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Helicobacter pylori and gastritis in patients with peptic ulcer and non-ulcer dyspepsia: ethnic differences in Singapore

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Abstract

Peptic ulcer occurs with different frequencies in the three main racial groups in Singapore. This study aimed firstly to determine the prevalence of *Helicobacter pylori* in peptic ulcer and non-ulcer dyspepsia patients of the different races and secondly, to assess the relation between *H pylori*, histological gastritis, patient diagnosis, and race. Gastric antral biopsy specimens from 1502 patients undergoing gastroduodenoscopy were studied and 892 (59%) were positive for *H pylori*. *H pylori* was strongly associated with gastritis: 873 of 1197 (73%) patients with gastritis were positive compared with 19 of 305 (6%) without gastritis ($p<0.0001$). The prevalences of *H pylori* and gastritis were similar in peptic ulcer patients of different races. Malay patients with non-ulcer dyspepsia, however, were less likely to be positive for *H pylori* (10 of 46 (22%)) or to have antral gastritis (17 of 46 (37%)) than Chinese (292 of 605 (48%) were positive for *H pylori* and 421 of 605 (70%) had gastritis) and Indians (35 of 61 (57%) were *H pylori* positive and 42 of 61 (69%) had gastritis). Patients with duodenal ulcer were more likely to be positive for *H pylori* than those with non-ulcer dyspepsia, even when subjects with gastritis were considered separately. While our results do not help to explain the observed racial differences in peptic ulcer frequency it may be that the pathophysiology of non-ulcer dyspepsia is different in the different races in Singapore.

The nature of the association between the occurrence of *Helicobacter pylori*, histologically proved gastritis, peptic ulcer, and non-ulcer dyspepsia remains unclear. Many authors believe that *H pylori* can cause gastritis[1 2 3]; others suggest that these organisms may also cause peptic ulcer and non-ulcer dyspepsia.[4 5] Another explanation for the association between *H pylori* and peptic ulcer and non-ulcer dyspepsia is that all these conditions are associated with antral gastritis.[6 7] Yet a further possibility is that *H pylori* is an opportunistic invader of gastric mucosa which has already been damaged by gastritis.[8]

The three main racial groups in Singapore show differences in peptic ulcer frequency.[9 10] The Chinese are the most susceptible, the Indians less so, and the Malays relatively immune. The reasons for these racial differences remain unclear but environmental factors are probably important.[9] A low prevalence of *H pylori* infection has been associated with a low frequency of peptic ulcer in Australian aborigines.[11] It is therefore possible that racial differences in peptic ulcer frequency are related to the prevalence of gastritis and *H pylori* in the various patient populations in Singapore too.

In this study we aimed to determine the prevalence of *H pylori* in patients of different racial groups with peptic ulcer and non-ulcer dyspepsia and to assess the relation between *H pylori*, histological gastritis, patient diagnosis, and race in Singapore.

Patients and methods

PATIENT SELECTION

We studied consecutive patients undergoing gastroduodenoscopy by one endoscopist (JYK) at the University Department of Medicine II, Singapore General Hospital between January 1984 and December 1985 and by four endoscopists (JYK, RG, HHT and IY) at the Department of Medicine, National University Hospital between July 1985 and December 1987. One gastric antral biopsy specimen was obtained from each patient provided there was no contraindication to this procedure and informed consent had been obtained. When focal abnormalities such as inflammatory changes, ulcers, or erosions were present the biopsy specimen was taken from the abnormal area. Otherwise the specimen was taken from the lesser curve antrum, midway between the incisura and the pylorus. The patients were divided into the following groups: duodenal ulcer, gastric ulcer, combined gastric and duodenal ulcer, gastric carcinoma, non-ulcer dyspepsia (defined as patients presenting with upper abdominal pain or discomfort but without peptic ulcer, gastric carcinoma, or macroscopic oesophagitis), and a miscellaneous group.

