Special Communication

Present Status and Future Concerns of Expanded Newborn Screening in Malaysia: Sustainability, Challenges and Perspectives

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Submitted: 18 Sep 2013
Accepted: 19 Dec 2013

Abstract

Newborn screening (NBS) program is an important tool for the early diagnosis and preventive treatment of life-long impairments. NBS is one of the strategies recommended by the World Health Organization to promote the primary prevention of congenital anomalies and the health of children with these conditions. However, NBS initiation and implementation in developing countries, especially South-East Asian and North African regions, are slow and challenging. Expanded NBS is not mandatory and has not yet been incorporated into the public healthcare system in our country. Limited funding, manpower shortages, inadequate support services, low public awareness, and uncertain commitment from healthcare practitioners are the main challenges in establishing this program at the national level. Involvement and support from policy makers are very important to the success of the program and the benefit of the entire population.

Keywords: *newborn screening, inborn error of metabolism, congenital disorders, Malaysia*

Introduction

Congenital anomalies affect approximately 1 in 33 infants. These anomalies cause approximately 3.2 million birth defect-related disabilities and an estimated 270,000 neonatal deaths annually (1). An increase in certified infant deaths from congenital anomalies has been observed in Malaysia even though the rate has declined as a result of improvements in nutrition and obstetric and neonatal services (2). Congenital abnormalities are the second leading cause of neonatal death in Malaysia (approximately 50%) according to Noraihan et al. (2). The World Health Assembly has recently called all member states to promote the primary prevention of congenital anomalies and the health of children with these conditions by (i) developing and strengthening registration and surveillance systems; (ii) developing expertise and building capacity; (iii) strengthening research and conducting studies on the etiology, diagnosis, and prevention of anomalies; and (iv) promoting international cooperation (1). Newborn screening (NBS) is one of the recommended preventive measures and involves clinical examination and screening for hematological, metabolic, and hormonal disorders. This program facilitates life-saving treatments and limits the progression of physical, intellectual, visual, and auditory disabilities.

NBS has been adopted worldwide as public health activity and has been well established in developed countries for over 40 years. NBS is recognized internationally as an essential, preventative health scheme that detects and treats inborn errors of metabolism (IEM) early prior to the onset of symptoms. Inherited metabolic disorders or IEM are genetic enzyme defects that cause the abnormal function of biochemical pathways (3). Patients with these disorders are unable to use or synthesize certain compounds, such as fatty acids, amino acids, organic acids, or other macromolecules (4). Acute or chronic symptoms of these conditions are frequently observed in infants and young children. The health of children with IEM often deteriorates suddenly, and the condition progresses rapidly as a result of severe, permanent brain damage (5). Individual IEM cases are rare but the collective prevalence of this condition is estimated to be 1 in 3,000 to 5,000 births in the general population. According to Raghuveer et al. (6), IEM has an incidence rate of a minimum of 1 in 1,500 persons in the United States. A number of reports on IEM in Malaysia have been published; however, the actual number of IEM patients cannot be derived from population-based studies (5).

NBS involves a comprehensive system

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of education, screening, follow-up, diagnosis, treatment/management, and evaluation which must be institutionalised and sustained within public health systems. This program often faces economic, political, and cultural challenges. For instances, the initiation and implementation of this program in developing countries, especially in South-East Asian and North African regions, are slow and limited by poor economies, unstable governments, unique cultures, geographic extremes, and varying public health priorities (7,8). A consensus regarding the disorders to include in screening panels has not been reached; therefore the coverage of congenital disorders is different among countries. However, most screening panels include various inborn errors in the metabolism of amino acids, fatty acids, and organic acids. We review the present status of and future concerns regarding expanded NBS in Malaysia in this paper. We also discuss some of the challenges in implementing and sustaining this program.

Current Status

NBS in Malaysia began with cord-blood screening for glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency) in 1980. In 2003, the Ministry of Health Malaysia implemented a nationwide, step-wise, congenital hypothyroidism (CH) screening program for all babies delivered in government hospitals. With the developing of audiological and intervention services for hearing-impaired children since the early 1990s, a few hospitals have implemented hospital-based newborn hearing screening in early 2000s. However, expanded NBS (inclusive of amino acid metabolism, fatty acid oxidation, and organic acid metabolism disorders) is not mandatory and has not yet been incorporated into the country's public healthcare system. At present, expanded NBS of IEM is being conducted mainly in two centers, namely Institute for Medical Research (IMR) and Centre for Advanced Analytical Toxicology Services (CAATS) on request by some of the private hospitals. IMR is under the auspices of Malaysian Ministry of Health, whereas CAATS (formerly managed by the Doping Control Centre) is a research and service laboratory under Universiti Sains Malaysia. Table 1 shows some of the statistics on NBS testing in CAATS. These data are obtained from routine samples sent by private hospitals with birthing and maternity facilities. The results provide an overview of the number of possible positive cases; however, the actual number of established IEM cases is not known because patient profiles are confidential and cannot be retrieved by the service centre.

