

Prevalence of peptic ulcer in *Helicobacter pylori* positive blood donors

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Abstract

This study aimed to determine the importance of raised antibodies to *Helicobacter pylori* in an asymptomatic population. A total of 128 asymptomatic blood donors who were seropositive for *H pylori* and consented to endoscopy were investigated. These subjects were from a population of 1010 blood donors screened for antibodies to *H pylori*. A questionnaire was completed to determine if any subjects had complained of symptoms, and they subsequently had endoscopy. Altogether 121 of 128 were positive for *H pylori* by histology and urease test and/or culture and all 121 had chronic active gastritis on histology. Twenty five of these subjects had peptic ulcer (20 duodenal, five gastric), a further 21 had erosive duodenitis, and two were found to have gastric cancer. *H pylori* associated peptic ulcer disease and duodenitis occur more frequently than previously recognised and this suggests that *H pylori* infection, even if asymptomatic, is of far greater clinical relevance than originally thought.

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Helicobacter pylori causes non-autoimmune gastritis and duodenal ulcer,¹ and infection is considered an important risk factor for the development of gastric cancer.^{2,3} Serological studies have shown that the prevalence of *H pylori* varies with age, social class, and country⁴⁻⁹ but the clinical importance of seropositivity is unclear. This study assesses the clinical, endoscopic, and histological importance of a positive ELISA IgG antibody to *H pylori* in asymptomatic blood donors.

Subjects and methods

SUBJECTS

Over one year (1990-91), blood was collected from 1010 Bologna residents attending the largest blood donor clinic in that city for the measurement of serum anti-*H pylori* IgG antibodies. Age, social class, smoking (>10 cigarettes/day), alcohol consumption (>75 g/day), blood groups, and IgG values were recorded. Subjects were stratified according to age (group I: 18-25 years, n=187; group II: 26-35 years, n=217; group III: 36-45 years, n=242; group IV: 46-55 years, n=207; group V: 56-65 years, n=157). Subjects were grouped into six social class categories based on their current or most recent occupation.¹⁰ In Bologna blood donors are screened, and anyone taking regular non-steroidal anti-inflammatory drugs,

antibiotics, or corticosteroids or who is found to have a biochemical abnormality is not allowed to donate blood. Men are allowed to donate blood every three months and women every six months.

METHODS

Specific anti-*H pylori* IgG antibodies were measured by a previously validated ELISA technique using anti-human peroxidase labelled IgG conjugate with a sensitivity and specificity of 94%.^{11,12} The results were expressed as the absorbance index (AI):

$$AI = \frac{\text{mean OD value (n=2) of patient serum}}{\text{mean OD value (n=2) of reference serum}}$$

where OD is the optical density at 405 nm. An AI >0.3 for the IgG to *H pylori* defined seropositivity. The serum from an *H pylori* positive duodenal ulcer patient was used as reference serum for all the assays.

The first consecutive 162 blood donors with high titres of IgG to *H pylori* were interviewed before endoscopy. They were questioned about the presence and frequency of upper gastrointestinal tract symptoms including indigestion, heartburn, nausea, and vomiting and about recent medication (consumption of antibiotics, H₂ antagonists, antacids, and NSAIDs within the previous three months). After interview, consent for endoscopy was sought. At endoscopy blood was taken for repeat serology. All endoscopies were performed under local anaesthesia (xylocaine), by the same investigator (DV), and using an Olympus videoendoscope GIF-100.

A gastric or duodenal ulcer was defined as mucosal ulceration >5 mm in diameter and erosive duodenitis as multiple, discrete, focal red spots <5 mm.¹³ Four antral biopsy specimens were taken with endoscopic biopsy forceps (Olympus FB 24Q) - two for histology (haematoxylin and eosin and Giemsa stains), one for culture, and one for the urease test (CP-TEST; Gist-Brocades Farma, SpA, Italy).¹⁴ Histology and culture were done without knowledge of the subject's *H pylori* status or the results of endoscopy. The histological appearances were graded according to Whitehead.¹⁵ *H pylori* was diagnosed by identification of the organism on histology and a positive urease test.¹⁴

A control group of consecutive and concurrent patients with dyspepsia (n=219; male/female: 123/96; age range 18-65, mean 46 years) endoscoped by the same operator (DV), were used as age and sex matched controls because it was clearly unjustified and unethical to use seronegative asymptomatic blood donors. The study

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was approved by S Orsola Hospital ethical committee and informed consent for endoscopy was obtained from all subjects.

Statistical analysis was by χ^2 test.

Results

Altogether 422 of 1010 blood donors (42%) had serological evidence of *H pylori* infection. The prevalence of high IgG titres increased with age (Fig 1), but was not correlated with cigarette or alcohol consumption, sex, blood group, or social class. None of the donors drank more than 75 g/day of alcohol, although 23% smoked >10 cigarettes/day.

