed to determine bone density changes in patients treated with alendronate using dual-emission X-ray absorptiometry (DEXA).

Methods: This was a prospective interventional study performed in Hospital Raja Perempuan Zainab II, Kota Bharu, over the period of 18 months. Samples were selected from the orthopaedic clinic among patients who were identified to have low bone density such as osteopaenia on radiograph and/or DEXA and patients with radiographic features of osteopaenia with pathological fracture as well as patients who fulfilled osteoporosis criteria by using DEXA. A total of 56 patients who had given a written informed consent underwent baseline DEXA. These patients were started with treatment of alendronate (70 mg weekly). Second DEXA scan was performed after 1 year of treatment. Only 38 patients came for second bone densitometry measurement. Bone density was measured at 3 different sites: the hip, the neck of femur, and the lumbar spine. Effects of other non-pharmacological factors such as supplements, exercise, milk consumption, hormone replacement therapy, caffeinated drinks, carbonated drinks, smoking, and family history of osteoporosis were also assessed in this study. The graphs of changes in bone density after treatment, the pattern of its changes, and the demographic pattern were obtained. Statistical analysis (paired t test, Wilcoxon signed rank test) were used to analyse the data in order to assess the significance of bone density increment after treatment as well as the effect of the non-pharmacological factors that may contribute to the changes of bone density.

Results: There were increases in bone density in all patients at all measured site (hip, neck of femur, and lumbar spine). The majority of patients (65.8%) showed 1% increment of bone density from baseline in the hip region, 52.6% showed 2% increment, whereas 47.4% showed 3% increment. Almost similar results were seen in the neck of femur (55.3% at 1% increment, 42.1% at 2% increment, and 31.6% at 3% increment) and in the lumbar spine (55.3% at 1% increment, 42.1% at 2% increment, and 31.6% at 3% increment). Increment in bone density was significant in the neck of femur (P = 0.045) compared with other sites, which did not show significance.

Conclusion: The majority of patients showed 1% increment of bone density in all measured part (hip, neck of femur, and lumbar spine). Increment of bone density is significant in the neck of femur region.

Supervisor:

Associate Professor Dr Noreen Norfaraheen Lee Abdullah Co-supervisors: Dr Md Ariff Abas Dr Anwar Hau Abdullah

IN VITRO EVALUATION OF BIOMEDICAL-GRADE CHITOSAN DERIVATIVES ON PRIMARY HUMAN SKIN FIBROBLASTS

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Introduction: Chitosan has been proposed for biomedical applications because of its biocompatibility and abundance in nature. However, many barriers still exist due to its physical and chemical limitations. Further work is needed to improve these properties, but any changes will influence its biocompatibility. Therefore, the biosafety of chitosan products, in terms of biocompatibility and cytotoxicity, requires an in vitro evaluation. The chitosan film that was tested has been locally processed as a chitosan derivative. Primary human dermal fibroblast, which plays a major role in the process of wound healing, was used for the evaluation.

Objective: The objective of this study is to evaluate the cytotoxicity of chitosan derivatives products and their ability to influence the proliferation of fibroblasts. This study also aimed to assess the effects of chitosan on interleukin 8 (IL-8) and transforming growth factor-\$\beta\$ secretion by primary fibroblasts in the culture system.

Methods: Comparative evaluation was done on four types of chitosan derivatives films, named as NO-CMC, O-CMC, O-C, and N-CMC.

Results: O-C and N-CMC were found to be non-cytotoxic against fibroblasts, as confirmed by 3(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. General observation using phase contrast microscopy showed no marked morphological changes on O-C and N-CMC treated cells at the initial period of incubation. Cultures incubated with NO-CMC were graded as slightly changed, whereby more than 20% of the cells were rounded and loosely attached, and occasional lysed cells were present. Minimal cell damage was observed on O-CMC treated cells. Similar results were obtained from quantitative approach assessment. Determination of cell proliferation using CellTiter 96® Aqueous Non-Radioactive Cell Proliferation Assay revealed no fibroblasts proliferation in the presence of high molecular weight chitosan derivatives after 5 days of treatment compared with untreated well. However, low molecular weight chitosan derivatives have the ability to induce the proliferation of fibroblasts. In addition, stimulation of proliferation increased with time exposure. This study also demonstrated that chitosan derivatives have an ability to influence the secretion of IL-8 by fibroblasts. In contrast, no TGF-ß secretion was detected.

Conclusion: Although in vivo experiments are anticipated, these current findings indicate the potential use of chitosan derivatives in wound management.

Supervisor: Professor Dr Ahmad Sukari Halim Co-supervisors: Dr Che Maraina Che Hussin Associate Professor Dr Shahrum Shamsuddin

TUMOUR NECROTIC VOLUME AND ITS ASSOCIATION WITH TUMOUR SIZE AND LUNG METASTASIS AMONG OSTEOSARCOMA PATIENTS USING MRI

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Introduction: Osteosarcoma is the most frequent skeletal malignancy in children and adolescent. Several recent studies indicate that hypoxia in solid tumours has a major prognostic effect. This has been demonstrated in head and neck cancers, gliomas, adult soft tissue sarcoma, and Ewing's sarcoma. Severe and long lasting hypoxia can result in necrosis; therefore, the presence of necrosis can be correlated with prognosis.

Objectives: This study was designed to determine the association and correlation between tumour volume and tumour necrosis with the risk of lung metastasis in osteosarcoma patients.

Methods: This was a cross-sectional study involving 33 confirmed osteosarcoma patients who were referred from tertiary centres or admitted to Hospital Universiti Sains Malaysia (HUSM) for investigation and management of osteosarcoma from October 2001 to September 2008. All patients who fit the inclusion criteria were selected and their data from patients' radiological, medical, and histopathological records were studied. Each patient had undergone magnetic resonance imaging in HUSM, using a standard imaging protocol. The measurement of tumour volume and tumour necrotic volume were done using OSIRIX software. Computed tomography of the thorax was done either in HUSM or in other hospitals. The association between tumour necrotic volume with lung metastasis and tumour volume were observed.

Results: The patients' age ranged from 6 to 28 years old, and the majority of them were males, with Malays being the major ethnic group. Femur was the most common site for osteosarcoma to occur. Out of the 33 cases, 70% presented with lung metastasis. The median tumour necrosis was 22.5cm^3 , and the median tumour volume was 280.5cm^3 . There was no statistically significant association between tumour necrotic volume and lung metastasis (P = 0.115). There was significant association between tumour volume and lung metastasis. Significant correlation was also noted between tumour necrotic volume and tumour volume (P < 0.001).

Conclusion: There was no association between tumour

necrotic volume and incidence of lung metastasis. However, there were association between tumour volume with tumour necrotic volume and lung metastasis.

Supervisor: Dr Nik Munirah Nik Mahdi Co-supervisor: Professor Dr Zulmi Wan

REMISSION AND RELAPSE OF PROLIFERATIVE LUPUS NEPHRITIS IN PATIENTS TREATED WITH INTRAVENOUS CYCLOPHOSPHAMIDE IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Although there are several reports on predictors of long-term outcomes of proliferative lupus nephritis, there is inadequate knowledge about predictors of remission and relapse among patients with proliferative nephritis treated with currently recommended intravenous cyclophosphamide regimen.

Objectives: We undertook a retrospective study on all eligible proliferative lupus nephritis patients treated with intravenous cyclophosphamide in Hospital Universiti Sains Malaysia from 1997 to 2007 to determine the timing and the rate of remission and relapse, and also to determine the predictors of the remission and relapse in those patients.

Results: Data from 70 patients were analysed: 38% had focal proliferative nephritis (Class III) and 62% had diffuse proliferative nephritis (Class IV). All of the patients were Malays, and the majority of patients were females. The mean age at presentation was 26 years (ranged 13-40 years). Out of 70 patients, 52 (74.3%) entered into remission; 26 (37%) of these patients had had relapse during follow-up. The overall median duration of treatment in our cohort was 24 months. The median time to remission was 3 months from the start of the intravenous cyclophosphamide regimen. The median time to relapse was 79 months from the start time of remission. In our study, central nervous system disease, proteinuria, creatinine level, systolic blood pressure, and type of renal histology at the time of the diagnosis of lupus nephritis were found to be significant independent predictive factors for relapse.

Conclusion: The majority of proliferative lupus nephritis patients had remission when treated with intravenous cyclophosphamide, and one third of them had relapse. Our study has confirmed several factors as predictors for relapse.

Supervisor: Associate Professor Dr Zainal Darus

THE EFFECT OF MONOCHROMATIC INFRARED ENERGY THERAPY ON DIABETIC FEET WITH PERIPHERAL SENSORY NEUROPATHY—A SINGLE BLINDED RANDOMISED CONTROLLED TRIAL

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Introduction: Peripheral diabetic neuropathy has been a burden to the health and economy with the increasing number of morbidity and mortality cases following foot ulcer and amputation. With foot ulcer being an irreversible disease, foot care and glycaemic control is the mainstay of treatment. Various adjunct treatments to improve neuropathy have been introduced to the market; among them is the monochromatic infrared energy therapy (MIRE), which claimed to produce promising results. This study focused on the effect of MIRE on the diabetic foot peripheral neuropathy. The main difference in comparison with other previous studies was the use of a neurometer, which is more quantitative and sensitive, for neuropathy assessment.

Objectives: The study aimed to assess the effect of MIRE on diabetic feet associated with peripheral neuropathy.

Methods: A randomised controlled single-blinded study was conducted at Hospital Universiti Sains Malaysia from February until October 2008, involving 30 lower limbs from 25 patients. The neuropathy was screened by Michigan Neuropathy Scoring Investigation followed by the assessment of the Current Perception Threshold using a neurometer at 2000 Hz, 250 Hz, and 5 Hz. The limbs were randomised to receive either daily MIRE or placebo treatment for a total of 12 treatments. The foot was reassesed again with neurometer within a week of completion of the treatment.

Results: The data obtained was analysed with non-parametric test to compare between the treatment and place groups. The inter-relationship of each result between these 2 groups was confirmed by chi-square test. We found no significant difference (P > 0.05) in the neuropathic foot of diabetic patients in the MIRE and placebo groups.

Conclusion: There was no improvement of neuropathy in the diabetic foot patient following MIRE treatment.

Supervisor: Dr Abdul Nawfar Sadagatullah

A PROSPECTIVE STUDY OF CERVICAL LENGTH MEASUREMENT IN PREDICTING PRE-TERM DELIVERY

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Objective: We aimed to study the cervical length measurement in relation to the outcome of pregnancy.

Methods: All patients who attended the antenatal clinic at Hospital Universiti Sains Malaysia and fulfilled all the set criteria were recruited in this study. The participants were subjected to transabdominal and transvaginal ultrasounds at 16, 20, 24, 28, and 32 weeks of gestation for cervical length measurement. At 28 weeks of gestation, high vaginal swab were taken, and subsequently the participants had routine antenatal follow-up as scheduled similar to other patients who are not involved in this study, until the time of delivery.

Results: A total of 183 pregnant women were recruited in this study; 61 of them had pre-term labour. The incidence of pre-term delivery was approximately 33.3%. Patients with history of pre-term delivery or miscarriage and short cervix were predisposed to pre-term delivery. In general, the average cervical length at 16, 24, 28, and 32 weeks of gestation were 2.82, 2.78, 2.73, and 2.69 cm, respectively. Both transabdominal and transvaginal methods in measuring the cervical length showed significant association in predicting pre-term delivery. At a cut off point of 2.5 cm, transvaginal cervical length showed positive predictive value of 100% in predicting pre-term delivery at all gestation periods, except at 32 weeks; this was far superior compared with the transabdominal method. Transvaginal ultrasound at 28 weeks demonstrated the highest predictive value in predicting pre-term delivery compared with other gestation periods.

Conclusion: Cervical length measurement can be used as important predictor for pre-term delivery, where the length of the cervix is inversely related with risk of pre-term labour. In predicting pre-term delivery, the measurement of cervical length by transvaginal ultrasounds is more superior to transabdominal ultrasound.

Supervisor: Dr Mohd Pazudin Ismail Co-supervisor: Professor Dr Nik Mohamed Zaki Nik Mahmud

PARAOXONASE 1 GLUTAMINE/ARGININE 192 POLYMORPHISMS IN THREE ETHNIC GROUPS IN MALAYSIA

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Introduction: Coronary heart disease (CHD) is the major cause of death globally, including in Malaysia. Despite of sharing almost similar environmental exposure, the prevalence of CHD was highest in the Indian population compared with the Malay and Chinese populations. We hypothesised that the Indians have genetic predisposition to CHD. Paraoxonase (PON) 1 / glutamine (Q) / arginine (R) 192 polymorphism has been shown to be associated with CHD.

Objective: This study was aimed to determine the distribution of lipid profile and genotype among the three ethnic groups (Malay, Chinese, and Indian), and to study the relationship of lipis profile and PON 1 genotype.

Methods: A total of 155 healthy blood samples were collected (54 Malays, 50 Chinese, and 51 Indians) for lipid profile estimation and PON 1 genotyping. The genotyping procedures involved DNA extraction, PCR amplification, Alw 1 digestion, and agarose gel electrophoresis. Statistical data were analysed by ANOVA, ANCOVA, chi-square, and Pearson's correlation tests.

Results: The mean concentrations of plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and TC to high-density lipoprotein cholesterol (HDL-C) ratio were significantly higher in Malays and Chinese than Indians (TC, P = 0.035; LDL-C, P = 0.039; TC:HDL-C, P = 0016). However, there were no significant differences in the plasma triglycerides (TG) and HDL-C concentrations (TG, P = 0.610; HDL-C, P = 0.225). The overall genotype compositions were 34% of QQ, 20% of QR, and 46% of RR. The allele frequencies for all subjects were 0.442 and 0.558 for Q and R, respectively. The frequencies of QQ, QR, and RR genotypes were 39%, 18%, and 43% for both Malay and Indian groups, and 24%, 24% and 52% for Chinese group, respectively. The allele frequencies for both Malays and Indians were 0.48 and 0.52 for Q and R allele, respectively, while they were 0.36 for Q and 0.64 for R in Chinese. PON 1 genotype (P = 0.483) and allele distributions (P = 0.134) were statistically not significant among the ethnic groups. After classification by National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines, the frequency of lower HDL-C were 2.2 times and 3.2 times more in Indians compared with Malays and Chinese, respectively. The mean concentrations of plasma TC, LDL-C, and TC:HDL-C were significantly higher in RR compared to QR and QQ (TC, P = 0.013; LDL-C, P = 0.019; TC:HDL-C, P = 0.03). The plasma HDL-C was also significantly different, but it was higher in QR than in RR and

QQ (P = 0.002). However, there was no significant difference in the plasma TG among the three genotypes (P = 0.292).

Conclusion: The highest CHD prevalence was observed in the Indian population in Malaysia; this might be because low HDL-C was more frequent among Indian subjects. The distribution of PON 1 glutamine / arginine polymorphism was independent of ethinicity. The PON 1 R allele was associated to elevation of 11.1% of TC, 16.5% of LDL-C, and 16.3% of TC:HDL-C. PON 1 Gin / Arg 192 polymorphism should be added as one of the risk factors to determination the progression of premature CHD among healthy Malaysian populations.

Supervisor: Associate Professor Hasenan Nordin Co-supervisor: Dr Win Mar Kyi

PRE-OPERATIVE SONOGRAPHIC PARAMETERS AND COMPARISON OF OUTCOME IN ARTERIOVENOUS FISTULA BETWEEN PRE-OPERATIVE VASCULAR MAPPING AND PHYSICAL EXAMINATION IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Haemodialysis access failure is the major cause of morbidity and multiple hospital admissions. Arteriovenous fistula (AVF) is recognised as a gold standard of haemodialysis access because of its long-term patency and lower infection and intervention rates. Recent evidence has questioned the preferred site of AVF creation in many patient groups. A pre-operative test that could reliably predict the outcome of a proposed AVF would be of great benefit. Ultrasonography is an excellent modality for haemodialysis access evaluation, as it is readily available, non-invasive, and inexpensive. Pre-operative ultrasound mapping (PUSM) has been advocated as more accurate to evaluate the vascular system in patients who required AVF creation. Because of PUSM success, it has become a common practice, and it has been suggested that this technique is used routinely for AVF creation every patient before regardless of their pre-operative physical examination (PE) findings.

Objectives: The study aimed to determine sonographic parameters of arteries and veins, to compare the success rate, and to identify the risk factors for failure of AVF in pre-operative ultrasound Doppler vascular mapping and pre-operative favourable examination findings.

Methods: This randomised controlled study was conducted at Hospital Universiti Sains Malaysia Kota Bharu, Kelantan, for 18 months, from 1 April 2008 until 30 September

2009. The eligible patients were then randomised into 2 groups: 1 group of patient had both pre-operative ultrasound Doppler vascular mapping and physical examination, whereas the other group had favourable physical examination only. The patients were followed-up for the outcome.

Results: A total of 180 patients with end-stage renal disease or chronic renal failure approaching end-stage renal failure were included in this study. The physical examination group consisted of 79 patients. In the other group, 101 patients underwent PUSM; however, only 79 patients underwent fistula creation, whereas the remaining 22 patients did not. The use of PUSM resulting in 8.91 times higher chances for thrills in AVF at day 1 post-operation, 4.60 times higher at 6 weeks, and 52 times higher at 3 months 3 than in patients who underwent PE alone. PUSM also enabled 2.60 times higher chances for suitable fistula for dialysis (functioning fistula) than PE. However, there was no significant difference in the presence of thrill immediately and 6 months post-operation; this showed that there was no difference of patency between both groups. Based on our study, when adjusted to age, sex, diabetes mellitus, hypertension, hypercholesterolemia, and ischemic heart disease, the use of PUSM had 5.70 times higher chances for functioning fistula at 6 weeks, and 3.76 times at 3 months, when compared with those only had PE, and PUSM also had 3.08 times higher chances for suitable fistula for dialysis (functioning fistula). No significant risk factors contribute to fistula failure in the study population.

Conclusion: Pre-operative sonographic vascular mapping results in a marked increase in patency of arteriovenous fistulas, as well as an improvement in the suitability/adequacy of fistulas for dialysis. This approach has resulted in a substantial increase in the proportion of patients dialysing with a fistula in our patient population. Implementation of routine pre-operative ultrasound mapping will be beneficial in management of dialysis patients in Hospital Universiti Sains Malaysia.

Supervisor: Dr Juhara Haron Co-supervisor: Dr Mohamed Ashraf Mohamed Daud

THE EFFECTIVENESS OF EPIDURAL 0.5% LEVOBUPIVACAINE PLUS CLONIDINE OR FENTANYL IN LOWER LIMB SURGERY

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Introduction: Epidural anaesthesia is one modality which provides surgical anaesthesia. It has been proven to offer numerous advantages. Usage of levobupivacaine

epidural anaesthesia was noted to have almost similar potency as bupivacaine with extradural adjuvants like fentanyl and clonidine as a bolus dose in epidural anaesthesia is still limited. Even the combination regime varies and focused mainly on post-operative analgaesia.

Objective: The study was conducted to determine the extent of clinical efficacy of combinations of levobupivacaine with clonidine or fentanyl in sensory and motor block.

Methods: In this randomised, double-blind study, 80 patients were allocated in to 3 groups: 0.5% levobupivacaine with 60 µg clonidine (LC) group, 0.5% levobupivacine with 50 μg fentanyl (LF) group, and 0.5% levobupivacine plus 1 mL of normal saline (LNS) as control group. Epidural anaesthasia performed were at the level of L3/4 or L4/5 for patients who underwent lower surgery. The drugs consisted of 3 mL of test dose plus 10 mL of study drug, which consisted of 9 mL of 0.5% levobupivacaine and 1 mL of adjuvant. Patients were assessed regarding the sensory block with Modified Bromage Scale (MBS). Another 5 mL of 0.5% levobupivacaine was added in incremental dose when sensory block is not achieved up to T10 within 30 minutes. Patients were monitored every 2.5 minutes in the first 30 minutes and, subsequently, every 30 minutes once T10 block has been achieved. Charges in haemodynamic parameters and any side effects were also observed in this study.

Results: All patients had completed the study. There were no significant among 3 groups in terms of the onset and the duration of motor block. The LF group was noted to have the fastest onset of sensory block, 4.90 minutes (SD 4.49), followed by the LC group, 6.88 minutes (SD 3.94), and the LNS group, 12.88 minutes (SD 28.39). For the duration of the sensory block, the mean time needed to regress to 2 dermatome levels were longest in the LC group, at 157.43 minutes (SD 40.23), followed by the LF group, at 148.29 minutes (SD 41.57), and the LNS group, at 138.37 minutes (SD 26.04). There was a significant difference in the onset of motor block, P = 0.03. The LF group had the fastest onset, 10.96 minutes (SD 10.66), followed by the LC group, 12.32 minutes (SD 8.97); the LNS group had the slowest onset, 20.67 minutes (SD 20.61). Charges in haemodynamics were noted to be significantly different (P < 0.001). The LC group had the most changes in systolic and diastolic blood pressure. The most common side effect was hypotension; other side effects such as nausea, vomiting, and pruritus occurred in lesser numbers or none at all.

Conclusion: We onserved that the LF group had faster onset of block and that the LC group had a longer duration of block. However, these findings were not statistically significant. The drugs' combination did not show haemodynamic instability, and the treatment was associated with lesser side effects. We concluded that the effectiveness of epidural anaesthesia with 0.5% levobupivacaine had improved with adjuvant combination.

Supervisor: Dr Mahamarowi Omar

FIVE-YEAR SURVIVAL AND PROGNOSTIC FACTORS OF CERVICAL CANCER PATIENTS TREATED IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: In Malaysia, cervical cancer has become the second most common cancer after breast cancer and the fourth leading cause of death in women. The research findings are expected to help in the management of cervical cancer as well as improving the survival rate.

Objectives: The study was conducted to determine the 5-year survival and to identify the prognostic factors that influence the risk of death among patients with cervical cancer treated at Hospital Universiti Sains Malaysia.

Methods: Data from 130 patients diagnosed with cervical cancer and treated at Hospital Universiti Sains Malaysia between 1 July 1995 and 30 June who fulfilled the inclusion criteria were analysed. The study design used was a retrospective record review where patients medical records were reviewed in detail, and important information on variables of interest and patients' survival status were collected and recorded using the data collection sheet prepared by the researcher. Univariable and multivariable analyses using Kaplan–Meier product limit estimates as well as simple and multiple Cox proportional hazard regression were perfomed to determine the 5-year survival and statistical significance of the prognostic factors.

Results: Overall 5-year survival was 39%, with a median survival time of 39.83 (95% CI 31.13–48.54) months. The survival according to stage was 49.6%, 43.8%, and 16.7% for stage I, II, and III-IV, respectively. The significant prognostic factors in this study were being diagnosed at stage III-IV (adjusted HR = 2.91, 95% CI 1.81–4.68, P = 0.004) and anaemia (adjusted HR = 2.49, 95% CI 1.35–4.61, P < 0.001). Prognostic factors such as ethnicity, age at diagnosis, lymph node involvement, histological type, bleeding, distant metastases, and primary treatment were not identified as prognostic factors in this study.

Conclusion: The 5-year survival of cervical cancer patients treated at Hospital Universiti Sains Malaysia was lower compared with other studies. Our findings showed that cancer stage III-IV and presence of anaemia influence cervical cancer patients's survival. Further studies with larger sample size are needed to identify more significant prognostic factors that influence the survival of cervical cancer patients.

Supervisor: Dr Muhammad Naeem Khan Co-supervisor: Professor Dr Syed Hatim Noor THE EFFICANCY OF IV PARECOXIB SODIUM AS AN ANALGAESIC ALTERNATIVE TO IV MORPHINE IN ACUTE TRAUMA PAIN: A RANDOMISED DOUBLE-BLINDED CONTROL TRIAL

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Introduction: Pain is the most common presenting complaint in any emergency department, occurring in more than 60% of the department's patients. Most of the patients with acute pain expect rapid delivery of pain medication after initial arrival in emergency department. The ideal analgaesic should have certain characteristics such as prompt onset of analgaesic activity, ease in administration, good efficacy, and no significant interference with evaluation of the underlying disease process. Even though morphine possess almost all the ideal characteristic of analgaesia and is considered as a gold standard for emergency acute pain relief, its side effects, especially nausea, vomiting, dizziness, depression of conscious level, hypotension, and respiratory depression, have lessened its usage in polytrauma patients with head injury. Analgaesic agents, such as COX-2 inhibitors, might be used as alternatives in the acute trauma setting. Parecoxib sodium is the first parenteral COX-2 inhibitor that is comparable to intravenous morphine. The COX-2 inhibitors' effectiveness had been proven in multiple studies, although most of them were postoperative pain studies. To date, no study has been conducted in the emergency department to evaluate COX-2 inhibitors' effectiveness and safety, especially in trauma patients. Thus, this study was undertaken to open a new pathway of the drug's usage in acute care setting and emergency department.

Objectives: The objective of the study was to compare between intravenous parecoxib sodium and intravenous morphine as an analgaesic for acute traumatic pain (fracture or soft tissue injuries) in the emergency department.

