Distribution of *Helicobacter pylori* colonisation and associated gastric inflammatory changes: Difference between patients with duodenal and gastric ulcers

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Abstract

Aims—To determine the gastric distribution of *Helicobacter pylori* in patients with duodenal and gastric ulcers; and to examine the mucosal inflammatory response.

Methods—Patients with newly diagnosed, uncomplicated duodenal and gastric ulcers were endoscoped and two biopsy specimens each taken from the antrum and the body. Specimens were evaluated blind by one pathologist to determine *H pylori* activity (scored 0–3) and inflammatory changes (according to the Sydney classification).

Results—Adequate biopsy material was obtained from 40 and 44 patients with gastric and duodenal ulcers, respectively. Although antral colonisation with *H pylori* was more common in the antrum of the latter, the organism was equally likely to be found in the body of both sets of patients; the density of colonisation was higher in those with gastric ulcers. Active gastritis and mucosal atrophy were more common in the body of those with gastric ulcers; intestinal metaplasia was also more common in the antrum of these patients.

Conclusions—Gastritis in patients with duodenal ulcers is mainly antral, but the incidence of gastric body colonisation with *H pylori* seems to be the same in patients with either type of ulcer. There is, however, a significant difference in colonisation density. The cause and importance of this are not obvious and may be related to either host or organism factors.

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Gastric *Helicobacter pylori* infection is strongly associated with duodenal ulcers and is also commonly found in association with gastric ulceration.¹ It is, however, an extremely prevalent infection and has been found in up to 88% of patients studied in Africa, making it the most common bacterial infection in that continent.² The organism is uniquely adapted to survive in the hostile gastric environment, and in fact seems able to colonise only gastric mucosa. This unique affinity for gastric mucosa is based on a specific receptor based mechanism,³ with the fibrillar haemagglutinin component of the organism acting as a “colonisation factor”.⁴ It has been postulated

that in duodenal ulcer disease the organism is found mainly in the antrum, but not in the body or fundal mucosa,⁵ thereby leading to hypergastrinaemia and acid hypersecretion. Gastric ulceration, on the other hand, occurs against the background of a more widespread gastritic process, which may reflect a more extensive colonisation with *H pylori*, or a difference in the immunological response of the gastric mucosa to the organism in these conditions.

Methods

Patients with newly diagnosed, uncomplicated gastric and duodenal ulceration were recruited from the gastroenterology outpatient services of the Groote Schuur and Tygerberg hospitals. All patients gave informed consent and the study was approved by the Ethics and Research Committee of the University of Cape Town.

All patients were subjected to a routine upper gastrointestinal endoscopy, using Xylocaine local anaesthetic with or without sedation with intravenous midazolam 2.5 mg. The ulcer site was defined as duodenal or gastric: pyloric channel ulcers were excluded from the study. Two biopsy specimens were taken from the antrum (less than 5 cm from the pylorus) and a further two from the posterior wall of the gastric body. Samples were preserved in formalin and evaluated by one pathologist, who had no prior knowledge of the ulcer diagnosis.

H pylori activity was determined histologically using Giemsa staining. The density of colonisation was scored semiquantitatively as: 0 (organisms not found after a thorough search using Giemsa stained material); 1 (organisms found only after a thorough search of more than one high power field of Giemsa stained material); 2 (organisms found in every high power field, present only in crypts); and 3 (organism abundant in crypts and mucus layer).

Gastritis was classified according to the guidelines of the Sydney classification system.⁶ Only samples incorporating muscularis mucosae (full thickness mucosa) were evaluated for atrophy. Gastritis was assessed as being either “predominantly antral” or “pangastritis” according to the presence of chronic inflammatory changes found in the samples from body and antral mucosa.

