Prevalence of *Helicobacter pylori* infection in patients with peptic ulcer diseases

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ABSTRACT

Objectives: To determine the prevalence of *Helicobacter pylori* (*H. pylori*) infection among patients presenting with peptic ulcer disease (PUD) and to establish the relationship between *H. pylori* infection and its diverse pathology. Secondly, we aimed to examine the effect of age, gender, and geographical distribution on the prevalence of the disease.

Methods: The study included patients with PUD who underwent upper gastrointestinal endoscopy at Hera General Hospital, Makkah, Kingdom of Saudi Arabia between January 2003 and February 2004. We tested the biopsies for the detection of *H. pylori* by *Campylobacter* like organism (CLO™) test, histopathology, immunoglobulin G (IgG) antibodies, culture, and antimicrobial susceptibility testing.

Results: The overall prevalence rate of *H. pylori* infection among 132 patients with PUD was 63%, while it was high among females (70%) as compared with males (58%). The *H. pylori* were mainly found in chronic active gastritis (89%) and severe active gastritis (96%). *Helicobacter pylori* were documented by CLO™ test in 73 (55.3%) cases, histopathology in 69 (52.3%) cases, microbiological culture in 59 (44.7%) cases, and IgG antibodies in 61 (46.2%) cases. The highest resistance (31%) was found in metronidazole, while lowest the (3%) in tetracycline and erythromycin.

Conclusion: The highest prevalence of *H. pylori* was found in the younger age group with female preponderance. The leading causes of multifocal pathology were chronic and severe active gastritis secondary to *H. pylori* infection.

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Helicobacter pylorus (*H. pylori*) is a gram-negative bacterium that colonizes the gastric mucosa of more than half of the world's population and plays a major role in the pathogenesis of peptic ulcer.[1] While most of stomach and duodenal ulcers are caused by the bacterium, not all infected individual develops ulcer.[2] Since its isolation in 1982, the association between *H. pylori* infection and the subsequent development of chronic active gastritis, peptic ulcer disease (PUD), gastric cell carcinoma, and B cell mucosa-associated lymphoid tissue lymphoma has been well established.[3] A better understanding regarding the epidemiology of *H. pylori* infection in relation to the geographical distribution is necessary to develop public health measures that will control the spread of the bacterium. The present study was planned to determine the prevalence of *H. pylori* infection among patients presented with PUD, and to establish the relationship between *H. pylori* infection and its diverse pathology. It was also aimed to evaluate the use of invasive and noninvasive tests in the diagnosis of *H. pylori* infection among patients with PUD and

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to determine the antibiotic susceptibility patterns of *H. pylori* isolated by culture.

Methods. This prospective study was conducted from January 2003 to February 2004 at Hera General Hospital, Makkah, Kingdom of Saudi Arabia. All patients with PUD who underwent upper gastrointestinal (GI) endoscopy were enrolled in the study. These patients were referred to a Gastroenterologists for upper abdominal pain, dyspepsia, or previous history of PUD. The demographic information included age, gender, socioeconomic group, and family size. A small family unit was defined as a husband and a wife with at least one child living in the same household.[4] A large family size was defined in comparison to a small unit namely more than one wife or more than one children. The socioeconomic groups (low, middle and high) were based on per capital income[5] and occupation of the patient or family head of the patient. Upper GI endoscopy was performed by an Olympus endoscope GIF-2T20 flexible and double channel. The initial diagnosis was made on the endoscopic findings of stomach and duodenum. The multiple biopsies were taken by using sterile biopsy forceps. The areas selected for biopsies were the gastric antrum and fundus, duodenum in addition to the specific site of lesion for the detection of *H. pylori* and other pathology. The invasive diagnostic tests for *H. pylori* included were the endoscopic biopsies taken from the stomach lining for rapid urease test *Campylobacter* like organism (CLO™) an old name for *Helicobacter*[6] histopathology and microbiological culture. The noninvasive test included was *H. pylori* antibodies IgG.