Methods: A randomised, double-blind controlled trial was performed from 1 September 2008 until 30 September 2009 in the emergency department of Hospital Universiti Sains Malaysia. A total of 32 patients who presented with complaint of acute traumatic pain requiring analgesia within 24 hours of event, fulfilled the set inclusion and exclusion criteria, and had given their consent were enrolled in the study. They were divided into 2 groups: soft tissue injury and bone fracture (16 patients each arm). The patients were randomised to receive either 0.10 mg/kg of morphine sulphate (14 patients) or 40 mg of parecoxib sodium (18 patients) intravenously. None of the patients had any history of analgaesic usage in the previous 6 hours. Focused history and physical examination were carried out, and the initial blood pressure, pulse rate, oxygen saturation, numerical pain score, and weight were recorded. Periodic assessment of blood pressure, pulse rate,

oxygen saturation, numerical pain score, sedation score, and side effects were taken at 0, 5, 15, and 30 minutes after the drug administration. Patients were asked by the researcher to rate their pain intensity on a 10-point verbally administered numerical rating scale, ranging from 0 (no pain) to 10 (worse possible pain). If the numerical pain score was still more or equivalent to 6 after 30 minutes, a rescue drug (0.1 mg/kg of intravenous morphine sulphate) were given. The patients' satisfaction was assessed using the scale of "poor", "fair", "good", and "excellence". The statistical analyses, including mean, standard deviation, percentage, paired t test, and repeated measure ANOVA, were performed.

Results: All 32 patients were Malays, with mean age of 35.6 years (SD 15.61); 26 were males and 6 were females. The majority of the patients (56.3%) weighed 61-80 kg, with a total mean of 62.2 kg (SD 11.49). The mean duration between trauma and treatment was 2 hours and 20 minutes. We found that 28.2% of patients had side effects of the medication. At the end of the study, 56.2% of the patients described the drugs as good. A majority (81.2%) do not require rescue medication after 30 minutes of drug administration. There is no significant difference in the mean numerical rating score, systolic blood pressure, diastolic blood pressure, and oxygen saturation between patients treated with parecoxib sodium and those treated with morphine in either the fracture or the soft tissue injury groups. However, the difference in the mean pulse rate between patients treated with parecoxib sodium and those treated with morphine in the soft tissue injury group were significant (P < 0.05). Comparison of mean numerical rating score reduction within the groups of patients treated with parecoxib sodium and those treated with morphine revealed significant difference in both fracture and soft tissue injury.

Conclusion: This study revealed no significant difference in the reduction of mean numerical rating score between patients treated with parecoxib sodium and those treated with morphine in both groups of injury, even though the mean numerical rating score reduction was greater in patients treated with morphine (P = 0.059 in fracture group and P = 0.672 in soft tissue injury group). Therefore, intravenous parecoxib sodium can be considered as an alternative analgaesic for the treatment of acute trauma pain in the emergency department, with no acute side effects.

Supervisor: Dr Kamarul Aryffin Baharuddin MORPHOMETRIC STUDY OF PEDICLE IN THE SUBAXIAL CERVICAL SPINE (C3–C7) IN A POPULATION TREATED IN HOSPITAL UNIVERSITI SAINS MALAYSIA—COMPUTED TOMOGRAPHY STUDY

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Introduction: Cervical pedicle diameter size differs between Asians and non-Asians. The transverse diameter of the pedicle is the determinant of the feasibility of transpedicular screw fixation (TPF). It has become a standard way to stabilise the spine in scoliosis surgery, degenerative conditions, trauma treatment, tuberculous spondylitis, and tumour reconstruction surgery. A successful pedicle screw placement in the cervical spine requires adequate threedimensional knowledge in morphology of cervical pedicles. Thus, a thorough understanding of cervical pedicle anatomy is important to avoid injury to vertebral artery, spinal cord, or nerve root. Data extracted from studies of non-Asians should be used with caution because they might not be applicable for our population. Thus, a study of morphologic features of cervical pedicles in Malaysian population is important before pedicle screw fixation of cervical spine is initiated.

Objective: The study was performed to measure and compare the dimensions and axes of subaxial cervical pedicles (C3–C7) in a population treated in Hospital Universiti Sains Malaysia using reformatted computed tomography (CT) images.

Methodology: This was a cross-sectional study performed in the Department of Radiology, Hospital Universiti Sains Malaysia, from 1 January 2006 until 28 February 2009. The sample size calculated was 74: 37 males and 37 females. All images of the CT scan were selected based on inclusion and exclusion criteria. Outer pedicle width (OPW), outer pedicle height (OPH), pedicle transverse angle, α (PTA), and transverse angle of safety zone of transpedicular screwing, γ (TASZ) were measured using reconstructed CT images. The height of each patient was also obtained.

Results: The majority of subjects in this study were Malays (94.6%); the rest were Chinese (5.4%). No Indian, Siamese, or other races were encountered. The mean OPW from C3 to C7 ranged 4.23–5.98 mm in males and 3.50–5.41 mm in females. The mean OPH from C3 to C7 ranged 4.74–6.07mm in males and 4.34–5.50 mm in females. The mean TPA from C3 to C7 ranged 38.14°–54.90° in males and 38.76°–54.03° in females. The smallest TPA was at C7 in both males and females. The mean TASZ from C3 to C7 ranged 18.90°–29.15° in males and 16.58°–28.84° in females. The height of the patients significantly correlated to the mean OPH at all levels of the subaxial cervical spine.

Conclusion: We found that the OPH, OPW, and TASZ increased in a stepwise manner from C3 to C7. These measurements were larger in males than in females, and were larger on the left side than on the right side. The TPA showed an increase from C3 to C4 levels, after which it decreased at subsequently lower levels. Only OPH was significantly correlated with height of the patient.

Supervisor: Dr Rohaizan Yunus Co-supervisor: Dr Win Mar @ Salmah Jalaluddin

BREASTFEEDING PRACTICE IN INFANTS DELIVERED IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introducton: In the past, breastfeeding has been the key survival for the human species and has been a symbol of motherhood. Unfortunately, in the era of modernisation, breastfeeding was not viewed as a key factor for survival anymore, but merely part of the lifestyle and mothers' personal choice. Despite the knowledge on the benefits of breastfeeding, the incidence of breastfeeding worldwide was still low. In Malaysia, it has been 15 years from the time of the first hospital being accredited as Baby Friendly Hospital by the World Health Organization. Thus, it was an appropriate moment to re-evaluate our breastfeeding practice.

Objectives: The main objective was to determine the proportion of exclusive breastfeeding on day 1, day 5, and week 6 of life in infants delivered in Hospital Universiti Sains Malaysia. The second objective was to determine the influence of socio-demographic factors on exclusive breasfeeding at week 6 of life.

Methods: A prospective cohort study was carried out, involving 422 mothers and their infants who were delivered in Hospital Universiti Sains Malaysia from May 2007 until September 2008. This study involved mothers who had delivered to a term infant weighing 2.5 kg and above. Both mothers and infants were well and able to practice breastfeeding. Mothers were interviewed in day 1, day 5, and week 6. The interview was based on structured questionnaire built from the literature review. The day 1 interview was to get the baseline data and socio-demographic background, along with the feeding practice at that time. Subsequent day 5 and week 6 interview were conducted through telephone calls. Data were analysed using SPSS version 12 software. Statistical methods used were chi-square test or Fisher-exact test, independent *t* test, and multiple logistic regression.

Result: The proportion of exclusive breastfeeding on day 1 of life was 96.7%. However, on day 5 of life, it declined to 78.4%; it dropped further to 54.5% at week 6. The main determinant factors for exclusive breastfeeding at week 6 were practice of exclusive breastfeeding on day 5 (OR = 7.20, 95% CI 3.99–13.01), mothers who were not working outside their houses or stay-at-home mothers (OR = 2.80, 95% CI 1.78–4.38), and 13 to 24 months of breastfeeding experience involving their previous child (OR = 2.35, 95% CI 1.44–3.84). Antenatal and post-natal counseling, educational level, and socio-economic status of the mothers were not the determinant factors for exclusive breastfeeding practice at week 6.

Conclusion: The proportions of exclusive breastfeeding practice in this study, especially on day 1, have increased compared with previous studies, which dated approximately 10 years back. However, it was far from the optimum suggested by World Health Organization, particularly because of the tremendous drop in the post-hospital discharge percentage. Thus, the problem was not in the initiation of breastfeeding but due to inability to sustain it. Therefore, the community intervention is the utmost important intervention in order to ensure the continuous exclusive breastfeeding practice among the mothers.

Supervisor: Dr Noraida Ramli

EVALUATION OF METHADONE MAINTENANCE THERAPY AMONG THE INTRAVENOUS DRUG USERS IN KOTA BHARU, KELANTAN, 2005–2008

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Introduction: In Malaysia, methadone maintenance therapy was among the harm-reduction activities launched in 2005 to combact the worsening drug addiction problems. Methadone is a synthetic opiate agonist, and the methadone maintenance therapy is indicated for those who are dependant on opiates for an extended period of time.

Objectives: The objective of this study was to evaluate the effectivess of the methadone maintenance therapy in Kota Bharu, Kelantan, and the factors that influence the outcome.

Methods: A retrospective record review was carried out to collect the data on all 117 the clients who fulfilled the set criteria at Hospital Raja Perempuan Zainab II. The opiates treatment index was used to evaluate the improvement of the program. Paired t test was used to compare the composite scores at intake and at 12 months after methadone maintenance therapy. A comparison of the employment status at intake and after 12 months of the methadone programme was carried out

using McNemar test. Multiple logistic regression was used to analyse the factors influencing the employment status after 12 months.

Results: The mean age of clients in this study was 31.38 years (SD 5.35) and the majority of them are males, Malays, and unmarried. The mean scores in all the opiate treatment index domains were lower after 12 months of methadone maintenance therapy. A total of 18.7% of subjects gained employment, and there was a 32.8% increase in subjects having full-time jobs. The self-perceived health problems and social functioning score at 12 months were found to be associated with the employment status.

Conclusion: This study demonstrated that the methadone maintenance program has contributed in reducing drug use, high-risk behaviour, crime, and self-perceived health problems, as well as improving social functioning. The employment status showed positive changes. Improvements of social functioning and health influence the employment status at 12 months.

Supervisor: Dr Azriani Ab Rahman Co-supervisor: Dr Wan Mohd Zahiruddin Wan Mohamad

WORK-RELATED FACTORS OF CARPAL TUNNEL SYNDROME IN COMPUTER USERS AMONG CLERICAL STAFF IN GOVERNMENT HEALTH FACILITIES, KOTA BHARU, KELANTAN

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Introduction: Carpal tunnel syndrome (CTS) is a group of signs and symptoms that manifest when the median nerve is compressed within the carpal tunnel. Uncertainty of the local prevalence and failure to eliminate contributory factors can result in the recurrence and progression of CTS, impaired use of the hand, and the need for surgical treatment.

Objectives: The aim of this study was to determine the prevalence of CTS and its and work-related associated factors in computer-using clerical staff in government health facilities, Kota Bharu, Kelantan.

Methods: A cross-sectional study was carried out at two government health facilities in Kota Bharu, Kelantan, from January until June 2008. Prevalence of CTS and its work-related factors in clerical workers were identified. Exposure to associated factors was assessed by workers' responses in a self-administered questionnaire, anthropometric measurement, and direct observation. Disease status was confirmed by history that was suggestive to the syndrome, and provocative test performed by hand surgeon or nerve conduction study.

Data was analysed by using simple and multiple logistic regression analyses.

Results: A total of 300 workers (180 CTS and 192 non-CTS) participated in the study. The prevalence of CTS was 36.0% (95% CI 31.5–41.5). The final model included 1 personal factor (family history) of CTS and 1 work-related factor (keyboard time in hours/day). A person with family history of CTS has 9.41 times the odds to get CTS (95% CI 1.09-81.65, P=0.39) as compared to those without a family of CTS, and an increase in 1 hour/day of keyboard time has a 1.11 times the odds to have CTS (95% CI 1.01-1.23, P=0.039), when adjusted for keyboard time and family history of CTS, respectively.

Conclusion: The prevalence of CTS in computer users was high, which indicated high morbidity in this type of occupation. The relationship of keyboard time and CTS showed that CTS in computer users was work-related. Health programmes, especially health educations and promotions, should be designed based on the factors that influenced the development of CTS.

Supervisor: Dr Zaliha Ismail Co-supervisor: Dr Sarimah Abdullah

A STUDY OF SYSTOLIC HEART FAILURE IN HOSPITAL UNIVERSITI SAINS MALAYSIA: A RETROSPECTIVE COHORT REVIEW

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Introduction: There have been many heart failure epidemiological studies worldwide, but local data, especially those that are exclusively echocardiographically-driven, are lacking. We studied the demographics, underlying aetiology, prevalence of co-morbidities, and factors associated with outcome in patients with systolic heart failure.

Methods: 230 adultpatients with echocardiographically-diagnosed systolic heart failure (left ventricular ejection fraction, LVEF, of less than 50%) in Hospital Universiti Sains Malaysia between 1 January 2005 and 31 December 2008 were selected from the echocardiography registry. Their respective case notes were reviewed retrospectively, and all relevant data were recorded. Their present functional status was determined via telephone call.

Results: Majority of the patients (77.8%) were males. The mean age was 6.04 years (SD 13.6), and the mean LVEF was 34.2% (SD 8.08). Out of 230 patients, 53.9% were overweight (pre-obese and obese), 54.8% were former smokers, and 10.9% were still actively smoking. At the time

of the study, 52.2% of the patients were still alive, and 47.8% were dead. Ischaemic cardiomyopathy accounted for 81.3% of the total heart failure patients, with the remaining nonischaemic or unknown etiology. In addition, 67.0% of the patients had hypertension, 60.0% had hyperlipidaemia, 44.3% had diabetes mellitus, 13.5% had chronic kidney disease, and 53.0% had anaemia. Multivariate analysis identified increasing age (OR = 1.026, 95% CI 1.000 to 1.053, P = 0.050), the presence of co-morbidities such as diabetes mellitus (OR = 2.068, 95% CI 1.006 to 4.252, P = 0.048) and/or chronic kidney disease (OR = 3.458, 95% CI 1.131 to 10.574, P = 0.030), increasing heart rate (OR = 1.044, 95% CI 1.018 to 1.071, P = 0.001), adecreasing haemoglobin level (OR = 0.853, 95% CI 0.721 to 1.008, P = 0.062), and the use of diuretics (OR = 3.955, 95% CI 1.711 to 9.142, P = 0.001) to be associated with higher chance of death. The use of angiotensin receptor blockers (OR = 0.225, 95% CI 0.067 to 0.756, P = 0.016) and/or beta-blockers (OR = 0.276, 95% CI 0.134 to 0.571, P = 0.001) was found to be independently associated with lower chance of death. Among patients with more severe left ventricular systolic dysfunction, there was no significant increase in mortality when compared with those with only mild dysfunction (P = 0.937).

Conclusion: A great majority of patients with systolic heart failure in Hospital Universiti Sains Malaysia were males, overweight, hypertensive, and hyperlipidaemic. Ischaemic cardiomyopathy was the predominant underlying aetiology of heart failure. Increasing age and heart rate, the presence of diabetes mellitus and chronic kidney disease, decreasing hemoglobin level, and the use of diuretics were all independently associated with a greater chance of death, while the use of angiotensin receptor blockers and beta-blockers was associated with more favourable outcome.

Supervisor: Dr Suhairi Ibrahim Co-supervisor: Associate Professor Dr Zurkurnai Yusof

THE EFFECT OF PRE-INDUCTION INTRAVENOUS DEXMEDETOMIDINE ON SYMPATHOADRENAL RESPONSES DURING INTUBATION

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Introduction: Dexmedetomidine is a highly selective alpha-2 agonist agent. The provision of anxiolysis and sedation with minimal effects on respiration has led to a wide range of clinical use of this agent, from monitored anaesthetic care and adjunct in general anaesthesia to post-operative sedation.

Objectives: The aim of this study was to evaluate the effects of a single bolus intravascular dexmedetomidine of 0.6 μ g/kg, 10 minutes before induction on sympathoadrenal responses during intubation.

Methods: A prospective, randomised double-blinded clinical trial was conducted on 112 patients planned for surgery who required tracheal intubation. The study was conducted in 12 months, between August 2008 and August 2009, at the operation theatre of Hospital Universiti Sains Malaysia. The patients were randomised to receive either dexmedetomidine (n = 56) or normal saline (n = 56) 10 minutes before induction of anaesthesia. They were then induced with intravenous fentanyl 2 µg/kg, propofol at a titrating dose, and rocuronium 1.0 mg/kg. Each patient's heart rate, blood pressure, oxygen saturation, and end-tidal CO2 were recorded from the time of induction until 2 minutes after intubation. The 2 groups were of similar age, weight, and sex. The mean baseline heart rate did not differ between the dexmedetomidine (67.91 beats per minute, SD 7.744) and the normal saline groups. Similarly, the mean baseline blood pressure in both groups was not significantly different.

Results: During the process of intubation in patients who received dexmedetomidine, the mean heart rate was not raised as compared with patients who received normal saline, at 60.06 beats per minute (95% CI 52.21 to 67.91) versus 68.89 beats per minute (95% CI 62.95 to 74.84). Dexmedetomidine group also had a significant reduction in the systolic blood pressure compared with the saline group, with a mean (95% CI) of 111.16 mmHg (98.50 to 123.82) versus 116.41 mmHg (110.30 to 122.52). This pattern of reduction was also observed in diastolic blood pressure, with a mean (95% CI) of 55.46 mmHg (46.89 to 64.04) versus 57.28 mmHg (51.70 to 62.86), and mean arterial pressure, with a mean (95% CI) of 58.54 mmHg (54.12 to 62.95) versus 58.23 mmHg (54.61 to 61.84). Furthermore, their propofol requirement was also decreased by 49.99% (SD 6.55).

Supervisor:

Associate Professor Dr Wan Aasim Wan Adnan

MORTALITY PREDICTION OF INTENSIVE CARE UNIT'S PATIENTS USING SIMPLIFIED ACUTE PHYSIOLOGY SCORE (SAPS II) IN A UNIVERSITY HOSPITAL

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Introduction: Outcome prediction and quantisation of the severity of illness has become an irreplaceable tool for the estimation of effectiveness and quality of intensive care unit (ICU). One of the most widely used scoring system for the general severity of illness and prognosis is the Simplified Acute Physiology Score (SAPS). The SAPS II has been shown to accurately stratify risk of death in a wide range of disease states and clinical settings. This experience has resulted in the widespread use of the SAPS II scoring system as a tool for ICU audit.

Objectives: Our objective was to assess the ability of the SAPS II system to predict patient's outcome and to determine the various factors that contribute to the prediction in our institution.

Methods: A retrospective database study was conducted in patients hospitalised in the ICU of Hospital Universiti Sains Malaysia between 1 April 2008 and 31 Mac 2009. A total of 342 patients were included in the study. The sum of the SAPS II points was used for calculating predicted mortality for each patient. The observed death rate was compared with predicted mortality calculated by SAPS II system. The ability of SAPS II prognosis system to predict probability of ICU mortality was assessed with discrimination (receiver operating characteristic [ROC] curve) and calibration (Hosmer–Lemeshow test) measures.

Results: The majority of the patients were Malay (95.3%). There were 62 deaths in the ICU (18.1%) during this 1-year study. The result showed the death mostly occurred in between March and May (83.4%) and mainly during the weekends, on Friday and Saturday (48.1%). Except for age and temperature, all the other variables in SAPS II showed significant differences between survivors and non-survivors. SAPS II showed a good ability to separate the patients predicted to live from those predicted to die, as shown by an area under the ROC curve of 0.865. The calibration curve demonstrated this system can accurately predict the mortality of the patients (Hosmer–Lemeshow goodness-of-fit test, C = 4.922, C = 4.922,

Conclusion: SAPS II performed well in predicting the mortality rate in our ICU, and it is a useful tool for the assessment of ICU performance.

Supervisor: Dr Mohd Nikman Ahmad Co-supervisor: Associate Professor Dr Wan Aasim Wan Adnan

EXPERIMENTAL ECONOMICS: TOWARDS THE IDENTIFICATION AND CHARACTERISATION OF NON-PROTEIN-CODING RIBONUCLEIC ACIDS IN PATHOGENIC AGENT, SALMONELLA TYPHI

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Introduction: Non-protein-coding RNA (npcRNA) is large class of riboregulators that act in complex with proteins (as ribonucleoproteins) in diverse regulatory pathways.

Objectives: This thesis focus on the experimental identification of small npsRNAs from *Salmonella enterica* serovar Typhi (*S. typhi*), the aetiological agent of typhoid fever

Results: By an experimental RNomics approach, 82 species of uncategorised novel npsRNA candidates were identified from a library generated from different growth phases of a clinically isolated S. typhi. From these 82 candidates, 28 were transcribed from the intergenic regions, 29 were transcribes in the antisense orientation of the open reading frames, and 18 were identified to overlap the open reading frames. Another 7 candidates were transcribed from repetitive regions and several non-repetitive locations. Eleven known npcRNAs were also detected. Interestingly, 55 candidates exhibit homology to Escherichia coli and were not previously annotated for both organisms. Using Northern blot analysis, the expression of 38 novel npcRNA candidates was confirmed. A total of 28 novel npcRNA candidates were growth phase regulated, where 14 candidates were growth phase regulated in both S. typhi USMo5 and E. coli K12, and 11 candidates were species-specific growth phase regulated, only in E. coli K12. A total of 8 npcRNA candidates were ubiquitously expressed, with 6 candidates ubiquitously expressed in both S. typhi USMo5 and E. Coli K12. There was no species-specific ubiquitously expressed candidate observed in E. coli K12. Two out of 38 candidates were shown to be growth phase regulated and ubiquitously expressed. The different features of expression pattern observed in this study can be associated with different classes of npsRNA that they might be grouped in, namely the housekeeping and the regulatory npcRNAs. A number of novel npsRNA candidates were shown to be located close to important genes that were conserved in E. coli K12 and Salmonella species.

Conclusion: Significantly, this study has set the understanding on the importance of the specific growth conditions to the expression of npsRNAs. The next phase of

challenge is to further characterise and elucidate the functions of these new classes of small RNA molecules. Considering that such regulators may be highly expressed upon induction, these molecules may be greatly enriched in cDNA libraries prepared from the relevant growth or stress condition.

Supervisor: Professor Dr M Ravichandran Co-supervisors: Associate Professor Dr Tang Thean Hock Associate Professor Dr Suraparaju Sivachandra Raju

MORPHANALYSIS OF NASAL ZONE TRAITS USING FACE PHOTOGRAPH AND 3D-CT SCAN IMAGES OF PATIENTS/ SUBJECTS ATTENDING HOSPITAL UNIVERSITI SAINS MALAYSIA TO PROVIDE BASIS FOR SKULL/ FACIAL IDENTIFICATION

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Introduction: Skull-face morphological correlations are important, and they are applied for forensic human identification and reconstructive surgery. The nasal zone of human skull shows a greater range of easily recognisable variations in multiracial population. Previous craniofacial studies employed various methods including cadaveric dissection, comparison between radiograph or cephalogram and photograph, or the use of non-real facial feature of the dead, magnification factor in radiography, and an unknown skull. With the CT scan technology, true correlations between the nasal zone traits of the skull and the nose features of an individual can be determined.

Objectives: The study aimed to determine correlation between nasal zone traits of the skull on 3D-CT image and the nose features on 2D-face photograph image of an individual.

Methods: A cross-sectional study was conducted in HUSM over 18 months, Research Ethics Committee (Human) approval was obtained in August 2007. Sample was selected from elective cases of ICT of the paranasal sinuses with normal bone findings; 15 patients were included (8 males, 7 females) who subsequently had 8 views of face photographs using stereophotogrammetric method. A 3D-CT skull image was reconstructed and 8 measurements were recorded (n rhi, mf mf, al al, rhi ac, NSW, NFA, NFcA, and NMA). The 2D measurements (NFA, NFcA, NTA, NLA, and CA) and 3D measurement (mf_mf, n_sn_prn, and al_al) of the face photograph were recorded. A trainee radiologist and a PhD student in Orthodontic record measurements according to the guidelines as single observer. The anatomical nasal index, nasal ridge, and nose index were calculated. The observational analysis of the nose was done by the trainee

radiologist according to the figure illustration given. Statistical analysis was performed using descriptive analysis, Spearman's correlation test, and Mann–Whitney test.

Results: There are 5 nasal traits in the skull that are significantly correlated with the nasal traits in the face photograph. The nasal length correlated with the nasofacial angle (P = 0.007). The piriform aperture width correlated with the nasofacial angle (P = 0.009) and the nasal root width (P = 0.047). The nasofacial angle of the bone correlated with the nasolabial angle (P = 0.036) and the columella inclination angle (P = 0.005). The nasomaxillary angle correlated with the nose height (P = 0.012) and the nose length (P = 0.004). The nasal ridge index correlated with the nasolabial angle (P = 0.043). The anatomical nasal index correlated with the piriform aperture height (P < 0.001). There are many statistically significant correlations among the nasal traits in the face photograph. The nose height correlated with the nose length (P < 0.001), the nose width (P = 0.031) and the nose tip inclination angle (P=0.011). The nose length correlated with the nose width (P = 0.025) and the nasal tip inclination angle (P = 0.017). The columella inclination angle correlated with the nasal root width (P = 0.003), the nasolabial angle (P < 0.001). However, there is no statistically significant relationship between the nasal trait measurement for each categorised nose features.

