

Reflux oesophagitis and *Helicobacter pylori* infection in elderly patients

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Summary

***Helicobacter pylori* is associated with gastritis, peptic ulcers and gastric malignancies. Little attention has been paid to the possibility that it may also have a role in the pathogenesis of reflux oesophagitis. This is especially true in elderly patients who have life-long infection and provide an ideal group to study the mucosal changes associated with the organism. The aim of this study was to determine if *H pylori* is associated with reflux oesophagitis in elderly patients. Consecutive gastroscopy patients were recruited. Multiple biopsies were taken from oesophagus, stomach, antrum and duodenum for histology and rapid urease tests. Patients also had IgG ELISA antibodies and ¹³C-urea breath tests performed. Patients with macroscopic or microscopic evidence of reflux oesophagitis were compared to patients with macroscopically normal upper gastrointestinal tracts and no microscopic evidence of reflux. A total of 114 patients were recruited, average age 78.9 years (\pm 5.4). There were 37 refluxers and 33 non-refluxers. We found no evidence for an association between the presence of *H pylori* and reflux oesophagitis in elderly patients. The high prevalence of *H pylori* in patients with reflux oesophagitis can be explained by the presence of incidental gastritis.**

Keywords: *Helicobacter pylori*, gastritis, reflux oesophagitis, elderly

The association between *Helicobacter pylori*, gastritis and peptic ulcer disease is well recognised and duodenal ulceration is now accepted as a curable infectious disease.^{1,2} The importance of *H pylori* in the pathogenesis of gastric carcinoma and mucosa-associated lymphatic tumours (MALTomas) is also being increasingly recognised.^{3,4} There have also been many studies describing the association of *H pylori* with gastritis and peptic ulcer disease in elderly patients.^{5–7} Little attention, however, has been paid to the possible role of *H pylori* in the pathogenesis of reflux oesophagitis and, to our knowledge, no study has specifically looked at this possibility in a group of elderly subjects.

H pylori is probably acquired in childhood and the duration of infection is life-long.^{8,9} A large proportion of the elderly population is

infected with the organism.^{10,11} These long-term infected elderly patients thus provide an ideal group to study the pathological changes associated with the infection. The aim of this study was to use a wide range of available tests; histology, rapid urease test (CLO test), IgG ELISA antibodies to *H pylori* and ¹³C-urea breath tests (¹³C-UBT) to determine if an association exists between *H pylori* and reflux oesophagitis in an unselected, consecutive group of elderly patients presenting for routine upper gastrointestinal endoscopy.

Patients and methods

Consecutive patients admitted for gastroscopy were recruited, regardless of the reason for the procedure. The protocol was passed by the ethics committee of Bolton Hospitals Trust and full informed consent was taken from each patient prior to recruitment. Patients were excluded if they had been on any antibiotic during the preceding three months as it was thought that this may interfere with *H pylori* detection.⁷ They were also excluded if they had had previous upper gastrointestinal surgery or had been on a proton pump blocker as there is evidence that this medication may also reduce *H pylori* detection.¹² Each patient had multiple biopsies taken from each of the following sites; the oesophagus, the body of stomach, the gastric antrum and the duodenum. The oesophagus was always biopsied prior to gastric biopsy to avoid contamination.¹³ Histological examination was by the Sydney system¹⁴ and all specimens were reported by a single histopathologist (MP). A rapid urease test was also performed. Patients subsequently had IgG ELISA antibodies and a European ¹³C-UBT performed.¹⁵ Using these methods, two groups were compared; those with either macroscopic or microscopic evidence of reflux oesophagitis

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Helicobacter pylori: features

- Gram-negative, non-sporing, spiral bacillus
- urease enzyme protects it from acid attack in the stomach
- able to survive within macrophages
- infection probably childhood acquired and lifelong
- world-wide distribution and increasing in third world
- associated with gastritis, peptic ulcer disease and gastric carcinoma

(the refluxers) and those who had macroscopically normal upper gastrointestinal tracts and no microscopic evidence of reflux oesophagitis (the non-refluxers). Statistical analysis was by χ^2 tests (with Fisher's exact or Yates corrections as appropriate) and Student's *t* tests (assuming unequal variance). Analyses were two-tailed, if appropriate, and $p < 0.05$ was taken as significant.