The CLO™ test was performed immediately after taking biopsy specimen by endoscope within the endoscopy unit. A single gastric biopsy was placed into a well of a CLO™ test slide containing urea. A positive result was indicated by a change in the pH indicator dye color from yellow to pink within 20 minutes. This change in color indicated the breakdown of urea in the presence of *H. pylori*. All negative CLO™ test slide specimens were also examined for any change in color after 24 hours to study the low urease activity.[7] The endoscopic biopsies were fixed in 10% buffered formalin, embedded in paraffin wax, serially sectioned, and stained with routine hematoxylin and eosin and periodic acid shift stain. Additional specific stains for *H. pylori* such as Giemsa were also performed. The histopathological lesions were described grossly and microscopically. The *H. pylori* were identified by its characteristic morphology in the specific location namely mucus layer or within the gastric pits.[8] The specimens for histopathology were taken in duplicate. The standard microbiological culture technique was used to isolate and identify *H. pylori*. The biopsies were cut into small pieces by using sterile scalpel and forceps and placed in sterile saline. The suspension was then inoculated within 24 hours on chocolate namely heated blood.[9] The plates were incubated using microaerophilic (5% oxygen), and hypercapnic (5% carbon dioxide-CO_2) at 35^{O}C for up to 10 days. Identity of *H. pylori* was confirmed by Gram's stain and production of urease, oxidase and catalase. Antimicrobial susceptibility was tested on 5 first line antibiotics against *H. pylori* infection: metronidazole (MTZ), erythromycin, amoxicillin, tetracycline, and ciprofloxacin by the National Committee for Clinical Laboratory Standards guideline.[10] Noninvasive test comprised the qualitative estimation of immunoglobulin G (IgG) antibodies for *H. pylori* by enzyme-linked immunosorbent assay that was performed on serum samples of all enrolled patients.

A patient with *H. pylori* infection was defined as a patient who was independently assessed by the attending Gastroenterologists based on clinical symptoms and a positive test for identification of *H. pylori* on biopsy specimens either by histopathology or by microbiology or any one of the 2 diagnostic tests.[11] This clinico-laboratory case definition was used as the comparator reference standard and evaluation of diagnostic performance. The statistical analysis; ± standard deviation, chi-square, student t-test, and correlation was made on the Statistical Package for Social Sciences version 10. Statistical significance was set as p values of <0.05.

Results. We studied 132 patients who fulfilled the study criteria; among them 129 (97.7%) were Saudis and 3 (2.3%) non-Saudis. There were 56 male (42.4%), and 76 female (57.6%). The male versus female ratio was 1:0.74. The age group distribution of our patients was as follows: 10-19 years 3 (2.3%), 20-29 years 38 (28.8%), 30-39 years 25 (18.9%), 40-49 years 26 (19.7%), 50-59 years 20 (15.2%), 60-69 years 15 (11.4%), and 70 years and above 5 (3.8%). The median age was 39.5, and ranged from 14-90 years. There was no significant association of age group with the prevalence of *H. pylori* infection. The family size of our patients was as follows; small 43 (32.6%), medium 65 (49.2%), and large 24 (18.2%). The association of family size and prevalence of *H. pylori* infection was not significant (p=0.66). There were 21 (15.9%) smokers and 111 (84.1%) non-smokers. The socioeconomic distribution was as follows; low 44 (33.3%), intermediate 85 (64.4%), and high 3 (2.3%).

The clinical features were assessed at the time of consultation prior to the endoscopic examination. The major clinical presentation was epigastric pain that was found in all 132 (100%) patients. The pain was sudden in the onset in 79 (60%) cases while slow onset in rest of the patients 53 (40%). The pain was relieved on taking meal in 33 (25%) and exacerbated with fasting in 30 (23%) cases. The other symptoms included were; bleeding 12 (9%), dyspepsia 99 (75%), stress 75 (57%), weight loss 12 (9%), tarry stool 5 (4%), coffee ground emesis 10 (8%), and chronic itching 3 (2%) cases. On examination, we found; tender board such as abdomen in 11 (8%), and succession splash 31 (23%) cases. **Table 1** shows the upper GIT endoscopic findings of patients with PUD and its association with *H. pylori* infection. Of 132 patients, *H. pylori* were identified in 83 upper GI biopsies; therefore, the overall prevalence rate of *H. pylori* infection among patients with PUD was 62.9%. In present study, we have analyzed the age-specific and gender-specific prevalence of *H. pylori* in order to see whether the prevalence of *H. pylori* varies in different age groups. **Table 2** shows the distribution of laboratory confirmed *H. pylori* cases in relation to gender and age groups.