Conclusion: The nasal traits on 3D-CT skull of an individual have many significant correlations with the nasal traits of the nose in the face photograph of the same individual. These findings can be used in future to the purpose of individual identification.

Supervisor: Associate Professor Dr Meera Mohaideen Abd Kareem Co-supervisor: Dr PT Jayaprakash

A STUDY OF RETINOPATHY AND VISUAL DISORDERS IN PREGNANCY

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Introduction: Hypertensive disorder is the most common medical complication of pregnancy and can rapidly progress to significant ocular changes especially in the retina. Hypertension has profound effects on structure and function of eye, which results in various non-blinding and potentially blinding conditions.

Objective: This study was conducted to determine the prevalence of retinopathy, the retinopathy changes, and the visual acuity in antenatal and postnatal women with hypertensive disorders in Hospital Universiti Sains Malaysia, Kubang Kerian.

Methods: This prospective study evaluated 154 pregnant women (308 eyes) at gestational period of 35 weeks and above with all types of hypertensive disorder. During antenatal and 6 weeks' postnatal periods, the patients' blood pressure and visual acuity were determined and thorough anterior and posterior segment eye examination was conducted. Data were recorded in separate forms for both antenatal and postnatal period, and both categorical and numerical analyses were performed.

Results: The prevalence rate of retinopathy in hypertensive disorders in pregnancy was 32.5%. The retinopathy changes noted during antenatal and postnatal periods were generalised arteriolar narrowing, arteriovenous nipping, silver wiring, and focal arteriolar narrowing. In addition to these changes, retinal haemorrhages, cotton wool spots, and serous retinal detachment were observed during antenatal period, and retinal hypopigmentation was observed during postnatal period. Based on Keith–Wagner–Barker classification, 50.0% of the patients were in group 1 hypertensive retinopathy, 41.0% in-group 2, 7.0% in group 3, and 2.0% in group 4. In our study, all patients had good visual acuity during antenatal (6/6 to 6/9) and postnatal (6/6) periods.

Conclusion: The prevalence rate of hypertensive retinopathy in our hospital-based study was 32.5%. The common retinal changes were generalised arteriolar narrowing, arteriovenous nipping, and focal arteriolar narrowing for both antenatal and postnatal periods. Our patients had good visual acuity during antenatal and postnatal periods.

Supervisor:
Dr Shatriah Ismail
Co-supervisor:
Dr Bakiah Shaharudin
Dr Nik Ahmad Zuky Nik Lah
Dr Zuraidah Mustari

PREVALENCE AND ASSOCIATED FACTORS OF SEXUAL DYSFUNCTION AMONG DIABETIC AND NON-DIABETIC PATIENTS IN HUSM

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Objective: The study was conducted to determine the prevalence of female sexual dysfunction among diabetes and non-diabetes women, to compare the sexual dysfunction domain in the 2 groups, and to identify the risk factors of female sexual dysfunction in both diabetic and non-diabetic group.

Methods: Data were collected from 178 diabetic women and 175 non-diabetic women in the Outpatient Clinic and the Diabetic Centre, Hospital Universiti Sains Malaysia, using

Malay-version Female Sexual Function Index. The sociodemographic characteristic, marital profile, medical illness, and husband health status of the participants were recorded. Glycaemic control was recorded based on HbA. level.

Results: The prevalence of sexual dysfunction among diabetic women was 26.4%, and among non-diabetic women, 20.0%. Arousal disorder was reported in 28.7% of diabetic women, and only 17.1% of non-diabetic women have the same problems (P = 0.040). Sexual satisfaction disorder was found in diabetic women (15.2%) and non-diabetic women (8.0%), and the difference was significant (P = 0.042). Age of more than 40 years, unhappy marriage, duration of marriage of more than 20 years, married to a husband with hypertension, and duration of diabetes of more than 10 years were the significant associated factors for sexual dysfunction among diabetic women. Among non-diabetic women, unhappy marriage, less sexual intercourse (less than 2 times per week), and presence of hypertension were the significant associated factors of sexual dysfunction.

Conclusion: The prevalence of sexual dysfunction among diabetic women was 26.4%, whereas among non-diabetic, it was 20.0%. Diabetic women significantly reported more sexual arousal and satisfaction problems compared with non-diabetic women. Associated factor for sexual dysfunction among diabetic women were age of more than 40 years, married to husband with hypertension, duration of diabetes of more than 10 years, duration of marriage of more than 20 years, and unhappy marriage. Among non-diabetic women, the associated factors for sexual dysfunction were less sexual intercourse, presence of hypertension, and unhappy marriage.

Supervisor: Dr Adibah Hanim Ismail Co-supervisors: Dr Norhayati Mohd Nor Professor Dr Hatta Sidi

A STUDY OF LUNG CANCER SURVIVAL AND ITS ASSOCIATED FACTORS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: The prognosis of lung cancer remains poor, with overall 5 year survival figures varying between 5% and 10% worldwide. Smoking is the most important risk factor for lung cancer, as supported by the epidemiologic evidence since 1950s. Smoking increases the risk of all histologic subtypes of lung cancer, as well as the rate of adenocarcinoma. Prognostic factors that independently predict survival outcome have been widely studied, such as

performance status, stage at diagnosis, histologic subtype, gender, age at diagnosis, and type of treatment.

Objective: The primary objective of this study was to determine the baseline characteristics at presentation and the survival of lung cancer patients treated at Hospital Universiti Sains Malaysia. The second objective was to determine survival and its affecting factors, and to compare our baseline characteristic of lung cancer patients with that of previous studies.

Methods: A total of 238 patients, who presented to the hospital from January 1996 until May 2008, were included in this retrospective cohorts study; 12 patients were surgically resectable (stages I, IIA, IIB, and IIIA), while 226 patients were non-surgically resectable (stages IIIB and IV). The patients were predominantly males (159 patients, 66.8%), with the overall mean age of 59.2 years (SD 11.5). Malays composed the majority of the patients at 80.7%, compared with non-Malays at 19.3%. There were 176 smokers (73.9%) and 62 non-smokers (26.1%). Among the non-smokers, 38.5% had adenocarcinoma, and 68.4% were women.

Results: Adenocarcinoma was the most common cell type in both men and women, as well as in smoker and those who had never smoked. Those patients with poor Eastern Cooperative Oncology Group (ECOG) performance status (ECOG score 2–4) had lower survival rate as compared to those with good performance status (ECOG score 0–1), with P < 0.01 and hazard ratio of 6.1. Patients who received only chemotherapy showed better survival than those who received only palliative treatment (P < 0.01 and hazard ratio of 0.11) while combination therapy of chemotherapy and radiotherapy proved to be a good prognostic factor to influence survival with a median time of 32 month (P < 0.01)

Conclusion: Overall median survival time for lung cancer patients treated at Hospital Universiti Sains Malaysia was 25 months. The performance status at presentation and the type of treatment were significant prognostic factors that influence survival in our lung cancer patients.

Supervisor: Dr Che Wan Aminud-din Hashim

A STUDY TO COMPARE THE CLINICAL AND HISTOPATHOLOGICAL REACTIONS TOWARDS BOVINE BONE HYDROXYAPATITE AND POROUS POLYETHYLENE ORBITAL IMPLANTS IN RABBIT

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Introduction: In anophthalmic patients, orbital implants are used to replace the volume lost and to improve their rehabilitation outcomes. As the bone-derived orbital

implant has not yet been studied widely, a study on locally synthesized bovine hydroxyapatite orbital implant would benefit much in terms of patient satisfaction and cost reduction.

Objective: The aim of this study was to compare the biocompatibility of bovine bone-derived hydroxyapatite (bone dHA) orbital implant and porous polyethylene (Medpor®) orbital implant in rabbits, and to compare the difference of histopathological changes and reaction towards the implants.

Methods: The bovine hydroxyapatite implant was prepared at National Tissue Bank, Hospital Universiti Sains Malaysia, Kubang Kerian. Evisceration with primary orbital implant (with either bone dHA or Medpor®) was performed in the right eye of 14 New Zealand white rabbits. Serial clinical examinations were performed at day 1, 7, 14, 28, and 42. The implanted eyes were enucleated on day 42. Histopathology assessment of inflammatory reaction and fibrovascular ingrowth were evaluated.

Results: Serial clinical examination demonstrated normal wellbeing of all subjects towards both implants. Histopathology examination revealed a significant difference in the depth of fibrovascular ingrowths in bone dHA. There was no significant different in inflammation reaction and fibrovascular ingrowth maturity in both implants.

Conclusion: Bone dHA appeared to be well tolerated. Bone dHA implant demonstrated deeper penetration of fibrovascular ingrowths compared with Medpor® implant. The inflammatory reaction and fibrovascular maturity are similar in both implants.

Supervisor:

Associate Professor Dr Shatriah Ismail Co-supervisors: Associate Professor Dr Wan Hazabbah Wan Hitam Associate Professor Dr Suzina Sheikh Abdul Hamid Dr Md Salzihan Md Salleh

EVALUATION OF ANGIOGRAPHY-INDUCED CEREBRAL VASOSPASM USING TRANSCRANIAL DOPPLER SONOGRAPHY IN PATIENTS WITH SUBARACHNOID HAEMORRHAGE

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Objective: The objectives of this study were to determine the proportion of of patients with spontaneous subarachnoid haemorrhage (SAH) who developed cerebral vasospasm following cerebral intra-arterial digital subtraction angiography (IADSA) and to identify the angiography-related risk factors that caused cerebral vasospasm following cerebral

IADSA by using the transcranial Doppler (TCD) criteria.

Methods: A prospective study was conducted over 18-month period from May 2007 until October 2008 in Hospital Universiti Sains Malaysia. A total of 8 patients above 12 years of age (5 males and 3 females; mean age 54.1 years, SD 13.1) who presented with spontaneous SAH were included in this study based on the selection criteria. They underwent IADSA examinations and mean blood flow velocity (mBFV) values of bilateral middle cerebral arteries (MCA) were obtained from the non-invasive TCD examination, which were performed within 6 hours before (as 1st TCD) and after (as 2nd TCD) cerebral IADSA. Non-ionic, water-soluble, iodinated, iso-osmolar contrast medium were used during the cerebral IADSA. The mBFV of more than 120 cm/s during the 2nd TCD examination was taken as indicator of angiography-induced cerebral vasospasm development.

Results: No patient in this study had developed angiography-induced cerebral vasospasm based on the TCD criteria, giving the rate of 0% of cerebral vasospasm. When the patients were compared according to changes in mBFV before and after IADSA, these was no statistical difference in mBFV for left and right MCA (P = 0.95 and P = 0.07, respectively).

Conclusion: This study suggested that with the use of non-ionic, iso-osmolar contrast medium combined with improved catheterisation techniques as well as application of digital technology, cerebral IADSA could be performed with a zero rate of angiography-induced vasospasm in patients with SAH. The patients were not at risk of vasospasm if radiology trainees were adequately trained and supervised by experienced angiographers. Cerebral IADSA would continue to be an important diagnostic imaging modality in managing patients with SAH in the years to come.

Supervisor: Dr Mohd Shafie Abdullah Co-supervisor: Professor Dr Jafri Malin Abdullah

PREVALENCE AND ASSOCIATED RISK FACTORS OF *CLOSTRIDIUM DIFFICILE* INFECTION IN TYPE 2 DIABETES MELLITUS PATIENTS TREATED WITH ANTIBIOTICS

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Introduction: Clostridium difficile infection (CDI) is one of the most common nosocomial infections and one of the leading causes for antibiotic-associated diarrhoea. CDI is currently on the rise, and it is associated with high morbidity and mortality, hence causing a financial impact in the healthcare system. Diabetes mellitus is associated

with increased susceptibility to infection; therefore, patients frequently receive antibiotics. These patients are at a high risk of developing CDI.

Objectives: The objectives of this study were to determine the prevalence of CDI among type 2 diabetes mellitus patients and to study the risk factors of developing CDI among these patients. We were also looking at the clinical features associated with CDI in this group of patients.

Methods: This was a cross-sectional study involving adults aged more than 30 years old with documented history of diabetes mellitus and had received antibiotics. A total of 159 patients had given their consent to participate in this study. Demographic and laboratory data were collected and recorded in a standard data collection sheet. Stool samples were collected and tested for *C. difficile* toxin. Variables were analysed and logistic regression test was used to identify significant association with CDI.

Results: A total of 159 stool samples were collected; out of these, 14 (8.8%) were tested positive for toxin A/B. Other than diarrhoea, abdominal pain was significantly associated with CDI with P = 0.001. Among antibiotic usage, imipenem and cefoperazone were significantly associated with CDI, with P = 0.006 (OR = 1.8, 95% CI 2.598 to 348.762) and P = 0.036 (OR = 9.5, 95% CI 1.163 to 76.965), respectively. Proton-pump inhibitor was also significantly associated with CDI, with P = 0.041 (OR = 13.7, 95% CI 1.110 to 169.220).

Conclusion: The prevalence of CDI in type 2 diabetes mellitus patients who received antibiotics was 8.8%. The use of imipenem, cefoperazone, and proton-pump inhibitor were strongly associated with CDI.

Supervisor: Dr Siti Asma' Hassan Co-supervisor: Dr Lee Yeong Yeh

A RETROSPECTIVE STUDY OF PERIOPERATIVE OUTCOME IN PATIENTS UNDERGOING LIVER TRANSPLANTATION IN SELAYANG HOSPITAL, MALAYSIA

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Objectives: This retrospective study was organised to evaluate the perioperative outcome in patients who underwent liver transplantation in Selayang Hospital, Malaysia.

Methods: The medical records of approximately 30 patients who underwent liver transplantation in 2002–2007 were traced and analysed for demographic details and incidences of perioperative outcome. Necessary information was charted into individual data collection sheets.

Data entry and analysis were done using SPSS version. Results were presented in the form of mean (SD). Statistical analyses were performed using descriptive and chi-square tests. Statistical significance is set at P < 0.05.

Results: In this study, we found that biliary atresia (53.3%) is the most common indication for liver transplantation in the paediatric population. There were no significant findings in the demographic data. About 90% of patients who underwent liver transplant survived and were successfully transfered out from intensive care unit; 20% of patients were transfered without serious complication. The incidence of graft dysfunction was only 3.3%, hypothermia, 30%, and sepsis, 43.3%. About 50% of recipients were successfully extubated within 24 hours; however, we could not conclude any factors that predict an increased risk for post-operative respiratory failure in liver transplant recipient. Sepsis appeared to be the only significant perioperative anaesthetic complication.

Conclusion: We were able to demonstrate a significant relationship between the development of post-operative sepsis and prolonged stay in the intensive care unit (P = 0.02).

Supervisor: Dr Shamsul Kamaruljan Hassan

FACTORS THAT DETERMINE PATIENT'S SATISFACTION POST-CORRECTIVE OSTEOTOMY OF MALUNITED PAEDIATRIC SUPRACONDYLAR HUMERUS FRACTURES

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Introduction: Patients suffering from cubitus varus due to malunited supracondylar humeral fracture during childhood may seek treatment, mainly for cosmetic reasons, yet there are not many studies conducted on the patient's satisfaction of the management of this fracture. A 3-dimensional correction is technically demanding and is associated with post-operative instability. There are contradicting evidences whether all cases require 3-dimensional correction.

Objectives: This retrospective review was performed to observe the factors that determine patient's satisfaction post-corrective osteotomy of malunited paediatric supracondylar humerus fractures.

Methods: Review of patients' records, radiological investigation, and interview of the patients and their parents were condected to gain information on the patient's clinical outcome and also their level of satisfaction on the outcome of their treatment. The hypothesis of this study is that the patient's satisfaction correlates with the adverse scar formation and varus correction rather than the lateral prominence and internal torsion.

Results: Out of the 40 patient who underwent corrective osteotomy at both centres during the stipulated time, only 14 were eligible for the study; the rest were encluded because of incomplete data or lost during follow-up. All patients underwent lateral close wedge osteotomy. The average age at osteotomy was 7.5 years. The patient's satisfaction score had a significant association with clinical outcomes score. Compiciations from corrective osteotomies are such as scar formation, lateral prominence, internal torsion, and, varus deformaty had negative correlation with patients' satisfaction score

Conclusion: In view that the surgery is essentially cosmetic, all the possible complications should be avoided by careful planning. As the results, the overrall patient's satisfaction score can be increased and the number of complications reduced. The patient's or parent's expectations should be addressed to make the procedure satisfactory and thus successful.

Supervisor: Dr Amran Ahmed Shokri

ANTI-CYCLIC CITRULLINATED PEPTIDE (ANTI-CCP) AUTOANTIBODY AS A USEFUL DIAGNOSTIC TEST FOR THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

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Introduction: Rheumatoid factor (RF) is currently used in the diagnosis of rheumatoid arthritis, and it is one of the classification criteria proposed by the American College of Rheumatology (ACR). However, RF positivity shows low diagnostic specificity because it is also present in patients with other autoimmune and infectious diseases and even in a proportion of normal healthy individuals. Another recent method of interest in the diagnosis of rheumatoid arthritis is the assay for anti-cyclic citrullinated peptide (anti-CCP) antibodies.

Objectives: The study aimed to determine the sensitivity and specificity of anti-CCP antibodies in the diagnosis of rheumatoid arthritis patients attending Hospital Universiti Sains Malaysia, using the ACR criteria as a gold standard, and to compare the sensitivity and specificity of anti-CCP and RF tests.

Methods: This was a cross-sectional study conducted from January until December 2008. The study consisted of 261 patients: 96 patients with rheumatoid arthritis (cases) and 165 patients with arthritis or arthralgia but did not fulfilled ACR criteria for rheumatoid arthritis (controls). Serum from each subject was tested for anti-CCP antibodies and IgG-RF by enzyme-linked immunosorbent assay (ELISA). However, both

tests were not done in 12 blood samples from the control group due to haemolysis. Sensitivity and specificity of the test were evaluated using the clinical diagnosis as the gold standard.

Results: The sensitivity of anti-CCP test was 69.8% and the sensitivity was 94.8% respectively. For RF test, the sensitivity was 84.5% and the specificity was 74.5%. The positive predictive value for anti-CCP was 89.3%, whereas for RF, it was 67.5%. The sensitivity and specificity of anti-CCP and RF tests were significantly different (P < 0.001).

Conclusion: Anti-CCP test has higher diagnostic specificity and positive predictive value that of RF test; however, its sensitivity was lower that of RF test.

Supervisor: Dr Adibah Hanim Ismail Co-supervisor: Dr Che Maraina Che Hussin

FACTORS INFLUENCING PERFORMANCE IN AUDITORY VERBAL LEARNING TEST (AVLT) AMONG SCHIZOPHRENIA PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: It is widely acknowledged that memory dysfunctions are of major prognostic importance for the course of the schizophrenia. Many studies have emphasised the significance of verbal memory for the functional outcome in schizophrenia. Further, a preserved capability to encode and recall verbal information is essential for the long-term efficacy of psychoeducational programmes and other psychological interventions, including cognitive-behavioural intervention, to ensure the successful transfer of newly acquired skills or knowledge into everyday life.

Objectives: This study aimed to determine the level of performance of schizophrenic patients in auditory verbal learning and memory test, and to determine the association between their performance in this test with their sociodemographic and clinical characteristics.

Methods: The study consisted of 2 stages. First, the validation of the Malay version of Auditory Verbal Learning Test (MVAVLT), followed by a cross-sectional study of factors influencing the test performance among schizophrenic patients in Hospital Universiti Sains Malaysia. The study involved 114 schizophrenic patients from in-patient and out-patient units. The following measures were taken: sociodemographic questionnaire, Brief Psychiatric Rating Scale (BPRS), and validated Malay-version Calgary Depression Scale for Schizophrenia (CDRS).

Results: The validation study showed that MVAVLT had a good validity and test-retest reliability and has been

shown to be sensitive in discriminating between normal and schizophrenic patients. In line with the previous research, schizophrenic patients performed significantly worse than healthy control in all indices measured in MVAVLT. However, the present finding were inconsistent with the previous studies where most of the sociodemographic characteristics measured in this study were unrelated to MVAVLT scores, except for occupation status and educational level. The results showed that illness duration, number of hospitalisation, medication compliance, use of anticholinergic drug, and type of antipsychotic prescribed did not have any significant association with the level of MVAVLT performance. The study did show that there was a significant relationship between severities of the illness, as measured by BPRS with the MVAVLT scores, but failed to identify a significant relationship with the depressive symptoms as measured by CDRS.

Conclusion: The present study found that schizophrenic patients performed significantly worse than healthy individuals on measures of verbal learning. Most of the patient's sociodemographic and clinical charecteristics were unrelated to the test performance except for patient's occupation status, educational level, and severities of the illness as measured by the BPRS. The screening of deficits in verbal learning and memory among the schizophrenic patients is important for early detection and treatment, since it can be helpful for clinician and psychologist in their counseling session and subsequently help patients to reduce such cognitive difficulties and their impact by using specific rehabilitation with the usage of newer antipsychotic agents.

Supervisor: Dr Zahiruddin Othman Co-supervisor: Associate Professor Dr Hasanah Che Ismail

EVALUATION OF ENERGY EXPENDITURE IN THE ACUTE CARE OF SEVERE HEAD INJURY PATIENTS: INDIRECT CALORIMETER VERSUS HARRIS—BENEDICT FORMULA

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Introduction: Management of comatose patients, especially those with severe head injury, is very crucial because secondary insults such as brain oedema, hypo- or hypertension, anaemia, and hypoxaemia may develop during this period. Such patients are managed in intensive care units and usually need ventilatory support and further neurosurgical interventions. Apart from the medical and surgical aspects of management, nutritional support plays an important role in patient's recovery. There are few literatures on head-injured patients' energy requirement or expenditure in the acute

setting. Adequate energy supply for head-injured patients is an important part of intensive care management in order to achieve optimal care and to avoid complications of hypo- or hypercaloric feeding. It is believed that patients with different grades of head injury have different energy requirements and hence different nutritional support in both acute and chronic settings.

Objectives: This study was undertaken to evaluate the energy expenditure in patients with severe head injury patients using indirect calorimeter and to compare the results to the predictive values by Harris-Benedict Equation. Specifically, we studied the difference in energy expenditure in different grades of severity of head injury based on a radiological classification of brain imaging, to compare the 24-hour energy expenditure among patients who underwent major operation or minor operation, and those who were conservatively managed in our intensive care unit. In addition, we aimed to determine the sensitivity and specificity of the Harris-Benedict formula as compared with the indirect calorimeter and to look for any association of the blood glucose levels within 24 hours post-injury with the severity of head injury according to Marshall's grading as well as with the treatment groups.

Methods: This was a prospective observational study involving severe head injury patients admitted to the Neurology Intensive Care Unit, Hospital Universiti Sains Malaysia. A total of 31 patients were selected for this study from January 2009 to March 2010 after fulfilling the inclusion criteria; they were divided into 4 groups according to severity as determined by Marshall's computed tomography grading (Marshall's grade 1-4). These patients' energy expenditures were measured by indirect calorimetry in an acute setting. The indirect calorimeter (Deltatrac II) was connected to each patient's ventilator and the measurement of energy expenditure were conducted for 24 hours. The measured energy expenditure (MEE) of each patient was compared with the predicted energy expenditure (BEE) obtained from the Harris-Benedict equation, and statistical comparisons were also made among the groups according to severity and type of treatment (major operation, minor operation, or conservative management).

Results: The lowest energy expenditure measured in this study was 740 kcal/day, and the highest was 2060 kcal/day, with a mean energy expenditure of 1498 kcal/day (SD 297). The comparable predicted value by Harris–Benedict equation was 755 kcal/day (lowest) and 2170 kcal/day (highest), with a mean of 1543 kcal/day (SD 268). By using Pearson's correlation test, there was strong positive correlation between MEE (by indirect calorimeter) and BEE (by Harris–Benedict equation), with r=0.789 and P<0.001. The mean energy expenditure in each groups of Marshall's grade 1, 2, 3, and 4 were 1440 kcal/day (SD 42), 1484 kcal/day (SD 349), 1358 kcal/day (SD 308), and 1595 kcal/day (SD 277), respectively. By using Kruskal–Wallis test, there was no significant difference of energy expenditure between these groups in the acute setting (P=0.343). The

mean energy expenditure in the major operation group was 1535 kcal/day (SD 265); in the minor operation group, 1113 kcal/day (SD 365); and in the conservative management group, 1565 kcal/day (SD 305). By using the one-way ANOVA test, there was no significant difference of energy expenditure between these treatment groups in the acute setting (P = 0.055). The lowest blood glucose level was 3.6 mmol/L, and the highest was 9.2 mmol/L, with a mean blood glucose level of 6.4 mmol/L (SD 1.4). Pearson's correlation showed no association between blood glucose level and MEE (r = 0.013, P = 0.943). The Kruskal–Wallis test and one-way ANOVA test showed that there were no significant differences of blood glucose level among Marshall's gradings (P = 0.432) and among major operation, minor operation, and conservative management groups (P = 0.830).

