The prevalence of *Helicobacter pylori* infection in Sherpa residents of the Upper Khumbu, an isolated community in eastern Nepal

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**Abstract**

**Aim** To determine the prevalence of *Helicobacter pylori* (*H. pylori*) among Sherpa residents of the Upper Khumbu region of Nepal and to test for associations between presence of *H. pylori* infection and lifestyle and health measures.

**Method** Written questionnaires were used to collect data from 383 individuals in randomly selected households in three villages of the region. Early morning stool samples were tested immediately for the presence of *H. pylori* antigen using standard rapid diagnostic Pylori strips. A descriptive data analysis was performed to estimate overall prevalence and its association with age, sex, dyspepsia, smoking, alcohol intake, diet, and medication use.

**Results** The overall prevalence of *H. pylori* in the study sample was 70.5%. The prevalence was high in all the three villages of Thame, Kunde and Fortse. Prevalence was high in all age groups, including a high prevalence of 78.1% in children aged <10 years. The presence of *H. pylori* was not significantly associated with any of the lifestyle and health measures collected, including dyspeptic symptoms, medication, smoking, alcohol intake and dietary factors like salt, smoked food, fruit/vegetable and pickle consumption.

**Conclusion** The overall prevalence of *H. pylori* in Upper Khumbu is high with the infection being acquired early in the first decade of life. This lifelong infection may explain the very high incidence of gastric cancer in this community. The rate of infection is not dependent on individual variables including demographic, social and dietary factors.

The upper Khumbu, located in the eastern Himalayas of Nepal, where many residents live above 3400 meters, is one of the highest permanently inhabited regions of the world. It is home to around 3300 indigenous Sherpa people. The region is isolated, more than a week’s walk from the nearest road-end. Kunde Hillary Hospital was built by Sir Edmund Hillary in 1966 and is the primary medical centre for the Upper Khumbu area.

Both dyspepsia and gastric cancer appear to be particularly prevalent in this Sherpa community. According to hospital records, dyspepsia accounted for more than 12% (1590) of the total (12,904) outpatient consultations made in the 2 years, July 2007 to July 2009. Over the same period 9 patients died of histologically proven gastric cancer, a mortality rate of 269 per 100,000 per annum (confidence interval (CI): 131.4, 530.2) in this Sherpa population.
By comparison, the International Agency for Research on Cancer (IARC) estimates the age-standardised worldwide mortality rate for gastric cancer as 10.3 per 100,000.\(^1\) There were no recorded deaths from other forms of cancer over the same period. Anecdotal evidence obtained from the resident doctors suggests that dyspepsia is much more common in the Sherpa community than in other ethnic groups in the region.

Current practice at Kunde Hillary Hospital is to treat all cases of dyspepsia with Histamine H2 receptor blockers and move to proton pump inhibitors should initial treatment fail. Triple therapy (omeprazole, clarithromycin and amoxicillin) for Helicobacter pylori (H. pylori) eradication is reserved for patients who present with upper gastrointestinal (GI) bleeding. Currently no testing for H. pylori is undertaken. Patients with symptoms and signs suggestive of stomach cancer are referred to the capital city, Kathmandu, for endoscopy and further management.

We postulated that this high incidence of upper GI disease could be explained by a correspondingly high prevalence of H. pylori and that determining this could guide treatment strategies. The link between H. pylori, chronic gastritis, peptic ulcer disease and malignancies including MALT lymphoma and gastric cancer is well established.\(^2–6\)

The Eurogast study group found an approximate six-fold increase in the incidence of gastric cancer in populations with 100% H. pylori infection compared to a population with no infection.\(^5\)

Infection with H. pylori is distributed worldwide but its prevalence is especially high in developing countries.\(^2,4,9\) The variation in H. pylori prevalence between different communities is mostly due to differences in the incidence of the bacterial infection during childhood.\(^11\)

In developing countries the infection is usually acquired during childhood and has been linked to low socioeconomic status, poor sanitation and dietary factors.\(^9,11–13,15,16\)

We aimed in this study to investigate whether H. pylori prevalence in the Upper Khumbu was high enough to suggest a change in clinical practice, and whether H. pylori was related to particular lifestyles of the Sherpa people in the region.

