

Dyspepsia, *Helicobacter pylori*, and peptic ulcer in a randomly selected population in India

P H Katelaris, G H K Tippett, P Norbu, D G Lowe, R Brennan, M J G Farthing

Abstract

There seems to be a worldwide geographic variation in the prevalence of peptic ulcer disease, although there are few reliable population based studies. This study aimed to determine the prevalence of peptic ulcer disease in a community in southern India and to evaluate the relationship between dyspeptic symptoms, *Helicobacter pylori* infection, gastritis, and peptic ulcer disease. A sample population was selected randomly from a rural monastic settlement in southern India. Subjects were interviewed using a standardised symptom and demography questionnaire then underwent upper endoscopy and antral biopsy for histology and CLO rapid urease test. Altogether 197 subjects from a population of 1499 (13.1%) were studied. All were male monks and ethnically Tibetan. The median age was 28 years (range: 21-81). None smoked or took NSAIDs. The six month period prevalence of dyspeptic symptoms was 68.5%. Current symptoms were present in 58.9% of subjects. Dyspepsia was more common in subjects aged 40 years or younger ($p < 0.0001$). *H pylori* was detected in 77.2% subjects. There was no association between dyspepsia and the presence of *H pylori* or histological gastritis, although there was a strong correlation between symptoms and ulcer ($p < 0.003$). The point prevalence of active peptic ulcer was 6.6% (13/197). All ulcers detected were either prepyloric or pyloroduodenal in location. A further 6.6% of subjects had definite evidence of scarring or deformity indicative of ulceration in the past. Subjects with past or present ulcers comprised 17.8% of dyspeptic subjects. *H pylori* was present in all subjects with active ulcers and in 12/13 of those with scarring. Dyspepsia, *H pylori* infection, gastritis, and peptic ulcer are all more common in this population than in those from developed countries. Ulcer disease, however, accounts for only a small proportion of subjects with symptoms and neither *H pylori* infection nor gastritis are significantly associated with the presence of dyspepsia.

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Peptic ulcer disease is common and is associated with considerable morbidity and mortality worldwide. There seems to be a wide geographical variation in its prevalence¹⁻³ but few studies defining prevalence within a population have been based on a randomly selected sample. Many studies have included subjects with known or undefined selection bias (such as presence of symptoms or hospital referral) that will not reflect the true prevalence of ulcer disease in a

population. Furthermore, many studies have relied on self reporting, government statistics, or suboptimal diagnostic methods rather than endoscopy for diagnosis.

Dyspepsia and peptic ulcer disease are considered to be common in India but there is little reliable information regarding prevalence. Available information is generally derived from studies of symptomatic subjects, post mortem findings, or hospital based surveys, none of which give a true indication of disease prevalence.³ Moreover, many studies have relied on single contrast barium studies or symptom assessment alone, methods that cannot now be considered acceptable for accurate diagnosis of gastroduodenal pathology. Nearly all of these studies were undertaken before the recognition of *Helicobacter pylori* as an important factor in gastroduodenal diseases and there are few data on *H pylori* prevalence in India. *H pylori* is accepted as the major cause of chronic gastritis and is increasingly linked aetiologically with peptic ulcer disease and gastric cancer.^{4,5} However, the relationship of *H pylori* to dyspeptic symptoms remains controversial.

There are over 100 000 Tibetans living in settlements throughout India. There are no data on disease prevalence in this population. From clinical observation, dyspepsia is thought to be a very common symptom. The aims of this study were to determine the prevalence of peptic ulcer disease in a Tibetan community in southern India and to evaluate the relationship between dyspeptic symptoms, *H pylori* infection, gastritis, and peptic ulcer in this population.

Methods

STUDY POPULATION

The Mundgod Tibetan settlement in Karnataka State lies on the western edge of the Deccan Plateau in southern India. The settlement has a population of 10 000 consisting of several small villages integrated with two Buddhist monastery complexes. This rural community is racially wholly Tibetan and relies on agriculture for subsistence. Villagers and monks share a similar diet, customs, and standard of living. The monasteries house 2544 monks, 98.3% of whom are male and 1499 aged 21 years or older at the time of the study.