Conclusion: Predictive formula (Harris–Benedict equation) can be used to determine the energy expenditure and the energy requirement of severe head injury patients who are fully sedated and ventilated, in order to achieve energy equilibrium. This preliminary study showed that there was no difference in energy expenditure among groups in the severe head injury patients regardless of their brain computed tomography findings and of whether they were operated or conservatively managed in the first 24 hours of injury.

Supervisor: Professor Dr Jafri Malin Abdullah Co-supervisors: Dr Mohammed Saffari Mohammed Haspani Dr Johari Siregar Adnan

IN VIVO EVALUATIONS OF WOUND HEALING AND ANTIMICROBIAL PROPERTIES OF TUALANG HONEY USING A FULL THICKNESS BURN WOUND IN SPRAGUE DAWLEY RATS

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Introduction: A burn wound may serve as a portal of entry for colonising opportunistic microorganisms, which can affect wound healing. The effect of Tualang honey on wound healing in the bacteria-contaminated, full-thickness burn wounds was evaluated in this study.

Objectives: The study was conducted to evaluate the wound contraction, the antimicrobial properties, and the histological aspects of Tualang honey in treating full-thickness burn wounds in a rat model in comparison with chitosan gel or Aquacel Ag.

Methods: The effect of Tualang honey on wound healing in full-thickness burn wounds was evaluated in 36 male Sprague Dawley rats. The rats were randomly divided

into 3 groups (12 rats per group). The rats were anaesthetised, and 3 full-thickness burn wounds were created on each rat using a modified metal screwdriver heated using flame from blowtorch. Each group of rats was inoculated with a different organism in the burn wounds: Group A was inoculated with *Pseudomonas aeruginosa*, Group B was inoculated with *Klebsiella pneumoniae*, and Group C was inoculated with *Acinetobacter baumanii*. One wound on each rat was dressed with either Tualang honey, chitosan gel, or Aquacel Ag. The rats were subjected to the evaluation period of 3, 6, 7, 9, 12, 14, 15, 18, and 21 days, where the wound size, microbiological and histological findings were assessed.

Results: The mean wound size of the Tualang honeytreated wounds was not statistically different from wounds treated with chitosan gel or Aquacel Ag when the wounds were compared throughout the entire experiment (P > 0.05); however, comparing the mean wound size on day 21 alone revealed that the Tualang honey-treated wounds were smaller. The quantitative and semi-quantitative methods showed that there was a significant reduction in bacterial growth in wounds treated with Tualang honey compared with those treated with chitosan gel or Aquacel Ag in Group A and C. There was no significant difference in the granulation tissue formation and epidermal thickness between the Tualang honey-, chitosan gel-, or Aquacel Ag-treated wounds when they were compared throughout the study. Nevertheless, early granulation tissue formation and epithelialisation was seen in Tualang honey-treated wounds at day 14 in burn wounds infected with P. aeruginosa.

Conclusion: Overall, the clinical examination of the wounds and the histological evaluation showed that Tualang honey gave the fastest rate of healing, the least inflammatory reaction, and the most rapid neovascularisation compared with the other treatments. Tualang honey also provided good evidence of the effectiveness of the antibacterial activity of honey on burn wounds infected with *P. aeruginosa* and *A. baumanii*.

Supervisor: Professor Dr Ahmad Sukari Halim Co-supervisor: Dr Kirnpal Kaur B Singh Dr Md Salzihan Salleh

THE UTILITY OF INITIAL CHEST RADIOGRAPH IN CHILDREN PRESENTING WITH SYMPTOMS OF RESPIRATORY TRACT INFECTION AT HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Sami Mohammed Ali Al-Ashwal MMed (Radiology)

Department of Radiology School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia **Objectives:** The aim of this study was to determine the utility of the first chest radiographs in the management of paediatric patients with symptoms of respiratory tract infection at Hospital Universiti Sains Malaysia.

Methods: The institutional ethics committee approved the study, with no informed consent required. The study was conducted in 6 months. A total of 378 chest radiographs of paediatric patients presented to the Family Medicine Clinic and Accident and Emergency Department with symptoms of respiratory tract infection were reviewed using high-resolution GE Pathspeed Workstation. Radiographic changes suggestive of lung infection were recorded in a specific form. Clinical data and line of management were collected from medical records in a different setting independent of the radiographic data. Clinical data was recorded in a different form.

Results: The prevalence of abnormal radiographs was 63.5% of all radiographs, while the normal radiographs were 37.5%. The prevalence of normal radiographs in the Family Medicine Clinic was 50.8%; in the Accident and Emergency Department, 29.4%. There were significant associations between radiographic changes and of the following clinical variables: fever, shortness of breath, pleuritic pain, tachypnea, retractions, grunting, decreased breath sounds, and crackles. Cough, coryza, and wheezing did not show significant association with radiographic changes. There was significant relationship between radiographic abnormalities and patient management. The majority of patients were discharged with antibiotic therapy; 72 (52.2%) of patients with normal radiographs were discharged and given antibiotic. Only 44.9% of patients who had normal radiographs were discharged without treatment. Only 16.9% of all patients were admitted to paediatric ward for management; they showed multiple clinical findings and radiographic abnormalities.

Conclusion: There was a high rate of normal chest radiographs among the study sample. Chest radiographs were good confirmatory tool for lung infection; however, it did not influence the management in 52% of patients with normal radiographs.

Supervisor: Dr Win Mar @ Salmah Jalaluddin

THE EVALUATION OF INTERVERTEBRAL DISC HEIGHT AND LATERAL FORAMEN SIZE IN SYMPTOMATIC DEGENERATIVE LUMBAR DISEASE IN POST-SURGICAL PATIENTS

Dr Samsuddin Mat Hassan MMed (Orthopaedic)

Department of Orthopaedic School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia Introduction: Degenerative lumbar disease is major cause of chronic disability in the adult working population and a common reason for referral to a magnetic resonance imaging centre. These patients are usually presented with lower back pain and radiating pain of the leg due to compression of the nerve root by changes of the intervertebral disc height, followed by reduced lateral foramen height. These compressions could be reduced by undergoing surgical intervention.

Objective: The primary objective in this study is to determine the intervertebral disc height and lateral foramen size in symptomatic degenerative lumbar disease. We also aimed to determine the correlation of the intervetebral disc height and lateral foramen size in degenerative lumbar disease in patients who underwent surgical intervention.

Methods: This was a cross-sectional study involving patients with degenerative lumbar disease who underwent operation between January 2004 until June 2009 at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. We studied the intervertebral disc height and lateral foramen size in symptomatic degenerative lumbar disease.

Result: The mean height of right foraminal of L3–4 was 15.6 mm (SD 3.6); L4–5, 14.0 mm (SD 2.8); and L5–SI, 12.9 mm (SD 3.2). The mean height of left foraminal of L3–4 was 15.6 mm (SD 3.4); L4–5, 14.5 mm (SD 3.9); and L5–SI, 12.9 mm (SD 2.9). There were correlation between the posterior intervertebral disc height with both lateral foramen width at the level of L3–4 (r = 0.46), but not at the level of L4–5 (r = 0.24, -00.5), and L5–SI (r = 0.16, -0.08). A correlation was found between the posterior intervertebral disc height with both the lateral foramen height at the level of L4–5 (r=0.55, 0.48), but not at the level of L5–@I (r=0.22, 0.13). There was a correlation between the posterior intervertebral disc height at the level of L3–4 with the right lateral foramen height (r = 0.40), but not with left lateral foramen of L3–4 (r = 0.24).

Conclusion: In degenerative lumbar diseases, the posterior intervertebral disc height was significantly correlated to the right and left lateral foramen.

Supervisor: Associate Professor Dr Mohd Imran Yusof Co-supervisor: Dr Mohd Shafie Abdullah

CHEST RADIOGRAPH IN ASSESSING THE SEVERITY OF PULMONARY TUBERCULOSIS AMONG HIV AND NON-HIV PATIENTS

Dr Santhi Varatharaja Pillai MMed (Radiology)

Department of Radiology School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia *Introduction:* Pulmonary tuberculosis (PTB) is the most common infectious disease in developing countries, and the development of complications remains a difficult diagnostic challenge. The proportion of tuberculosis in immunocompromised hosts is especially high, and PTB is one of the leading causes of morbidity and mortality.

Objectives: The study aimed to determine the association between the chest radiograph depicting the severity of PTB and human immunodeficiency virus (HIV)-infection status (non-HIV and HIV). We also evaluated the differences in various chest radiograph appearances of pulmonary tuberculosis among the two study groups.

Methods: The study focused on adult PTB patients with or without HIV co-infection, from Hospital Raja Perempuan Zainab II, Kota Bharu. Patients who had clinical symptoms and signs of PTB with positive result in either AFB sputum smear or MTB culture were recruited in this study.

Result: Mean age of the patients in both non-HIV and HIV groups were 46.5 and 32.6 years, respectively. During pretreatment phase, 93% of non-HIV and 94% of HIV patients demonstrated abnormal chest radiograph; whereas 6 month after the recommencement of treatment, 18% of non-HIV and 31% of HIV patients demonstrated normal chest radiograph findings. There was no significant difference between the two groups in the chest radiograph severity or extent of PTB during pre-treatment (P = 0.668) and post-treatment (P = 0.135) phases. Comparison of the 2 groups showed HIV patients with PTB had higher incidences of pleural effusion (23% versus 14%, P = 0.081) and military tuberculosis (7% versus 3%, P = 0.196), although the differences were not significant. Hilar or mediastinal lymphadenopathy demonstrated significant higher incidence in the HIV group (32% versus 4%, P < 0.001), whereas in non-HIV group, there were more cases of pleural thickening (36% versus 11%, P < 0.001), bronchiectasis (16% versus 5%, P = 0.007), and lung fibrosis (41% versus 17%,P < 0.001). Lesser incidence of chest radiograph presentation with cavitations were found in the HIV group (33% versus 24%); however, there difference was not statistically significant (P = 0.177).

Conclusion: There was no statistically significant finding between the two study groups in the chest radiograph depicting the severity of PTB during pre-treatment (P = 0.668) and post-treatment (P = 0.135). This study also demonstrated significant difference between the PTB patients with and without HIV co-infection, in that there is more number of normal chest radiograph in the various chest radiograph presentations, specifically in hilar/mediastinal lymphadenopathy, in the non-HIV patients; however, pleural thickening, bronchiectasis, fibrosis, and consolidation were found more commonly in non-HIV patients.

Supervisor: Dr Nik Munirah Nik Mahdi

VISUAL ANALOGUE SCALE FOR DYSPNEA (VAS) CORRELATION WITH PEAK FLOW METER IN ASSESSING SEVERITY OF ACUTE ASTHMA

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Introduction: Asthma is a common disease presented to emergency departments; the majority of cases presented with dyspnea. Peak flow meter is a standard measurement to assess asthma severity; however, peak flow monitoring has several limitations. Peak expiratory flow is effort-dependent, therefore respitory muscle strength and patient's motivation affect the peak flow. Variation in the predicted peak expiratory flow values in the normal population is largely due to age, sex, race, height, and smoking. Researchers are trying to measure dyspnea as indicator for grading of asthma severity. Visual analogue scale for dyspnea (VAS) is a reasonable tool for measurement and monitoring of severity of asthma in individual patients, and it maybe used when more objective tests are not available. The limitation of peak flow monitoring with encouraging discovery of VAS as tool for measurement and monitoring of severity of asthma in individual patients had trigger the idea for this study.

Objective: The study aimed to quantify VAS with asthma severity and to determine whether social factors (such as age, gender, and level of education) and asthma chronicity factors (such as duration of asthma, history of admission, and regularity of asthma attack) make significant difference in VAS during acute asthma. We also aimed to determine the correlation between VAS with peak flow meter in assessing acute asthma.

Methods: This was a cross-sectional study of patients presented at Asthma Bay, Emergency Department, Hospital Kuala Lumpur. Selection of patients was made according to the inclusion and exclusion criteria. Selected patients were asked to mark a vertical line on the VAS according to their perception of dyspnea. Peak expiratory flow was also measured. The data collection forms were filled and subjected to analysis.

Results: The P values for comparison of VAS mean differences in dissimilar social and asthma chronicity factors were more than 0.05. The Pearson's correlation value was -0.212, which indicated negative correlation between VAS and peak expiratory flow (%); this was significant with a 2-tailed significance of P < 0.05.

Conclusion: There is no significant VAS mean difference within social or asthma chronicity factors. There is a poor correlation between VAS with peak flow meter.

Supervisor: Dr Rashidi Ahmad

99mTc-MIBI SCINTIMAMMOGRAPHY IN DIAGNOSING BREAST CANCER: A COMPARISON WITH MAMMOGRAPHIC FINDINGS

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Introduction: Breast cancer is the most common malignancy in women, and newly diagnosed cases are increasing each year. Scintimammography has been proposed as an adjunct to mammography to assist in the evaluation of breast lesion in patients with intermediate mammogram, to reduce the number of negative biopsies. It may also be use as an alternative in patients suspected of having breast cancer, but refused to undergo mammogram.

Objectives: The study aimed to determine the diagnosis accuracy of ^{99m}Tc-MIBI Scintimamography and mammography in diagnosing breast cancer in Hospital Universiti Sains Malaysia, by means of comparing the results with histopathological or cytological findings.

Methods: This cross-sectional study was conducted within 12 months, from October 2007 until October 2008, in Hospital Universiti Sains Malaysia. A total number of 10 patients were recruited in the study. Mammogram, followed by scintimammogram, was performed after consent was obtained from each patient. The mammogram and scintimammogram was compared with the histopathological/cytologyical report. The sensitivity specificity, positive, predictive value, negative predictive value, and accuracy were calculated.

Results: The sensitivity, specificity, and accuracy of scintimammogram were each 100%, 80%, and 90%, respectively. Scintimammogram had higher specificity than mammography, but the sensitivity was the same. No significant difference was observe in scintimammography images taken at 5 and 10 minutes (P = 1.000).

Conclusion: Scintimammograpy is useful in differentiating benign and malignant lesions and is useful as an adjunct to mammogram.

Supervisor: Dr Nik Munirah Nik Mahdi Co-supervisor: Associate Professor Dr Hasnan Jaafar

ULTRASONOGRAPHY MEASUREMENT OF INFERIOR VENA CAVA DIAMETER OF BLOOD DONORS IN HUSM. KELANTAN

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Introduction: Early detection of hypovolaemic shock is a challenge in trauma patients. Adequate resuscitation of hypovolaemic shock early in the emergency department (ED) is essential to ensure improved patients' outcome. Inferior vena cava (IVC) diameter measurement is a potential tool to diagnose hypovolaemic shock. This study examined the use of ultrasound to measure the difference in IVC diameter in blood donors, as a predictor of blood loss.

Objective: The study aimed to determine the baseline diameter of IVC in relation to factors such as body mass index, age, and sex, as well as to determine the changes of IVC diameter in donors with blood loss (during blood donation) using ultrasound by measuring the IVC diameter pre- and post-blood donation.

Methods: This was a prospective observational study involving blood donors at Blood Bank, Hospital Universti Sains Malaysia. The inferior vena cava diameters during both inspiration (IVCi) and expiration (IVCe) were measured in volunteers before and after 450 mL blood donation. Donors aged 18 years and above who agreed to participate were enrolled in this study. All examinations were performed in the supine position with the ultrasound transducer placed in a subxyphoid location. Horizontal sections of the IVC 2 cm from the right atrial point were imaged, and the maximal diameter of the IVCe and the minimal diameter of the IVCi were measured. Statistical analysis included normality test, paired t test, Wilcoxin rank test, and multiple linear regression test.

Results: There were 42 blood donors enrolled; all of them were males, with mean age 32.3 years (range 21–54). Mean IVCe measurement before blood donation was 18.49 mm (95% CI 18.23 to 18.74), and after blood donation, 16.55 mm (95% CI 16.35 to 16.76). The mean IVCi before blood donation was 17.09 mm (95% CI 16.89 to 17.30), and after blood donation, 15.62 mm (95% CI 15.43 to 15.81). The difference of IVCe before and after blood donation was 1.94 mm (95% CI 1.75 to 2.13, P < 0.001). The difference of IVCi before and after blood donation was 1.51 mm (95% CI 1.34 to 1.68, P < 0.001. No significant correlation was observed between age and IVCe (P = 0.553) as well as IVCi (P = 0.994). Similarly, no significant correlation was found between body mass index and IVCe (P = 0.601) as well as IVCi (P = 0.149).

Conclusion: There is significant association between IVC diameter before and after blood donation, as well as between age and body mass index with inferior vena cava during expiration or inspiration.

Supervisor:

Dr Nik Hisamuddin Nik Abdul Rahman

CHARACTERISTIC, ACCURACY, AND OUTCOME OF HYSTEROSALPINGOGRAM IN HUSM

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Introduction: In Malaysia, infertility affects 1 out of 7 couples. Over the decades, infertility rates in the country have been increasing between 10% and 15%. Despite this figure, awareness of this subject and its available treatments are still lacking. Many are not aware that infertility is a disease of the reproductive system that, in the majority of cases, can be treated. Tubal factor accounts for 15%-30% of infertility in all women in developing countries with high rates of pelvic inflammatory disease. Hysterosalpingogram (HSG) is an important diagnostic test in the evaluation of intrauterine abnormalities and tubal patency in the infertility workup of female patients. Many studies had been done to assess the accuracy of hysterosalpingogram as compared to laparoscopy as the gold standard. The recent study showed good concordance rate of the findings investigated by both modalities.

Objectives: The study aimed to identify the characteristics, accuracy, and outcome of hysterosalpingography in HUSM.

Methods: This was a cross-sectional study on retrospective data over a period of 6 years starting from January 2003 until December 2008. A total of 197 patients who fulfilled the inclusion criteria were studied. List of eligible patients were obtained from PACS and the patient's medical records were reviewed; data needed were entered in the data collection sheet. Reports of HSG were taken from PACS and Radiology Information System.

Results: Out of 197 patients, 171 (86.8%) were Malays, 16 (8.1%) were Chinese, 5 (2.5%) were Siamese, 1 (0.5%) was Indian, and 4 (2%) were of other races. The mean duration of infertility was 5.21 years, and the mean age was 32.38 years. More than half of the patients in our study had primary infertility (56.3%). The most common pathology detected at HSG was tubal occlusion, either one-sided or twosided occlusion (17.8% and 3.6%, respectively). The diagnostic accuracy of HSG was based on sensitivity, specificity, positive predictive value, and negative predictive value. In our study, HSG is shown to have a very high specificity (100%) and a moderate sensitivity (58.3%) in detecting tubal patency and has low sensitivity (15.38%) in the detecting pelvic pathology. A total of 12.7% of our patients were pregnant within 6 months following normal HSG examination, with 2.35 higher chances of conception than those with abnormal HSG.

Conclusion: In this study, we conclude that the diagnostic performance of HSG in the diagnosis of pelvic pathology is poor. HSG has a limited use for detecting tubal patency because of its low sensitivity; however, its high specificity makes it a useful test for ruling in tubal obstruction. It should be placed as first-line screening investigation of tubal patency. HSG has low prognostic value, and the findings at HSG do not contribute much in predicting the occurrence of pregnancy.

Supervisor: Dr Juhara Haron Co-supervisor: Associate Professor Dr Nik Hazlina Nik Hussain

PREVALENCE OF PTSD AND ITS ASSOCIATED RISK FACTORS AMONG TRAUMA PATIENTS ATTENDING ORTHOPAEDIC CLINICS AND WARDS IN HUSM AND HRPZII

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Introduction: Post-traumatic stress disorder (PTSD) is prevalent among the trauma patients in orthopaedic wards and clinics. An easy, inexpensive, and reliable screening tool is needed to screen possible PTSD symptoms in order to provide early intervention and to prevent further complication.

Objectives: This study aimed to validate the Malay version of the Treatment Summary Questionnaire (TSQ) in order to determine the prevalence of PTSD and its associated risk factors among trauma patients who attended orthopaedic wards and clinic in Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II.

Methods: This was a cross-sectional study conducted in 2 stages: the first stage was the validation of the Malay-version TSQ, and the second stage was a prevalence study. Data were collected from each of the 201 patients by using the validated Malay-version TSQ, a sociodemographic data form, and the Clinician Administered PTSD Scale (CAPS). CAPS was used as a gold standard to diagnose PTSD and for comparison with the Malay-version TSQ.

Results: Malay-version TSQ has good internal consistency ($\alpha=0.733$) and good concurrent validity with CAPS. At cut-off score of 5 or more, the sensitivity and specificity were 0.8 and 0.85, respectively. The negative predictive value was 0.96, but the positive predictive value was low, at 0.48. The prevalence of PTSD among the trauma patients was 24.9%. Fear during trauma was shown to be a significant risk factor of developing PTSD (OR = 2.41, 95% CI 1.11 to 5.20). Praying was a significantly common means used by respondents to cope with trauma. There was also significant

association between support received from professionals and PTSD symptoms.

Conclusion: Malay-version TSQ is a valid, inexpensive, and reliable tool for screening PTSD. In our study, 24.9% of trauma patients in orthopaedic wards and clinics in Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II were diagnosed with PTSD.

Supervisor: Dr Zarina Zainan Abidin

A STUDY ON *GJB2* AND *GJB6* GENE MUTATIONS AMONG MALAYS WITH NON-SYNDROMIC HEARING LOSS

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Introduction: Hearing loss is the most common congenital sensory defects in human. About 1 in 1000 neonates in the world is born with the abnormality, which may vary from mild to profound hearing loss. This condition can be caused by 2 factors: genetic and environmental factors. More than 50% of the defect is due to genetic causes. It has been proven that multiple genes are involved in non-syndromic hearing loss (NSHL), a type of hearing loss without other symptoms, which was covered in this study. Mutations in GJB2 gene have been shown to be a major role for congenital NSHL. A related gene, GJB6, which is located adjacent to GJB2, might be related and associated with NSHL.

Objectives: The objectives of this study were to identify the mutations in the 2 genes and study their associations with NSHL.

Methods: Buccal cell samples were taken from 91 NSHL patients and 91 normal volunteers in Kelantan. Polymerase chain reaction (PCR) was used to amplify the coding region of *GJB2* gene. The PCR product of *GJB2* coding region was proceeded with screening for mutations using denaturing high performance liquid chromatography (dHPLC), and mutations detected were confirmed by DNA sequencing.

Results: Eleven sequence variations including mutations and polymorphisms were found in 32 patients and 37 control subjects; however, none of the variations showed any statistically significant association with NSHL and its severity. For GJB6 XX gene coding region, the deletion was identified by multiplex PCR assay in which β-globin gene was used as the internal control. All 182 subjects were found to have no deletion of the GJB6 coding region irrespective of whether they have genetic variation in GJB2 or not.

Conclusion: It is believed that a larger sample size and screening of all regions in *GJB2* and *GJB6* as well as other related genes are necessary to verify the possible association

between the mutations and polymorphisms and the severity of hearing loss in patients.

Supervisor: Dr Zilfalil Alwi Co-supervisors: Dr Mohd Khairi Md Daud Dr Zafarina Zainuddin

A COMPARISON OF THE CORPUS CALLOSUM SIZE IN THE DEVELOPMENTALLY DELAYED AND TYPICALLY DEVELOPED CHILDREN PRESENTED IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN, KELANTAN

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Introduction: Corpus callosum is the major interhemispheric structure in the human brain crucial for unified motor, sensory, and cognitive perfomances. The thickness of the corpus callosum may reflect the abnormalities that may originate in the cerebral cortex and can act as indicator of the cerebral cortical state. When the normal development of the corpus callosum is affected, it may be reflected in the development of the motor, sensory and cognitive functions.

Objectives: The study aimed to determine and compare the size of the corpus callosum in the developmentally delayed children and typically developed children.

Methods: This was a comparative cross-sectional study of the thickness of the corpus collasum in developmentally delayed children and typically developed children. A total of 34 children with developmental delays who underwent magnetic resonance imaging of the brain were included in this study. Similar number of controls was included in this study. The thickness of the corpus callosum was measured manually. The mean and standard deviation of the corpus callosum thickness of both groups were calculated.

Results: The mean and standard deviation of the length of genu and splenium of the corpus callosum in the developmentally delayed children were significantly low than those in typically developed children (P < 0.001). The midbody of the corpus callosum showed no significant reduction in both groups.

Conclusion: There is significant reduction of the corpus callosum size in the developmentally delayed children.

Supervisor: Dr Noreen Norfaraheen Lee Abdullah

BIOCOMPATIBILITY AND ANGIOGENESIS EVALUATIONS OF BIOCHEMICAL GRADE CHITRON DERIVATIVE FILM IN RABBITS

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Introduction: of Chitosan is composed glucosamine and N-acetylglucosamine, which are constituents of mammalian tissues. Chitosan is a nontoxic, biocompatible, and biodegradable polymer, and it has been proposed for use as a topical agent in tissue repair. SIRIM Berhad has developed three new types of chitosan films: N-carboxymethychitosan (N-CMC), N,O-carboxymethylchitosan (NO-CMC), and Oligo Chito.