**Methods**

**Sampling method and sample size**—The Upper Khumbu region has a population of 3,335 (digital Himalaya Census of Nepal), with people living in small seasonal settlements and larger permanent villages scattered throughout the region.

Only Sherpas were included in the study. Members of other ethnic groups form a transient population group who live and work in the Khumbu, mostly during the trekking seasons. They are not registered in the local population databases. Only Sherpa households are included in the databases that were used to find participants. Participants were drawn from three of the largest villages – Thame (population 299), Fortse (population 322) and Kunde (population 292). These three villages provide a reasonable representation of the Upper Khumbu both geographically and socioeconomically.

A sample size of 384 was established, based on the sample size formula: 

\[
n = \frac{Z^2 \times P \times (1-P)}{d^2}
\]

where \(n\) = sample size, \(Z\) = Z statistics for level of significance, \(P\) = expected prevalence or proportion and \(d\) = precision.\(^17\) This was calculated using a H. pylori prevalence assumption of 50% with a 95% confidence interval and a precision of 5%. Households, rather than individuals, were randomly selected for practical and cultural reasons.

All households in the three villages were allocated specific numbers and the numbers were randomly selected using an online sample generator. All members of the selected households were included in
the study. 33, 32 and 35 households were needed from Thame, Kunde and Fortse, respectively, in order to give the desired sample size of 128 participants from each village.

The size of families living in selected houses ranged from one to nine members with an average of four. Individuals who were absent at the time of data collection and not expected to be home during the nine months study duration were excluded from the study.

**Questionnaire**—The *de novo* written questionnaire was piloted on 30 patients visiting Kunde Hillary Hospital. The data collection was undertaken by the community medical assistants employed by Kunde Hillary Hospital and the principle investigator. Written informed consent was sought from all eligible candidates and from the family heads in the case of children.

The questionnaires contained the following information: 1) demographics including age and sex, 2) medical history of upper GI disorders including dyspepsia, upper GI bleeds and stomach cancer, 3) medication intake in the form of antacids, histamine H2-receptors antagonists and proton-pump inhibitors, 4) family history of gastric cancer and history of gastric surgeries, 5) dietary history including salt, smoked food, fruit and vegetable and pickle intake, and 6) history of alcohol, cigarette and chewing tobacco consumption.

Ethical approval was obtained from the Nepal Health and Research Council (NHRC).

Households were visited to explain the study, seek consent and collect data. Study participants were given clean, leak proof plastic containers without preservatives and were asked to bring two loops of early morning stool samples to the villages’ clinic laboratory. Participants were asked to stop taking antibiotics and proton pump inhibitors for four weeks and to stop taking H2 receptor blockers and antacid for two days prior to providing a sample. The stool samples were stored in icepacks and study tests were performed on the day of stool collection.

**H. pylori stool antigen test**—Most *H. pylori* prevalence studies have been based on serological testing. However, the sensitivity and specificity of serology is low and serology tests do not distinguish between past and current infection. Endoscopy and biopsy followed by culture is considered the gold standard for establishing *H. pylori* infection but this can be performed only in specialized centres and is not practical for population based studies. The 13C-urea breath test (UBT) has a high sensitivity and specificity but is expensive and difficult to perform. In a resource limited setting like ours the stool antigen test appeared to be a valuable alternative. The stool antigen test is highly sensitive and specific.

A systemic review of 43 studies in 2001 found that the sensitivity, specificity, positive predictive value and negative predictive value (weighted mean) were, 92.4 % (95% CI: 91.0%, 93.0%), 91.9% (CI: 91.0%, 92.0%), 92.1% (91.0%, 93.0%), and 90.5% (90.0%, 91.0%) respectively. In view of its high diagnostic accuracy and ability to determine current infection, the stool antigen test can be a favoured approach in prevalence studies. Moreover the test is non-invasive, cost effective and simple to perform, and therefore was considered most appropriate for use in our study.

Commercially available test kits manufactured by Coris Biocept were used in accordance with the manufacturer recommendations. According to the manufacturers specifications the kits have a sensitivity of 97.1% and specificity of 96.7%. It is a spot test that is based on the homogeneous membrane system technology with latex microspheres.

