

## ORIGINAL ARTICLE

# HELICOBACTER PYLORI RELATED FUNCTIONAL DYSPEPSIA IN A DEFINED MALAYSIAN POPULATION

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The objective of the study was to determine the prevalence of *H. pylori* in functional dyspepsia among the three main races in Malaysia. Gastric antral biopsies from 233 (98 males, 135 females; age range: 17-75 years, mean age 39.5 years) patients attending the Universiti Kebangsaan Malaysia (UKM) gastroenterology clinic were assessed for the presence of *H. pylori* by culture and histology. About a third of the cases (79 of 233 (34%); 34 males, 45 females; mean age 42.6 yrs) were positive for *H. pylori*. The presence of *H. pylori* was always associated with antral gastritis. Malay patients were least likely to be positive for *H. pylori* (10 of 88 (11.4%); 5 males, 5 females; mean age 35.7 yrs) compared to the Chinese (43 of 95 (45%); 19 males; 24 females; mean age 40.2 yrs) and Indian patients (23 of 41 (56%); 10 males, 13 females; mean age 48.1 yrs). We found that *H. pylori* were most common among Chinese followed by Indians. However, the relative risk for the Indians was 8.58 and 6.29 for the Chinese compared to Malays. We conclude that the prevalence of *H. pylori* in patients with functional dyspepsia differs considerably with respect to ethnic groups.

*Key words : Helicobacter Pylori, dyspepsia, Malaysia*

### Introduction

Functional dyspepsia (FD) is a complex entity of disorders in which their genes are many and varied but not proven. It is common throughout the world including Malaysia. FD constitutes a significant percentage of upper gastrointestinal disorders and it is at least twice as common as peptic ulcer disease (1,2). In Malaysia, the magnitude of FD is impressive. Kudva et al. (1988) showed that 63% of males and 83% of females referred for endoscopic examination were diagnosed as FD.

The three groups of races, which form major components of the Malaysian population, are the Malays, Chinese and Indians. In Kuala Lumpur,

where the present study was conducted; the ethnic proportions are 33% Malay, 53% Chinese and 14% Indians (1). All three races show differences in FD frequency. The Malays are most susceptible and the Indians the least. The reasons for the differences are unclear. Among the numerous attributes implied to cause FD, *Helicobacter pylori* is now recognised as an etiology (2). Our previous findings had shown that a third of FD patients attending the gastroenterology clinic had *H. pylori* (3). We report here the detailed findings on the relationship between *H. pylori* and age, sex and have made particular reference to the prevalence of *H. pylori* in the main ethnic groups among the patients presenting at the gastroenterology clinic in UKM.

## Methods

### Patients

We studied 233 cases that were diagnosed as functional dyspepsia at endoscopy. Patients with gastric or duodenal ulcers, reflux esophagitis, irritable bowel disease, cancer of esophagus or stomach, and previous gastrectomies were excluded. Patients who had a recent history (up to 4 weeks before endoscopy) of antiulcer agents, corticosteroids, non-steroidal antiinflammatory drugs and antibiotic ingestion were also excluded. Patients that were included in the study were patients who did not have any of the exclusion criteria and who were diagnosed as FD which was taken to mean dyspepsia where clinical evaluation and basic laboratory tests failed to reveal an obvious structural cause for the symptoms and in which endoscopy was normal or there was visual evidence of non-erosive gastritis or non-erosive duodenitis. Patients selected were aged between 17 and 75 years. Informed written consent was obtained from these patients. This project was approved by the Ethics Committee of Universiti Kebangsaan Malaysia.

### Endoscopies

Endoscopies were done with an Olympus GIF – P2 fiberoptic endoscope. Biopsies were taken from the prepyloric antral area, corpus and duodenal bulb. Biopsies were usually taken from an inflamed area if present, otherwise any part of the mucosa was used. After each patient the biopsy forceps would be sterilised with gluteraldehyde and subsequently rinsed with saline.

