Prevalence of *Helicobacter pylori* infection in epilepsy patients in a teaching hospital in Malaysia

Megat Razeem Abdul Razak *MMed*, Hui Jan Tan *MMed*, Hamizah Razlan *MMed*, Norlinah Mohamed Ibrahim *MRCP*, *Rosnah Sutan MPH*

1Department of Medicine, *Department of Public Health, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

**Abstract**

*Background & Objective:* *Helicobacter pylori* infection has been associated with extradigestive diseases including epilepsy. The main aim of the study was to determine the prevalence of *Helicobacter pylori* using 13C urea breath test (UBT) in epilepsy patients in a teaching hospital in Malaysia and compared to control. **Methods:** The study subjects were epilepsy patients from the neurology clinic in a teaching hospital. The study was conducted from August 2010 to February 2011. The control consisted of healthy individuals matched for age and gender, not on any acid suppression medications and antibiotics. All subjects underwent UBT as per protocol. Variables such as age, race, household income, types of epilepsy, duration of epilepsy, number of antiepileptic drugs, prognosis were analysed. Good prognosis was defined as seizure free for 3 years. **Results:** Forty eight epilepsy patients and 47 control subjects were studied. Prevalence of *H. pylori* infection in the epilepsy patients was 37.5% (n=18) and was 36.2% (n=17) in control. There were significantly more subjects in the epilepsy group with lower income. There were also more smokers in the epilepsy group but there was no association between smoking and positive UBT. Epilepsy patients with poor prognosis have a higher UBT positive rate compared to the good prognosis group (64.3% vs 35.7 %). However the difference was not statistically significant. **Conclusion:** The prevalence of *H. pylori* infection in epilepsy patients is similar to that of the control in this study involving Malaysian subjects.

**INTRODUCTION**

*Helicobacter pylori* (*H. pylori*) cause multiple gastrointestinal and non gastrointestinal diseases which include gastritis, peptic ulcer disease, gastric cancer and mucosa associated lymphoid tissue (MALT) lymphoma,1-3 acute coronary syndrome, autoimmune diseases, Alzheimer’s disease, Parkinson’s disease and epilepsy.2,4-6 Although the exact mechanism is unknown, the immunological response has been postulated to be cytokine mediated by interleukin -6 and TNF α in a study by Crabtree et al.9

*Helicobacter pylori* infection is characterized by apparent geographical and time variations in the incidence of acute infection, a low rate of spontaneous loss or eradication of infection, and hence prolonged duration of infection in most people.10 Goh et al showed that there was a large variation in the prevalence rates occur between and within different population subgroups in Malaysia.10,15 The overall prevalence of *H. pylori* ranges from 26.4% to 55%.14

Recent studies showed that there is a higher prevalence of *H. pylori* in epilepsy patients.2,3 Okuda et al of Japan reported that the seroprevalence of *H. pylori* is substantially higher in idiopathic generalised epilepsy patients than in those with chronic disease.3 Furthermore, the seroprevalence rate of the good prognosis idiopathic generalised epilepsy patients (defined as seizure freedom for 3 years) was lower than the poor prognosis group i.e. 40.9% vs. 7%.3 The authors concluded that *H. pylori* infection, possibly through inflammatory response and production of anticardiolipin antibodies, is associated with certain types of epilepsy.3

Ozturk et al in Turkey studied the presence of *H. pylori* in epilepsy patients using *H. pylori* stool antigen (HPSA), serum Ig G and Ig M. The positive rates of HPSA, *H. pylori* Ig G and Ig M were significantly higher in the epilepsy group as compared to control, and between the poor versus good prognosis epilepsy patients.2 They concluded that there may be an association
between acute *H. pylori* infection and epilepsy, especially those with poor prognosis. Ozturk et al also suggested that *H. pylori* might trigger epilepsy by immunologic events via elevation of TNF-α and IL-6, and recommended that *H. pylori* infection should be investigated especially in poor prognosis epilepsy patients.

We thus aim to re-examine these associations in Malaysian epilepsy patients.