Helicobacter pylori were documented by CLO™ test in 73 (55.3%) cases; histopathology in 69 (52.3%) cases, serology *H. pylori* antibodies IgG in 61 (46.2%) cases and microbiological culture in 59 (44.7%) cases. On antimicrobial susceptibility of 59 isolates of *H. pylori*; MTZ was found the least sensitive and its sensitivity rate was 41 (69%). The sensitivity rate of other antimicrobial tested was as follows; erythromycin 57 (97%), amoxicillin 54 (92%), tetracycline 57 (97%), and ciprofloxacin 55 (93%). **Table 3** shows the histopathological diagnosis of total 132 biopsies and the distribution of *H. pylori* infection among the patients. **Table 4** elucidates the correlation of *H. pylori* infection with the clinical features and examination finding of patients. The association of socioeconomic factors and the *H. pylori* infection is given in **Table 5**.

Discussion. Infection with the bacteria generally occurs in childhood, with ulcers appearing much later in life. In fact, approximately half of all adults in the United States[12] over the age 60 are infected with *H. pylori*, but only a small percentage of those infected develop an ulcer. However, the situation in Saudi Arabia is different from that of USA and other developed countries. In our study, the peak prevalence of *H. pylori* infection was at the age of 20-29 years. There were 38 patients in age group 20-29 years, among whom 25 (66%) were positive. This high prevalence in younger age group is comparable to other studies in Saudi Arabia,[13] but in southern area of Saudi Arabia researchers demonstrated that the incidence of *H. pylori* infection is virtually the same in different age groups.[14] Our female patients showed high prevalence of *H. pylori* infection (70%) as compared with male (58%). This female preponderance of *H. pylori* infection cannot be proved by any other local study. It may be a coincident or required another study with large sample size. The number of nonsmoker was higher 111 (84.1%) as compared with smokers 21 (15.9%) in our PUD patients. Therefore, the number of smokers and PUD has given us the conflicting result. This fact can be explained that smoking is more restricted in the Kingdom of Saudi Arabia as compared with many other countries. In contrast to number of smokers among PUD patients, the *H. pylori* infection was more common in smokers (61%) than nonsmokers (52%) as shown in **Table 5**. This positive correlation of smoking and *H. pylori* infection is comparable to many local[15,16] and international studies.[17,18] The negative association was reported in another study[19] in contrary to data presented in current study. Therefore, we were unable to prove this association, as there was only one case of gastric cancer out of 132 patients of PUD. This cancer patient was nonsmoker and no *H. pylori* compatible structure seen on any of his histopathology specimens. We found the inverse association found between *H. pylori* infection and family size as high prevalence rate was found among those individuals who had small family size. Similarly, no positive association of *H. pylori* infection and economic levels was found. This can be explained that the socioeconomic factors such as housing conditions, water supply, and family size had not played any role in the predisposing factor of *H. pylori* infection.

Our study revealed that of *H. pylori* was most commonly present in severe active gastritis cases 91% followed by in chronic gastritis 55% cases comparable to one of the local study.[20] Histology should not any longer be considered a gold standard test for *H. pylori*.[21] It has been suggested that a combination of 3 separate diagnostic tests is needed to confirm the presence or absence of *H. pylori* infection. The comparison of results for the *H. pylori* using 4 tests used in our study is summarized in **Table 6**. On microbiological culture *H. pylori* was isolated on 59 (44.7%) biopsies while on histopathology 69 (52.3%). Negative microbiology cultures showed the presence in histopathology in 10 cases and CLO™ test in 14 cases. Failure of organism to grow possibly due to its reduced viability after patient's ingestion of topical anesthetic, prior treatment with antibiotics, proton

Table 1 - Endoscopic findings of patients with peptic ulcer diseases and its association with *Helicobacter pylori* infection.