SUBJECT SELECTION AND ASSESSMENT

The subjects for inclusion in the study were selected from the monastery population registers of male monks 21 years or older. Randomisation was achieved by using a table of random numbers. The only exclusion criteria were a

Departments of
Gastroenterology and
Pathology,
St Bartholomew's Hospital,
London
P H Katelaris
G H K Tippett
D G Lowe
R Brennan
M J G Farthing

Doeguling Tibetan
Hospital, Mundgod,
Karnataka State, India
P Norbu

Correspondence to:
Dr P Katelaris, Department of
Gastroenterology,
St Bartholomew's Hospital,
West Smithfield, London
EC1A 7BE

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serious illness or other contraindication to upper gastrointestinal endoscopy. Informed consent for this study was obtained from the Doeguling Hospital Administration, heads of monasteries, and each individual subject.

Symptoms in each subject were assessed by two interviewers, one of whom was a Tibetan physician. A structured symptom questionnaire was used. There is a specific Tibetan phrase in common use which describes dyspepsia and translates as 'epigastric burning pain.' This phrase was included in the questionnaire. Details of the duration, frequency, and type of symptom as well as associated features and response to treatment were also sought. Dyspepsia was defined as any intermittent or persistent pain, nausea, or discomfort referable to the upper alimentary tract that had been present for one month or more and was unrelated to exertion. Patients with jaundice or bleeding were excluded.⁶ Any available medical records and previous investigations were also assessed. On the basis of this information, subjects were regarded as having dyspeptic symptoms currently or recently (within six months) or as not having dyspeptic symptoms.

All subjects had a physical examination and a blood sample was taken for a differential white cell count and blood grouping. After this all subjects underwent an upper gastrointestinal endoscopy with an Olympus XQ10 panendoscope. All endoscopic examinations were performed by a single endoscopist who was unaware of the clinical symptom status of each subject. Endoscopic findings were recorded using standard definitions.⁷ Past ulceration was inferred if there was definite evidence of scarring or deformity such as a pseudodiverticulum. Endoscopic appearances of gastritis were classified according to the Sydney system classification of gastritis: endoscopic division.⁸ A biopsy specimen was taken 2 cm from the pylorus anteriorly for a rapid urease test for the detection of *H pylori* (CLO test, Delta West, Western Australia). Two biopsy specimens were taken from 2 cm anterior and posterior to the pylorus for histological examination using haematoxylin and eosin, periodic acid Schiff alcian blue, and cresyl fast violet stains. Gastritis and the presence of *H pylori* were assessed on these sections using the Sydney system classification of gastritis: histological division⁹ by a pathologist unaware of the endoscopic findings. Lesions found on endoscopy were biopsied for histological diagnosis where appropriate. As the CLO tests and histology are both sensitive and specific, the subject was considered positive for *H pylori* if the CLO test or histology, or both, was positive, and negative for *H pylori* if both the CLO test and histology were negative.

The point prevalence of peptic ulcer was defined as the frequency of active peptic ulcer disease in the sample population at this examination. Cumulative prevalence was defined as the proportion of the population who had evidence of peptic ulcer at some time in their lives, either at the time of the study or in the past.

To ascertain whether the prevalence of *H pylori* among monks was representative of that in the community as a whole, randomly selected

villagers were interviewed and 28 consecutive subjects with dyspeptic symptoms underwent endoscopy and had *H pylori* status determined. The prevalence of *H pylori* in these subjects was compared with that in an equal number of age matched, randomly selected monks with dyspepsia.

STATISTICAL ANALYSIS

Data were analysed using the χ^2 test or Fisher's exact test for difference between variables and the Wilcoxon rank sum test where appropriate.