Objectives: This study was conducted to evaluate the biocompatibility and angiogenesis of these types of chitosan derivative films on rabbits, using implantation and partial-thickness wound models.

Methods: In implant model, empty pockets served as control, and in partial-thickness wound models, Aquacel (commercial dressing) served as control.

Results: Historical examination revealed that inflammations elicited in all chitosan derivative implants were higher than that observed in control because of the presence of the implants in tissue. However, these reactions were organised and did not deviate from the course of inflammation associated with healing process, as observed in partial-thickness wound model, rendering these materials biocompatible. Macroscopic evaluation of the dressing and wounds demonstrated that all three types of chitosan derivative films, namely O-C, N-CMC and NO-CMC, process the necessary basic attributes to be employed as wound dressing comparable to the commercial dressing, Aquacel. In angiogenesis evaluation, results of the microvessel densities demonstrated that the test materials were able to promote the angiogenesis, as higher densities were observed in chitosan derivatives compared with control in implant model, and comparable to Aquacel in partialthickness wound model. All chitosan deritative implants were also able to promote the endogenous expression of VEGF in both models. Relationship between VEGF expressions of the chitosan derivatives with their respective microvessel density and fibrous capsule thickness in the implant model showed positive correlations, except for NO-CMC, which showed no correlation in microvessel density. No correlation was observed between VEGF expression with microvessel density and granulation index in all chitosan derivatives-treated wounds, except for granulation index in Aquacel and O-C.

Conclusion: The results signify that all chitosan derivatives do promote the angiogenesis, and this process may be enhanced by VEGF or other angiogenic factors.

Supervisor: Professor Dr Ahmad Sukari Halim Co-supervisors: Associate Professor Dr Hasnan Jaafar Dr Wan Azman Wan Sulaiman

EXPRESSION OF TUMOUR MARKERS AND DETERMINATION OF MICROVESSEL DENSITY IN MNU-INDUCED BREAST TUMOUR

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Introduction: Angiogenesis plays an important role in breast tumour development. The association of this phenomenon with the expression of breast tumour markers has not been fully elucidated.

Methods: In this study, breast tumour was induced by injecting 21-day-old rats intraperitoneally with 1-methyl-1-nitrosurea (MNU) at a dose of 70 mg/kg body weight for 3 consecutive days. The breast tumours were the subjected to intratumoural angiogenesis promotiom using basic fibroblast growth factor (bFGF), or inhibition using platelet factor 4 (PF40), at dose 10 μg/tumour. The size of the tumours was monitored. The excised tumour tissues were subjected to quantitative RT-PCR for ER, PR, EGFR, c-erbB2, E-cadherin, and LR expression. Angiogenesis was determined by microuniversal density with immunohistochemical staining for FVII-RA. Histological findings showed that most of the MNUinduced breast tumours were malignant, where the cribiform type predominated the apilary type. Benign and pre-neoplastic lesions were seen mainly in tumours of size less than 1.2 cm. Promoted angiogenesis appear to have similar histological features with the control group. We noted the suppression of ductal carcinoma of no special type.

Results: It was clearly seen that tumour growth in the control group shows dependency on peritumoural and intratumoural blood vessels compared with peritumoural blood vessel. As tumour grew, there was significant increase of ER, PR, EGFR, and c-erbB2 expressions. The expressions of EGFR and c-erbB2 continue to increase irrespective of whether angiogenesis is increased or suppressed. We also noted that the invasiveness of breast tumours was increased in PF4-treated group by the decrease expression between increased MVD and overexpressions of ER, PR, EGFR, c-erbB2, and LR mRNAs and the downregulation of E-cadherin mRNA expression in the control group. This association occurs irrespective of whether the MVD is in peritumoural or intratumoural regions. There was also significant association between the peritumoural MVD and the expression of ER, PR, and LR seen in the bFGF-treated group. There was a significant association between intratumoural MVD and the expressions of ER and PR seen in the PF4-treated group.

Conclusions: Our findings have shown the reduction of blood supply to breast tumours, as illustrated by the presence of more aggressive phenotypes in the PF4-treated group, with downregulations of ER and PR in the intratumoural region. Even though tumour phenotype in the angiogenis promoted group was similar to the control group, the growth rate was faster, and this was supported by significant associations with increased expressions of ER, PR, and LR in the peritumoural region. We also noted that expressions of EGFR and c-erbB2 in promoting tumour growth and downregulation of E-cadherin were independent of angiogenesis.

Supervisor: Associate Professor Dr Hasnan Jaafar Co-supervisor: Dr Md Tahminur Rahman

A COMPARATIVE STUDY ON STUDENT'S
PERCEPTION OF EDUCATIONAL ENVIRONMENT
BETWEEN A PUBLIC AND PRIVATE MEDICAL
ASSISTANT COLLEGE, MALAYSIA

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Introduction: The educational environment is an important determinant for producing quality graduates. It also plays an important role in effective teaching and learning in an institution. Besides that, evaluation is essential to ensure that a programme in a college is following the criteria or guidelines of international standard. There is no educational environment measurement study conducted for Medical Assistant programme in Malaysia so far. It is a need to study the educational environment of Medical Assistant programme to see the standard and quality of the programme. To ensure the customers' satisfaction, it is important to get information from different aspects of a programme.

Objective: The study aimed to measure and compare the students perception of educational environment between 2 colleges.

Methods: A cross-sectional study was carried out among 123 and 52 final year students from Kolej Pembantu Perubatan Seremban and Kolej Islam Sains dan Teknologi, respectively. The perception of students towards their educational environment was measured using the Malay version of Dundee Ready Educational Environment Measurement (DREEM) tool. Ethical issues were taken into consideration during the process of implementation of the study.

Results: Total DREEM mean score for Kolej Pembantu Perubatan Seremban was lower (128.91/200) compared to Kolej Islam Sains dan Teknologi (130.07/200) with standard deviation of 16.72 and 17.70, respectively. There are 5 weak areas for Kolej Pembantu Perubatan Seremban compared with 6 weak areas for Kolej Islam Sains dan Teknologi; these need to be explored further. The total DREEM score was slightly higher in the private collage compared with the public college. However, in individual item analysis, the public college was in slightly better position than private collage.

Conclusion: The study concludes that, for both colleges, the total DREEM score ranged 101–105, which was a positive indication in the aspect of educational environment. However, there were many individual items that scored below 2.00 and need further exploration for remedial measures. In terms of educational measurement score, both the collages should learn from their weak and strong areas and take remedial measures to improve their educational environment. The small number of participants, only involving students from the final year, was identified as one of the major limitations in this study.

Supervisor: Dr Hafiza Arzuman Co-supervisor: Professor Ab Rahman Esa

EFFECTS OF COMBINED JUMPING EXERCISE AND HONEY SUPPLEMENTATION ON BONE PROPERTIES AND BONE METABOLISM IN YOUNG FEMALE RATS

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Introduction: Physical activities and nutritional factors play vital roles in the prevention of osteoporosis. However little is known about the combination effects of exercise and honey supplementation on bones.

Objective: This study was carried out to investigate the effects of combined jumping exercise, as a high impact exercise, and honey supplementation on bone properties and bone metabolism in young female rats.

Methods: In this study, 48 12-week-old Sprague Dawley female rats were divided into 4 groups: sedentary without supplementation control group (8C), sedentary with honey supplementation group (8H), jumping exercise without supplementation group (8J), and combined jumping exercise and honey supplementation group (8JH). Jumping exercise consisted of 40 jumps/day for 5 days/week at the height of 40 cm. Honey as a supplementation was given to the rats at the dosage of 1 g/kg body weight/rat/day, for 7 days/week via force feeding. After 8 weeks of experimental period, blood samples were collected in order to measure serum total calcium, serum phosphate, serum alkaline phosphatase (bone formation marker), and serum C-terminal telopeptide of type 1 collagen

(1CTP, bone resorption marker) concentrations. Right hind leg tibiae and femurs or the rats were harvested for measurements of bone mass (wet and fat-free dry weight), bone mechanical property (maximal load), and bone physical dimensions (length, mid shaft maximal and minimal diameters).

Results: Combination of jumping exercise and honey supplementation significantly increased tibial wet weight and fat-free dry weight, tibial and femoral maximal load, tibial minimum diameter, and femoral maximum diameter. We also found significant increase in serum total calcium and reduction in serum 1CTP. However, these discernable improvements in bone could not be observed with jumping exercise or honey supplementation alone.

Conclusion: From the present study, it is concluded that combination of jumping exercise and honey supplementation elicited discernabled beneficial effects on lower extremity bone properties and bone metabolism in young female rats as compared with jumping exercise, honey supplementation, and control groups.

Supervisor: Dr Ooi Foong Kiew Co-supervisor: Dr Oleksandr Krasilshchikov

COST EFFECTIVENESS IN MANAGEMENT OF OPEN FRACTURE TIBIA GRADE 3A

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Introduction: Economic analysis is one of the tools that is becoming popular among health care providers in assessing or evaluating the method of treatment, but it is less popular among orthopaedic surgeons. Considering the economic burden shouldered by our government, economic analysis should be given serious consideration in our day-to-day orthopaedic practice. One of the common fractures being managed by orthopaedic surgeons is open fracture tibia grade 3A. The standard practice in managing open fracture tibia grade 3A is early surgical intervention (debridement and stabilisation), which should be carried out within 6 hours after injury; however, this could not be practiced at all time because of many factors, especially in our government hospital set up. Due to this problem, delayed surgical intervention occurs, resulting in many complications.

Objectives: The study aimed to show it is always more cost effectiveness to treat open fracture tibia grade 3A within 6 hours after injury.

Methods: This study was conducted over a period of 2 years. The parameters studied were the cost (hospital admission fee, surgical fee, and antibiotic fee) and the time

taken for union to occur. This study was conducted at Hospital Universiti Sains Malaysia, Hospital Raja Perempuan Zainab II, and Hospital Sungai Petani. Ethical approval was obtained from the ethical committee of Universiti Sains Malaysia. The records of 128 patients who sustained open fracture tibia grade 3A were traced from the record office; 66 records belonged to those who were treated within 6 hours after injury, whereas another 64 records belonged to those treated more than 6 hours after injury. Data collected from the case records include the admission fee, surgical fee, antibiotic fee, and time to achieve union. Total cost was calculated and effectiveness was measured by time taken for union to occur. Data obtained was then analysed and conclusion made.

Results: There was a statistically significant difference in the total cost in both groups (P < 0.001). The total cost was RM73.92 (SD 29.04) in the group treated within 6 hours after injury, whereas the total cost in the group treated more than 6 hours after injury was RM 239.40 (SD 81.40). Three gross costs were analysed separately to give account for the total cost: hospital admission fee, surgical fee, and antibiotic fee. All of the three costs showed statistically significant difference from one another (P < 0.001). Another parameter compared, time taken for union, also showed significant difference (P < 0.001) in that those treated within 6 hours after injury had earlier union (19.9 weeks, SD 5.08) compared with those treated more than s6 hours after injury (35.4 weeks, SD 8.4).

Conclusion: Treating open fracture tibia grade 3A within 6 hours after injury was more cost effective than treating it more than 6 hours after injury.

Supervisor: Dr Nor Azman Mat Zin

EXPRESSSIONS OF BCL-2 AND BAX IN BREAST CANCER CELLS AND ITS BLOOD VESSELS AND THEIR ASSOCIATION WITH TUMOUR ANGIOGENESIS

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Objective: Breast cancer development and progression have been largely related to anti-apoptotic activity and angiogenesis. In relation to that, this study was designed to compare the expression of anti-apoptotic Bcl-2 and pro-apoptotic Bax proteins on the endothelial cells of blood vessel supplying the tumour and the tumour cells of invasive ductal carcinoma. In relation to that, we also compared the microvessel density intratumourally and peritumourally. The relationship between apoptotic and angiogenic activity in invasive ductal carcinoma of the breast was also studied.

Methods: A cross-sectional study was conducted from December 2007 to October 2008 with 96 cases of invasive

ductal carcinoma of breast included in the study. Tissue sections that were retrieved from archived tissue blocks were stained with immunohistochemistry stain for Bcl-2 and Bax expressions, and CD34 for microvessel density.

Results: Higher expression of Bax in tumour cells (93%) was observed compared with expression of Bcl-2 (66%), though the difference was statistically not significant. There was significant association (P < 0.001) between the expression of Bax of the endothelial cells with the expression of Bax of tumour cells, whereas the expression of Bcl-2 of the endothelial cells was inversely associated with the expression of Bcl-2 of tumour cells (P < 0.001). Our study also demonstrated that the expression of Bcl-2 of tumour cells was strongly associated with hormonal receptor status (oestrogen and progesterone receptors) of tumour cells (P = 0.003and P = 0.004, respectively). Intratumoural microvessel density was significantly higher than of the peritumoural region (P < 0.001). However, the microvessel density was not associated with the expression of pro-apoptonic Bax and anti-apoptotic Bcl-2, tumour size, tumour grade, hormonal receptor status, and overexpression of c-erbB2.

Conclusion: This study suggests that anti-apoptotic activity plays important role in breast cancer development and is associated with the hormonal receptors, oestrogen, and progesterone. The large portion of cancer cells undergoing apoptosis was directly associated with the number of endothelial cells undergoing apoptosis. Tumour angiogenesis was promoted especially at the intratumoural region. However, the angiogenic activity was independent from anti-apoptotic activities.

Supervisor: Associate Professor Dr Hasnan Jaafar

ANXIETY AND DEPRESSION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Introduction: Chronic obstructive pulmonary disease (COPD) is recognised by the World Health Organization as one of the major public health problems. Psychological disturbances, such as anxiety and depression, are recognised as the major factors that worsened the quality of life (QOL) of COPD patients.

Objectives: The aims of the study were to assess the prevalence of anxiety and depression in COPD patients and in subgroups, according to severity of COPD, and to study the associations between anxiety and depression with the psychosocial and relevant clinical factors, severity of COPD, and QOL of the patients.

Patient and Method: This is a cross-sectional study conducted at the respiratory clinic, Hospital Universiti Sains Malaysia, involving 110 COPD patients. Data were collected using self-administered general questionnaire, the Malay versions of Hospital Anxiety and Depression Scale and St George's Respiratory Questionnaire. Lung function test using spirometer was done to determine the severity of COPD. The main outcome measures were anxiety, depression, and health-related QOL of the COPD patients.

Result: Prevalence of anxiety, depression, and mixed psychological disturbance (both anxiety and depression) were 6.4%, 28.2%, and 29.1%, respectively. A higher prevalence of anxiety and depression were reported in those with more severe COPD. Among the psychosocial variables, being no longer in marriage showed a significant association with anxiety and depression in COPD. The presence of frequent exacerbations was significantly associated with depression and mixed anxiety and depression. QOL-impact and QOL-total were strongly related to depression, whereas all dimensions of St George Respiratory Questionnaire were strongly related to mixed anxiety and depression. Furthermore, deterioration in QOL pertaining to health was strongly related to anxiety and depression rather than to the severity of COPD.

Conclusion: Anxiety and depression are common in COPD patients, especially when the disease was severe. Being no longer in marriage was a single psychosocial factor significantly associated with anxiety and depression in COPD. The presence of frequent exacerbations was the only clinical factor associated with both depression and mixed anxiety and depression. Patients with more severe COPD were more likely to have anxiety and depression as compared to those with mild and moderate severity. Health-related QOL of the patients was much affected by the presence of anxiety and depression rather than the severity of COPD.

Supervisor: Associate Professor Dr Hasanah Che Ismail Co-supervisor: Dr Che Wan Aminuddin Hashim

A RANDOMISED CONTROL TRIAL ON EPIDURAL INFUSION WITH INITIAL BOLUS AND CONTINUOUS EPIDURAL INFUSION WITHOUT INITIAL BOLUS IN COMBINED SPINAL EPIDURAL ANAESTHESIA IN CAESAREAN SECTION

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Objective: The aim of this study was to compare whether continuous epidural infusion without an initial dose can decrease post-operative pain as well as continuous

epidural infusion with an initial dose. The haemodynamic changes and occurrence of side effects of both groups were explored.

Methods: A total of 118 patients were recruited. Standard anaesthetic management was provided during the pre-operative and intra-operative period. Combine spinal epidural (CSE) were performed on all patients prior to initiation of the caesarean section. The patients were divided into 2 groups. The initial dose group consisted of 59 patients who were given 4 mL of 0.2% plain ropivacaine as an initial dose through the epidural catheter 45 minutes after the spinal dose; this was immediately followed by epidural continuous infusion of 4 mL/hour of 0.2% plain ripivacaine. The remaining 59 patients were placed in the continuous dose group where 4 mL/hour of 0.2% plain ropivacaine was started for epidural continuous infusion without the prior initial dose. Haemodynamic changes consisting of heart rate and systolic, diastolic, and mean arterial pressures were charted on arrival to the operation theatre (baseline) and at 1, 3, 10, and 45 minutes after the spinal dose. All patients received the continuous epidural infusion for at least 24 hours. Postoperative pain was treated with intravenous sodium diclofenac 50 mg and 50 mL of intravenous normal saline as a first choice upon patient's request. If this was not effective, intravenous tramadol 50 mg and 50 mL of intravenous normal saline were added 30 minutes later. The usage of these medications and patients' pain scores at first skin incision, last skin stitch, and 12 and 24 hours post-operation were documented. Incidences of complications were also noted. Haemodynamic variables, pain scores, and usage of sodium diclofenac and tramadol were analysed by independent t test, whereas complication data were analysed by chi-square test.

Results: Demographic data were comparable in all groups. There was no difference in the baseline haemodynamic parameters. Both groups demonstrated a significant decrease in haemodynamic parameters at 1 minute, immediately after performing combine spinal epidural. However, all changes were transient and subsequently recovered to baseline. This study showed no significant differences of pain scores in both groups. Also, patients maintained a good pain score throughout the caesarean section. There were no significant difference in the frequency of usage of sodium diclofenac and tramadol in both groups. The mean usage of sodium diclofenac was 1.4 (SD 1.1) in the initial dose group compared with 1.42 (SD 1.2) in the continuous dose group. The mean usage of tramadol was 0.15 (SD 0.45) to 0.22 (SD 0.53) respectively. No major complications were noted.

Conclusion: Epidural initial dose was unnecessary for providing pain relief in CSE for caesarean section. CSE without initial dose was able to provide adequate anaesthesia for caesarean section and for post-operative analgaesia. However, it is still unclear whether the haemodynamic fluctuations and side effects are similar for CSE with initial epidural dose and without epidural initial dose.

Supervisor: Associate Professor Dr Kamarudin Jaalam A STUDY ON THE RELATIONSHIPS BETWEEN
CENTRAL CORNEAL THICKNESS AND RETINAL
NERVE FIBRE LAYER THICKNESS, MEAN CUP
DEPTH, AND VISUAL FIELD PROGRESSION IN
PRIMARY ANGLE CLOSURE AND PRIMARY ANGLE
CLOSURE GLAUCOMA

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Objectives: The study aimed to determine the mean central corneal thickness (CCT), the mean retinal nerve fibre layer (RNFL) thickness, and the mean cup depth (MCD), as well as the correlations between CCT with RNFL thickness and MCD, and the relationship between CCT and visual field (VF) progression in primary angle closure (PAC) and primary angle closure glaucoma (PACG).

Methods: A cross-sectional and cohort studies were conducted among PAC and PACG patients. The CCT was measured by non-contact specular microscopy. The patients were divided into thin and thick CCT groups and followed-up for 12 to 18 months to monitor VF progression by mean advanced glaucoma intervention study (AGIS) score. Heidelberg laser tomography II was used to measure the RNFL thickness and the MCD.

Results: A total of 35 eyes were studied in each group. The CCT in Asian eyes in the PAC (516.8 μ m, SD 26.0) and the PACG (509.7 μ m, SD 27.4) groups were significantly lower (P < 0.001) than in the control group (540.3 μ m, SD 27.8). PACG was associated with thinner RNFL and higher MCD, but these characteristics were not seen in PAC. The CCT was not correlated with RNFL and MCD in both PAC and PACG. There was a statistically significant increase of the mean AGIS score after 12.9 months (SD 1.7) of follow-up in PACG patients with lower CCT (P = 0.002). There was no significant increase of the mean AGIS score after similar follow-ups in the PACG patients with higher CCT and in all PAC patients. However, the CCT was not a significant factor in VF progression in PACG patients when other associated factors were considered together.

Conclusion: The PACG group has significantly lower mean CCT, thinner mean RNFL, and higher MCD compared with PAC group. The CCT is not correlated with RNFL and MCD in both PAC and PACG groups. Lower CCT is associated with VF progression based on mean AGIS score in PACG, but not in PAC.

Supervisor: Associate Professor Dr Wan Hazabbah Wan Hitam Co-supervisor: Dr Shatriah Ismail

A STUDY ON CORNEAL ENDOTHELIAL CELL MORPHOLOGY OF CORNEAL ARCUS PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Objective: Objective: The study aimed to determine the central corneal endothelial morphology among patients with corneal arcus in Hospital Universiti Sains Malaysia.

Methods: A total of 152 walk-in and warded patients who had given their consent were recruited in the study; these patients were without any previous history of intraocular surgery, intraocular trauma, glaucoma, corneal diseases, and contact lens usage. The clear-cornea group showed absence of arcus, whereas the corneal arcus group showed presence of arcus that was graded into mild, moderate, and severe under slit-lamp biomicrosciope, according to a previous unpublished manuscript. The patients' medical status of diabetes mellitus and dyslipidaemia were ascertained. A non-contact specular microscope Topcon SP 2000P was used to measure the corneal endothelial morphometric assessment of the endothelial cell would be analysed by the machine-based algorithm.

Results: The mean central corneal endothelial cell density (ECD) among the corneal arcus group was 2390 cells/ mm2 (ranged 2336-2444 cells/mm2 with 95% CI), which was statistically lower than in clear-cornea group, 2507 cells/mm2 (ranged 2413-2600 cells/mm2 with 95% CI), after adjustment to the demographic factors. However, when the corneal arcus was graded into 3 grades, the adjusted mean central ECD among the different grades of corneal arcus was statistically insignificant (P = 0.054). The adjusted mean cell size among the corneal arcus patients (422 µm², 95% CI 412 to 431) was also significantly larger than among the clear-cornea patients (403 µm², 95% CI 387 to 420). When the adjusted mean cell size among the corneal arcus was graded, only the mild-severe grade of corneal arcus showed significant results, with a mean difference of -25.3 μm² (95% CI -49.89 to -7.74). Furthermore, both means of minimum and maximum endothelial cell size were statistically significant between the clear-cornea group and the corneal arcus group prior to adjustment. These findings were, however, statistically insignificant after demographic factors were adjusted. The coefficient variation of endothelial cell size was statistically insignificant between the clear-cornea group and the corneal arcus group, and also among the different grades of cornea arcus, when demographic factors were adjusted.

Conclusion: This study showed that the corneal arcus patients had lower endothelial cell density and higher mean endothelial cell size than the clear-cornea patients. The mild and severe grades of cornea arcus also had statistically

different mean endothelial call size.

Supervisor: Associate Professor Dr Mohtar Ibrahim

TREATMENT OUTCOME OF SUPERFICIAL CEREBBRAL ABSCESS: AN ANALYSIS OF TWO SURGICAL METHODS (BURR HOLE ASPIRATION AND CRANIOTOMY EXCISION)

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Introduction: With the advance development of new and more potent antibiotics and earlier diagnosis, we are seeing less intracebral abscess in our country. However, treatment of this disease remains a challenge, as it may result in significant morbility and mortality.

Objectives: The objective of this study was to determine the association between 2 surgical methods, burr hole and craniotomy, in the treatment of superficial cerebral abscess (SCA) with survival of the patients, improvement of neurological status, radiological clearance of abscess, re-surgery, and morbidity.

Methods: This was a retrospective case review of all the patients who had undergone surgery for brain abscess in 2 hospitals, HKL and HAS, in 4 years (2004–2007); we identified 78 cases, but only 51 cases were included in the study. These patients were broadly categorised into 2 groups based on their first surgical method performed. The case notes and brain computed tomography films of these patients were analysed with respect to their clinical, radiological, surgical treatment, and outcome data. Statistical analysis was determined using chi-square tests to study these associations.