The stool samples were diluted with 0.5 ml of buffer (HC) solution (Saline solution buffered to pH 7.5 with Tris-EDTA, NaN3 (<0.1%), a detergent, and charged proteins) until a homogenous solution was obtained. The test strip was then dipped into the faecal suspension and allowed to stand for up to 10 minutes. The interpretation of the test depends on the appearance of coloured lines on the strip (one green line = negative; one green line AND one red line = positive; no line = invalid). Invalid tests were repeated again for reconfirmation.

**Statistical analysis**—The statistical analysis used SPSS (Statistical Package for the Social Sciences) and Stata 11 software. Comparison of the variables used Pearson’s Chi-squared test, Fisher’s exact test for smaller values and a test for trend. Logistic regression analyses were run with age, sex, heartburn history, family history of gastric cancer and village (± dietary variables) in the models, run both taking into account household clustering and without clustering.

Participants who requested it were provided with the results of their test.
Results

The total sample size was 383; 174(45.4%) males and 209(54.6%) females. No one refused to join the study and only one person was dropped from the study (failure to provide a stool sample). Overall 270 (70.5%) participants were positive for *H. pylori*. There was no significant difference in prevalence between sexes.

The sample was divided into age groups with 108(28.2%) children under 19 years, 201 (52.5%) adults aged 19 to 59 years and 74(19.3%) elderly over 60 year old. The prevalence (95% CI) in these three age groups was 72.2% (62.6, 80.2), 70.7% (63.7, 76.6) and 67.6% (55.6, 77.7) in children, adults and elderly respectively, as shown in Figure 1.

Children aged <10 years had higher *H. pylori* prevalence than other age groups (78.1%) but none of the differences between age groups reached statistical significance (p-value for trend = 0.509). *H. pylori* prevalence in Fortse, Thame and Kunde was 62.2%, 72.7% and 76.6 % respectively. The difference between the villages was statically significant (p=0.034).

Figure 1. *H. pylori* results according to age group

A history of dyspepsia was reported by 154(40.20%) participants, 15(3.91%) had a history of upper GI bleeding, and 18 (4.93%) had a family history of stomach cancer. No statistically significant association was identified between *H. pylori* infection and dyspepsia, upper GI bleeding or family history of stomach cancer, as shown in Table 1. Likewise there was no statistically significant association between *H. pylori* and diet, tobacco use or alcohol consumption.
Table 1. Association of medical history, lifestyle factors and dietary factors with *H. pylori* infection

<table>
<thead>
<tr>
<th>Medical and lifestyle variables</th>
<th>Total</th>
<th>N (%) <em>H. pylori</em> positive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History of dyspepsia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No</td>
<td>229</td>
<td>167(72.9)</td>
<td>0.204a</td>
</tr>
<tr>
<td>- Yes</td>
<td>154</td>
<td>103(66.9)</td>
<td></td>
</tr>
<tr>
<td><strong>History of upper gastrointestinal bleeding</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No</td>
<td>368</td>
<td>261 (70.9)</td>
<td>0.363a</td>
</tr>
<tr>
<td>- Yes</td>
<td>15</td>
<td>9 (60.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Family history of stomach cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No</td>
<td>365</td>
<td>260(71.2)</td>
<td>0.155a</td>
</tr>
<tr>
<td>- Yes</td>
<td>18</td>
<td>10(55.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
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<td></td>
</tr>
<tr>
<td>- Never smoked</td>
<td>368</td>
<td>259(70.4)</td>
<td>0.937b</td>
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<tr>
<td>- Ex-smoker</td>
<td>2</td>
<td>2(100.0)</td>
<td></td>
</tr>
<tr>
<td>- Current smoker</td>
<td>13</td>
<td>9(69.2)</td>
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<tr>
<td><strong>Chewing tobacco use</strong></td>
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<td></td>
</tr>
<tr>
<td>- No</td>
<td>371</td>
<td>263(70.9)</td>
<td>0.348a</td>
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<tr>
<td>- Yes</td>
<td>12</td>
<td>7(58.3)</td>
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<tr>
<td><strong>Alcohol consumption</strong></td>
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</tr>
<tr>
<td>- Never</td>
<td>247</td>
<td>178(72.1)</td>
<td>0.237b</td>
</tr>
<tr>
<td>- Social</td>
<td>110</td>
<td>75(68.2)</td>
<td></td>
</tr>
<tr>
<td>- Daily</td>
<td>19</td>
<td>14(73.7)</td>
<td></td>
</tr>
<tr>
<td>- Heavy drinker[^d]</td>
<td>7</td>
<td>3(42.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Dietary variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Smoked food intake</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Low</td>
<td>381</td>
<td>269(70.9)</td>
<td>0.504c</td>
</tr>
<tr>
<td>- High</td>
<td>2</td>
<td>1(50.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Salt intake</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Low</td>
<td>335</td>
<td>235(70.2)</td>
<td>0.694a</td>
</tr>
<tr>
<td>- High</td>
<td>48</td>
<td>35(72.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Fruit/vegetable intake</strong></td>
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<td></td>
<td></td>
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<tr>
<td>- Low</td>
<td>344</td>
<td>239(69.5)</td>
<td>0.194a</td>
</tr>
<tr>
<td>- High</td>
<td>39</td>
<td>31(79.7)</td>
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</tbody>
</table>

