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## Prevalence of non-*Helicobacter pylori* duodenal ulcer in Karachi, Pakistan

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### Abstract

**AIM:** To determine the prevalence of non-*Helicobacter pylori* (*H pylori*)-related duodenal ulcer in patients with acid-peptic diseases.

**METHODS:** Medical records of patients who attended the Gastroenterology Department at Aga Khan University Hospital from 1999 to 2001 and had endoscopic diagnosis of duodenal ulcers were reviewed. Duodenal ulcer associated with *H pylori* was diagnosed on the basis of endoscopy, rapid urease test and histopathology whereas histories of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) related duodenal ulcers. Non-*H pylori*, non-NSAID duodenal ulcers were those without *H pylori* infection and history of NSAID intake. Co-morbid conditions associated were noted.

**RESULTS:** Of 2 260 patients, 10% (217/2 260) had duodenal ulcer. Duodenal ulcer related to *H pylori* infection accounted for 53% (116/217), NSAID-related 10% (22/217), non-*H pylori* non-NSAID 29% (62/217), and 8% (17/217) had both *H pylori* infection and histories of NSAID intake. Fifteen percent (18/116) patients had past histories of peptic ulcer disease in *H pylori* infection, while 8% (5/62) in non-*H pylori* non-NSAID ulcer. Co-morbid conditions in *H pylori* infection were seen in 23% (27/116) and 34% (21/62) in non-*H pylori* non-NSAID ulcer.

**CONCLUSION:** Incidence of *H pylori* infection related with duodenal ulcer is common. In the presence of co-morbid, non-*H pylori* and non-NSAID duodenal ulcer is likely to be present.

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**Key words:** *H pylori*; Acid-peptic diseases

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### INTRODUCTION

Peptic ulcer is a leading cause of morbidity and mortality. *Helicobacter pylori* (*H pylori*) infection and nonsteroidal anti-inflammatory drugs (NSAIDs) are recognized as the most important causes of peptic ulcer disease. *H pylori* infection is considered as a prerequisite for duodenal and gastric ulcers<sup>[1,2]</sup>. The widespread use of NSAIDs has led to an increased incidence of ulcer complications. There has been an increase in admission for ulcer related complications among elderly people, which is attributed to the increased use of NSAIDs and low-dose aspirin<sup>[3]</sup>. An estimated 16 500 patients with arthritis die from the gastrointestinal toxicity of NSAIDs every year<sup>[4]</sup>. The decline in prevalence of *H pylori* infection in developed countries has changed the pattern of peptic ulcer diseases<sup>[5]</sup>. Studies from North America showed that 11-44% of peptic ulcers were not related to either of the two factors<sup>[6,7]</sup>. In a meta-analysis of duodenal ulcer trials in North America, 20% of patients had ulcer recurrence within 6 mo after the eradication of *H pylori*<sup>[8]</sup>. This is in contrast with studies from Asia where the prevalence of *H pylori* infection is high and that of ulcers not related to *H pylori* or NSAIDs is very low<sup>[9,10]</sup>. In Pakistan, *H pylori* exposure rate increases with advancement of age and lowering of socio-economic status<sup>[11]</sup>. In a study, the overall exposure rate to *H pylori* in children was 33% while in a group of adult dyspeptic patients undergoing upper gastrointestinal endoscopy, the prevalence of *H pylori* infection investigated by histology and rapid urease test revealed that *H pylori* was associated with 85% cases of duodenal ulcer<sup>[11,12]</sup>. The pattern of duodenal ulcer in Karachi, Pakistan, extending over 13 year from June 1976 to June 1989, demonstrated that duodenal ulcer occurred predominantly between the 3<sup>rd</sup> and 5<sup>th</sup> decade of life with a male-female ratio of 6:1<sup>[13]</sup>. History of NSAID intake was present in only 5% of these cases<sup>[13]</sup>. The aim of this study was to determine the prevalence of non-*H pylori*-related duodenal ulcer in our patients.

### MATERIALS AND METHODS

This retrospective study was conducted at Aga Khan University Hospital, Karachi, Pakistan. It is a tertiary care center and used as a referral center for patients from all over the country. Medical records of patients who attended the endoscopy unit of Gastroenterology Department at Aga Khan University Hospital from 1999 to 2001 and ICD-9-