**METHODS**

This was a case control study conducted in a teaching hospital in Kuala Lumpur, Malaysia from August 2010 till February 2011. Approval was obtained from the ethics committee of the university. Forty eight epilepsy patients were recruited from the Neurology Clinic. The control group consisted of 47 healthy subjects with no history of dyspepsia, gastritis, or peptic ulcer disease. Patients on any histamine2 antagonist, proton pump inhibitor or antibiotics for the last 4 weeks, prior UBT, pregnant patients, and those who were unable to perform the UBT were excluded. The demographic data and clinical history of epilepsy were obtained from the subjects. Subjects then underwent 13C urea breath test (UBT) as per protocol. If the UBT was positive, patient was counseled for *H. pylori* eradication therapy.

Subjects were advised to fast for at least 4 hours prior to the test. Subjects were asked to blow into the first chamber of IRIS Twin Chamber Inflatable Bag as the base value. They were given orange drink ‘Tang’ with 75 mg 13C urea and blew their into the chamber bags at an interval of 10 minutes for 30 minutes. The collected 13C breath contained in the IRIS Twin Chamber Inflatable Bags would then be couriered to the Breath Centre for analysis with IRIS 13C Breath Analyser.

IRIS-2 (Infra Red Isotope) analyser measured the 13CO2 and 12CO2 concentrations from sequences of breath samples, and related their ratios to the (Pee Dee Belemnite) PDB-13C stable isotope standard. Measurements were made at breath samples from the sample bags. Standard breath bags had a volume of 120 ml breath gas, which would allow for two measurements per sample. The IRIS-autosampler would accept sixteen sample bags to be run in automated sequence at a cycle of two minutes per sample. IRIS software version 2.3 was based on Windows operating system (95, 98, 2000 and XP) and did provide routines for calibrations, for sample definitions and measurement control. It also provided a database to define and organized standardised breath test procedure, to note and store patient’s data, and to collect and administrate patient’s test results. Standardised graph allow comparison of patient’s mean 13C exhalation as measured by mean 13C exhalation. The results were considered positive when delta over baseline (DOB) was 4.0‰.

**RESULTS**

The 48 epilepsy patients and 47 controls consisted of 51 males and 44 females. The ethnic composition was Malays (70.5%), Chinese (21.0%), Indians (5.3%), and others (3.2%). The median age in the epilepsy group was 29.0 (21.3-33.8) years, and that of the control group was 29.0 (24.0-34.0) years. The number of smokers was significantly higher in the epilepsy patients (n=10) compared to the controls (10/48 vs 1/47, p=0.04). There was also significantly more subjects in the epilepsy patients who had income of less than RM 3,500 per month (p=0.009) (USD 1 = RM 3.2).

Table 1 shows the characteristics of the epilepsy patients. As shown, the median age of onset of epilepsy was 15.0 years, the median duration of epilepsy was 10.0 years, most had no neurological deficit, about half the patients had an abnormal imaging on computed tomography (CT) or magnetic resonance imaging (MRI), and 37.5% had abnormal electroencephalography (EEG). The median frequency of seizure was 2.5 per year. The median number of antiepileptic drugs was 1.0; 39.6% had generalised epilepsy, and 70.8% (n=34) had poor prognosis.

The percentage of positive UBT was 37.5% (n=18) in the epilepsy patients and 36.2% (n=17) in the controls, which was not statistically different (X2=0.18, df=1, p=0.893). There was no significant difference in age, gender and race in the UBT positive or negative epilepsy group. Of the 19 patients with generalised epilepsy, 5 patients (26.3%) had positive UBT. This was lower than the 44.8% (13/29 patients) in partial epilepsy. The difference was not statistically significant. The number of medications also did not have any significant association with positive UBT results. Epilepsy patients with poor prognosis have higher UBT positive rate compared to the good prognosis group. However the difference was not statistically significant (64.3% vs 35.7%, p = 0.87).
DISCUSSION

In spite of numerous studies and reviews reporting the association of \textit{H. pylori} and extradigestive diseases\textendash{19-22}, only limited studies investigate its relationship with epilepsy. Higher prevalence of \textit{H. pylori} has been reported to occur more in cryptogenic or idiopathic generalised epilepsy patients compared to chronic disease patients or normal controls\textendash{2,3} Both these studies (which were conducted in Japan and Turkey), used \textit{H. pylori} stool antigen (HPSA) or serology as a tool in detecting \textit{Helicobacter pylori}. In our study, we used the UBT to detect the prevalence of \textit{H.pylori} infection. UBT has been around for more than 15 years. As serum and stool antigen for \textit{H. pylori} is not widely available in Malaysia, hence our study used UBT which is a non invasive technique and has a very good specificity and sensitivity\textendash{10-12,23-25}.