Results

A total of 114 patients (79 women, 35 men) were recruited over a nine-month period, average age was 78.9 years (± 5.4). The main reasons for endoscopy were iron deficiency anaemia, reflux symptoms and epigastric pain accounting for over 60% of referrals.

Twenty-nine patients had macroscopic evidence of reflux oesophagitis (six of whom had histological features of reflux) and a further eight had histological evidence of reflux only, giving a total of 37 (table 1). They were compared to 33 patients who had neither macroscopic nor histological evidence of reflux oesophagitis as described above. In fact, the entire upper gastrointestinal tract of these 33 patients was normal. As expected more patients with evidence of reflux oesophagitis had heartburn as their primary symptom than in those without, 15/37 vs 5/33, $p = 0.03$. Of the 37 refluxers, 28 (75.5%) were positive for *H pylori* on at least one test compared to 27 (81.8%) of the non-refluxers, $p = 0.7$.

Gastric histology was available on 33/37 of the refluxers and 32/33 of the non-refluxers. The incompleteness of the histological data was due to inadequate biopsy samples in some patients and inability to pass the scope into the stomach in the patients with oesophageal strictures. Twenty-four (72.7%) of the refluxers had histological evidence of gastritis compared to 25 (78.1%) of the non-refluxers, $p = 0.8$. There was no significant difference in the site, severity or *H pylori* positivity of the gastritis in the refluxers compared to the non-refluxers (table 2).

With respect to the non-invasive tests for *H pylori* detection, the mean IgG ELISA antibody levels in the refluxers was 37.6 (± 22.3) compared to 44.2 (± 27.4) in the non-refluxers, $p = 0.29$. Likewise the mean ^{13}C -UBT levels were 13.3 (± 17.2) in the

Table 2 Histological findings and pattern of gastritis. There were no statistically significant findings between the two groups

	Reflux oesophagitis (n = 37)*	Normal (n = 33)**
Gastritis	24	25
Antral	7	5
Body	3	4
Pan	14	16
Mild	8	5
Moderate	9	10
Severe	7	10
<i>H pylori</i> positive	16	16

*This is the total number of patients with oesophagitis (macroscopic and microscopic). Histology available on 33/37. **Histology available on 32/33.

non-refluxers, $p = 0.29$. Likewise the mean ^{13}C -UBT levels were 13.3 (± 17.2) in the refluxers compared to 14.3 (± 13.4) in the non-refluxers, $p = 0.8$.

Twelve patients had macroscopic evidence of a hiatus hernia. Biopsies from oesophageal/hernial sac mucosa of these patients revealed evidence of *H pylori* in one patient while two others had histological evidence of Barrett's oesophagus; *H pylori* was not identified in the oesophageal mucosa in either case.

There was no statistically significant difference in the numbers of patients on either aspirin or nonsteroidal anti-inflammatory drugs.

Discussion

The pathogenesis of inflammatory oesophageal diseases shows many similarities to the pathogenesis of gastritis and peptic ulcer disease and they have been considered as types of 'acid-peptic' disorders.^{16,17} Acid and pepsin have long been thought to be the major cause of mucosal damage caused by the reflux of gastric contents into the oesophagus, but other factors may also influence the severity of reflux oesophagitis, perhaps mucosal resistance, motility disorders¹⁸ and theoretically infectious agents. It is possible therefore that *H pylori* may be involved in the pathogenesis of reflux oesophagitis.

