PREVALENCE AND PREDICTORS OF HELICOBACTER PYLORI INFECTION IN CHILDREN AND ADULTS FROM THE PENAN ETHNIC MINORITY OF MALAYSIAN BORNEO

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Abstract. To determine the prevalence of Helicobacter pylori antigen carriage in stool in the Penan ethnic minority in Malaysian Borneo, we studied 295 Penans 0.6–89.0 years of age from 1) the remote Limbang Division, 2) Mulu regional center, and 3) Belaga village. Overall, 37.7% of the subjects tested positive. Peak prevalence was reached by 10 years of age. There were no differences in age, sex, body mass index, and socioeconomic/domestic variables between antigen-positive and antigen-negative subjects. In a logistic regression analysis, subjects from Limbang were least likely to be antigen-positive (odds ratio [OR] = 0.23, 95% confidence interval [CI] = 0.12–0.44 versus other sites, \( P < 0.001 \)). Availability of a flushing toilet was protective against \( H. pylori \) carriage (OR = 0.51, 95% CI = 0.27–0.95, \( P = 0.031 \)). Infection with \( H. pylori \) among the Penan was less than reported in other low socioeconomic groups. The lowest prevalence in the most remote setting suggests that the infection has been a recent arrival in previously isolated communities.

INTRODUCTION

Although infection with Helicobacter pylori is a global health problem, developing countries have generally higher rates of \( H. pylori \) carriage than those found in industrialized countries, especially in children.\(^1\)-\(^4\) This difference reflects socioeconomic factors including large families, crowded living conditions, and poor sanitation.\(^5\)-\(^8\) but ethnicity may contribute independently.\(^8\),\(^9\) There are limited epidemiologic data from southeast Asia regarding this issue. In a study from Singapore,\(^10\) Indian Asians had a higher prevalence of antibodies to \( H. pylori \) than either Chinese or Malays with, for example, 43%, 23%, and 20% seropositivity, respectively, in the 11–20-year-old age group. Nevertheless, peninsular Malays appear to have particularly low rates of \( H. pylori \) carriage,\(^11\) with only 13.5% of symptomatic adult patients referred for upper gastrointestinal endoscopy proving to be seropositive.\(^12\) It could be argued that these southeast Asian studies have involved subjects from relatively wealthy communities, while there are other minority ethnic groups in the region that do not enjoy the same standard of living and might therefore be at greater risk of \( H. pylori \) infection.

The Penan minority were, until relatively recently, jungle nomads living in Malaysian Borneo.\(^13\)-\(^15\) Most of the estimated 10,500 Penans are now semi-nomadic or live in remote settlements in the interior of Sarawak as part of Malaysian government plans to facilitate assimilation. Those who are settled are hunter-gatherers and subsistence farmers whose families inhabit crowded single-room longhouses. Illiteracy rates remain high, and understanding of personal hygiene and sanitation has been rudimentary. Property is largely shared and this extends to cooking and eating implements. Because their communities are in remote areas, health care is basic and treatment is commonly through medicinal plant extracts. Access to antibiotics has been limited. As with other poor communities in developing countries, the conditions under which the Penan live could foster the spread of \( H. pylori \) infection.

A major barrier to obtaining \( H. pylori \) prevalence data from remote communities is a lack of facilities for obtaining and processing laboratory samples including gastric biopsies and even sera. The recent development of stool antigen test-
In the remote Limbang region (Figure 2), settlements at Long Napir (∼17 families), Long Balau (∼20 families), Rumah King (∼7 families), Long Sulong (∼5 families), and Long Rayeh (∼8 families) were visited. Long Napir, the most readily accessible of these settlements, is four hours by air/four-wheel-drive vehicle from Kuching. The remaining four settlements are an additional 1−3 hours away by four-wheel-drive vehicle/walking trail. In the case of Mulu (Figure 3), Long Iman (∼32 families) and Batu Bungan (∼20 families) in Mulu National Park were accessed by air/four-wheel-drive vehicle/boat/walking trail. These settlements were 2.5−3.5 hours from Kuching. For the Belaga region (Figure 4), the settlements Sungai Asap (∼35 families), Long Ketueh (∼32 families), and Long Urun (∼6 families) were 2.5−6 hours from Kuching by air/four-wheel-drive vehicle.