Results: Brain abscess was one of the most common type of intracranial suppurations operated in HKL and HAS from 2004 to 2007, accounting for 31.7% of surgery for intracranial infection. There was a male predominance, with male-to-female ratio of 1.8:1. The mean age was 36.6 years old. Twenty-five patients (49.0%) presented with good functional level (Modified Rankin Scale of grade 1 or 2). The source of infection was established in 80.4% of the cases, most commonly from the heart (31.4%). Only 38 out of 51 patients (74.5%) had their culture and sensitivity results available. Out of these, the pus obtained during the surgery was sterile in 22 patients (57.9%), and only 16 (42.1%) had organism isolated. Patients who underwent craniotomy showed better results initially, with 20 patients (71.4%) having significant early neurological improvement and 25 (89.3%) had satisfactory radiological clearance of the abscess following the first operation. The need for a repeat surgery was more

commonly seen in the burr-hole group (47.8%). However, 5 patients died in this series, making the mortality rate 9.8% among the surgically-treated superficial cerebral abscess. Among the 46 survivors, 40 (87.0%) were able to perform their activities of daily living and had Modified Rankin Scale of 2 or below. Chi-square test revealed a significant association between the initial surgical method used for abscess and computed tomography (P < 0.001). Hence, craniotomy excision was found to be the better surgical methods for superficial cerebral abscess compared with burr-hole aspiration, as it gave a higher rate of early neurological improvement (P = 0.004), a better clearance of the abscess (P < 0.001), and a lower rate of repeat surgery (P < 0.001). Nevertheless, there was no significant difference in the survivors in both groups.

Conclusion: The initial surgical method used was found to be associated with the treatment outcome of superficial cerebral abscess in terms of improvement in the neurological status, clearance of the abscess, and resurgery. From this study, we concluded that craniotomy and excision is probably a better surgical method in the treatment of superficial cerebral abscess compared with burn hole aspiration, as it has been shown to improve neurological status in a shorter duration, has better abscess clearance, as well as reduce rate of re-surgery.

Supervisor: Dr Johari Siregar Adnan

A RANDOMISED CONTROLLED TRIAL OF PATIENT-CONTROLLED ANALGAESIA COMPARED WITH BOLUSES OF ANALGAESIA FOR THE TREATMENT OF ACUTE PAIN IN THE EMERGENCY DEPARTMENT

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Introduction: Pain is the physiologic response to a noxious stimulus, whereas suffering reflects the perception of pain. In the emergency department, pain appears to be one of the most frequent complaints, but pain control is often suboptimal, as seen by many recent audits. The usage of patient-controlled analgaesia (PCA) has been reported to provide effective pain relief, often results in lesser opioid consumption, but gives greater patient satisfaction when compared with other techniques of analgaesia delivery. However, while there are many data regarding its usage in post-operative pain, cancer pain, burns pain, and so forth, there is very little research done regarding its usage in the emergency department.

Objectives: This study was done to compare the effectiveness of pain relief and patient satisfaction between

PCA and conventional boluses of analgaesia for acute pain of traumatic origin in the emergency department.

Methods: This study was conducted by in the emergency departments of Hospital Universiti Sains Malaysia and Hospital Kuala Lumpur over a period of 1 year. All patients suffering from acute traumatic pain (moderate to severe in intensity) were approached for consent, after fulfilling the inclusion and exclusion criteria. The patients were then randomised into 2 groups after given a bolus of analgaesia. The study group was then given analgaesia via the PCA system, whereas the control group was given the conventional method of boluses of analgaesia via titration. Pain levels were measured using the visual analogue scale, together with their vitals signs and Glasgow Coma Scale at intervals of 0, 15, 30, 45, 60, 90, and 120 minutes. Any adverse events were also noted. Finally, within 24 hours, these patients were given questionnaires regarding their experience of pain relief.

Results: A total of 37 patients were enrolled. The study showed significant difference in terms of pain relief between groups; the PCA group experiencing faster and better pain relief. No life-threatening event was encountered. The satisfaction questionnaire also revealed that the PCA group has higher level of satisfaction with the method used.

Conclusion: PCA provides a more effective pain relief and better patient satisfaction when compared with the conventional method of titrated bolus intravenous injection for the relief of traumatic pain in the emergency department setting.

Supervisor:

Dr Nik Hisamuddin Nik Abdul Rahman

THE OUTCOMES OF ISOLATED THORACOLUMBAR BURST FRACTURES WITHOUT NEUROLOGICAL DEFICIT: COMPARING BETWEEN OPERATIVE AND NON-OPERATIVE TREATMENTS

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Introduction: Thoracolumbar fractures make up 40% of all spine fractures, usually arising from high-energy trauma. This is includes the region from thoracic 11 to lumbar 2 vertebrae. The thoracolumbar junction is situated between the rigid thoracic spines, predisposing it to injury. The treatment for burst thoracolumbar fractures with no neurological deficit has always been a controversy.

Objectives: The study aimed to evaluate the functional outcomes in operative versus non-operative treatment in thoracolumbar burst fractures at a single level, with no neurological deficit.

Methods: The study was conducted over the period of 1 year; the parameters studied were pain, time taken to return to previous job, and progression of Kyphotic deformity. This study was conducted at Hospital Tengku Ampuan Afzan, Kuantan, Pahang, and Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. Discharged records were traced from both hospitals. All cases fulfilling the set criteria were analysed after obtaining informed written consent. A total of 15 cases, 10 treated non-operationally and 5 treated operatively, were included in the study. Data including kyphotic index were collected from radiographs at 3 intervals: before treatment and 6 and 12 months after treatment. Pain score at 12 to 16 months post-treatment was measured using the visual analogue score. Time, in months, to return to job was also noted. Data obtained were analysed and conclusion made.

Results: No significant difference of pain at 12 to 16 months was observed in patients treated non-operatively versus operatively (P = 0.263). In terms of kyphotic deformity reduction, the operated cases fared better than the non-operated cases (P = 0.020). However, the time taken to return to work was less in the non-operatively treated cases (P = 0.031).

Conclusion: Isolated burst thoracolumbar fracture with no neurological deficit had better short-term functional outcome when treated non-operatively.

Supervisor: Dr Abdul Halim Yusof

COMPARISON OF INTRACEREBRAL AND SYSTEMIC HAEMODYNAMICS IN SEVERE TRAUMATIC BRAIN INJURED PATIENTS RECEIVING DEXMEDETOMIDINE OR PROPOFOL AS SEDATIVE AGENT

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Introduction: Sedation in neurosurgical intensive care unit is crucial, as the practice does not merely overcome patient's anxiety and facilitate ventilation, but it may prevent deleterious changes in intracranial pressure and cerebral perfusion pressure.

Objective: The aim of this study was to test the efficacy of dexmedetomidine, compared with propofol, for sedation in severe traumatic brain injured patients. This study focused on the effects of dexmedetomidine, compared with propofol, on the cardiovascular haemodynamics, cerebral haemodynamics, and sedation on severe traumatic brain injured patients.

Methods: A prospective and randomised trial was conducted on post-craniectomy patients with severe traumatic

brain injury who were ventilated in neurosurgical intensive care unit. A total of 30 patients were randomised to receive either dexmedetomidine (n=15) or propofol (n=15). The infusion rate was titrated to achieve bispectral index (BIS) of 60 to 70. Cardiovascular and cerebral haemodynamics, analgaesic requirement, and extubation time were measured and compared.

Results: Demographic data were comparable in both groups. Titration of sedation in both groups was able to achieve the same mean Sedation–Agitation Scale and mean BIS. There were no significant differences in mean blood pressure, mean arterial blood pressure, intracranial pressure, and cerebral perfusion pressure between dexmedetomidine and propofol groups. Heart rates were found to be significantly lower in the dexmedetomidine group (58.08 beats per minute, 95% CI 51.54 to 64.62) compared with the propofol group (77.06 beats per minute, 95% CI 70.52 to 83.60), with P < 0.01. The analgaesic requirement were marginally lower in the dexmedetomidine group compared with in the propofol group (P = 0.06). There were no differences in terms of extubation time between the 2 groups.

Conclusion: This study showed that dexmedetomidine was comparable to propofol in the provision of sedation in post-craniectomy in severe traumatic brain injured patients. Dexmedetomidine was comparable in terms of cardiovascular and intracerebral haemodynamics, except that patient treated with dexmedetomidine has lower heart rates. There was also reduction in the needs for additional analgaesia with dexmedetomidine, although this observation was not statistically significant.

Supervisor: Dr Ahmad Nizam Alias Co-supervisor: Dr Wan Mohd Nazaruddin Wan Hassan

ASSOCIATION BETWEEN COMMON ALLERGENS AND SYMPTOMS AMONG ALLERGIC RHINITIS PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN

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Introduction: Allergic rhinitis is one of the most common manifestations of clinical diseases following exposure to allergens. It is also the most common form of atopic disease in primary care practice, affecting 10% to 25% of the general population. In Allergic Rhinitis and Its Impact on Asthma (ARIA) criteria, allergic rhinitis is clinically defined as a symptomatic disorder of the nose induced by immunoglobin E (IgE)-mediated inflammation after allergen exposure to the

membrane of the nose. IgE-mediated inflammation is also the mechanism of underlying atopic allergies (e.g., asthma and atopic dermatitis), systemic anaphylactic reaction, allergic urticaria (hives), as well as helminthic infection.

Objectives: The study aimed to evaluate the prevalence of common allergens and the symptoms among allergic rhinitis patients. Specific IgE level was measured to evaluate its association with the severity of allergic rhinitis symptoms.

Methods: This cross-sectional study was conducted from January to December 2007 involving 128 patients from the Otorhinolaryngology-Head and Neck Surgery Clinic, Hospital Universiti Sains Malaysia. All patients who fulfilled the inclusion and exclusion criteria and had given their written consents were recruited. Interviewer-guided questionnaire was administered to gather information from each patient. Blood samples were taken and analysed for IgE specific to 28 allergens: soybean, cow milk, egg white, egg yolk, shrimp, crab, tuna, chicken, beef, citrus, wheat, peanut, cat, dog, cockroach, house dust mites (Dermatophagoides faraine and Dermatophagoides pteronyssinus), house dust, latex, Candida, Mucor, Aspergillus, Penicillium, Cladosporium, Alternaria, Bermuda grass and Johnson grass. The blood was analysed by using chemiluminescence assay. Low positive class was defined as 1 or less, and high positive class was defined as 2-4.

Results: In univariate analysis, house dust mites, D. farinae (75.8%, 95% CI 68.0-83.0), was the most common allergen in the aeroallergen group, followed by D. pteronyssinus (64.8%, 95% CI 56.0-73.0), and house dust (33.6%, 95% CI 25.0-42.0). Among the food allergen group, shrimp (28.9%, 95% CI 21.0-37.0) was found to be the most common allergen, followed by soybean (26.6%, 95% CI 19.0–34.0), crab (23.4%, 95% CI 16.0-31.0), clam (22.7%, 95% CI 15.0-30.0), wheat (21.9%, 95% CI, 15.0-29.0), peanut (20.3%, 95% CI 13.0-27.0), egg yolk (18.1%, 95% CI 12.0-26.0), cow's milk (18.0%, 95% CI 11.0-25.0), citrus mix (18.0%, 95% CI 11.0-25.0), beef (14.1%, 95% CI 8.0-20.0), egg white (12.5%, 95% CI 7.0-18.0), tuna (11.7%, 95% CI 6.0-17.0), and chicken (11.7%, 95% CI 6.0-17.0). Among the fungal allergen group, Aspergillus (23.4%, 95% CI 16.0-31.0) was the most common allergen, followed by Candida (20.3%, 95% CI 13.0-27.0), Alternaria (16.4%, 95% CI 10.0-23.0), Mucor (14.8%, 95% CI 9.0-21.0), Penicillium (12.5%, 95% CI 7.0-18.0), and Cladosporium (10.9%, 95% CI 5.0-16.0). Meanwhile, for animal allergen group, cockroach (49.2%, 95% CI 40.0-58.0) was found to be the most common allergen, followed by cat (44.5%, 95% CI 35.0-53.0), and dog (43.0%, 95% CI 34.0-52.0). The prevalence of latex allergy was 42.2% (95% CI 33.0-50.0). Allergy to Barmuda grass (28.9%, 95% CI 21.0-37.0) was found to be more common than allergy to Johnson grass (21.9%, 95% CI 15.0-29.0). Regarding the symptoms, sneezing (99.2%, 95% CI 98.0-100.0) was found to be the most common clinical symtomps among allergic rhinitis patients, followed by rhinorrhoea (94.5%, 95% CI 91.0-99.0), nasal or eye itchiness (94.5%, 95% CI 91.0-99.0), and nasal

obstruction (86.7%, 95% CI 81.0–93.0). Most patients had moderate–severe allergic rhinitis (53.9%), while the remainder (46.1%) had mild reactions. Chi-square analysis showed that there were significant associations between the specific IgE class and the severity of symptoms for house dust mites, D. farinae (P = 0.038), D. pteronyssinus (P = 0.039), cockroach (P = 0.038), cat (P = 0.042), and latex (P = 0.044). However, there was no significant association between the specific IgE class and the severity of symptoms for other allergens.

Conclusion: This study showed that the most common allergen in allergic rhinitis patients was from aeroallergen group (*D. farinae*). Sneezing was found to be the most common clinical symptoms, and majority of the patients had moderate to severe allergic rhinitis symptoms. There were significant association between the specific IgE class and the severity of allergic rhinitis symptoms for house dust mites, cockroach, cat, and latex. However, there was no significant association between the specific IgE class and the severity of symptoms for other allergens.

Supervisor: Dr Nurul Khaiza Yahya

THE VALIDATION OF THE TRANSLATED, MALAY-VERSION ATTENTION DEFICIT HYPERACTIVITY DISORDER RATING SCALE-IV (ADHD RS-IV) AS A SCREENING TOOL FOR DETECTION OF ADHD AMONG PRIMARY SCHOOL CHILDREN AGED 7 TO 12 YEARS IN KOTA BHARU

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Introduction: Attention-deficit hyperactivity disorder (ADHD) is the most commonly diagnosed childhood disorder. It is charecterised by behaviour disturbances and poor attention. They may present with either hyperactive-impulse or inattention. ADHD affects children in their mental and physical development. Thus, early diagnosis of ADHD helps the patients and their family significantly. ADHD Rating Scale-IV (ADHD RS-IV), originally developed by Dr George J Du Paul, is a set of 18-item scale to be completed by the parents and teachers of 4- to 20-year-old respondents. To date, there is no validated Malay version of the rating scale to screen ADHD. Currently, the condition is diagnosed based on the Diagnosis and Statistical Manual of Mental Disorder, 4th edition (DSM IV-TR)'s criteria. This study will help to screen ADHD among schoolchildren before being seen by child psychiatrists. The availability of the validated Malay version of ADHD RS-IV can help in further researches on ADHD to be conducted in Malaysia.

Objectives: The study aimed to validate the Malay version of ADHD RS-IV as a screening tool for detection of ADHD, and to determine the rate of possible ADHD cases among primary school children aged 7 to 12 years old in Kota Bharu.

Methods: Phase 1 was essentially a cross-sectional study conducted from August 2007 until September 2008 at the Child Psychiatry Clinic, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. In this phase, the ADHD RS-IV questionnaire underwent forward and backward translation. The reliability and validity of the translated, Malay version of the questionnaire were determined. A total 30 patients were used for test-retest reliability within the interval of 1 week. Result from 68 children with ADHD and 136 children without ADHD was analysed for internal consistency, factor analysis, sensitivity, and specificity; ADHD samples were taken from the clinic, whereas non-ADHD samples were taken from a primary school in Kota Bharu. The instruments used were the DSM IV-TR criteria and the ADHD RS-IV. Phase 2 was a descriptive study to determine the rate of possible ADHD cases, and the samples were taken from 1259 pupils and 566 teachers from 10 primary schools in Kota Bharu. The subjects were randomised using systematic random sampling. The rate of possible ADHD cases was determined using the validated Malay version of ADHD RS-IV. Data were analysed using SPSS version 12.

Result: The translated, Malay version of ADHD RS-IV showed consistent indication with the original version. The realibility study showed that the intraclass correlation coefficient of 0.67 (95% CI 0.535 to 0.799) for the home version. Internal consistency showed a good result, with Cronbach's alpha of 0.939 for the home version and 0.944 for the school version. Factors analysis revealed 2 domains, which was indentified as inattention and hyperactivity—impulsivity subtype. The cut-off score for the home version of the translated Malay version of ADHD RS-IV was 23.5, with 83% sensitivity and 84% specificity. The effect size of translated, Malay version of ADHD RS-IV was 0.56. The rate of possible ADHD cases among primary school children in Kota Bharu was 6.9%.

Conclusion: The translated, Malay version of ADHD Rating Scale-IV was a valid and reliable tool for screening of ADHD children.

Supervisor: Associate Professor Dr Mohd Jamil Yaacob

EFFECTS OF ADJUVANT HONEY THERAPY ON DISEASE ACTIVITY, LYMPHOCYTE FUNCTION, AND LYMPHOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Systemic lupus erythematosus (SLE) is a prototype autoimmune disease that can affect many tissues and organs of the body. Current treatments with anti-inflammatory and immunosuppressive drugs are able to suppress disease activity, but they are also associated with significant short-term and long-term side effects. Honey has been shown to have anti-bacterial and anti-inflammatory properties. However, the role of honey in autoimmune diseases has not been elucidated. We studied the effects of honey, as an adjuvant to conventional treatment, in disease activity, and its immunological effects on lymphocyte subsets and function.

Objectives: The study aimed to compare the effects of adjuvant honey therapy versus conventional therapy alone on disease activity, to determine the effects of adjuvant honey therapy versus conventional therapy alone on lymphocyte subsets and function in SLE patients.

Methods: This was a prospective randomised study. Sixty SLE patients were randomised into two groups: group 1 receiving conventional treatment with low dose of steroid and cyclophosphamide or azathioprim, and group 2 receiving the same treatment with the addition of honey (20 g) twice a day. Disease activity was measured in all patients every 3 months by means of SLE Disease Activity Index (SLEDAI) score and the levels of C3, C4, antinuclear antibody (ANA), dsDNA antibody, and C-reactive protein (CRP). The function of T lymphocyte was determined at baseline and after 6 months by measuring the expression of 3 lymphocyte-activation markers (HLADR, CD45RO, and CD25) using flow cytometer. Enumeration of lymphocyte subsets (CD3, CD4, CD8, CD19, and CD16/56) was done by immunofluorescence staining method using flow cytometer at baseline and after 6 months.

Results: SLEDAI score was significantly decreased in the group 2 compared with group 1 after 3 and 6 months of follow-up (P < 0.0001, P = 0.023, respectively). C3 and C4 showed significant increases within group 2 (P = 0.002, P = 0.017, respectively). The level of dsDNA antibody decreased significantly within group 2 (P < 0.05). CRP level was significantly decreased within group 2 compared with group 1 after 6 months follow up (P = 0.016). For ANA titre, the mean differences between the groups after 3 and 6 months follow-ups were statistically not significant. For the expression of lymphocyte activation markers, there were significant decreases in the expression of CD8CD45RO and CD8CD25 within group 2 compared with group 1 after 6 months follow-up (P = 0.04, P = 0.021, respectively). Regarding lymphocyte

subsets, there were significant increases in CD3 and CD16/56 percentages in group 2 after 6 months follow-up compared group 1 ($P=0.021,\ P=0.038,$ respectively). Patterns of increment for CD4 and of decrement for CD8 and CD19 were observed in group 2, but the changes were not statistically significant.

Conclusion: The use of honey therapy as adjuvant to conventional treatment in patients SLE was found to be useful in suppressing disease activity and enhancing lymphocyte subsets and functions.

Supervisor: Associate Professor Dr Kamaliah Daud Co-supervisors: Dr Che Maraina Che Hussin Dr Azreen Syazril Adnan

A STUDY ON THE EFFECTIVENESS OF NEW FOOD BASKET BY MINISTRY OF HEALTH, MALAYSIA, IN THE REHABILITATION OF MALNOURISHED CHILDREN PROGRAMME IN KELANTAN

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Objective: The study was conducted to compare the effectiveness of new food basket programme with the previous food basket programme by the Ministry of Health, Malaysia, for malnourished children in Kelantan by observing the progress of nutritional status of these children aged 1–5 years old.

Methods: Anthropometic measurements, nutritional intake details, and food basket information were taken from 97 children who were the recipients of the new food basket, whereas the control group district allocated the previous food basket to 101 children. Knowledge, attitude, and dietary practices of the parents or caregivers were also assessed.

Results: Anthropometric measurements demonstrated that the mean z score of weight-for-height had improved after intervention in both groups. Mean z scores in the intervention group had improved from -2.79 to -2.60 (P < 0.001); likewise, the control group had also shown improvement from -1.90 to -1.67 (P < 0.001). Z score for weight-for-age and weight-for-height also improved in the intervention and control groups, with mean z score of -2.69 to -2.50 (P < 0.001) and -1.73 to -1.54 (P < 0.001), respectively. However, there were no significant improvements in height-for-age in both groups. Comparison of anthropometric outcomes between both groups showed no significant difference in weight-for-age (0.04; -0.9, 0.17; at 95% confidence interval). Dietary intake of calories, protein, fat, vitamins, and minerals exceeded the levels of Recommended Nutrient Intake for Malaysia. However, intake of calcium and vitamin A were below the recommended levels. According to food preferences in the new food basket, it was revealed that respondents prefered sweet biscuits to family cereals. Generally, level of knowledge of all respondents assessed was good. However, there are significant difference between intervening district (Tumpat) and control district (Pasir Mas) by taking into consideration of its education factor. Most of the respondents had a positive perception on nutrition. However, only 25% of respondents had positive view in monitoring their children weight.

Conclusion: Overall, this study revealed that there was no significant difference in the measured indicators between recipients of new food basket and the old ones. Food type was not found to be a major factor in the improvement of nutritional status of malnourished children. Malnourishment is caused by various socioeconomic factors, such as caregivers' nutrition knowledge, household income, and household size. Co-operation with other ministries and non-governmental bodies is believed to improve nutritional status among malnourished children.

Supervisor: Dr Wan Nudri Wan Daud Co-supervisor: Professor Dr Zulkifli Ahmad

INFLUENCE OF CYPD2D6 POLYMORPHISM ON THE CLINICAL OUTCOME OF PATIENTS WITH SCHIZOPHRENIA

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Introduction: CYPD2D6 enzyme is involved in the metabolism of many centrally acting as well as cardiovascular drugs, and polymorphism of *CYPD2D6* gene has been reported in the literature. Dopamine D2 receptor gene (*DRD2*) is another candidate gene implicated in the efficacy of antipsychotic drugs.

Objective: The study aimed to develop PCR methods for detection of *DRD2* polymorphisms and to investigate the association of the *CYPD2D6* and *DRD2* polymorphisms with the treatment outcome in patients with schizophrenia.

Methods: The protocol for the study was approved by the Research and Ethical Committee, Universiti Sains Malaysia, Kelantan, Malaysia. The subjects were patients with schizophrenia (DSM-IV) on antipsychotic treatment or had been treated with antipsychotic drugs in the past. Written informed consent was obtained from the subjects after full explanation of the study procedure. The selected patient was then called for interview and further assessment. The psychopathological severity was evaluated using the Positive and Negative Symptoms Scale (PANSS). The extrapyramidal

side effects and akathisia were assessed with the Simpson–Angus Scale (SAS) and the Barnes Akathisia Rating Scale (BARS), respectively. DNA was extracted from blood taken from the patients, using salting out procedure, and subjected to PCR-genotyping. Specific primers were designed to develop PCR methods for detection of polymorphisms. The PCR methods were specific and sensitive to detect *CYPD2D6* and *DRD2* genotypes. These methods were used for genotyping analysis of 156 subjects enrolled in this study of *CYPD2D6* and *DRD2* polymorphisms.

Results: The frequencies for *CYPD2D6*1*, *4, *5, *10, and *DRD2* duplication were 39.1%, 1.3%, 3.8%, 46.8%, and 3.2%, respectively: while *CYPD2D6*3*, *6, *14, and *17 were absent. The frequencies for *DRD2* variants *Ser310*, *Cys311*, *Taq A1*, -141C *Del* and -241G were 0.3%, 3.2%, 42.3%, 14.7%, and 17.6%, respectively. There was no patient tested positived for *Ala96*, *Leu141(T)*, and *Ile154* variants. We founds that *CYPD2D6* polymorphism was significantly associated with subtotal negative PANSS scores than those without the *Cys311* allele. We also found that *CYPD2D6* and *DRD2* polymorphisms were not related to the side-effects of antipsychotic therapy as well as the SAS and BARS score.

Conclusion: The results suggested that *CYPD2D6* and *DRD2* polymorphisms may have implications in the treatment and the occurance of neuroleptic-included side-effects. Therefore, CYPD2D6 and DRD2 polymorphisms may be a predictor for the treatment outcomes of patients with schizophrenia.

Supervisor: Professor Dr Mohd Razali Salleh Co-supervisor: Dr Teh Lay Kek

COMPARISON BETWEEN VISCOUS LIGNOCAINE AND RECTAL DICLOFENAC FOR IMMEDIATE POST-OPERATIVE ANALGAESIA IN PAEDIATRIC TONSILLECTOMY

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Introduction: Tonsillectomy is a common surgical procedure in children. Pain after tonsillectomy is inevitable and causes not only distress, but also dehydration, difficulty in eating, and delayed post-operative recovery. Previous studies in the paediatric population have demonstrated a significant decrease in post-operative pain and morbidity by using local analgaesic, but the effectiveness in relieving pain has not been formally assessed, and there is no study done using viscous lignocaine for the pain reduction following tonsillectomy. It is very important to determine if topical drug can replace

other form of medication in the management of immediate post-operative pain.