CM coded as duodenal ulcers diagnosed by esophagogastrroduodenoscopy (EGD) were reviewed. These patients included all referrals from both outpatient and hospital inpatient services. All the patients were included only once for analysis. Of these, 49% (1 115/2 260) patients had chronic gastritis, 9% (198/2 260) gastric ulcer, 32% (730/2 260) duodenitis and 10% (217/2 260) duodenal ulcer. *H pylori* infection was confirmed by rapid urease test and histopathology, which was later used as the gold standard for the diagnosis. Age, sex, co-morbid conditions, history of aspirin, NSAIDs, proton pump inhibitor (PPI), histamine-2 receptor blocker (H<sub>2</sub>-RB), antibiotics usage, *etc.*, were noted. Co-morbid conditions included hypertension, ischemic heart disease, diabetes mellitus, dyslipidemia, arthritis, *etc.* NSAID/aspirin usage was defined as ingestion of at least one dose within 4 wk before endoscopy. The current treatment of duodenal ulcer and symptomatic relief that followed was noted. The treatment consisted of a PPI alone or in combination of clarithromycin and amoxicillin at a recommended dose for 1 wk<sup>[14]</sup>. Complete relief was defined requiring no further medication while partial relief required maintenance treatment with a PPI or H<sub>2</sub>-RB. The risk factors associated with peptic ulcer diseases such as smoking and alcoholism were also noted. The endoscopic lesions were defined as duodenal ulcer with a break of  $\geq 5$  mm in the mucosal surface with an apparent depth, duodenitis and signs of active bleeding such as oozing and visible blood vessels. Rapid urease test and histopathology results were also noted. Histopathology documented *H pylori* infection in the presence of Gram negative curved bacilli on staining with hematoxylin-eosin (HE) in the presence of inflammation that was graded according to Sydney classification. In doubtful cases, Giemsa stain was used to stain the slides.

### Statistical analysis

Results were expressed as mean $\pm$ SD, with median range for all continuous variables (age, dose, *etc.*) and number (percentage) for categorical data (gender, *etc.*). Univariate analysis was performed using Pearson's  $\chi^2$  test, Fischer-exact test and the difference in mean was evaluated by independent sample *t* test wherever appropriate.  $P < 0.05$  was considered statistically significant. Statistical interpretation of data was performed using the computerized software program SPSS version 10.0.

## RESULTS

The number of EGDs performed for upper gastrointestinal symptoms over this period was 9 000. Of these, 2 260/9 000 had gastroduodenal diseases with *H pylori* infection-related duodenal ulcer 53% (116/217), NSAID related 10% (22/217), non-*H pylori* non-NSAID 29% (62/217), and both *H pylori* and NSAID related 8% (17/217) (Table 1). Those with NSAID-related duodenal ulcer had the highest mean age of  $62 \pm 16.2$  years and lowest of  $41 \pm 14.3$  years in *H pylori* infection. In all groups there was a male dominance.

### Duodenal ulcer related to NSAID use and *H pylori* infection

Patients with NSAID-related duodenal ulcers had a higher male: female ratio of 4:1 with mean age of  $62 \pm 16$  years (Table 1). Abdominal pain was common in *H pylori* infection 54% (63/116) however, symptoms of abdominal pain, hematemesis and melena were relatively more in those with NSAID related duodenal ulcer covering 36% (8/22) (Table 1). Endoscopic duodenitis and signs of active bleeding were seen in those with *H pylori* infection-related and NSAID-related duodenal ulcers (Table 1). Patients with both *H pylori* and NSAID-related duodenal ulcers had no

**Table 1** Clinical detail of the patients with duodenal ulcer (mean $\pm$ SD)

Variables	<i>H pylori</i> infection (n = 116)	NSAIDs related (n = 22)	Non- <i>H pylori</i> non-NSAIDs related (n = 62)	<i>H pylori</i> and NSAIDs related (n = 17)
Gender				
Male	80	18	42	11
Female	36	4	20	6
Mean age $\pm$ SD	41 $\pm$ 14.3	62 $\pm$ 16.2	42 $\pm$ 17	53 $\pm$ 13.6
Symptoms				
Abdominal pain	63	6	30	8
Non-specific	10	4	7	3
AHM	10	8	12	6
Bloating	33	4	13	3
Past history				
Peptic ulcer	18	4	5	1
Co-morbid	27	13	21	11
Endoscopy				
Duodenitis	42	6	24	4
Active bleed	8	4	4	2
Therapy				
Triple therapy	74	5	14	11
PPI	37	14	43	6
H <sub>2</sub> -RB	3	2	4	-
Symptom relief				
Complete	69	$P = 0.09$ 17	47	12
Partial	47	5	15	5

AHM = abdominal pain with hematemesis and melena.

**Table 2** Co-morbid conditions associated with duodenal ulcer in different groups

Co-morbid	<i>H pylori</i> infection (n = 27)	NSAIDs related (n = 13)	Non- <i>H pylori</i> non-NSAIDs related (n = 21)	<i>H pylori</i> and NSAIDs related (n = 11)
HTN	12	3	9	1
DM	5	1	3	2
IHD	4	3	8	4
Arthritis	6	6	1	4

distinguishing features.