Statistical analysis of categorical data was carried out using Fisher’s exact and the Mantel-Haenszel χ^2 tests and continuous

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Table 1 *H pylori* activity

	Gastric ulcers	Duodenal ulcers	p Value
Patients	40	44	
Age: mean (SD)	52(13)	42(15)	<0.01†
<i>H pylori</i> distribution	+/-	+/-	
Antrum	31/9	43/1	<0.01*
Body	29/11	30/13	NS*
Antrum and/or body	35/5	43/1	NS*
Density of colonisation			
Antrum	0 + 1 12	6	
	2 + 3 28	38	NS‡
Body	0 + 1 22	36	
	2 + 3 18	7	<0.01‡

†Student's *t* test; *Fisher's exact test; ‡ χ^2 .

Table 2 Gastric morphology

	Gastric ulcer	Duodenal ulcer	p Value
	+/-	+/-	
Neutrophil activity:			
Antrum	36/4	40/4	NS*
Body	11/29	4/40	<0.05*
Mucosal atrophy:			
Antrum	31/2	28/5	NS*
Body	8/31	0/43	<0.01*
Intestinal metaplasia:			
Antrum	15/25	3/41	<0.001*
Body	3/37	0/44	NS*

Student's *t* test; *Fisher's exact test; ‡ χ^2 .

variables were evaluated using Student's *t* test, both using the EPISTAT statistical package. A *p* value of <0.05 was considered significant.

Results

The results are summarised in tables 1–4.

Adequate antral and fundic biopsy specimens were obtained from 40 of 43 patients with gastric ulcer and from all 44 with duodenal ulcers. The patients with gastric ulcer were significantly older than the other group (mean (SD) age 52(13) years for gastric ulcers and 42(15) years for duodenal ulcers; *p* < 0.01). The overall incidence of *H pylori* infection was 88% (35/40) in gastric ulcer patients and 98% (43/44) in duodenal ulcer patients. This was not significant.

H pylori was found more frequently in the antrum of patients with duodenal ulcers than in those with gastric ulcers: 43/44 *v* 31/40; *p* < 0.01. The pattern of *H pylori* colonisation

also differed in the two groups of patients. Antral colonisation was more common in patients with duodenal ulcer than body colonisation—43/44 positive in the antrum, 30/43 positive in the body; *p* < 0.001. No difference was found in the distribution of the organism in patients with gastric ulcers—31/40 (antrum) *v* 29/40 (body).

The pattern of distribution differed, but the incidence of body colonisation did not differ in both groups of patients—30 of 43 patients with duodenal ulcer were colonised in the body of the stomach, compared with 29 of 40 with gastric ulcers. There was, however, a significant difference in the density of body colonisation, with the group with gastric ulcers containing significantly more subjects in the 2 and 3 density categories (18 of 29 with gastric ulcers *v* seven of 30 with duodenal ulcers; *p* < 0.01).

Differences were noted in the gastritic characteristics of the two ulcer groups (tables 2–4). Active gastritis (neutrophil activity) was found more often in the body of patients with gastric ulcers and atrophy was also more common (eight of 39 *v* 0 of 43; *p* < 0.01). The incidence of antral intestinal metaplasia also differed noticeably between the groups—15 of the 40 patients with gastric ulcers showed evidence of antral intestinal metaplasia, compared with three of 44 patients with duodenal ulcers; *p* < 0.001. When patients were stratified into three arbitrarily chosen age groups (15–40 years, 40–60 years, and over 60 years), and the data analysed by the Mantel-Haenszel χ^2 test controlling for age, the differences in prevalence of both antral intestinal metaplasia (*p* < 0.01) and body atrophy (*p* < 0.05) remained significant, although less so, and only marginal in the case of body atrophy.

The gastritic process tended to be predominantly antral in duodenal ulceration: in gastric ulceration a pangastritic process was more common. The gastritis was deemed to be predominantly antral in 39 of the patients with duodenal ulcers, compared with 23 of those with gastric ulcers, and pangastritic in five of the former and 17 of the latter; *p* < 0.01.