Endoscopic findings	No. of *Helicobacter pylori* infections (%)		Total no. of patients
	Present	Absent	
Esophagus			
Normal	59 (64)	33 (36)	**92**
Esophagitis	16 (57)	12 (43)	**28**
Mucosal congestion	0 (0)	1 (100)	**1**
Hiatus hernia	3 (100)	0 (0)	**3**
ILOS	5 (62)	3 (38)	**8**
Stomach			
Normal	49 (68)	23 (32)	**72**
Acute gastritis	12 (50)	12 (50)	**24**
Mucosal congestion	10 (65)	8 (44)	**18**
Gastric erosion	7 (64)	4 (34)	**11**
Gastric polyp	2 (100)	0 (0)	**2**
Nodular erosion	2 (67)	1 (33)	**3**
Gastric ulcer	1 (50)	1 (50)	**2**
Duodenum			
Normal	58 (56)	45 (44)	**103**
Duodenitis	11 (79)	3 (21)	**14**
Duodenal ulcer	6 (86)	1 (14)	**7**
Mucosal congestion	7 (100)	0 (0)	**7**
Nodular erosion	1 (100)	0 (0)	**1**

ILOS - incompetent lower esophagus sphincter

Table 2 - Distribution of laboratory confirmed *Helicobacter pylori* infection in relation to gender and age groups (n=83).

Age groups Years	*Helicobacter pylori* infections		
	Male N (%)	Female N (%)	Total N (%)
10-19	0 (0)	1 (1.2)	**1 (1.2)**
20-29	10 (12)	15 (18.1)	**25 (30.1)**
30-39	7 (8.4)	7 (8.4)	**14 (16.9)**
40-49	5 (6.2)	13 (15.7)	**18 (21.7)**
50-59	10 (12)	6 (7.2)	**16 (19.3)**
60-69	6 (7.2)	1 (1.2)	**7 (8.4)**
≥70	1 (1.2)	1 (1.2)	**2 (2.4)**
Total	**39 (47)**	**44 (53)**	**83 (100)**

Table 3 - *Helicobacter pylori (H. pylori)* infection in the lesions on histopathological examination (n=132).

Histopathological diagnosis	Presence of *H. pylori* infection N (%)	Absence of *H. pylori* infection N (%)	Total no. of patients
Normal	3 (20)	12 (80)	**15**
Acute gastritis	3 (60)	2 (40)	**5**
Chronic gastritis	42 (70)	18 (30)	**60**
Chronic active gastritis	8 (89)	1 (11)	**9**
Severe active gastritis	23 (96)	1 (4)	**24**
Congestion	1 (9)	10 (91)	**11**
Atrophic gastritis	1 (100)	0 (0)	**1**
Gastric polyp	0 (0)	1 (100)	**1**
Chronic duodenitis	0 (0)	1 (100)	**1**
Erosive gastritis	1 (33)	2 (67)	**3**
Adenocarcinoma	1 (100)	0 (0)	**1**
Reflux gastritis	0 (0)	1 (100)	**1**
Total	**83 (63)**	**49 (37)**	**132**

Table 4 - Clinical features of patients in association with *Helicobacter pylori* (*H. pylori*) infection (n=132).

Clinical features	No. of *H. pylori* infections (%)		
	Present	Absent	Total
Onset of pain			
Sudden	46 (58)	33 (42)	**79**
Slow	37 (70)	16 (30)	**53**
Bleeding			
Yes	9 (75)	3 (25)	**12**
No	74 (62)	46 (38)	**120**
Stress			
Yes	46 (61)	29 (39)	**75**
No	37 (65)	20 (35)	**57**
Coffee ground emesis			
Yes	7 (70)	3 (30)	**10**
No	76 (62)	46 (38)	**122**
Dyspepsia			
Yes	61 (62)	38 (38)	**99**
No	22 (67)	11 (33)	**33**
Weight loss			
Yes	7 (58)	5 (42)	**12**
No	76 (63)	44 (37)	**120**
Tender board like abdomen			
Yes	5 (46)	6 (54)	**11**
No	78 (64)	43 (36)	**121**
Tarry stool			
Yes	5 (100)	0 (0)	**5**
No	78 (61)	49 (39)	**127**
Succession splash			
Yes	18 (58)	13 (62)	**31**
No	65 (64)	36 (36)	**101**
Chronic itching			
Yes	2 (67)	1 (33)	**3**
No	81 (63)	48 (37)	**129**