### *H pylori* and non-*H pylori* non-NSAID duodenal ulcer

*H pylori* and non-*H pylori* non-NSAID duodenal ulcer had a similar male:female ratio and mean age (Table 1). Co-morbid conditions were more common in non-*H pylori* non-NSAID, which were 34% (21/62) and 23% (27/116) in *H pylori*, respectively (Table 2). In the presence of co-morbid conditions, the likelihood of non-*H pylori* non-NSAID duodenal ulcer was twice that of *H pylori* infection odds ratio: 1.7; 95%CI: (0.8-3.5). Symptoms, endoscopic duodenitis and signs of active bleeding were almost equally common in both groups (Table 1).

### Treatment of duodenal ulcer related to *H pylori* infection, NSAIDs use and non-*H pylori*, non-NSAIDs

Triple therapy was administered to 64% (74/116) patients with *H pylori* infection, while PPI was used in 69% (43/62) non-*H pylori* non-NSAID ulcers and in 68% (15/22) NSAID-related ulcers (Table 1). These forms of treatment were associated with complete symptom relief of *H pylori* infection in 59% (69/116), NSAID-related ulcer in 77% (17/22) and non-*H pylori* non-NSAID ulcer in 76% (47/62), with partial relief in 41% (47/116), 23% (5/22) and 24% (15/62), respectively ( $P = 0.09$ , Table 1).

## DISCUSSION

It is known that not all ulcers are caused by *H pylori* and that there is evidence that the proportion of non-*H pylori* ulcers is common. The present study demonstrated that *H pylori* infection related duodenal ulcers accounted for 53% and those associated with NSAIDs 10% (Table 1). The NSAIDs used were conventional and not selective COX-2 inhibitors. The mean age and the male to female ratio of patients with NSAID-related duodenal ulcer were comparatively higher than those of other three groups (Table 1). We did not find any association between risk factors such as smoking and alcohol intake with duodenal ulcer in any group. Abdominal pain was frequent in all groups, the combination of abdominal pain, hematemesis and melena was prominently seen in association with non-*H pylori* non-NSAIDs. Past history of peptic ulcer diseases was present in *H pylori* infection, none of these patients with past histories of peptic ulcer diseases was found to be on maintenance PPI or H<sub>2</sub>-RB. In keeping with other studies, co-morbid conditions were commonly associated with non-*H pylori* non-NSAID-related duodenal ulcer<sup>[9,15]</sup>. As the sample size was small, it was not sufficient to compare these co-morbid conditions individually in each of the four groups. Endoscopic duodenitis and signs of active bleeding on endoscopy were

not prominent in any particular group (Table 1). Duodenal ulcer related to *H pylori* was treated with triple therapy but only 56% became completely symptom free (Table 1). This might be attributed to yet undefined proportion of non-ulcer dyspepsia patients with co-existent carriage of *H pylori*.

The implications of this study are that in this group of patients the incidence of *H pylori* infection related duodenal ulcer compared with previous study by Kazi *et al*<sup>[12]</sup>, was low, this might be attributed to the eradication therapy of *H pylori* infection, improvement of socio-economic and living conditions. Also, practice of indiscriminate use of antibiotics in our society might have contributed to this. Non-*H pylori* non-NSAID duodenal ulcers were also present in our population where there is a high incidence of *H pylori* infection. Non-*H pylori* non-NSAIDs-related duodenal ulcers were found in 29% (Table 1). However, a high incidence of non-*H pylori* non-NSAIDs duodenal ulcer on a retrospective study needs confirmation prospectively. Also, some cases of *H pylori* infection might have been missed on both rapid urease test and histopathology. It is also known that in some of the critically ill patients with co-morbid conditions, stress-related ulcers may occur. However, none of our patients was critically ill or from intensive care units. The mean age of our patients with *H pylori* infection and non-*H pylori* non-NSAID duodenal ulcer was the same in contrast to studies in the West where non-*H pylori* non-NSAID duodenal ulcer patients were of a higher age<sup>[9]</sup>. This can be explained by *H pylori*, host and environmental factors all having a role in peptic ulcer diseases. Etiological factors for the development of non-*H pylori* non-NSAID duodenal ulcer remain to be identified. In the presence of effective prophylactic agents, ulcer complications related to NSAIDs were high in our elderly patients.

In conclusion, *H pylori* infection-related duodenal ulcer is still common while NSAID-related duodenal ulcers occur in older age group. In the presence of co-morbid conditions, non-*H pylori* non-NSAID duodenal ulcers are likely to be present.

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