Newborn screening Implementation Challenges

The population of the Asia Pacific constitutes over half of the total world population and births in this region comprise 49% of annual births worldwide (9). However, NBS coverage in some of the developing countries in the Asia Pacific remains very low (< 1%) (10). Several factors critical to a successful national NBS program have been identified in a survey conducted among

Table 1: Statistics on newborn screening testing at Centre for Advanced Analytical Toxicology Services from 2007–2013

Year	Number of samples	Number of positive samples*	Findings
2007	39	–	–
2008	745	3	Slight elevation of tyrosine & C16
2009	2081	3	Slight elevation of amino acid & acylcarnitine profiles
2010	966	1	Slight elevation of phenylalanine
2011	1211	7	Slight elevation of tyrosine, alanine, methionine, ornitine & C3
2012	801	–	–
2013**	501	–	–
Total	6284	14	

*Positive sample is referred to the sample that exceeded the cut off value.
**Samples counted up to 31 August 2013.

NBS managers in Asian countries: (i) government prioritization; (ii) full or partial government financing; (iii) public education and acceptance; (iv) health practitioner cooperation/involvement; and (v) government participation in NBS system institutionalisation (7). The challenges faced by NBS in Malaysia are similar to those of other developing countries and the main limitation is the high infrastructure cost required by this program. The cost of the instruments and manpower training used in the screening program is a significant issue in the establishment of this national program. The lack of medical or laboratory staff given the increased workload is another factor. Malaysia has a shortage of doctors and other support staffs at present: the current doctor-to-patient ratio in West Malaysia is 1:800, whereas the ratio in East Malaysia is approximately 1:1700. These ratios are lower than the recommended ratio of 1:600 set by the World Health Organization (11,12). Follow-up treatments and confirmation regarding positive NBS diagnosis requires experienced and knowledgeable personnel and medical or technical support is critical to sustainable NBS. However, very few specialists to whom referrals can be made once a positive disease diagnosis has been confirmed in newborns are practicing in this region (7). In the survey conducted by CAATS to investigate NBS awareness and acceptance levels among parents, clinicians, and hospital administrators in Malaysia, only approximately 20% of all registered private hospitals with birthing and maternity facilities sent samples for free expanded NBS testing (13). This finding reveals that public awareness of NBS is low and that clinicians and hospital administrators lack interest in this program. Perceived expenses and long turn-around time may also account for low IEM-screening rates. Insufficient knowledge, commitment, and the lack of ability to conduct NBS follow-up treatments/services in healthcare providers have also caused the discontinuation or initiation of the program.

Parental concern and perception play an important role in the choice to undergo screening. Parents normally obtain information regarding NBS from either pediatricians, gynecologists, or printed materials from clinics or hospitals. The majority of parents who consented to screening understand the principle behind metabolic testing according to Biswas et al. (14). The reasons cited by parents who opted not to undergo screening are either related to processes (IEM screening is being unimportant because it is optional), or understanding (the previous child is unaffected and well; the present child appears healthy; NBS is a research tool). Parents' judgment on risk assessment (IEM is deemed uncommon) and their emotional states also affect decision-making regarding screening (the test is too painful or the baby is too young to be tested) (14). However, Biswas et al. (14) found that cost is not the main barrier to the choice to undergo screening, even for parents from low socio-economic strata. Unnecessary worries may be one of the parental concerns because false-positive diagnoses are inevitable (15).

NBS tests face challenges different from those of other biochemical analyses. The test is time-sensitive, and the screening must be conducted in the first week of birth. Specimen-collection time frame is important because timely treatment before four weeks of age helps to prevent irreversible mental retardation, physical disability, and death in most cases (16). In normal practice, dried blood-spot NBS specimens are collected from infants before 72 hours of age or prior to hospital discharge. However, this process is logistically difficult for home deliveries or for mothers who return to their rural hometowns for a post-delivery confinement period of up to 42 days. Not all of these places have a dedicated public health facility to accommodate testing. Thus, following up and calling babies back to the facility for blood sampling or re-sampling for confirmation purposes or as a result of unsatisfactory and invalid samples is difficult.

Sustainability and Future Perspective

Integrating this program into the national health delivery system is the most critical element to its success and sustainability. Innovative and well-planned financial strategies (for example inclusion in health insurance schemes) enhance program sustainability. The extent of government involvement and the successful handling of all limitations have a direct impact on the implementation of expanded NBS and its coverage. Although additional expenses and difficult techniques are required, NBS has proven to be cost-effective in reducing neonatal mortality and morbidity in both developed and developing countries. For instance, the implementation of expanded NBS in Texas is reported more cost-effective than unexpanded NBS because the screened population benefited from greater quality-adjusted life-years (QALYs) (17). Good partnership among all sectors must be empowered to participate in program implementation. This partnership involves all pediatricians, obstetricians, midwives, neonatologists,

geneticists, endocrinologists, nurses, community health workers, hospital administrators, and policy makers.

Conclusion

NBS is an important tool in early diagnosis and treatment. Even though the prevalence of IEM may be low, this problem must be addressed early to avoid life-long impairments. Numerous published studies on expanded NBS have demonstrated that the program is feasible and beneficial. However, limited funding, manpower shortage, inadequate support services, low public awareness, and uncertain commitment by healthcare practitioners to NBS initiation and implementation are the typical obstacles encountered by several developing countries, including Malaysia. To ensure a better life especially for the next generation, the involvement and support from the policy makers are very important for the implementation of expanded NBS in the country.

Acknowledgement

A special thanks to Prof Dato' Mohamed Isa Abdul Majid for his guidance.

Conflict of Interest

None.

Funds

None.

Author Contribution

Drafting of the article: YHL
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