Table 5 - Association of *Helicobacter pylori (H. pylori)* infection with socio-economic factors of patients (n=132).

Socioeconomic factors	No. of *H. pylori* infections (%)		
	Present	Absent	Total
Economic condition			
Low	29 (66)	15 (34)	**44 (33.3)**
Intermediate	52 (61)	33 (39)	**85 (64.4)**
High	2 (67)	1 (33)	**3 (2.3)**
Family size			
Small	30 (70)	13 (30)	**43 (32.6)**
Medium	39 (60)	26 (40)	**65 (49.2)**
Large	14 (58)	10 (42)	**24 (18.2)**
Smoking habit			
Smokers	14 (67)	7 (33)	**21 (16)**
Nonsmokers	69 (52)	42 (48)	**111 (84)**
Nationality			
Saudis	81 (61)	48 (39)	**129 (97.7)**
Non-Saudis	2 (67)	1 (33)	**3 (2.3)**

Table 6 - Result of 4 tests performed for identification of *Helicobacter pylori* among patients with peptic ulcer diseases (n=132).

Name of test	Result of *Helicobacter pylori* detection (%)	
	Positive	Negative
CLO™ test	73 (55.3)	59 (44.7)
Histopathology	69 (52.3)	63 (47.7)
Serology (IgG)	61 (46.2)	71 (53.8)
Microbiology culture	59 (44.7)	73 (55.3)

CLO - *Campylobacter* like organism, IgG - immunoglobulin G

pump inhibitors or specimen transport in room air.[22] The identification rate of *H. pylori* on histopathology and microbiology is comparable to similar study conducted in the western area of Saudi Arabia.[14] The highest resistance was found in MTZ (31%) and same resistant pattern was found in Europe and the United States[23] ranging from 33.1-36.9%. The lowest resistant was found in tetracycline and erythromycin (3%).

Epidemiological studies have shown that areas with high gastric cancer rates often have a correspondingly high prevalence of *H. pylori*. In our study, there was only one case of malignancies (adenocarcinoma mucin type) that was associated with *H. pylori* infection. It was documented that stomach cancer ranks sixth in all malignancies in the southern region of Saudi Arabia and stands second among GI malignancies.[24,25] The data of the current study did not support the above statement; furthermore; the number is not adequate to discuss the casual relationship between *H. pylori* infection and gastric cancer. Most likely that gastric cancer may be the result of a sequence of changes, some of which may have been initiated by *H. pylori*. Therefore, *H. pylori* could be considered as a co-factor in gastric carcinogenesis in this patient and exposed to other unknown carcinogenic factors. The clinical features such as epigastric pain, stress, coffee ground emesis, bleeding, dyspepsia, weight loss, tender board such as abdomen, tarry stool, succession splash, and chronic itching was more common compared with a to study conducted in Saudi Arabia.[15] The clinical presentation was statistically different in *H. pylori* positives compared with those of negatives. Most other people harboring *H. pylori* will not have any symptoms or problems as a result of infection. In

17% of cases, we did not yet understand what were the etiological factors of PUD.

In conclusion, we studied that *H. pylori* infection was acquired early in life of our patients, leading to multifocal pathology of the upper GIT and thus predisposing the patients to develop chronic gastritis. The clinical presentation and examination findings have a positive correlation with *H. pylori* infection while surprisingly, we were unable to prove any significant role of transmission of *H. pylori* infection among the established predisposing factors. The mode of transmission of *H. pylori* in our population is still uncertain; therefore, authors recommend a population based on the study of Makkah population.

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