Postal questionnaires were sent to the first 180 consecutive blood donors, 162 responded (90%) and 128 (79%) (M/F: 88 of 40, age range 18–65, mean 48 years) consented to endoscopy. Twenty four of 34 refused endoscopy on the advice of their general practitioner and 18 subjects were no longer resident in Bologna and could not be contacted.

At endoscopy, *H pylori* infection was confirmed in 121 of 128 (95%) seropositive donors by both Giemsa staining and urease test, and in 97 of 121 (80%), culture was also positive. Only seven of 128 previously seropositive donors (4%) (age range 31–63 years, median 48 years) had no evidence of *H pylori* and all had normal histology. On repeat serology five of seven had an AI of <0.3, while in two of seven the titre was similar to the previous level. None of the five patients had been investigated previously for

dyspepsia or received anti-*H pylori* therapy, nor were they taking antibiotics or bismuth containing compounds at the time of endoscopy, suggesting that spontaneous clearance of *H pylori* had probably occurred.

Endoscopy of 121 patients with confirmed chronic *H pylori* infection showed gastritis/antral erosions in 58 (45%), erosive duodenitis in 21 (16%), duodenal ulcer in 20 (16%), gastric ulcer in six (5%), and gastric cancer in two patients (one leiomyosarcoma (T1, N0, M0), one adenocarcinoma (T3, N2, M1)). In 21 of 121 (16%) seropositive subjects the endoscopic findings were normal. In the seven donors with no evidence of *H pylori* infection endoscopy was normal in five and showed antral gastritis in two. No correlation was found between the IgG titres and the endoscopic findings or between blood group status and duodenal ulcer (0+ n=6, 0- n=2, B+ n=2, A+ n=8, A- n=2). The endoscopic findings in the age matched *H pylori* positive controls with dyspepsia (n=120; M/F: 71/49, age range 18–65, mean 46 years) were broadly similar (Fig 2). Compared with seropositive blood donors, however, erosive duodenitis was significantly less frequent (n=8, 7% v 16%, $p<0.05$). In the *H pylori* negative controls with dyspepsia (n=99; M/F: 52/47; age range 18–65, mean 46 years), 51 of 99 (51%) had a normal endoscopy compared with 16% and 21% of seropositive donors and *H pylori* positive patients with dyspepsia respectively ($p<0.001$), and only three (3%) had duodenal ulcers – significantly fewer ($p<0.001$) than either seropositive donors (16%) or *H pylori* positive patients with dyspepsia (n=18, 15%). There were no significant differences in age, social class, and cigarette or alcohol consumption in seropositive endoscoped blood donors, seronegative and seropositive donors, nor between *H pylori* positive dyspeptic and *H pylori* negative dyspeptic controls. Table I shows the social class distribution in the study population. No significant differences were found between the antibody responses of the seropositive blood donors and the *H pylori* positive controls with dyspepsia (Fig 3).

Only two of 20 seropositive blood donors with a duodenal ulcer complained of dyspepsia at the time of endoscopy. At interview, a further six donors later found to be seropositive complained of current dyspepsia, but endoscopy showed only antral gastritis (n=4) or erosive duodenitis (n=2). All eight patients had been investigated for dyspepsia in the previous year and none had been taking NSAIDs; a further 35 patients had also been investigated previously for dyspepsia by their general practitioner (barium meal n=25, upper gastrointestinal endoscopy n=18) a median (range) of 4 (1–32) years previously. Table II shows the previous findings compared with present ones.

Discussion

This and previous studies have shown the accuracy of serology in detecting *H pylori* and that seropositivity is associated with chronic non-autoimmune gastritis.¹⁶ The earlier validation studies were done using sera from dyspeptic

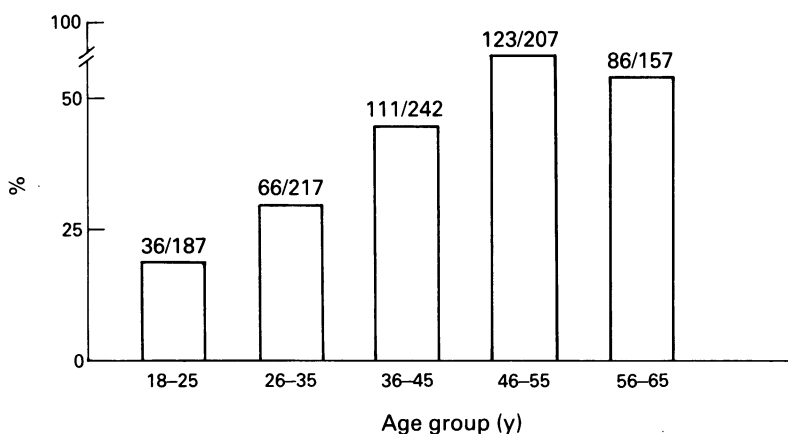


Figure 1: IgG seroprevalence of *Helicobacter pylori* in 1010 blood donors.