STUDY DESIGN

Histological gastritis was diagnosed according to the criteria of Whitehead.[12] The gastritis was classified as acute, chronic, or acute-on-chronic depending on whether the cellular infiltrate was predominantly neutrophilic, lymphoplasmacytic, or both. The presence or absence of *H pylori* was assessed by light microscopic examination of sections stained with haematoxylin and eosin. A blinded review by the same pathologist of 24 consecutive antral biopsy specimens stained with haematoxylin and eosin and read on two separate occasions showed agreement in all cases. Another blinded comparison of serial sections of 126 consecutive antral biopsy specimens stained with haematoxylin and eosin and

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TABLE I *Demographic characteristics of patients studied*

Diagnosis	Total no	Age (yrs) (mean (SD))	Sex (M:F)	Race			
				Chinese	Malays	Indians	Others
Gastric ulcer	195	57 (15)	130: 65	173	10	11	1
Duodenal ulcer	422	44 (16)	303:119	352	18	49	3
Gastric and duodenal ulcer	28	64 (14)	16: 12	27	1	0	0
Gastric carcinoma	15	61 (10)	9: 6	12	2	0	1
Non-ulcer dyspepsia	729	42 (17)	388:341	605	46	61	17
Miscellaneous	113	52 (18)	59: 54	99	5	9	0
All	1502	46 (17)	905:597	1268	82	130	22

with Giemsa[13] showed agreement in 123 (98%). Although bacterial culture was not performed as part of this study, we had previously cultured *H pylori* from gastric biopsy specimens in which spiral organisms were identified histologically.[14]

STATISTICAL CONSIDERATIONS

Categorical data were analysed by the χ^2 test, with Yates's correction when appropriate. Numerical data was analysed by the Student's *t* test. Because multiple comparisons were being made, only p values below 0·01 were considered significant.

Results

Gastric antral biopsy specimens were taken from 1502 patients. Their diagnoses and demographic characteristics are summarised in Table I.

SEX AND H PYLORI

Men were more likely to be positive for *H pylori* than women (562 of 905 (62%) *v* 330 of 597 (55%), p<0·01). This was due, however, to a greater proportion of men with peptic ulcer (449 of 905 (50%)) and a smaller proportion with non-ulcer dyspepsia (388 of 905 (43%)) when compared with women (196 of 597 (33%) and 341 of 597 (57%) respectively). When individual diagnoses were considered, there was no sex difference.

H PYLORI AND GASTRITIS

Histological gastritis was present in 1197 (80%) of the antral biopsy specimens. *H pylori* was present in 873 of 1197 (73%) of biopsy specimens that showed gastritis compared with 19 of 305 (6%) of those without gastritis (p<0·0001) (Table II). When biopsy specimens showing only gastritis were considered, *H pylori* was found to occur more commonly in those showing acute and acute-on-chronic gastritis than those showing chronic gastritis alone (Table III). Of 567 biopsy specimens showing atrophic gastritis, 437 (77%) were positive for *H pylori* compared with 436 of 630 (69%) showing superficial gastritis (p<0·01). Of 298 biopsy specimens in which intestinal metaplasia was detected, 201 (67%) were positive for *H pylori* compared with 672 of 899 (75%) specimens showing gastritis but no intestinal metaplasia (0·01 <p<0·02).

TABLE II *Helicobacter pylori (HP) and gastritis*

Diagnosis	No (%) with HP	
	Gastritis	No gastritis
Gastric ulcer	124/183(68)	4/12(33)†
Duodenal ulcer	359/405(89)*	3/17(18)
Gastric and duodenal ulcer	21/27(78)	0/1(0)
Gastric carcinoma	1/7(14)	2/8(25)
Non-ulcer dyspepsia	333/489(68)*	10/240(4)†
Miscellaneous	35/86(41)	0/27(0)
All	873/1197(73)‡	19/305(6)‡

* *v* *, † *v* †, ‡ *v* ‡:p<0·01.

TABLE III *Helicobacter pylori (HP) and type of gastritis*

	All	No with HP	% with HP
Acute gastritis	243	190*‡	78
Chronic gastritis	772	531*†	69
Acute-on-chronic gastritis	182	152†‡	84

* *v* * p<0·01; † *v* † p<0·001; ‡ *v* ‡ NS.