Objective: The goal of this study was to find out the effectiveness of viscous lignocaine for immediate paediatric post-tonsillectomy pain in comparison to rectal diclofenac. Specific objectives of the study include determining peri-operative viscous lignocaine effectiveness in reducing immediate incisional pain in tonsillectomy patients, using visual analogue score (VAS), and observing the reduction in post-operative analgaesic requirement as a rescue analgaesic in paediatric tonsillectomy patients. The study was also performed to assess the ability of the patients to start oral feeding following tonsillectomy.

Methods: In this study, 130 patients aged between 5 to 12 years old were randomly allocated into 2 groups to receive either viscous lignocaine or rectal diclofenac as post-operative analgaesic, using computer generated simple random sampling. 65 patients were assigned into group A (viscous lignocaine), and the remaining 65 were assigned into group B (rectal diclofenac). Group A was given 3 mL of viscous lignocaine 2% or maximum of 4 mg/kg body weight whereas group B was given rectal diclofenac 1 mg/kg. All patients will be pre-oxygenated with oxygen and induced with intravenous fentanyl 1.5 μg/kg, propofol 2 mg/kg, and rocuronium 0.5 mg/kg as muscle relaxant. In the recovery room, vital signs were charted and pain assessment was done using VAS at 0.5-hour and before discharge to ward. In the ward, patients were then followed-up for 24 hours by Acute Pain Service team, and the time of oral feeding resumption and the total rescue medication is recorded at 1-hour, 2-hour, 4-hour, 12-hour, and 24-hour. If the patients complained of intolerable pain, rescue medication, intravenous pethidine 0.5 mg/kg, will be given, and the time, the frequency, and the total doses will be recorded at the same time interval.

Results: All 130 patients completed the study. The result showed that, although not statistically significant (P=0.479), the VAS score was lower in viscous lignocaine group at the first 4 hours post-operation. Haemodynamically, the mean arterial pressure was significantly reduce in viscous lignocaine group after 4-hour (P=0.043), at 12-hour (P=0.040), and at 24-hour (P=0.044). The dose of rescue medication was significantly reduced at 2-hour post-operation (P=0.023), and the dose was also reduced at 4-hour post-tonsillectomy. The time for resumption oral feeding were also significantly reduced for oral fluid and oral soft diet in viscous lignocaine group (P=0.016) and P=0.007, respectively).

Conclusion: From our study, we conclude that viscous lignocaine is comparable to rectal diclofenac for post-tonsillectomy analgaesia in paediatric patients. Viscous lignocaine significantly reduced immediate post-operative pain and resulted in early return of oral feeding. Thus, it is concluded that viscous lignocaine is safe and can reduce the unnecessary complication of systemic analgaesia.

Supervisor: Associate Professor Dr Wan Aasim Wan Adnan

ANXIETY, DEPRESSION, FEMALE SEXUAL DYSFUNCTION IN WOMEN SEEKING INFERTILITY TREATMENT IN TWO MALAYSIAN HOSPITALS

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Introduction: Infertility is defined as inability to conceive after 1 year of unprotected sex. It is associated with substantial level of stress. Previous literature has reported that infertile women reported higher level of depressive and anxiety symptoms than women in the fertile population did. Another consequence that has been reported in the infertile women is increased level of sexual dysfunction; studies have reported that infertile women have an increased risk of developing sexual dysfunction compared with in controls.

Objectives: The aim of the study was to determine the prevalence of anxiety, depression, and sexual dysfunction in women seeking infertility treatment. This study also aimed to determine the association between anxiety, depression, and reproductive characteristics in women seeking infertility treatment and to determine the correlation between sexual dysfunction and anxiety as well as depression in these women. In addition, this study compared the level of anxiety, depression, and sexual dysfunction between different groups of sociodemographic factors in infertile female patients.

Methods: This was a cross-sectional study involving 159 women seeking infertility treatment in infertility clinics in Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II. They were selected through nonprobable sampling method. Anxiety and depression were assessed using the Malay version of Hospital Anxiety and Depression Scale (HADS) and sexual dysfunction was assessed using the Malay version of Female Sexual Function Index (MVFSFI). Subjects that scored above the cut off points for depression and anxiety in HADS questionnaire underwent the Mini International Neuropsychiatric Interview (MINI) to diagnose anxiety and/or depression according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). The outcome measures were the percentages of patient who had anxiety, depression, and female sexual dysfunction, the association between anxiety and depression with the type of infertility, as well as the cause and duration of infertility. The correlations between anxiety and depression with female sexual dysfunction were determined. Descriptive analysis, Fisher's exact test, Cramer's V test, Pearson's correlation test, and Mann-Whitney U test were appropriately used in data analysis.

Results: From the HADS questionnaire, 4.4% of the subjects was found to have anxiety, and 0.6% (1 subject) had depression. None of the subjects who had reached the HADS cut-off point for anxiety and depression and had undergone MINI was diagnosed to have any anxiety or

depressive disorder according to DSM IV criteria. Only 3.1% had sexual dysfunction as detected by MVFSFI. There were no association between anxiety and depression with the type, cause, and duration of infertility. However, there were significant correlations between anxiety and depression with female sexual dysfunction. There was no significant difference in anxiety level between different groups of sociodemographic factors, but there were significant difference in depression between different groups of race, education level, and income, as well as in sexual dysfunction between different durations of marriage.

Conclusion: The level of anxiety, depression, and female sexual dysfunction were low in women seeking infertility treatment. It appeared that the level of anxiety and depression have not led to clinical impairment. However, there were significant correlations between anxiety and depression with female sexual dysfunction. There was no significant difference in anxiety level between different groups of sociodemographic factors, but there were significant difference in depression between different groups of race, education level, and income, as well as in sexual dysfunction between different durations of marriage.

Supervisor: Dr Zarina Zainan Abidin Co-supervisor: Associate Professor Dr Nik Hazlina Nik Hussain **Abstracts**

Abstracts of Theses Approved for the MSc and PhD at the School of Health Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia

THE EFFECT ON MALE RATS' REPRODUCTIVE FUNCTIONS AFTER LONG-TERM ADMINISTRATION OF METHAMPHETAMINE HYROCHLORIDE AND ITS WITHDRAWAL

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Objectives: This experiment aimed at investigating the effect of methamphetamine hydrochloride (MA) administration and its withdrawal on the male rat reproductive functions. We studied the serum gonadotrophins, namely follicle stimulating hormone (FSH), luteinising hormone (LH), and testosterone; relative weight of reproductive organs; testis morphology; and sperm count and morphology.

Methods: A total of 120 12-week-old male Wistar rats were divided into 3 groups: control, placebo, and MAtreated. MA-treated group received 5 mg/kg body weight of MA daily intraperitoneally, whereas the placebo group were administered normal saline. Each group consists of 5 subgroups (M12, W2, W4, W8, and W2) that were assigned with 5 different withdrawal weeks: 0, 2, 4, 8, and 12 weeks, respectively. At the end of the withdrawal period, the rats were anaesthetised by ether and sacrificed by cervical dislocation, followed by laparotomy. The blood was obtained from inferior vena cava, and the serum concentrations of FSH, LH, and testosterone were analysed. The isolated right epididymis was gently pressed and sperms were collected. The epididymis was minced and mixed with the collected sperms and subsequently filtered. The filtered material was stained with 1% eosin for sperm count and sperm morphology assessment. The testes, left epididymis, prostate gland, and seminal vesicle were weighed and their relative organ weights were determined. The testes were stained with haematoxylin and eosin for histological analysis. Consequently, seminiferous tubular diameter (STD) and seminiferous epithelial height (SEH) were measured using image analyser.

Results: The W8 and W12 subgroups of MA-treated rats had significantly reduced serum FSH and LH concentration. The serum testosterone concentration in W2 and W4 were also significantly reduced. The testis and epididymis relative weight of W2, W4, and W8 were significantly reduced. However, the prostate gland and seminal vesicle relative weight were not affected by MA treatment. The STD of W2 and W4, and SEH of W2, W4, and W8 demonstrated significantly reduced measurement. The sperm morphology and count were also

significantly lowered in W2, W4, W8, and W12 groups. After 12 weeks of withdrawal, the serum FSH and LH returned to normal level. Serum testosterone concentration was restored following 4 weeks of withdrawal. The relative weight of testis and epididymis returned to normal range after 8 weeks of withdrawal. The STD and SEH measurement also returned to normal range after 8 and 4 weeks of withdrawal, respectively. Sperm count and morphology also improved after 12 weeks of withdrawal.

Conclusion: The administration of 5 mg/kg body weight of MA at 12 weeks appears to be harmful to the male rat reproductive function. However, after certain withdrawal weeks, the functions were restored to normal; thus, damages are reversible.

Supervisor:

Associate Professor Dr Mohammed Nasimul Islam

THE IMPACT OF RECONSTRUCTION FILTERS ON 99mTc MYOCARDIAL SPECT IMAGING

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Objectives: This prospective and retrospective study was undertaken to investigate the effect of filtering on image quality and functional parameters in myocardial single-photon emission computed tomography (SPECT) using various reconstruction filters and their associated parameters.

Materials and Methods: In the prospective study of image quality, a cardiac phantom system (with 1.10 cm cold defect in myocardium) for different 99m Tc radioactivity concentration as background was used in the SPECT procedure. The target–background concentration ratio (T/B) of 5.3, 4.0, 3.3, 2.7, 2.0, 1.3, and 1.0 were used to acquire SPECT images. Based on the SPECT studies, the calculated background count to target count ratio (BTR) for each T/B was 0.2, 0.4, 0.6, 0.7, 0.8, and 0.9, respectively (T/B = 1.0 was excluded). The image quality was analysed based on image contrast, signal-to-noise ratio (SNR), defect size accuracy, and total grade (trade-off between contrast, SNR, and defect size accuracy).

Results: Different filters produce different values of contrast, SNR, and defect size. The increase in cut-off frequency and order of filter resulted in the increase in contrast and SNR, but the accuracy of defect size was reduced. Butterworth filter has the ability to balance between contrast, SNR, and defect size accuracy, while Gaussian filter is good

in producing image with high contrast and SNR. This study suggests that Butterworth filters can be used to analyse SPECT images, while Gaussian filter can be used as an alternative. Based on total grade, the Butterworth filter parameters of (0.40 Nq; n = 12), (0.45 Nq; n = 8), (0.75 Nq; n = 12), (0.80 Nq; n = 8), (0 .80 Nq; n = 11), and (0.80 Nq; n = 11) were found to be optimum for BTR = 0.2, 0.4, 0.6, 0.7, 0.8, and 0.9 respectively. For Gaussian filter, the filter parameters of (0.60 Nq; n = 10), (0.65 Nq; n = 12), (0.65 Nq; n = 14), (0.70 Nq; n = 14), (0.75 Nq; n = 14), and (0.50 Nq; n = 20)were found to be optimum for BTR = 0.2, 0.4, 0.6, 0.7, 0.8, and 0.9, respectively. The optimum cut-off frequency of Butterworth and Gaussian filters showed linear relationship with BTR. For Butterworth filter, cut-off frequency = 0.227 + (0.715 \times BTR), R2 = 0.864, P < 0.01; and for Gaussian filter, cut-off frequency = $0.538 + (0.236 \times BTR)$, R2 = 0.876, P < 0.05. These 2 equations were used to predict the functional parameters of 4 patients who underwent 99mTc myocardial SPECT based on their BTR values (a retrospective study based on the patient data taken in 2003). End diastolic volume (EDV), end systolic volume (ESV), stroke volume (SV), and ejection fraction (EF) were calculated. The results showed that EDV and ESV values depend on the filter types applied during the reconstruction process. Butterworth filter produced lower EDV and ESV compared with Gaussian filter did.

Conclusion: It is recommended that only one filter type need to be used during reconstruction process to ensure correct interpretation.

Supervisor: Professor Dr Ahmad Zakaria

DETERMINATION OF HEAVY METALS CONTENT IN SEAFOOD FROM EAST COAST OF PENINSULAR MALAYSIA

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Methods: Seafood samples obtained from 3 main markets in the East Coast Peninsular, Malaysia were analysed for the content of heavy metals, using Graphite Flame Atomic Absorption Spectrophotometer (GF-AAS) for copper (Cu), zinc (Zn), chromium (Cr), cadmium (Cd), and arsenic (As), and Flame Injection Mercury System (FIMS) for mercury (Hg). The 3 locations of interest were Pasar Siti Khadijah, Kelantan, Pasar Payang, Terengganu, and Pasar Besar Kuantan, Pahang. Statistical analyses were applied using two-way ANOVA with Duncan's multiple range tests to identify significant differences among species. Comparisons were made of metal concentrations in muscle, bone, and organ of various species of marine fishes.

Results: All samples showed different heavy metal contents. Higher metal content was observed in the organ and bone compared with in the muscle. Concentrations of the heavy metals (in mg/kg dry weight) in muscle samples of fish species ranged as follows: Cu 1.14–10.22, Zn 10.03–42.97, Cd 0.01–1.32, As 0.01–0.28, and Pb 0.01–0.09.

Conclusion: The results indicated that, in the edible parts of 13 species of marine fishes from marine coastal of East Coast Peninsular Malaysia, the heavy metal concentrations were well below the permissible amount according to Malaysian Food Act 1983 and Food Regulations 1985. Their contribution to the body burden could be considered as negligible and deemed safe for human consumption. However, Cd and Zn in the bones and organs were significantly above permissible limit (*P* < 0.05).

Supervisor: Associate Professor Dr Shariza Abdul Razak

BELIEFS, ATTITUDES, AND PRACTICES OF PARENTS IN FEEDING OBESE SELECTED PRIMARY SCHOOL CHILDREN IN KOTA BHARU, KELANTAN

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Introduction: The increasing prevalence of obesity among children in Malaysia is becoming a major problem because childhood obesity can result in many diseases in adulthood. Thus, parents play an important role in determining their children's food intake.

Objective: This study was conducted to evaluate parents' belief, attitudes, and practices in child feeding among obese and overweight primary school children.

Methods: This was a cross sectional study involving 175 Standard 2 children at 3 schools in Kota Bharu. Height, weight, and triceps skin-fold thickness were measured. Questionnaires, which include socio-demography questionnaire, Child Feeding Questionnaire (CFQ), and International Physical Activity Questionnaire (IPAQ), were distributed to the parents. Qualitative study was also carried out on predictor variables of body mass index (BMI) and child obesity. Eight parents of obese children were involved in an in-depth interview.

Results: This study showed that the prevalence of weight problems among children was 13.2%, of which 6.9% was overweight and 6.2% was obese. All the children in the study were Malays. Significant difference between obese and normal-weight child was found in father's occupation, where 52.2% of fathers of obese children were self-employed and 47.8% were paid employees. Scores on perceived parent's own weight (P < 0.05) and their children's weight (P < 0.001) were

higher among parents of obese children compared with among parents of normal-weight children. Pressure on children to eat (P < 0.05) among obese children was less than among normalweight children. Total days of moderate physical activity of parents showed significant correlation (P < 0.05) with child anthropometry (weight, height, and triceps skin-fold thickness). This study also found that perceived child weight and pressure to eat were the predictor variables of child BMI. Only perceived child weight was the predictor for obesity among children. Qualitative research showed that most parents perceived their children were overweight or obese since their children were 5 years old, and the pressure to eat was less among overweight or obese child because the parents realised that their children have high appetite. However, the way parent identified their child as obese or overweight was not accurate because they did not refer to any growth chart or correct indicator.

Conclusion: This research showed that parents play a major role in preventing obesity among children.

Supervisor:

Professor Dr Wan Abdul Manan Wan Muda

PHARMACOLOGICAL ANALYSIS, MORPHOLOGICAL AND IDENTIFICATION OF BIOACTIVE COMPOUNDS OF THE EDIBLE BIRD'S NEST

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Introduction: The edible bird's nests (EBN) are made by the swiftlets using their saliva. In the traditional Chinese medicine, EBN is considered as one of the top health foods and is claimed to have many therapeutic effects. Although some of the in vitro effects of EBN have been studied, a study looking at the pharmacological effects of EBN on the vital body system is not available.

Methods: In the present study, the morphology of the beak of the swiflets and EBN, the bioactive compounds, and the cardiovascular system (CVS) effect of the EBN water extract (EBN-WE) were analysed. Two experimental procedures were executed to determine the effect of the EBN-WE on the CVS of anaesthetised normotensive rats: (1) the direct effect of the intravenously administered EBN-WE on the mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR); and (2) the effect of the intravenously administered EBN-WE on the responses of MAP, SBP, DBP, and HR to endogenous chemicals, namely acetylcholine (Ach), noradrenaline (NA), adrenaline (Adr), histamine (His), and serotonin (5-HT).

Results: The swiftlet's tongue sections revealed the presence of intralingual and sublingual salivary gland structures, which may be the main source of the salivary secretion used in nest building. Presence of other structures such as the intrinsic skeletal muscle and cartilaginous structures showed the relationship between the function of these structures and nest-building ability. The morphology of the EBN showed solidity and uniformity of the nest building material. Gas chromatography-mass spectrometry (GC-MS) analysis of the EBN-WE revealed the presence of amino acids and its analogues, biogenic amine analogues, and amphetamine analogues. The intravenous administration of the EBN-WE (0.01, 1, and 100 mg/kg) caused transient decreased in the blood pressure and HR. The effects of the EBN-WE on the MAP and DBP were inversely proportional to the dose level and were found significant at 0.01 mg/kg. Following EBN-WE injection, SBP was decreased by 3 times as the dose level was increased, without change in the HR. MAP and SBP responses to Ach after EBN-WE injection were significantly increased at the dose of 1 mg/kg EBN-WE, and no significant changes were observed on the DBP and HR responses to Ach. There were no significant changes on the degree of responses of MAP, SBP, DBP, and HR to Adr and NA after EBN-WE injection. The change in DBP response to His after EBN-WE injection was only significant at the dose of 0.1 mg/kg. There were no significant changes observed in MAP, SBP, and HR responses to His administration after EBN-WE injection. MAP and DBP responses to 5-HT showed significant increased after EBN-WE injection at the dose of 1 mg/kg. The change in SBP response to 5-HT after EBN-WE injection was significant at the doses of 0.1 and 1 mg/kg of EBN-WE. No significant changes were observed on HR. Based on the observation throughout the experiment, no toxic effect was apparent due to intravenous injections of EBN-WE. The test substance was successfully administered directly through the blood circulation without deterring the haemodynamics of the blood pressure in the rats. The EBN-WE did not cause much alteration in the responses of MAP, SBP, DBP, and HR to endogenous chemicals.

Conclusion: The present findings may be the first report that provides an overall aspect of the EBN, which include the source of the salivary secretion, the morphological structure of the EBN, the composition of the bioactive compounds, and the pharmacological effects of the EBN-WE on the cardiovascular system of an in vivo rat model. This study had also provided substantial data to verify that the EBN is safe for human consumption.

Supervisor:

Professor Dr Syed Mohsin Syed Sahil Jamalullail Co-supervisor: Associate Professor Dr Syed Waliullah Shah

EFFECT OF ZINC SUPPLEMENTATION ON THE MORPHOLOGY AND PERMEABILITY OF THE SMALL INTESTINE MUCOSA SECONDARY TO CHRONIC MILD STRESS IN RATS

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Introduction: Psycho-physiological stress has widely attracted researchers to investigate the effects of stress on physiological system. However, no study on the beneficial role of zinc in stress-induced physiological alterations has been established.

Objectives: This study examined the effect of zinc supplementation on the physiological parameters, morphology, permeability, and inflammatory cell infiltration of the small intestine mucosa secondary to chronic mild stress in rats.

Methods: A total of 40 male Sprague Dawley rats aged 6 weeks with a mean body weight of 49.69 g (SD 3.92) were divided into 4 groups (n = 10 each): control (C), control with zinc supplement (CZ), stress (S), and stress with zinc supplement (SZ). The rats were exposed to water avoidance stress 1 hour daily for 10 consecutive days. Body weight gain, food and water intake, and number of stool pellet after every stress session were documented throughout the study. On the 11th day, after an overnight fasting, rats were anaesthetised with diethyl ether, and fluorescein isothiocyanate dextran solution was injected into a loop of small intestine. One hour later, rats were re-anaesthetised, and blood was collected from the abdominal agrta to measure the intestinal permeability. Rats were then sacrificed, and ileum and jejunum were taken for histological evaluation and inflammatory cell assay. Statistical comparisons were made by one-way analysis of variance, followed by post hoc Tukey test.

Results: Daily stress sessions in this study had significantly reduced the body weight gain of the S group compared with that of the C group's, although no significant difference was seen in the comparison of food and water intake between the 2 groups. However, the SZ group had significantly increased body weight gain and food intake compared with those of the S group's. The number of stool pellet was significantly higher in the S group compared with in the C group, and in the SZ group compared with in the CZ group. The S group had significantly shorter crypt depth in the ileum, lower villus height in the jejunum, lower number of goblet cell in the crypt of the ileum and the jejunum, and lower number of goblet cell in the villus of the jejunum compared with those of the C group's. The SZ group had significantly longer crypt depth, higher villus height, and higher number of goblet cell in the crypt as well as in the villus of the ileum and the jejunum compared with those of the S group's. The S group had significantly higher permeability of FITC in the small intestine

and higher inflammatory cell infiltration in the ileum and the jejunum compared with those of the C group's. However, SZ group had significantly lower permeability of FITC in the small intestine and lower inflammatory cell infiltration in the ileum and the jejunum compared with those of the S group's.

Conclusion: Chronic mild stress compromised the small intestinal mucosal morphology, permeability, and inflammatory cell infiltration, which were attenuated by zinc supplementation. These findings suggest that zinc might be involved in the prevention of small intestinal barrier dysfunction secondary to chronic mild stress and possibly be a promising nutrient for diseases related to intestinal barrier dysfunction.

Supervisor: Dr Jesmine Khan Co-supervisor: Professor Dr Zalina Ismail

ANALYSIS OF BIOLOGICAL, BEHAVIOURAL, AND ENVIRONMENTAL DETERMINANTS OF MALNUTRITION: A STUDY OF MALNOURISHED CHILDREN IN TUMPAT, KELANTAN, MALAYSIA

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Introduction: Many studies have shown that poor growth in children is associated with malnutrition. The contributing factors are diverse, multi-sectoral, and interrelated, including biological, social, cultural, and economical factors. As poor growth is one of the most serious health issues in the world, it is important for policymakers to understand the determinants in order to design more concise and effective public health intervention programmes.

Objective: The purpose of this cross-sectional study was to examine the relationships between biological, behavioural, and environmental factors and malnutrition in children aged 5 years and below.

Methods: The instrument used in this study was based on a previously described conceptual framework for malnutrition in children (Sastry 1996) and was tested for its psychometric component, using both qualitative and quantitative methods. In addition to the use of a questionnaire, anthropometric and dietary data were collected from 295 children who were randomly selected from clinics in Tumpat, Kelantan, Malaysia. The proposed model was tested and modified using Structural Equation Modelling. The modified model was adequately fitted with the data.

Results: The results demonstrate that the environmental construct with its factors (total household income, $\beta = 0.68$, P < 0.01; total expenditure, $\beta = 0.67$, P < 0.01; number of rooms in house, $\beta = 0.46$, P < 0.01; socio-economic status,

 β = 0.71, P < 0.01), had a significant effect on malnutrition. None of the biological and behavioural constructs showed any significant effects.

Conclusion: These findings provide useful insights into the importance of focusing on environmental factors as the main target in designing intervention programmes, particularly in the area that can promote economic growth. The adoption of 'pro-poor growth', establishment of social and physical infrastructure, and execution of public policy that directly helps the poorest groups should be continued to the main agendas of the government in eradicating malnutrition among children. Nevertheless, the existing health intervention on behavioural change and infrastructure support should be continued to maintain the current nutritional status of the children. Moderate malnutrition among children 5 years and below in rural communities is still an area of importance. The findings also have implications for the use of multiple techniques in anthropometry for screening the nutritional status of children. Future efforts should focus on promoting public awareness on poverty and child malnutrition among the rural communities, developing partnership between private sectors and non-governmental agencies with the government in eradicating poverty and child malnutrition, empowering communities in the implementation of intervention programmes, and capacity building among the communities to take care of themselves.

Supervisor: Professor Dr Wan Abdul Manan Wan Muda Co-supervisor:

Professor Dr Zabidi Azhar Mohd Hussin

DEVELOPMENT OF A GLASS FIBRE MEMBRANE— BASED LATERAL FLOW BIOSENSOR FOR THE DETECTION OF LABELLED PCR AMPLICONS USING VIBRIO CHOLERAE AS THE MODEL ORGANISM

Chua Ang Lim PhD Biomedicine

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Introduction: In recent years, molecular techniques have played an increasing role in the diagnosis of infectious diseases, and polymerase chain reaction (PCR) is one of the predominant techniques used. However, major setbacks such as requiring trained personnel, cold-chain storage, and cumbersome detection protocols hampered the general use of PCR in place of conventional methods. Furthermore, PCR products are commonly detected using agarose gel electrophoresis methods, involving carcinogenic ethidium bromide and harmful ultraviolet illumination.