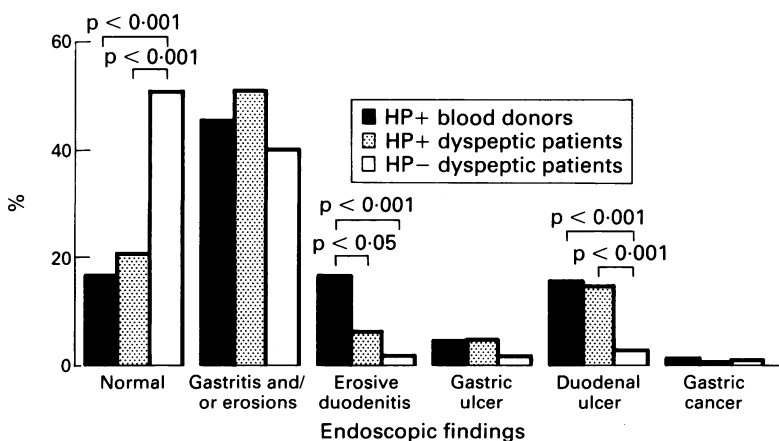


Figure 2: Endoscopic findings in *Helicobacter pylori* (HP) positive blood donors compared with *H pylori* positive and *H pylori* negative dyspeptic patients.

TABLE I Distribution in social classes (%)

Social class grouping	Seronegative blood donors	Seropositive blood donors	Seropositive endoscoped blood donors	H pylori positive controls	H pylori negative controls
I	18 (3)	13 (3)	4 (3)	4 (3)	4 (4)
II	55 (9)	40 (9)	12 (9)	10 (8)	9 (9)
IIIN	217 (37)	155 (37)	47 (37)	42 (35)	35 (35)
IIIM	69 (12)	49 (12)	15 (12)	14 (12)	12 (12)
IV	229 (39)	165 (39)	50 (39)	50 (42)	39 (39)
V	0	0	0	0	0
Total	588	422	128	120	99

ulcer to be 6%, while a similar study from India has suggested that the point and lifetime prevalences of duodenal ulcer were 5% and 11% respectively.¹⁸ These early studies, however, antedate the discovery of *H pylori* and appreciation of its role in the aetiology of duodenal ulcer. Thus, differences in and between populations in ulcer prevalence may have been due to differences in the prevalence of *H pylori* infection.

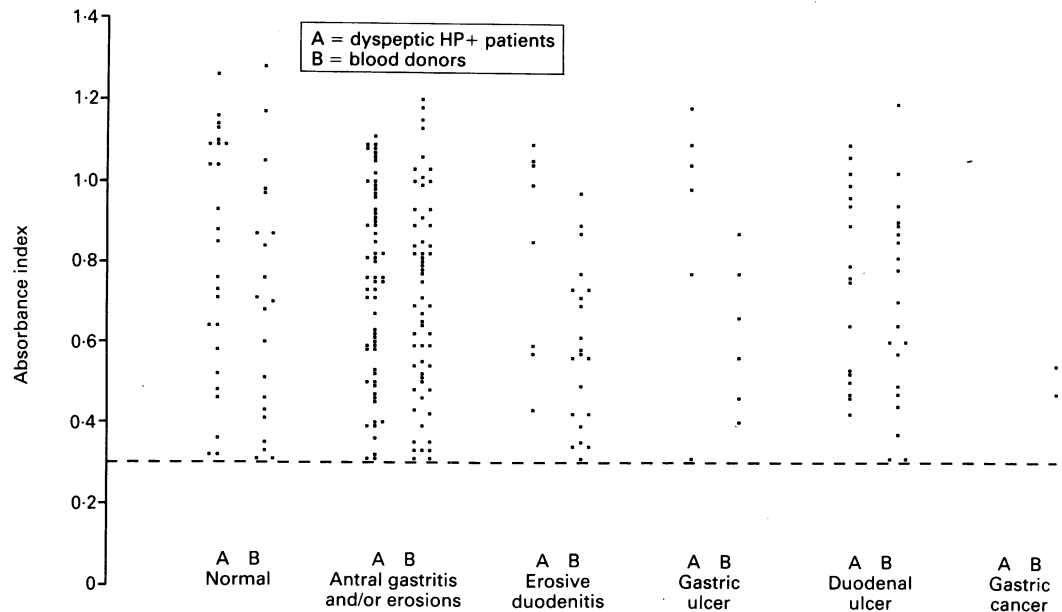


Figure 3: IgG absorbance index in relation to different endoscopic findings in *H pylori* (HP) positive blood donors and *H pylori* positive dyspeptic patients.