Subjects were identified through village elders (who approved the study) and local medical assistants. We conducted three screening periods of up to seven days during 2001 and 2002, and Penans resident in the communities during these periods were recruited. Because of problems with literacy, verbal informed consent was obtained after explanation of study procedures and children were recruited only after parental consent was given. The study was reviewed and approved by the Universiti Malaysia Sarawak Faculty of Medicine and Health Sciences Research and Ethics Committee. 

Methods. A detailed questionnaire was administered to each subject through a Penan interpreter. The questionnaire included 1) age and sex; 2) employment status, educational level, and family income; 3) accommodation type, including number of resident family members, number of rooms, access to water and electricity, and toilet facilities; 4) history of smoking, diabetes, and other vascular risk factors; and 5) gastrointestinal symptoms (anorexia, nausea, vomiting, epigastric pain, epigastric reflux, abdominal distension, hematemesis and melena, weight loss, and previous endoscopies).

Height and weight were measured and the body mass index (BMI) was calculated. All stool samples for a H. pylori antigen assay were collected into airtight sterile containers that were put immediately in ice. The ice was replenished as necessary in settlements and major centers during transportation. The maximum times from when the stool samples were placed in ice and then transferred to freezer storage at −20°C in Kuching were 24 hours for Mulu and 36 hours for both Belaga and the remote Limbang region. Sample handling was therefore in accordance with that recommended by the assay manufacturer (Meridian Diagnostics, Inc., Cincinnati, OH).

Each stool sample was tested for the presence of H. pylori antigen using a commercially available enzyme-linked immunosorbent assay (ELISA) (Premier Platinum HpSA; Meridian Diagnostics, Inc.). A 5-mm³ aliquot of stool was added to 200 µL of diluent, mixed in a vortex, and 50 µL of the resultant suspension was pipetted into an ELISA plate well containing enzyme conjugate. After incubation and drainage, each well was washed five times with buffer and substrate was added. After further incubation, the reaction was terminated by acidification and the plates were read spectrophotometrically at a wavelength of 450 nm.

Statistical analysis was performed using the computer package SPSS for Windows version 11.5 (SPSS, Inc., Chicago, IL). Data are presented as proportions, mean ± SD, geometric mean (SD range) or, in the case of variables that did not conform to a normal or log-normal distribution, median (in-
FIGURE 3. Detailed map showing the settlements in Mulu (Long Iman and Batu Bungan) accessed in the present study.

FIGURE 4. Detailed map showing the settlements near Belaga village (Sungai Asap, Long Ketueh, and Long Urun) accessed in the present study.
terquartile range). The Student’s t-test was used for comparison of two means, Fisher’s exact test for two proportions, and the chi-square test for multiple proportions. Two-group non-parametric comparisons were made by the Mann-Whitney U test. Comparison of multiple groups was done by analysis of variance and the Scheffé post-hoc test. Linear and logistic regression were used to assess independent associations between variables. A two-tailed significance level of P < 0.05 was used throughout.

RESULTS

Subject characteristics. We recruited 295 subjects ranging in age from 7 months to 89.0 years. There were approximately equal numbers of males and females (50.2% males). The majority of subjects were from families with more than five members (52.8%) and lived in single-room communal longhouses (58.0%). Most had access to electricity (56.9%), a piped water supply (58.7%), and septic tank toilet facilities (70.5%). Of the 124 subjects more than 18 years old, 31.5% were current smokers while only 2.5% of those < 18 years old smoked. There was only one case of diabetes in the sample.

Prevalence of H. pylori antigen in stool. Overall, 37.7% of the subjects tested positive for H. pylori antigen. The age-specific prevalence of H. pylori positivity in the total sample is shown in Figure 5. The peak prevalence was reached in the first few years of life, with a relatively stable prevalence thereafter. This pattern was seen at each of the three sites (data not shown). In univariate comparisons, there were no significant differences in age, sex, or BMI in those who were antigen positive compared with those who were antigen negative (P > 0.30 in each case). In relation to socioeconomic and domestic circumstances, there were no significant differences by H. pylori stool antigen status in educational level (no formal schooling versus some education), income bracket (< Malaysian Ringit (RM) 300/month, equivalent to < US $80/month versus ≥ RM 300/month), residence in a longhouse versus other accommodation, number of household members, or access to piped water, electricity, or septic tank toilet facilities (P > 0.06 in each case). We also examined the relationship between variables relating to gastrointestinal symptoms and history and H. pylori stool antigen status (Table 1). No significant differences were seen (P > 0.07). When we considered subjects less than 14 years old as a separate group, there was no association between antigen status and height, weight, or BMI after adjusting for age (P > 0.25 in each case).