Results

Two hundred and five subjects 21 years of age or older were randomly selected for the study. Eight were excluded – in five selection was not random, one was too ill, one declined investigation, and one was unable to be endoscoped. All 197 evaluable subjects were male monks and racially Tibetan. The median age was 28 years (range: 21–81). None of the sample population smoked, consumed alcohol or NSAIDs, or had had previous upper gastrointestinal surgery.

Endoscopic findings are summarised in Table I. Active chronic peptic ulcers were found in 13/197 subjects, a point prevalence of 6.6%. All ulcers were either duodenal, pyloric, or immediately prepyloric in location. No chronic gastric ulcers were seen more proximally. A further 13 subjects (6.6%) had definite evidence of scarring or deformity, or both, without evidence of a concomitant active ulcer. The cumulative prevalence of peptic ulcer could thus be estimated as 13.2%. Oesophagitis was rare. Two gastric adenocarcinomas were detected, both in symptomatic subjects.

The six month period prevalence of dyspepsia was 68.5%. Current symptoms were present in 58.9%. Dyspepsia was more common in younger subjects (Table II). Subjects with past or present ulceration comprised 17.8% of the dyspeptic group. This figure increased to 29.6% when subjects with duodenitis, acute gastric ulcer, adenocarcinoma, and oesophagitis were included. However, the prevalence of active chronic peptic ulcer among subjects with dyspepsia was only 10.3%.

TABLE I Endoscopic findings in 197 randomly selected subjects

<i>Duodenum and pylorus:</i>	
Chronic duodenal ulcer	7*
Chronic pyloric channel ulcer	4
Pyloroduodenal scarring/deformity (with no active ulcer)	12
Duodenitis (with no active ulcer)	10
<i>Stomach:</i>	
Chronic prepyloric ulcer	3
Other chronic gastric ulcer	0
Acute gastric ulcer (denuded epithelium >5 mm)	3
Scar/deformity	1
<i>Macroscopic gastritis:</i>	
Erythematous	30
Erosive	11
Haemorrhagic	8
Bile reflux	1
Cancer	2
Polyp	1
<i>Oesophagus:</i>	
Oesophagitis	1
Barrett's epithelium	1
Cancer	0

*1 subject had duodenal and pyloric channel ulcers.

H. pylori was present by urease test or histology, or both, in 77.2% of subjects. There was no association between the presence of dyspeptic symptoms (either current or recent), and infection with *H. pylori* or with symptoms and histological gastritis (Table II). There was a strong association between symptoms and ulcer and all subjects with active ulcers and 12/13 with evidence of past ulceration were positive for *H. pylori*. There was no association between blood group and the presence of ulcer disease in this population sample. Eosinophilia was present in 16.2% of the group but was not significantly associated with dyspepsia.

Histology showed that gastritis was very common – it was present in 89.7% of biopsy specimens – and was predominantly of mild-moderate severity. *H. pylori* infection was strongly correlated with the presence of histological gastritis ($p < 0.0001$). Endoscopic gastritis underestimated the presence of histological gastritis, but was a reliable indicator when present (sensitivity 28%, specificity 90%, positive predictive value 96%, negative predictive value

13%). Diffuse mild erythema was common ($n=60$), but was not considered as endoscopic gastritis as this does not meet minimal diagnostic criteria.⁸

The prevalence of *H. pylori* in the 28 village subjects with dyspepsia (median age 50 years, range 28–66; male/female, 12/16) was not different to that in the same number of age matched dyspeptic monks (82.1% *v* 71.4%, $p=0.5$) suggesting that the findings in the study population are representative of the community as a whole. The inclusion of women in this comparison is unlikely to affect the prevalence of *H. pylori*.¹⁰

Discussion

The prevalence of peptic ulcer has been shown to rise with age in many studies, peaking between the fourth and seventh decade.^{11–13} The high prevalence of peptic ulcer disease in this community is emphasised by the low median age of the study population – only 28 years. Furthermore, the population is devoid of other risk factors associated with peptic ulcers such as NSAID use and cigarette smoking. The high ratio of pyloric and duodenal ulcers to gastric ulcers and the overall paucity of gastric ulcers is similar to other reports from India.^{3,11} Oesophagitis was rare in this population. This is probably due to the lack of risk factors for oesophageal reflux and oesophagitis in the community. Obesity is very uncommon and other known promoters of reflux such as cigarettes, alcohol, and caffeine containing food and beverages are rarely consumed by this population. To determine accurately the prevalence of gastric carcinoma would require a greater sample size than that in this study. However, finding two carcinomas among 197 randomly selected subjects suggests a high prevalence of this disease and is in accord with clinical observations (Dr Norbu, personal communication) in the community.