TABLE II Present findings in 43 blood donors previously investigated for dyspepsia

	Current status						Symptoms
	N	AG	AE	ED	GU	DU	
Those who had previously undergone upper gastrointestinal endoscopy:							
Past findings	N=5	3	1	1			1 burning pain, 1 heartburn, 1 nausea
	AG=7	2	1	2		2	1 burning pain
	ED=1					1	1 burning pain
	DU=5	1	2			2	
Those who had previously undergone x ray:							
Past findings	N=13		6	4	2	1	1 heartburn
	AG=5	3				1	
	ED=0						
	DU=7	2	1	1	1	2	1 burning pain, 1 heartburn nausea

N=normal; AG=antral gastritis; AE=antral erosions; ED=erosive duodenitis; GU=gastric ulcer; DU=duodenal ulcer.

outpatients referred for endoscopy, however, and therefore only limited conclusions could be drawn about the clinical importance of a positive result in the general population. Seropositivity (or a positive breath test) in an asymptomatic subject was generally assumed to be clinically irrelevant and did not need further investigation. Indeed, seropositivity or a positive breath test in an asymptomatic individual has been used as sufficient inclusion criteria for control groups in clinical research. Our results suggest that these previous assumptions are no longer valid and challenge our understanding of the natural history of *H pylori* infection and duodenal ulcer.

Previously, the cumulative life time risk of duodenal ulcer for any individual (based mainly on radiological diagnosis and without considering *H pylori* status) was considered to be about 10%.¹⁷ More accurate endoscopic data from random samples of an Estonian population have shown the cumulative 10 year risk for duodenal

Therefore the Estonian endoscopic biopsy material has been re-examined and it has been shown that 95% of the study population were infected with *H pylori*. A more recent study, from a population with an *H pylori* prevalence of 55% and of a similar mean age to that in our study, found a duodenal ulcer in 24 of 171 (14%) *H pylori* positive dyspeptic patients referred for endoscopy.¹⁹ Similarly, a large study of dyspeptic patients undergoing upper gastrointestinal endoscopy in China, where the *H pylori* prevalence is 65%, found that 19% had a duodenal ulcer²⁰ and there was a 3:1 male preponderance. All these recent studies were on patients referred for dyspepsia, however, and are therefore not representative of the general population.

Although blood donors may not be representative either, because of self selection or financial reward for donation (unlikely for Italy), we consider our study population valid because the age and social class distributions were similar to those in the general population of Bologna and because only 6% had complained of dyspepsia in the preceding 12 months, a figure similar to that in other reports on the prevalence of dyspepsia in the community. In contrast to the data of Sitas *et al*,⁸ we did not find any correlation with social class. This could be due to the fact that the standard of living in the city of Bologna is not related to the economic status of the inhabitants.

Recent Norwegian data, which took into account both the presence and absence of either dyspepsia or *H pylori* infection, compare strikingly with our own and other data. Bernersen *et al*^{21,22} found that in dyspeptic subjects, 48% of whom had *H pylori*, endoscopy showed duodenal

ulcer in only 3.8% v 1% of asymptomatic subjects, 36% of whom had *H pylori*. Different endoscopic criteria for duodenal ulcer, NSAID usage, or observer variation may account for some of the variation in ulcer prevalence. Similarly, in a study of Tibetan monks with a high prevalence of dyspepsia (69%) and *H pylori* infection (75%), Katelaris *et al* found a 6.6% endoscopic point prevalence for peptic ulcer.²³

Intrapopulation comparison of our data shows that duodenal ulcer is as common in *H pylori* patients with dyspepsia as in the asymptomatic seropositive blood donors. Moreover, the AIs were identical in all positive subjects, regardless of symptoms or endoscopic findings (Fig 3).

A history of peptic ulcer is not an exclusion criterion for giving blood in Italy and indeed peptic ulcers were present in 12 of 43 (28%) donors investigated previously for dyspepsia. Five of 12 were found to have a duodenal (n=4) or gastric ulcer (n=1) (Table II). If we exclude these five subjects the prevalence of peptic ulcer in the asymptomatic *H pylori* positive donors is still 16%, a prevalence considerably higher than that previously reported.

Finally, these results also suggest that the measurement of IgG antibodies to *H pylori* are helpful in detecting 'silent' peptic ulcer, which confirms previous reports that screening for *H pylori* infection is an effective way of reducing the endoscopic workload and that dyspepsia is a poor guide to the diagnostic value of endoscopy.^{19,24}

Although it is now generally accepted that *H pylori* is a pathogen and not a commensal infection, sceptics still claim that *H pylori* is not clinically important, because only a very small proportion of infected patients develop duodenal ulcer.

H pylori associated peptic ulcer occurs more frequently than previously recognised and suggests that *H pylori* infection, even in the absence of symptoms, is of far greater clinical relevance than originally thought.

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