Study site and prevalence of H. pylori antigen in stool. Because subjects were drawn from different geographic areas, we divided them into three groups based on study site (Limbang, representing the more mountainous and remote areas of the Division, Mulu and Belaga; Table 2). Subjects from Limbang were approximately half as likely to be H. pylori antigen positive compared with the other two groups (P < 0.001, by chi-square test). The subjects from Belaga were significantly older, had a higher BMI, were more likely to be female, and were more likely to be smokers than those at the other two sites (P < 0.05, by Scheffé test). Residence in a longhouse was lowest in Belaga and highest in Mulu, and Belaga subjects were also more likely to have a family income > RM 300/month (P < 0.001, by chi-square test in each case). Access to piped water was greater in Mulu than the other two sites, but septic tank toilets with mechanical or manual flush-

DISCUSSION

The Penan ethnic minority provides a unique group in which to study the prevalence and predictors of H. pylori.
infection. The Penan people live in relative isolation, are usually domiciled in single-room longhouses, use communal cooking and eating utensils such as bamboo forks, may not have a reliable water supply or toilet facilities, and have limited access to antibiotic therapy that could facilitate eradication of the organism.\textsuperscript{13–15} We studied Penans living in three different situations. The prevalence of \textit{H. pylori} antigen positivity was least in those living in the most remote region (the mountainous jungle of the Limbang Division of Sarawak Province), a finding that persisted after adjustment for other possible contributory variables. The 77% lower adjusted prevalence in this setting suggests that \textit{H. pylori} infection has been a relatively recent arrival, and that earlier integration with other cultures such as Malays and Chinese has occurred at the other two sites. The Malaysian Government has implemented a program of resettlement of Penan communities with provision of basic housing, reliable electricity and water supplies, and sanitation. Interestingly, the Limbang people in the present study had the highest availability of septic tank toilets despite being the most geographically isolated. This proved an independent determinant of the low \textit{H. pylori} prevalence, albeit relatively minor compared with study site.

The prevalence of \textit{H. pylori} infection is strongly correlated with socioeconomic status but there are also wide differences between and within countries.\textsuperscript{1–4} Infection rates > 90% by five years of age have been reported in the developing world.\textsuperscript{19} Consistent with other studies,\textsuperscript{1–4} our data from children suggest that the infection is acquired in the first years of life, reaching a prevalence approaching 50% by 10 years of age. We are not aware of any prospective study that has tracked \textit{H. pylori} prevalence in isolated communities with initially low infection rates, but it is possible that greater numbers of Penan will carry \textit{H. pylori} in future unless living conditions improve further. Several studies have provided evidence of transmission of \textit{H. pylori} within families.\textsuperscript{20,21} Due to the fact that one or both parents were away during the screening of children, we were not able to gather valid data on clustering of antigen carriage within Penan families.

We found that use of septic tank toilets with mechanical or manual flushing had an independent protective association with \textit{H. pylori} prevalence compared with other methods of fecal waste disposal including pit latrines and defecation directly into the jungle and rivers. This suggests that greater attention to sanitation associated with toilet use led to reduced fecal-oral transmission. Although evidence for fecal-oral transmission of \textit{H. pylori} is inconsistent,\textsuperscript{22} acute diarrhea significantly increases fecal shedding of the organism into the environment\textsuperscript{23} and diarrheal diseases are relatively common in low socioeconomic communities such as the Penan.

Despite detailed questioning relating to the common gastrointestinal manifestations of \textit{H. pylori} infection, we did not show any association between antigen carriage and symptoms. This is consistent with past studies\textsuperscript{2} and the fact that the lifetime risk of peptic ulcer disease and gastric malignancy are only 15% and 0.1%, respectively, in infected individuals.\textsuperscript{24} There is no indication to treat asymptomatic carriers of the organism and, in the case of children,\textsuperscript{25} screening of those with dyspeptic symptoms using non-invasive tests is not currently recommended. Studies in the literature have not shown a consistent effect of \textit{H. pylori} infection on growth and development in children,\textsuperscript{26} and we did not find an association between \textit{H. pylori} antigen carriage and markers of growth in the subjects in our study who were younger than 14 years of age.