Unlike the previous studies\textendash{2,3}, we did not find an association between epilepsy and \textit{H. pylori}. The prevalence rate of \textit{H. pylori} infection in our epilepsy patients and controls at 37.5\% and 36.2\% respectively, was comparable to 35.9\% reported by Goh and Parasakthi in 2001 among the Malaysian population\textendash{14}.

We also did not find an association between gender and UBT positivity. The relationship between gender and prevalence in the literature has not been consistent\textendash{14,15,17,18,27,29,30} In the study by Okuda \textit{et al}, they found that idiopathic generalised epilepsy patients was associated with higher prevalence of \textit{H. pylori}\textendash{3} In our study, 39.6\% (n=19) had generalised epilepsy. Only 5 patients with generalised epilepsy (26.3\%) had a

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=48</th>
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<tbody>
<tr>
<td>Age of onset (years)\textsuperscript{a}</td>
<td>15.0 (8.3-23.8)</td>
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<tr>
<td>Duration of epilepsy (years)\textsuperscript{a}</td>
<td>10.0 (4.3-18.8)</td>
</tr>
<tr>
<td>Neurological exam, abnormal, n (%)</td>
<td>3 (6.4%)</td>
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<tr>
<td>Radiological exam, abnormal (CT brain or MRI), n (%)</td>
<td>21 (43.8%)</td>
</tr>
<tr>
<td>EEG findings, n (%)</td>
<td>Abnormal 18 (37.5%), 1. Partial 16 (88.9%), 2. Generalised 2 (11.1%)</td>
</tr>
<tr>
<td>Frequency of seizures per year\textsuperscript{a}</td>
<td>2.5 (0-10.0)</td>
</tr>
<tr>
<td>History of status epilepticus, n (%)</td>
<td>2 (4.2%)</td>
</tr>
<tr>
<td>Family history of epilepsy, n (%)</td>
<td>7 (14.6%)</td>
</tr>
<tr>
<td>History of febrile convulsion, n (%)</td>
<td>15 (31.2%)</td>
</tr>
<tr>
<td>Epilepsy classification, n (%)</td>
<td>Generalised 19 (39.6%), Partial 29 (60.4%)</td>
</tr>
<tr>
<td>Number of medications \textsuperscript{a}</td>
<td>1.0 (1.0-2.0)</td>
</tr>
<tr>
<td>Antiepileptic agents, n (%)</td>
<td>Sodium valproate 24 (50.0%), Carbamazepine 15 (31.2%), Levetiracetam 9 (18.8%), Phenotoin 8 (16.7%), Lamotrigine 8 (16.7%), Topiramate 3 (6.3%), Phenobarbitone 2 (4.2%), Gabapentin 1 (2.1%)</td>
</tr>
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\textsuperscript{a}: median (25\%, 75\% percentiles)
positive UBT. There was no significant difference between the types of epilepsy and positive UBT. However, our sample size was small.

In our study, 70.8% (n=34) had epilepsy with poor prognosis. Although there was a trend showing epilepsy patients with poor prognosis having a higher UBT positive rate as compared to the good prognosis group; the difference was not statistically significant. As mentioned above, both Okuda et al and Ozturk et al have demonstrated correlation between epilepsy with poor prognosis and positive H. pylori serology. The difference between our results and the previous studies could also be due to small sample size and differences in the tools used in detecting H. pylori.

In conclusion, using UBT to detect H. pylori infection, we fail to find a significant association between epilepsy and higher prevalence of H. pylori infection, and the association poor prognosis epilepsy patients and seropositive rate of H. pylori. However, the study sets the platform for further studies using a larger sample size to detect the significance of H. pylori in epilepsy patients.

REFERENCES

18. EUROGAST. Epidemiology of, and risk factors for, Helicobacter pylori infection among 3194 asymptomatic subjects in 17 populations. Gut 1993; 34.