H PYLORI IN VARIOUS CONDITIONS

The frequency of *H pylori* varied considerably between patients in the different diagnostic groups. For example, 86% of patients with duodenal ulcer were positive for organisms compared with 47% of patients with non-ulcer dyspepsia and 31% of patients in the miscellaneous group (Table IV). These differences were partly due to different frequencies of gastritis in the different diagnostic groups. Thus 96% of duodenal ulcer patients had histological gastritis compared with 67% of patients with non-ulcer dyspepsia and 76% of patients in the miscellaneous group (Table V). Even when the presence or absence of gastritis was taken into account, however, *H pylori* occurred more commonly in ulcer patients than in patients with non-ulcer dyspepsia (Table II).

H PYLORI AND RACE

H pylori occurred most commonly among Indians (69%) followed by Chinese (60%), and Malays (37%) (Table IV). This was partly due to racial differences in the frequency of the various diagnoses (Table I). Relatively few Malay subjects had peptic ulcer (29 of 82 (35%)) when compared with Chinese (522 of 1268 (44%)) and Indians (60 of 130 (46%)). In contrast, 46 (56%) Malay subjects presented with non-ulcer dyspepsia compared with 605 (48%) Chinese and 61 (47%) Indians.

There were no racial differences in the prevalence of *H pylori* and gastritis among patients with gastric ulcer, duodenal ulcer, or those with miscellaneous diagnoses (Tables IV and V). Among non-ulcer dyspepsia patients, however, 48% of Chinese were positive for *H pylori* compared with 57% of Indians and only 22% of Malays (Malays *v* Chinese or Indians p<0·01, Table IV). Some 70% of Chinese with non-ulcer dyspepsia had gastritis compared with 69% of Indians and 37% of Malays (Malays *v* Chinese or Indians p<0·01, Table V).

AGE, DIAGNOSES, RACE, H PYLORI, AND GASTRITIS

Overall, there was no difference in the mean (SD) age of patients with and without *H pylori* (46·2 (16·7) years *v* 45·1 (18·1) years, NS). Patients with gastritis were older than those without (47·5 (17·1) years *v* 38·6 (17·2),

TABLE IV *Helicobacter pylori (HP), diagnosis, and race*

	No (%) with HP				
	Chinese	*Malays*	*Indians*	*Others*	*All*
Gastric ulcer	115/173(66)	4/10(40)	8/11(73)	1/1(100)	128/195(66)
Duodenal ulcer	300/352(85)	15/18(83)	45/49(92	2/3(67)	362/422(86)
Gastric and duodenal ulcer	20/27(74)	1/1(100)	–	–	21/28(75)
Gastric carcinoma	3/12(25)	0/2(0)	–	0/1(0)	3/15(20)
Non-ulcer dyspepsia	292/605(48)*	10/46(22)*†	35/61(	6/17(35)	343/729(47)
Miscellaneous	33/99(33)	0/5(0)	2/9(2	–	35/113(31)
All	763/1268(60)‡	30/82(37)‡§	90/1	9/22(41)	892/1502(59)

*v *, †v † } p<0·001
‡v ‡, §v § }

1(0)
6/17(35
–
9/22(

p=0·0001). W individual diagnoses were considered, n cer dyspepsia patients with *H pylori* were o than those without this diagnosis (43·8 ndivi 5) years *v* 39·9 (17·2) years, p=0·002) r dys -ulcer dyspepsia patients with gastritis an t also older than those without gastritis (yea (16·8) years *v* 35·5 (15·8) years; p=0·0001). In contrast, the occurrence of *H pylori* or gastritis in patients with gastric ulcer and duodenal ulcer was not influenced by age.

Non-ulcer dyspepsia patients did not differ in age from duodenal ulcer patients (43·9 (16·1) *v* 41·7 (17·0) years), even where patients with gastritis only were considered separately (43·6 (16·0) *v* 44·8 (16·8)). Gastric ulcer patients were, in contrast, older (57·1 (14·7) years).

The age distributions of non-ulcer dyspepsia patients in the three main races were not significantly different. The relation between age and positivity for *H pylori* and gastritis in non-ulcer dyspepsia patients occurred only among Chinese. Among non-ulcer dyspepsia patients of Malay and Indian origin, patients with and without *H pylori* and gastritis did not differ in age.