### Histopathology

Biopsies were immersed in 10% formalin. Sections were stained with hematoxylin and eosin and the presence and severity of gastritis were graded

according to the modified Whitehead's criteria (6) and assessed by a histopathologist. The Warthin-Starry stain was used for confirmation when the H & E sections examined were doubtful for the presence of *H.pylori*.

### Statistical Analysis

Dichotomized data was compared using the chi-square test. A logistic regression model was used to determine the association of *H.pylori* with subjects' characteristics after adjusting for age and race. Adjusted odds ratios and 95% confidence intervals were calculated from this logistic model.

## Results

*H.pylori* was demonstrated in 79 of 233 (34.4%) cases studied. The demographic data of the total number of patients studied is summarised in Table 1.

### Sex and *H.pylori*

There was no difference in the gender ratio in each age or ethnic groups. The percentage of *H.pylori* positive patients was comparable in both genders (43.7 % males versus 33.3 % females).

### Age and *H.pylori*

The age specific prevalence rates of *H.pylori* are 26% in those aged less than 30, 29% in those between the ages of 30 and 49 and 41% for those above 50 years of age. The prevalence of *H.pylori* was noted to be higher in patients more than 50 years of age compared to those below 30 years ( $P=0.027$ ). The mean age of patients with *H.pylori* were older than those without the organism (43.2 (13.3) years versus 35.9 (12.4) years,  $P=0.002$ ). The relative risk of patients in the older age (50 years) groups to get the infection is greater compared to those aged less

Table 1. Demographic data of all subjects

<i>H.pylori</i> status	Total no	Age (yrs) (mean (SD))	Sex M:F	Race			
				Malays	Chinese	Indians	Others
Positive	79	43.2 (13.3)	34:45	10	43	23	3
Negative	154	35.9 (12.4)	64:90	78	52	18	6
All	233	35.6 (12.4)	98:135	88	95	41	9

than 30 years (Table 2). After adjustment for race, in comparison to patients less than 30 years, the relative risk of those aged between 30 and 40 years increased slightly but remained unchanged for the group more than 50 years (Table 2).

#### Race and *H.pylori*

The Indians had the highest race specific prevalence rates (56%) followed by the Chinese (45%). The Malays were the least likely to be positive for *H.pylori* (11.4%). The percentage distribution of infection by race showed that *H.pylori* occurred most commonly in the Chinese followed by the Indians and the Malays (Table 2). Having adjusted for age, the relative risk was increased for the Indians and the Chinese but low in the Malays (Table 2).

#### *H.pylori* and gastritis

Endoscopic gastritis was found in 82 of 233 (35%) patients studied. *H.pylori* was detected in 35 of 82 (43%) patients.

Histologic evidence of gastritis was detected in 38% (88 of 233 patients) of the total antral biopsy specimens examined. All 79 of 233 or 100% of patients who were positive for *H.pylori* showed histologic gastritis compared to only 9 of 154 (5.8%) *H.pylori* free patients. *H.pylori* was more commonly found in biopsy specimens that showed acute-on-chronic gastritis than those showing chronic gastritis alone but the reverse was true in *H.pylori* free specimens with gastritis.

The overall findings showed that the association between *H.pylori* and gastritis is highly

significant ( $P < 0.001$ ) and confirm the widely observed close relationship between the two. Endoscopic gastritis underestimated the presence of histological gastritis but was a reliable indicator of *H.pylori* associated gastritis when present.