Peptic ulcer disease is perceived to be common in India but there are few reliable epidemiological data. In a vast and diverse developing country it is to be expected that prevalence data for peptic ulcer will vary between areas. Much of the data available have been derived from selected groups such as hospital based surveys, surgical series, or post mortem studies that are not comparable or representative.^{3,14,15} Moreover, the few population studies reported^{16–18} relied on single contrast barium studies which underestimate the frequency of ulcer and may not reliably distinguish active ulcers from scarring. The prevalence rates from these studies vary between 0.6–1.2% and are almost certainly underestimates. In the only other endoscopic survey of a randomly selected population in India,¹¹ the point prevalence of active peptic ulcer in urban Kashmir was 4.7%, with a high duodenal to gastric ulcer ratio (17:1:1). In this population the point prevalence of peptic ulcer in men was 6.4%, a figure remarkably similar to the result from the present study of men in the south. The cumulative or 'lifetime' prevalence in the current study was 13.2% and it was 15.0% in the Kashmir study. Both of these figures are undoubtedly underestimates as peptic ulcers may

TABLE II Relationship of dyspepsia to age, Helicobacter pylori status, histological gastritis, and peptic ulcer

	Total (n=197)	Dyspepsia (n=135)	No dyspepsia (n=62)	p*
Age: median (range) (yr):	28 (21–81)	27 (21–69)	50 (21–81)	<0.002
21–40	133	104	29	<0.0001
41–60	46	24	22	
61+	18	7	11	
<i>H. pylori</i> :				
All subjects:				
HP+	152	105	47	NS
HP–	45	30	15	
No ulcer disease				
HP+	127	82	45	NS
HP–	44	29	15	
Peptic disease:				
Absent	171	111	60	<0.003
Present	26	24	2	
Histological gastritis:				
All subjects:				
Gastritis	174	124	50	NS
No gastritis	20	11	9	
Not available	3	–	3	
No ulcer disease:				
Gastritis	149	101	48	
Atrophy/metaplasia only	9	6	3	
Chronic active gastritis	140	95	45	NS
No gastritis	19	10	9	
Gastritis grade:				
Mild	72	51	21	
Moderate	56	36	20	NS
Severe	12	8	4	

HP+ = *H. pylori* positive, HP– = *H. pylori* negative.
*Comparison of subjects with and without dyspepsia.

TABLE III Comparison of peptic ulcer prevalence from different geographic areas

	Country	No	Subjects	Method	Prevalence (%)		
					GU	DU	PU
Monsen 1969 ^{3a}	USA	7460	Male physicians, >25 yr	Mail survey	0.04	0.29	0.33*
NHI Survey 1985 ^{3b}	USA	34 844 homes large nos.	General population	Self-reported			2.0†
Kawai 1989 ¹²	Japan	Male adult patients	General population	Hospital survey			0.5‡
Ihamaki 1979 ¹⁷	Finland	358	General population	Endoscopy	0.28	1.40	1.68‡
Khuroo 1989 ¹¹	N India	370	General population >15 yr	Endoscopy	0.50	4.22	4.72‡
Katelaris 1992	S India	203	Males >15 yr	Endoscopy	0.80	5.62	6.42‡
		197	Males >21 yr	Endoscopy	–	6.60	6.60‡

(PU=peptic ulcer, GU=gastroic ulcer, DU=duodenal ulcer and usually includes prepyloric ulcers as in the present study).