Table 3 Categorisation of histological characteristics, antrum

	Duodenal ulcer				Gastric ulcer			
	0	1	2	3	0	1	2	3
Chronic inflammation	0	3	33	8	0	2	30	8
Neutrophil activity	4	28	11	1	4	14	21	1
<i>H pylori</i> density	1	5	20	18	9	3	16	12
Mucosal atrophy	5	11	16	1	2	7	21	3
Intestinal metaplasia	41	1	2	0	25	5	4	6

Table 4 Categorisation of histological characteristics, body

	Duodenal ulcer				Gastric ulcer			
	0	1	2	3	0	1	2	3
Chronic inflammation	25	18	1	0	11	19	9	1
Neutrophil activity	40	2	2	0	29	6	5	0
<i>H pylori</i> density	13	23	7	0	11	11	14	4
Mucosal atrophy	43	0	0	0	31	2	5	1
Intestinal metaplasia	44	0	0	0	37	2	0	1

Discussion

This study confirms that the gastritis in duodenal ulcer disease is predominantly antral in nature, while it is more widespread in gastric ulceration. The finding that gastric ulcer disease is more commonly associated with antral intestinal metaplasia is consistent with the findings of earlier studies,^{7,8} but seems to be at variance with a recent study,⁹ in which this difference was not found when the data were analysed controlling for age.

The almost identical incidence of *H pylori* in the body of the stomach in the duodenal and gastric ulcer disease groups may be construed as contradicting the established view that patients with duodenal ulcers have fundal "sparing" of *H pylori* colonisation.⁵ The fundal inflammatory morphological changes

were, however, associated with a significantly higher colonisation density in the group with gastric ulcers. In this regard, the findings of our study agree with earlier reports suggesting a correlation between the magnitude of the inflammatory response and the density and depth of *H pylori* colonisation,¹⁰⁻¹² rather than the presence of *H pylori* itself.

Several factors may be important in determining the difference in the colonisation density gradient in duodenal and gastric ulcers. Firstly, this may merely reflect the duration or chronicity of the infection. This seems to be borne out by the finding of a significantly older mean age, as well as the presence of markers for chronic gastritis (atrophy and intestinal metaplasia) in the gastric ulcer group. The relation of age to the chronicity of gastritis is not simple, however, and the duration of the gastritis may be better assessed by the chronicity of symptoms, an approach used in earlier studies.⁸ Studies on the natural history of duodenal ulcer associated type B gastritis have claimed that the inflammatory changes do not progress to include the body or fundus, whereas the gastritis in patients with gastric ulcer or gastritis without peptic ulcer disease is progressive.¹³⁻¹⁴ It thus seems unlikely, based on current data, that *H pylori* infection spreads proximally up the body of the stomach from the antrum in patients with duodenal ulcers. Suitably designed longitudinal studies, however, should address this important question as the controversial phenomenon of duodenal ulcer "burnout", first suggested by Fry,¹⁵ may be explained by proximal spread of the gastritic process, with resultant hypochlorhydria.

Secondly, as gastric colonisation with *H pylori* seems to be mediated by specific *H pylori* colonisation factors for gastric glycerolipid receptors,³ it is conceivable that either the affinity of the organism's colonisation factor may vary, or that the distribution of these glycerolipid receptors in patients may differ, giving rise to either organism or host differences in colonisation patterns and resulting in, or associated with, different gastroduodenal diseases. There is some evidence that strain differences may exist between organisms found in different gastroduodenal disease states: Crabtree *et al* have shown a strong association between the presence of a strain of *H pylori* containing a 120 kilodalton membrane protein and duodenal ulcer disease.¹⁶ There is at present no information to suggest that the distribution of the glycerolipid receptor differs among individuals.

Finally, patients with duodenal ulcers may be resistant to colonisation of the oxyntic mucosa by *H pylori* by virtue of the increased

acid secretion found in this group of patients, which in turn may protect the oxyntic mucosa from bacterial colonisation.¹⁷

In summary, this study confirms the established finding with regard to the distribution of gastritis in duodenal and gastric ulcer disease. It shows, however, that in the population studied, colonisation of the gastric body by *H pylori* is equally common in gastric and duodenal ulcer disease, but that the density of colonisation and the inflammatory changes are less noticeable in patients with duodenal ulcer, as is the case in non-ulcer subjects with type B gastritis.¹⁸ These differences seem to be linked to differences in colonisation density, but other host or organism factors could be relevant.

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