[^a]: Pearson's Chi^2^ test;[^b]: Test for trend;[^c]: Fisher's exact test (if cell count <5).
[^d]: Daily consumption starting in the morning.

Discussion

We found in this study that the prevalence of *H. pylori* infection in the Upper Khumbu region of Nepal was 70.5%. The methods used for this study may be unusually robust in that samples were collected from almost 100% of Sherpa people living in a random sample of households of remote villages, using a test that is specific for active disease.

In most other prevalence studies the samples groups have been selected by other means (e.g. blood donors) and tested using serology, which does not differentiate between active and past infection.

*H. pylori* prevalence is known to be related to poor socioeconomic status, household crowding, education, hygiene and sanitation.\[12,13,15,16\] These are all common in isolated
rural communities in developing countries. H. pylori prevalence in this study was higher than that found in a rural village of Nepal, Kyotang in 1998 (41.5%) but it is comparable to the prevalence found in isolated rural communities in other parts of the world. A prevalence of 69% was observed among residents of a rural community in the Columbian Andes. Similarly, high prevalence’s of 72.3% and 91% were found in a rural Beninese population and an indigenous, rural community in Western Australia, respectively.

A surprising result from this study was the very high prevalence amongst children - at least as high as it was in older age groups. Once acquired, H. pylori infection usually persists in a chronic form. While most infections in developing countries are acquired in childhood the prevalence in children is still usually lower, gradually increasing as age advances.

Studies in children of Peru and Pakistan revealed a prevalence of 50% and 47% (respectively) - considerably lower than our figure of 78%. However a very high H. pylori prevalence, similar to that shown here, was found in school children of Iran and children aged less than 8 years in Bangladesh.

A study of Japanese American men provides evidence that the early acquisition of H. pylori infection is associated with an increased incidence of gastric cancer and gastric ulcers later in life. The early acquisition and long duration of H. pylori infection may explain the very high incidence of gastric cancer and chronic gastritis in the Sherpas of the Upper Khumbu.

These results mandate a change in practice for the management of dyspepsia in the area. When the prevalence of H. pylori in the community is greater than 30% authorities recommend a ‘test and treat strategy’. Instead of treating patients empirically with H2 blockers, patients presenting with dyspeptic symptoms in the Upper Khumbu should be tested for H. pylori and if positive treated with triple therapy to eradicate the infection. There is also evidence suggesting that H. pylori eradication in high risk populations can reduce the incidence of gastric cancer.

A new treatment strategy has the potential to reduce the burden of upper GI disorders including gastric cancer. While it may be more expensive in the short term it may be cost effective in the long term by providing a cure for what are otherwise chronic problems. The Himalayan Trust is looking at funding options. The incidence of upper GI disorders in the Khumbu should be monitored long term to evaluate the effectiveness of this strategy.

Competing interests: Nil.

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Funding: The study was funded by the University of Otago, New Zealand and the Sir Edmund Hillary Foundation of Canada (Toronto) – [www.thesiredmundhillaryfoundation.ca](http://www.thesiredmundhillaryfoundation.ca)

Acknowledgments: We thank all the participants for their willingness and cooperation and the local community medical assistants who helped us in the data collection process. We are also very grateful to Kunde Hillary Hospital in Nepal for helping us with the logistics.

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