Borkent and Baker demonstrated that colloidal bismuth subcitrate together with cimetidine gave better results than cimetidine alone in healing ulcerative reflux oesophagitis.¹⁹ They also found that oesophagitis was accompanied by *H pylori* infection in nine of 20 patients and concluded that *H pylori* may have a role in the pathogenesis of reflux oesophagitis. This is supported by McCallum *et al* who suggested that patients with reflux oesophagitis had a higher incidence of *H pylori* in the stomach.²⁰ In their retrospective study of 21 consecutive patients with gastro-oesophageal reflux disease, 75% had gastritis and 60% had *H pylori* identified in the antral biopsy specimens, significantly more than the findings in healthy controls (10% and 5%, respectively). They proposed that patients with gastro-oesophageal

Table 1 Patients with reflux oesophagitis

Oesophagitis grade	n	Other macroscopic findings			
		Hiatus hernia	Oesophageal stricture	Gastritis	Duodenitis
Grade 1	11	4	0	2	1
Grade 2	6	4	0	1	0
Grade 3	8	2	0	1	0
Grade 4	4	0	2*	1	0
Microscopic only	8**	2	0	0	1
Total	37	12	2	5	2

*Both these patients had histological evidence of Barrett's oesophagus. **One patient with microscopic oesophagitis also had a gastric carcinoma.

reflux disease may be at increased risk of colonisation by *H pylori* as a result of raised intragastric pH with chronic antacid consumption, and also speculated that *H pylori* may be involved in the pathophysiology of the disease. It is also interesting to note that Marshall and Warren's original study included 34 patients with abnormal oesophagi by endoscopic appearance and that 14 (41%) of the 34 had *H pylori*-like organisms identified in the antral biopsy specimens.²¹ However, more recent studies have found no such association between *H pylori* and reflux oesophagitis. O'Connor and Cunnane prospectively studied 93 patients with reflux oesophagitis and found no association between *H pylori* and grade of oesophagitis.²² Similarly, Coelho *et al* found that oesophageal infection was not significant in a group of 246 patients with a wide range of upper gastrointestinal tract disorders. They felt that oesophageal infection was simply due to gastrointestinal reflux.²³

The present study is the first, to our knowledge, to investigate the possible association between *H pylori* infection and reflux oesophagitis in elderly patients, who have a higher prevalence of infection. We found no convincing evidence for such an association. There was, as expected, a high overall rate of gastritis (over 75%) in these patients but no statistically significant difference in the site, severity or *H pylori* positivity of this gastritis when patients with evidence of reflux oesophagitis were compared to those who have macroscopically normal upper gastrointestinal tracts and microscopically normal oesophagi. Likewise ¹³C-UBT levels and IgG ELISA antibody levels were similar in both groups. We used multiple diagnostic modalities for *H pylori* detection to maximise pick-up rates and minimise false negative results. Using these methods *H pylori* was as likely to occur in those

Summary/learning points

- lack of data regarding *H pylori* and reflux oesophagitis
- elderly patients have high prevalence of life-long *H pylori* infection
- elderly are ideal group to study *H pylori* induced mucosal changes
- 75% of elderly with reflux oesophagitis have *H pylori* infection
- 80% without reflux oesophagitis have *H pylori* infection
- no differences exist in the site, severity or *H pylori* positivity of gastritis in elderly with and without reflux oesophagitis
- there is no evidence for a role for *H pylori* in the pathogenesis of reflux oesophagitis

with no evidence of reflux as in those with definite evidence.

Only two of our patients had evidence of Barrett's oesophagus and in neither of these was *H pylori* detected in the mucosa. This is in keeping with the work of Paull and Yardley who found no direct association between *H pylori* and Barrett's oesophagus in a group of 26 patients with the condition.²⁴ Other authors have reached similar conclusions.²²

We conclude that extensive investigation of a group of elderly patients with a high overall level of *H pylori* infection has revealed no evidence of an association between *H pylori* and reflux oesophagitis. The high prevalence of *H pylori* infection in patients with evidence of reflux can be fully explained by the presence of incidental gastritis.

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