Infections that involve only humans comprise those that can persist in an individual for a prolonged period and those that are infectious only in the acute phase.\textsuperscript{27} The former exhibit high endemicity and the latter die out quickly. \textit{Helicobacter pylori} is likely to fall into the first category, especially given the living conditions in Penan communities. This implies that the low prevalence of \textit{H. pylori} carriage in the remote settlements of the Limbang Division is due to relatively recent introduction of the organism. Consistent with this suggestion, a study of amebic infection in the Orang Asli ethnic minority in Peninsular Malaysia showed a relatively low seroprevalence in an isolated village in the deep jungle compared with that in peri-urban settlements.\textsuperscript{28}

The present study had limitations. Because of logistic problems with communication, transportation, and access, we recruited a convenience rather than a random sample. There was a disproportionate number of children, primarily because adults in Penan communities spend periods away from their settlements gathering food for their families. Even with the services of an interpreter, complete questionnaire data were not always obtainable, especially when children and adolescents were interviewed without their parents being present. Although the detection of \textit{H. pylori} antigen in stool has a sensitivity and specificity of 90–95%, other tests (such as the urease test and culture of the organism from gastric biopsies) or test combinations may have improved our detection rate.\textsuperscript{16–18} Nevertheless, these cross-sectional data are the first from such a unique ethnic group and do provide insights into the epidemiology and modes of transmission of \textit{H. pylori} in the Penan.

Knowledge of the health status of the Penan people is limited. The present study adds to the current knowledge base, but prospective data on \textit{H. pylori} carriage are required to validate our hypothesis that the more remote Penan communities have been only relatively recently exposed to the organism. In addition, longitudinal data on \textit{H. pylori}-related
clinical events such as peptic ulcer disease, and perhaps also growth and development in children, would allow an assessment of the impact of \textit{H. pylori} in remote ethnic communities such as the Penan, and highlight situations in which screening and treatment should be considered.

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REFERENCES


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TABLE 2
Details of subjects classified by study site*

<table>
<thead>
<tr>
<th></th>
<th>Limbang</th>
<th>MuIu</th>
<th>Belaga</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>142</td>
<td>96</td>
<td>57</td>
</tr>
<tr>
<td>Age (years)†‡</td>
<td>13.2 (4.5–39.1)</td>
<td>14.0 (4.7–41.5)</td>
<td>20.2 (7.5–54.5)</td>
</tr>
<tr>
<td>Sex (% males)†</td>
<td>53.4</td>
<td>55.2</td>
<td>33.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)‡</td>
<td>18.1 ± 3.7</td>
<td>18.4 ± 4.5</td>
<td>20.2 ± 4.0</td>
</tr>
<tr>
<td>Current smokers (%)§</td>
<td>10.5</td>
<td>0</td>
<td>51.8</td>
</tr>
<tr>
<td>Domiciled in longhouse (%)§</td>
<td>53.4</td>
<td>82.3</td>
<td>28.1</td>
</tr>
<tr>
<td>No formal education (%)</td>
<td>61.1</td>
<td>67.0</td>
<td>67.9</td>
</tr>
<tr>
<td>Monthly family income &lt; RM300</td>
<td>96.2</td>
<td>99.0</td>
<td>74.5</td>
</tr>
<tr>
<td>(%)§</td>
<td>53.0</td>
<td>69.4</td>
<td>56.1</td>
</tr>
<tr>
<td>Access to piped water (%)§</td>
<td>91.2</td>
<td>54.2</td>
<td>56.1</td>
</tr>
<tr>
<td>Septic tank toilet (%§</td>
<td>55.6</td>
<td>59.7</td>
<td>56.1</td>
</tr>
<tr>
<td>Access to electricity (%)</td>
<td>25.4</td>
<td>51.0</td>
<td>47.4</td>
</tr>
<tr>
<td>% \textit{Helicobacter pylori} positive (%)§</td>
<td>25.4</td>
<td>51.0</td>
<td>47.4</td>
</tr>
</tbody>
</table>

* Values are the geometric mean (SD range), mean ± SD, or median [interquartile range] as indicated.
† P < 0.05 by analysis of variance or chi-square test.
‡ P < 0.01 by analysis of variance or chi-square test.
§ P < 0.001 by analysis of variance or chi-square test.

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