*Annual incidence rate; †12 month prevalence; ‡point prevalence.

heal without scarring or deformity and the median age of subjects in both studies was low, before the years of peak prevalence of ulcer. Longitudinal studies incorporating endoscopy are needed to assess this further.

Areas in the south and east of India and Kashmir in the north have been reported to have a higher prevalence of peptic ulcer than other regions.³ However, these regional differences have not been confirmed by later studies.¹⁶⁻¹⁷ More endoscopic studies of randomly selected subjects from various regions are required to establish any geographical variation in ulcer prevalence in India. In the past a variety of hypotheses has been forwarded to account for these purported differences. These have included differences in diet,¹⁹ masticatory habits,²⁰ socioeconomic status,¹⁵⁻²¹ and religion.²² However, the missing data in these hypotheses has been information on the frequency of *H pylori*. The association throughout the world between *H pylori* and peptic ulcer, especially duodenal ulcer, is incontrovertible and the organism is increasingly accepted by many as directly implicated in aetiology. This current study documents a high prevalence of *H pylori* in a population with a high prevalence of ulcer. The few other studies of *H pylori* epidemiology in India involve selected symptomatic patients and the results are not relevant to the population in general. In a study from north India, 64% of dyspeptic subjects were found to be infected with *H pylori* but only 24% of subjects with gastritis and peptic ulcer were found to be positive in another report from Bombay.^{23,24} More data on the prevalence of *H pylori* in general populations are required. It may be that the prevalence of peptic ulcer varies with the rate of *H pylori* infection but is modulated by the factors mentioned above. The high prevalence of peptic ulcer in this randomly selected population contrasts with the results of surveys from the developed world. These are summarised and compared in Table III. The prevalence of peptic ulcer disease in the developed world seems to vary between 0.3-2%, although there are very few endoscopic studies in randomly selected subjects. The prevalence of *H pylori* is also much lower than the prevalence reported in the present study. Although these populations are disparate in many demographic variables it is tempting to speculate that the difference in *H pylori* prevalence is a dominant factor in the observed differences of ulcer prevalence between these populations. The age at which *H pylori* is acquired is probably also critical to the ulcer diathesis. This is supported by the high rate of *H pylori* infection but low ulcer prevalence in a study from Peru where acquisition of the organism is thought to occur early in life.²⁸

Although the association between gastritis, peptic ulcer, and *H pylori* is strong, the relationship between *H pylori* infection and symptoms in those without ulcer is less clear. In the west the association between *H pylori* and dyspepsia and the effect of suppression or eradication of *H pylori* on non-ulcer dyspepsia has yielded both negative^{29,30} and positive findings.³¹⁻³³ In this study there was no correlation between symptoms (in patients without an ulcer) and the

presence of *H pylori* infection. Furthermore, only a minority of dyspeptic subjects in this study had evidence of ulcer disease yet current symptoms were present in 58.9% of the study population. In a developed country up to 27% of the general population may complain of dyspepsia when questioned.³⁴ The reasons for the much higher frequency of dyspeptic symptoms in this study are unclear. Upper gut pathogens such as *Giardia lamblia*, hookworm, and other parasites are commonly diagnosed in this population. Such organisms are reported to cause dyspepsia and mimic peptic ulcer symptoms and may be the cause of symptoms in some subjects without ulcers. The prevalence of eosinophilia in the study subjects is further, indirect evidence of parasitism. Nothing is known about the role of stress, the cultural definitions of pain, or the pattern of functional symptoms in this community. The settlement is a community of displaced people: most live in suboptimal conditions and face an uncertain future. The stresses generated by this environment may influence the frequency with which symptoms occur and affect the reporting of them.³⁵

Dyspepsia *H pylori* infection, gastritis, and peptic ulcer are all more common in this population compared with similarly selected and studied populations from developed countries. However, only a small proportion of subjects with symptoms have ulcer disease and neither *H pylori* infection nor gastritis are associated with the presence of dyspepsia in this population.

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