## DISCUSSION

Our study shows that about a third of FD patients are infected with *H.pylori*. This finding is in agreement with other reports (7,8). However, many have reported higher frequencies of infection among FD cases, ranging from 50 – 87% (4, 8-10). This is probably due to the difference in the definition of FD used in the various studies and the different population evaluated. The gastric mucosa did not always show gross abnormality even in the presence of *H.pylori*. A previous report (11) had also stated that the findings at gastroscopy cannot be related to the presence of *H.pylori*. Definitive studies on the presence of *H.pylori* should rely on histology. In contrast to endoscopic findings of the gastric mucosa, all *H.pylori* positive cases had histological gastritis. Only a minority of negative cases had histological gastritis. Our data thus suggest that histological gastritis is closely related to the presence of *H.pylori*. The histologic structural changes that occur in the mucosa of infected individuals provide evidence to support the role of this bacterium in a subset of patients with FD. If *H.pylori* were merely an opportunistic pathogen colonising an already abnormal mucosa, the frequency of gastritis would be similar irrespective of *H.pylori* infection. Instead our findings show that the prevalence of gastritis is definitely higher in subjects with *H.pylori*. The clinical improvement and mucosal restoration in

Table 2. Results of Analysis using Logistic Regression.

Factors	% Positive <i>H.pylori</i>	% Negative <i>H.pylori</i>	Odds Ratio	Odds Ratio (Adjusted for race)	95% Confidence Interval
<b>Age (years)</b>					
<30	20.3*	29.2	1	1	
30-49	22.8	28.6	1.15	1.33	0.95-1.86
>50	56.9*	56.9	1.95	1.94	0.88-4.28
<b>Race</b>					
Malays	12.7	50.3	1	1	
Chinese	54.4**	33.8	9.96	6.29	2.90-13.66
Indians	29.1**	11.7	6.45	8.58	3.42-21.52

The prevalence of *H.pylori* is higher in the older age group \* $P=0.027$ .

The Indians and the Chinese have a higher prevalence of *H.pylori*, \*\* $P=0.001$  compared to the Malays.

subjects freed of the organism after treatment shown in our previous report (12) further support the contention that the organism may have a pathogenic role in a subset of FD patients.

Previous studies have reported that females have a higher frequency of FD (3, 13). In this study, we found that the subset of *H.pylori* related FD indicated no sex preponderance. This confirms the findings of others (14 -15). A study conducted in Singapore (17) showed that *H.pylori* associated FD was more common in the older group. This difference was observed in groups with only a slight age difference (43.8 (16.5) years versus 39.9 (17.2) years,  $P=0.002$ ). Due to the marginal difference in the age compared, it would be difficult to say with absolute certainty that the infection is more common in the older age group compared to the younger age group. More over, this age related frequency was without the adjustment for race. We found a similar age-related frequency but this relationship was no longer strong on multivariate analysis taking into account race, the range of confidence interval included the value 1. Thus, our study did not show any strong association between age and the frequency of infection. We conclude that at present, there is no overwhelming evidence that *H.pylori* is more common in the older age group. This is in agreement with other studies conducted in the European population (4, 16).

Our cohort study shows that the Malays are the most frequent race afflicted by FD (3). However, we found that the Malays were the least likely to be affected when *H.pylori* related FD was considered. We noted that in Malaysia, the prevalence was notably higher in Indians and the Chinese compared to the Malays. Similar findings were observed among Singaporeans (14). There certainly exist ethnic variation, with rates of 11% in Chinese aged between 30-49 years, and only 2% in Indians of the same age group. To adjust for the potential confounding between age, sex and race, a logistic regression model was fitted in our study with age, sex and race as independent variables. Race was found to be significant but not sex. From this model, the relative risks (Malays as reference) adjusted for age was only slightly reduced for the Indians and the Chinese. It can therefore be concluded that the higher risk of being positive for *H.pylori* in the Indians and Chinese compared to the Malays is real and not likely to be due to age. Others (17-19) have also observed ethnic variation.

Factors that can probably affect *H. pylori* carriage rates are socio-economic status,

sociocultural practice and religious dietary taboos practiced by the different races. The Malays appear to be relatively protected against the infection even though they make up a large percentage of FD patients. This further verifies FD as a heterogeneous disorder. Studies to evaluate the above mentioned factors are required for a clearer understanding on the ethnic variation as more reliable comparisons can be made between the different races.

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