Discussion

The importance of *H pylori* in gastric mucosa is not fully understood. Although associations with gastritis, peptic ulcer, and non-ulcer dyspepsia are now clearly established, it is still unclear whether *H pylori* is the cause or the effect of these conditions. Several lines of evidence suggest that *H pylori* actually causes gastritis. Firstly, its eradication from the gastritic stomach results in improvement of the gastritis.[15] Secondly, both in humans and animals, experimental inoculation of the stomach results in the development of gastritis.[16 17] Further, specific local and systemic immune responses to *H pylori* have been described.[18] It has also been suggested that *H pylori* is a cause of peptic ulcer or non-ulcer dyspepsia.[4 5] An alternative possibility, however, is that its association with gastritis, ulcer, and non-ulcer dyspepsia merely represents an opportunistic infection of an abnormal mucosa.[8] Against the latter view is the observation that *H pylori* is uncommon in antral gastritis associated with duodenogastric reflux[19] and also in that associated with pernicious anaemia.[20]

Our results also argue against the view that *H pylori* is merely an opportunistic agent colonising already abnormal mucosa. If this were so, its prevalence in patients with gastritis would be similar, irrespective of the primary diagnosis. We have shown that the prevalence of *H pylori* in gastritic mucosa of non-ulcer dyspepsia patients is considerably lower than in subjects with duodenal ulcer. Our results also mean that if *H pylori* causes gastritis, it is probably only one of several causes.

In a recent study an isolated group of Australian aborigines, in whom peptic ulcer is virtually unknown, was found to have *H pylori* antibody values comparable with white Australians known not to be infected.[11] Age-matched 'healthy' white Australians as well as duodenal ulcer patients had higher values of *H pylori* antibody. It was suggested that the low frequency of peptic ulcer in Australian aborigines may therefore be due to the rarity of *H pylori* infection.

Racial differences in peptic ulcer frequency have been shown in Singapore.[9 10] Chinese, for example, have up to seven times the risk of ulcer surgery than Malays. Gastric acid secretion seems to be similar in the different races. Although available data suggest that environmental factors probably account for at least some of the racial differences,[9] these factors remain unidentified. An assessment of the prevalence of *H pylori* and gastritis in peptic ulcer patients of different races is therefore of interest. Our finding that gastritis and *H pylori* infection are similar in peptic ulcer patients of different races gives no further clues on the aetiology of peptic ulcer.

Non-ulcer dyspepsia is thought to be a heterogenous disorder in which different pathophysiological factors act in different subsets of patients.[21] It has been suggested that dyspeptic patients infected with *H pylori*, but not those without infection, experience improvement of their symptoms after antibacterial treatment.[22 23] Therefore infection with *H pylori* may be one cause of non-ulcer dyspepsia. Both *H pylori* and gastritis are less common in Malays than in Chinese and Indians. These differences could not be explained by differences in age. The pathophysiology of non-ulcer dyspepsia may therefore vary between the three races in that different proportions of patients may be infected with *H pylori*.

In studies in which both histology and culture were used to assess the occurrence of *H pylori*, a proportion of biopsy specimens negative for *H pylori* on histology would be positive on culture (and vice versa).[24 25] Since culture was not used in the present study, the prevalences of *H pylori* in our various patient populations are likely to be underestimated. Since different diagnostic and racial groups were likely to have been affected to a similar extent, however, our various comparisons should remain valid.

TABLE V *Histological gastritis, diagnosis, and race*

	No (%) with gastritis				
	Chinese	*Malays*	*Indians*	*Others*	*All*
Gastric ulcer	161/173(93)	10/10(100)	11/11(100)	1/1(100)	183/195(94)
Duodenal ulcer	340/352(97)	15/18(83)	48/49(98)	2/3(67)	405/422(96)
Gastric and duodenal ulcer	26/27(96)	1/1(100)	–	–	27/28(96)
Gastric carcinoma	5/12(42)	1/2(50)	–	1/1(100)	7/15(47)
Non-ulcer dyspepsia	421/605(70)*	17/46(37)*†	42/61(69)†	9/17(53)	489/729(67)
Miscellaneous	74/99(75)	4/5(80)	8/9(89)	–	86/113(76)
All	1027/1268(81)‡	48/82(59)‡§	109/130(84)§	13/22(59)	1197/1502(80)

*v *, †v † } p<0·01
‡v ‡, §v § }

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