Objective: The objective of this study was to develop and evaluate a thermostabilised PCR assay and a lateral flow-based device for detection of amplicons.

Methods: Vibrio cholerae was used as a model organism to develop a molecular detection kit named the cholera PCR-ICT-DNA assay. A multiplex PCR with an incorporated internal amplification control (IC) and utilising haptenmodified primers was developed and optimised. The PCR was thermostabilised and evaluated for analytical specificity. Concurrently, a lateral flow device was developed and optimised using FUSION 5 glass fibre membrane (Whatman, UK). Capture reagents were coupled to carrier beads and detector reagent bioconjugated to gold nanoparticles. The device consisted of a conjugate pad embedded with detector reagents, a reaction pad immobilised with capture reagents, and a wicking zone. Dispensing, blocking, and drying parameters were refined to produce a stable ICT-DNA dipstick prototype. Analytical sensitivity and specificity of the ICT-DNA dipstick were also determined. The cholera PCR-ICT-DNA assay kit was then evaluated for analytical sensitivity. Clinical evaluation was also performed using spiked stool specimens (n = 174). The shelf life of the kit was then estimated using elevated temperature-based accelerated aging techniques. The cholera PCR-ICT-DNA assay translated PCR results of the kit into visual signals on the ICT-DNA dipstick. The test line of the ICT DNA dipstick detected target amplicons, while the IC line detected IC amplicons. Control line provided the chromatographic control element for the ICT-DNA dipstick.

Results: The analytical specificity of thermostabilised PCR component and the ICT-DNA dipstick component was at 100% each. The ICT-DNA dipstick reported a limit of detection (LoD) of 0.5 ng/µL at the DNA level for both monoplex and duplex PCR products, which was 2 times more sensitive than agarose gel electrophoresis analysis. The cholera PCR-ICT-DNA assay recorded a LoD of 106 CFU/mL at bacterial cell level and 10 pg at genomic DNA level. Clinical evaluation yielded 100% for sensitivity, specificity, positive predictive value, and negative predictive value. The kit was estimated to be stable for at least 3 months at ambient temperature.

Conclusion: A novel molecular detection kit for cholera was developed. The detection kit provided an easy and rapid format to perform PCR that requires no cold-chain, coupled with a PCR amplicons detection device that can translate results into visual signals within 10 minutes. The versatile detection kit can be easily modified for PCR amplicon detection of other infectious diseases.

Supervisor: Professor Dr Lalitha Pattabhiraman Co-supervisor: Dr Lim Boon Huat INFLUENCE OF RAIN, MALATHION, SUNLIT, AND SHADED HABITATS ON THE DURATION OF DEVELOPMENT AND MOLECULAR IDENTIFICATION OF CHRYSOMYA MEGACEPHALA (FABRICIUS) (DIPTERA: CALLIPHORIDAE) IN KELANTAN, MALAYSIA

Naji Arafat Mahat PhD Forensic Science (Toxicology Forensic)

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Introduction: Chrysomya megacephala (Fabricius) is the earliest and the most prevalent necrophagous species infesting dead bodies in Malaysia and thus, may provide the best estimate of minimum post-mortem interval (PMI). In Malaysia, heavy and/or incessant rain is a commonplace occurrence, and malathion is the most prevalent poison used for committing suicide.

Methods: In this research, the independent and combined influences of the rain and the presence of malathion in whole rabbit carcasses decomposing in sunlit and shaded habitats on oviposition and development of *C. megacephala* were studied over a period of 1-year in Kelantan, Malaysia, to provide baseline data for the estimation of PMI. Base sequence of *CO1* gene was used for species identification, and the influence of malathion on the sequence of *CO1* gene of *C. megacephala* was determined. The possible use of larvae and pupae of *C. megacephala* for detecting malathion in diagnosing the cause of death, especially when visceral organs have liquefied, was also investigated.

Results: In general, rain, depending on its intensity, delayed initial oviposition by 1 to 2 days and prolonged the pupation period by 1 to 3 days. The presence of malathion in the carcasses delayed initial oviposition by 1 to 3 days and prolonged the pupation period by 2 to 3 days. Presence of rain and malathion cumulatively prolonged pupation period that extended to a maximum of 8 days. It was found that malathion did not impede the accuracy of species identification while using the base sequence of CO1 gene fragment amplified by CI-J-2495/CI-N-2800 primers.

Conclusion: The detection of malathion in larvae and pupae *per se* may prove useful in diagnosing the cause of death, since malathion is a poison unlike other drugs that are abused. These findings deserve consideration in estimating PMI in decomposed bodies recovered in Malaysia during both rainy and dry months, as well as when malathion poisoning is suspected.

Supervisor: Associate Professor Dr PT Jayaprakash Co-supervisor: Dr Zafarina Zainuddin INTERACTION OF CTCF AND ITS INTERACTING PARTNERS IN HYPERTROPHIC SCAR AND NORMAL FIBROBLASTS FOLLOWING CHITOSAN DERIVATIVES TREATMENT

Mohammad Syaiful Bahari Abdull Rasad PhD Biomedicine (Molecular and Cellular Biology)

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Introduction: Chitosan, a deacetylated form of chitin with excellent biological properties implicated in wound healing activity via well-regulated regulators.

Methods: In this study, primary human skin keratinocytes and fibroblasts of both normal and hypertrophic scars were established in order to assess the cytocompatibility of novel chitosan derivatives sheets and pastes, carboxymethyl chitosan and oligochitosan, as well as the involvement of multivalent transcription factor, CTCF, with its interacting partners in wound healing mechanism.

Results: The establishment of primary cell was confirmed by immunocytochemistry and Western blot approaches using specific markers, involucrin and cytokeratin 6 for keratinocytes and fibroblast surface protein and heat shock protein 47 for fibroblasts. All tested chitosan showed appropriate cytocompatibility properties as judged by colourimetric tetrazolium salt (MTT) assay, whereby SH120 (N, o-carboxymethyl-chitosan) was considered the most cytocompatible, with stimulation of the normal fibroblast cell growth and inhibition of the overgrowth of hypertrophic scar. Using Western assay, CTCF and its associated proteins (YB-l, c-Myc, and p53) were found to be differently expressed in both normal (pNHDF) and hypertrophic scar (pHSDF) fibroblasts, including cells treated with chitosan. These factors most probably play different roles in cell cytocompatibility, proliferation, and apoptosis. Using in vitro and in vivo biochemical interaction assays, YB-l has been found to interact physically with CTCF N-terminal domain. This interaction was further characterised using both cognate sequence of YB-l and AP-l via electrophoretic mobility shift assay. This study showed that the physical protein-DNA interaction may act as an activator of the matrix metalloproteinase (MMP-13) promoter activity of normal and hypertrophic scar fibroblasts, which may further regulate cell proliferation and MMP-13 activity in the wound healing pathway.

Supervisor: Associate Professor Dr Shaharum Shamsuddin Co-supervisor: Professor Dr Ahmad Sukari Halim FACTORS INFLUENCING THE USAGE OF MULTIMEDIA FOR TEACHING AMONGST HEALTH SCIENCES LECTURERS IN MALAYSIAN PUBLIC UNIVERSITIES: TOWARDS THE DEVELOPMENT OF A MULTIMEDIA REPOSITORY SYSTEM

Zar Ni Wynn PhD Health Informatics

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Introduction: In higher institutions worldwide, the integration of multimedia for teaching medical and health sciences (HS) has been limited owing to organisational and individual factors. Organisational factors identified were insufficient organisational support in terms of teaching resources, facilities, information technology training programmes, and technical support. Individual factors include attitude and knowledge of academics on technology integration into their lectures.

Objectives: This study was conducted to explore the current status of multimedia usage among HS lecturers in Malaysian public universities, to conduct a situational assessment study in order to observe the current system of organisation support for HS lecturers, and to design, implement, and evaluate the acceptance of a new Multimedia Repository System (MRS).

Methods: This study was conducted in 2 phases. Phase I consisted of 2 substudies: an exploratory study and a situational assessment study. For the exploratory study, a cross-sectional survey was conducted, from January until August 2006, among the HS lecturers from 10 Malaysian public universities. An English version of a validated questionnaire was sent to 190 participants, and 90% responded. The Mann-Whitney test, Kruskal-Wallis test, and multiple linear regression analysis were carried out using SPSS version 15. The situational assessment study investigated the perceptions of training and workshop organisers, as well as the organisation support in the Universiti Sains Malaysia Health Campus. Consequently, in Phase II of the study, a new MRS was developed in conformance with Health Education Assets Library metadata schema standard. In January 2008, a User Evaluation Workshop was conducted among 35 HS lecturers in the School of Health Sciences, Universiti Sains Malaysia. An English version of the validated questionnaire was given to participants at the end of the hands-on section. Structural Equation Modeling was used for the path analysis using AMOS 7. To test MRS acceptance, a web-based System Acceptance Model (WebSAM) was developed, comprising 6 determinants to predict the intention to use (IU) of MRS in the future: perceived ease of use (PEU), perceived usefulness (PU), web experience (WE), technical support (TS), computer experience (Com_Exp), and compatibility (COM).

Results: Although HS lecturers' technology usage was high on computer and the Internet, their use was just above average on hardware and library materials, and low on software, digital repositories, and sharing digital materials (DM) among them. Their practice was significantly associated with their technological knowledge ($R^2 = 0.34$; $F[df_1, dt_2] =$ 79, 46; P < 0.0001), attitudes towards sharing DM via the Internet ($R^2 = 0.40$; F[df1, dt2] = 51, 44; P < 0.0001), working experience ($R^2 = 0.43$; F [df1, dt2] = 37, 44; P < 0.0001), perceived organisational support on teaching materials $(R^2 = 0.44; F[df_1, dt_2] = 30, 06; P < 0.0001)$, and the teaching facilities ($R^2 = 0.45$; F [df1, df2] = 24, 95; P < 0.0001). The findings from the situational assessment study indicated that the Universiti Sains Malaysia Health Campus was lacking in information technology training programmes and workshops that foster HS lecturers' technology integration into teaching, as well as the need for a repository to support them with sharable DM resources. The results from the acceptance study showed that PU ($\beta = 0.68, P < 0.01$), COM ($\beta = 0.41, P < 0.05$), and Com_Exp (β = 0.15, P < 0.01) were the direct determinants of HS lecturers' IU of MRS for their lecture preparations. TS had a significant direct effect on COM ($\beta = 0.71, P < 0.01$), and COM had a significant direct effect on the PU ($\beta = 0.43$, P < 0.01). The proposed Web-SAM accounted for 59% of the variance explained on IU. When it was tested on Davis' original Technology Acceptance Model (TAM) with 2 determinants (PEV and PU), the variance explained of IU was only 45%. The greater proportion of the Web-SAM model proved that it is more robust than the original TAM.

Conclusion: In the future, this study can be replicated in other fields and the proposed Web-SAM will be useful for evaluating the acceptance of other Web-based systems. MRS can be further enhanced to incorporate more features and functions to support the lecturers need.

Supervisor:

Associate Professor Dr Sharifah Mastura Syed Mohamad

Abstracts

Abstracts of Theses Approved for the MSc at the School of Dental Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia

THE STUDY OF DENTAL PULP STEM CELLS FOLLOWING RESTORATIVE PROCEDURES ON DECIDOUS MOLARS

Dr. Alaa Nasser Abed Al Rahman Lutfi MSc Dentistry

Paediatric Dentistry Unit School of Dental Sciences, Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia

Introduction: The biological examination of pulp injury, repair events, and the response of dental pulp stem cells to dental restorative materials are of paramount importance for the understanding of the post-operative development and the use of these repair activities in restorative treatment.

Objectives: The objectives of this study were to compare the stem cells proliferative activity using colorimetric proliferation reagent alamarBlue[™], and to evaluate their response by comparing the tertiary dentin thickness (TDT) formation following restorative procedures on the teeth using haematoxylin and eosin staining for histological section and microscopic viewing using the Image-Pro Express software.

Methods: Healthy paediatric dental patients aged 9 to 11 years were selected; these patients attended the Paediatric Dental Clinic, School of Dental Sciences, Universiti Sains Malaysia Health Campus, for dental treatment, with carious teeth on deciduous molars without pulpal exposure. The patients' teeth were divided into 2 groups: Group 1 comprised of 29 teeth filled with glass ionomer cement (GIC) alone, and Group 2 comprised of 29 teeth lined with Ca(OH)₂ cement and filled with GIC. The teeth were reviewed for up to 6 months before being extracted according to standardised procedures based on the selected criteria.

Results: A total of 34 teeth were extracted (17 teeth per group). In each study group, 7 teeth were assigned for stem cell culture and 10 teeth were subjected to histological sections. The results showed that stem cells from human extracted deciduous teeth (SHED) were positive for surface antigenic markers CD105 and CD166 following immunocytochemistry test. The proliferative activity (median, IQR) for Group 1 (38, 19) was significantly less (P > 0.05) compared with in Group 2 (41, 19). However, the TDT area (median, IQR) in Group 2 (0.15, 0.03) was significantly higher (P < 0.001) compared with in Group 1 (0.05, 0.01).

Conclusion: The pulp of deciduous teeth contained stem cell population, which responded well and maintained proliferative activity following restorative procedures using Ca(OH)₂ cement and GIC. However, these materials created different responses of SHED in tertiary dentin deposition, where the reactionary dentin deposition appeared to be

more under restorations lined with ${\rm Ca(OH)}_2$. Thus ${\rm Ca(OH)}_2$ cement has high credibility to be used in deep cavities for pulp protection.

Supervisor: Dr Siti Noor Fazliah Mohd Noor Co-supervisors: Dr TP Kannan Dr Saidi Jaafar

IN VITRO CYTOTOXICITY EVALUATION OF PROCESSED NATURAL CORAL ON HUMAN FIBROBLAST AND OSTEOBLAST CELL LINES

Nor Shamsuria Omar MSc Molecular Biology

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Introduction: The development of bone-graft substitutes has evolved from the understanding of how autografts and allografts are used intra-operatively and how they are remodelled by the body after transplantation. The research on natural coral as a bone substitute has been reported in many experimental studies. Natural coral has been proven to be biocompatible and biodegradable. All newly developed biomaterials must fulfil stringent criteria laid out by government authorities and international agencies, before receiving approval for clinical application. Standard cell-based cytotoxicity assay are performed in vitro and high-risk materials are removed at early stage.

Objective: The aim of this study was to evaluate the in vitro cytotoxicity of the locally produced (Universiti Sains Malaysia Health Campus, Malaysia), processed natural coral (PNC) from the *Porites* species in terms of proliferation, apoptosis study, and cell attachment, by using human osteoblast (HOS) and fibroblast (MRC-5) cell lines.

Methods: The in vitro cytotoxicity of PNC was evaluated using test on extract and direct contact as per ISO 10993-5 (1999). HOS cells were used to study the magnitude of proliferation when exposed to the extraction medium of 2 different particle sizes of PNC: granules (0.5–1.0 mm) and powder (1–50 μ m). The proliferation of HOS cells was analysed using tetrazolium-based colourimetric assay (MTT) and neutral red assay (NR). The material is considered toxic if the proliferation rate was less than 50%. For the apoptosis study, HOS cells were exposed to the extraction medium of PNC powder at a concentration of 200 mg/mL for 48 and 72 hours. Then, the cell pellet (1 × 10 6 cells) was resuspended in Annexin-V-FLOUS labelling solution and subjected to flow

cytometric analysis. Proliferation study via direct contact of PNC disc was carried out using HOS and MRC-5 cell lines. Both cell lines were exposed to the PNC material at 1, 24, 72, and 168 hours and analysed using NR assay; the medium was never changed through out the incubation periods. The material is considered toxic if the proliferation rate was less than 50%. For the cell attachment study, MRC-5 cells and HOS cells were cultured on the PNC discs and rubber latex (positive control) and observed under inverted microscope after 72 hours of incubation period. For the Scanning Electron Microscopic analysis, HOS cells were cultured on the PNC disc and thermanox plastic (negative control) and observed after 72 hours of incubation period.

Results: Proliferation study of HOS cells on the extraction of PNC granules and powder showed that both particles were not cytotoxic. Also, both PNC granules and powder did not induce any cytotoxicity, as was evident from their proliferation rate, which was above 50%. The flow cytometry analysis showed that the viable cell percentage for the HOS cells was high and the apoptotic cell percentage was low, indicating that PNC did not cause a remarkable damage to the cells. The results of the magnitude of proliferation of HOS and MRC-5 cells when exposed to the PNC material at different incubation periods using NR assay indicated that there was no cytotoxicity until an incubation period of 72 hours. The cell attachment study showed that both MRC-5 and HOS cells were attached on the edge of the PNC disc, which later grew into the pores of the PNC disc.

Conclusion: All the above results show that the locally produced PNC material by Universiti Sains Malaysia Health Campus is non-cytotoxic and favours the growth of HOS and MRC-5 cells.

Supervisor: Professor Dr Abdul Rashid Ismail Co-supervisors: Professor Dr Ab Rani Samsudin Associate Professor Dr Suzina Sheikh Ab Hamid Associate Professor Dr Thirumulu Ponnuraj Kannan

Abstracts

Abstracts of Theses Approved for the MSc at the Institute for Research in Molecular Medicine (INFORMM) Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia

DEVELOPMENT OF DNA-BASED DIAGNOSTIC TESTS FOR THE DETECTION OF SHIGELLA DYSENTERIAE, SHIGELLA FLEXNERI, AND SHIGELLA SONNEI

Nik Noorul Shakira Mohamed Shakrin MSc Molecular Medicine

Institute for Research in Molecular Medicine (INFORMM), Universiti Sains Malaysia Health Campus, 16150 Kelantan, Malaysia

Introduction: Shigellosis or bacillary dysentery caused by Shigella spp. remains as significant health problem worldwide. Current detection and identification methods of the pathogens from stool specimens by culture method is relatively insensitive, generally time consuming (approximately 2–5 days) and laborious.

Objectives: In this study, thermostabilised polymerase chain reaction (PCR) assays were developed for the detection of *ompA* genes in *Shigella dysenteriae*, *Shigella flexneri*, and *Shigella sonnei*. The tests contained specific primers for the detection of *S. dysenteriae*, *S. flexneri*, and *S. sonnei*, respectively, freezed-dried or thermostabilised PCR reagents with internal control (IC), and gel loading dye.

Methods: Primers targeting *ompA* genes for *S. dysenteriae, S. flexneri*, and *S. sonnei* were designed. Optimisation of PCR parameters including concentration of IC DNA template, annealing temperature, and MgCl₂ concentrations was performed. In assessing specificity and sensitivity, the primers were challenged with known *S. dysenteriae, S. flexneri, S. sonnei*, and other enteric pathogens. Thermostabilised PCR-mix periodic stability assessment for each test was done at ambient temperature (25–26 °C) and 4 °C. Optimisation of stool culture in Gram Negative broth (GNB) was done in order to measure optimum incubation time prior to PCR assay. Preliminary evaluation of the developed tests was done using children seeded stool culture in GNB with *S. dysenteriae, S. flexneri, S. sonnei*, and other enteric bacteria (n = 50).

Results: None of the DNA template from non-targeted organisms was amplified. After optimisation of IC DNA template concentration was done, 5 pg/μL of IC was incorporated into the assays. Minimum concentration of genomic DNA that could be detected by the assays was 0.39 ng/μL for *S. sonnei* and *S. flexneri*. As for the detection of S. dysenteriae, the minimum concentration was 0.78 ng/μL. At bacterial level, the sensitivity was found to be 4.0 × 10^3 CFU/PCR reaction for the test developed for the

detection of $S.\ dysenteriae$, and $4.0 \times 10^4\ CFU/PCR$ reaction for $S.\ flexneri$ and $S.\ sonnei$. Results suggested that the reagent is stable until 6 months of storage at both temperatures. The optimum time for stool culture in GNB was 8-12 hours for all tests. Preliminary evaluation using seeded stool culture gave 100% for PCR sensitivity and specificity, with 100% positive predictive value (PPV) and negative predictive value (NPV) for the test developed for the detection of $S.\ dysenteriae$ and $S.\ sonnei$. As for the detection of $S.\ flexneri$, the sensitivity was found to be 100%, and for specificity, 92.8%. Therefore, the PPV and NPV was 92.8% and 100% respectively.

Conclusion: We have developed simple, rapid, sensitive, specific, and cost-effective tests with built-in control for the detection of *S. dysenteriae*, *S. flexneri*, and *S. sonnei*. However, further studies with a larger set of sample, probably using adult stool, need to be done to evaluate the true performance of the developed tests.

Supervisor: Profesor Dr Asma Ismail Co-supervisor: Associate Professor Dr Mohd Zaki Salleh

UTILISATION OF FERMENTATION AND PURIFICATION STRATEGIES TO ENHANCE THE YIELD OF *Bm*R1 ANTIGEN

Norsyahida Arifin MSc Molecular Medicine

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Introduction: Brugia Rapid is an established diagnostic test that is commercially available to detect both *Brugia malayi* and *B. timori* infections (brugian filariasis). The test is a dipstick lateral flow test format that utilises *Bm*R1 recombinant antigen expressed by the clone *Bm*17DIII/pPROEXTMHT/TOP 10. Due to a significant demand for the test in the market, there is a need to scale up the production of the recombinant antigen and increase the purification efficiency to reduce the production cost of the test.

Objectives: The objectives of this study were to increase the cell mass of *Bm*17DIII/pROEXTMHT/TOP10 recombinant bacteria and to enhance the expression of *Bm*R1 recombinant antigen. In addition, the study aimed to improve the purification strategy in order to obtain a high yield of *Bm*R1 recombinant antigen.

Methods: The cultivation of the recombinant bacteria was performed using fed-batch fermentation, where cells were grown in modified Terrific broth medium and glucose and fed exponentially at a controlled rate, using Multifermenter Control Software for automated feeding, during pre-induction and post-induction feeding. Parameters of fed-batch culture, such as the medium composition, growth conditions, feeding, and induction methods, were varied in order to increase the cell mass and produce minimum metabolite inhibition. More specifically, the effects of key fermentation parameters in fermenter, namely pre-induction feeding specific growth rate and the volumetric feed rate of post-induction, were studied. The expression of BmR1 recombinant antigen was enhanced by varying the protein induction parameters, namely IPTG concentration, frequency, and time point of induction. Efficient purification method was developed in order to increase yield and purity of BmR1 recombinant antigen by varying the imidazole, salt concentration, and volume of wash buffer used during the affinity chromatography. Lastly, the sensitivity and specificity of BmR1 recombinant antigen produced in this study were evaluated using ELISA and rapid test.

Results: Varying the specific growth rate (µ) prior to induction showed that a final cell concentration of 24.3 g/L was obtained at specific growth rate of 0.15 h-1 with feeding at high rate during post-induction. However, further increase of the specific growth rate during pre-induction feeding does not produce a higher cell mass; in fact, it decreased the BmR1 recombinant protein production. It was found that the highest BmR1 production of 9.82 g/L was obtained when the feeding was carried out at low constant rate (1.9 mL/min), combined with the specific growth rate controlled at 0.075 h-1. At this feeding rate, it was also observed that the overall specific productivity, the fermentation yield coefficients, was the highest amongst all the runs tested. This strategy has successfully controlled the accumulation of acetic acid inhibitory by-product below the reported growth inhibitory level of 1.26 g/L. The expression of BmR1 recombinant antigen was found to be optimal with twice induction of 1 mM of IPTG concentration. Initiation of expression at mid log had generated significant amounts of the soluble protein. Therefore, the BmR1 recombinant antigen was then purified under non-denaturing conditions using immobilised metal affinity chromatography. In order to increase the efficiency of purification process, various volumes of wash buffer, imidazole, and salt concentration were performed. Imidazole at 20 mM was found to be the best concentration that gave the best yield of BmR1 recombinant antigen while achieving sufficient purity. When 5 column volumes (CV) of washing buffer was used in the purification step, the production of BmR1 recombinant antigen was 5.14 mg/L compared with 2.84 mg/L when 10 CV of washing buffer was employed. The overall production of the target protein was improved 7-fold compared with using the conventional flask cultivation method. The sensitivity and specificity of the purified BmR1 recombinant antigen produced in this study was confirmed by Western blot and 2 other immunoassays techniques, namely

ELISA and immunochromatographic rapid test. In ELISA, it was found that the BmR1 recombinant antigen produced in this study retained its antigenic property, as it was recognised by sera of filariasis patients (100% sensitive) and not reactive when tested with sera in other infections or from healthy individuals (100% specific). When applied to the rapid dipstick, the BmR1 recombinant antigen also reacted with the anti-filarial antibodies in the sera of patients' infected with $B.\ malayi$, with 100% sensitivity.

Conclusion: The *Bm*R1 recombinant antigen produced in this study is useful to for the production of Brugia Rapid kit. This study provided an improved method of higher efficiency at a lesser cost for mass-production and downstream processing of *Bm*R1 recombinant antigen, and this method would be useful for industrial applications.

Supervisor: Profesor Dr Rahmah Noordin Co-supervisor: Dr Ahmad Ramli Mohd Yahya

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Patient consent

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