Prevalence and risk factors for *Helicobacter pylori* infection among Yemeni dyspeptic patients

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ABSTRACT

Objective: *Helicobacter pylori (H. pylori)* is one of the world's most common human bacterial infections. Acquisition of *H. pylori* infection may be associated with chronic gastritis, peptic ulceration and gastric cancer. This study was aimed at investigating the prevalence of *H. pylori* infection among dyspeptic patients, any correlation with dyspeptic symptoms and endoscopic findings and, any socioeconomic and environmental risk factors.

Methods: The study was conducted between September 1997 and October 1998 in one Endoscopy Unit, Sana'a city, Yemen. A total of 275 consecutive patients with chronic dyspepsia were enrolled in the study. Endoscopic examination was conducted, gastric biopsies were obtained from the antrum and corpus, and *H. pylori* infection was diagnosed at the time of endoscopy using the rapid urease test.

Results: The prevalence of *H. pylori* infection in our patients was 82.2% (95% confidence interval (CI) 78 to 87%). Independent variables associated with infection were age >40 years (odds ration (OR)=2.2; 95% CI: 1.0-4.64; P=0.043); the presence of ≥ 5 children under 14 years per household (OR=6.62; 95% CI: 2.245 to 19.5; P= 0.001); and duodenal ulcer disease (OR=3.7; 95% CI: 1.38 to 10.0; P=0.009).

Conclusion: The prevalence of *H. pylori* infection in dyspeptic patients in Yemen seems to be high. Advancing age, 5 or more children per household and duodenal ulcer disease were found to be significantly associated with *H. pylori* infection.

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Helicobacter pylori (H. pylori) is one of the world's most common human bacterial infections as more than 3 quarters of the population in the developing countries are infected from an early age.[1] Its reservoir is essentially human and the transmission seems to be direct from person-to-person, which may be by the oro-oral or faeco-oral route.[2] Recent studies indicate that intrafamilial transmission of *H. pylori* infection is more important than child-to-child transmission outside the family, and that the prevalence in the parental generation may be a crucial determinant for a child's risk of contracting the infection.[3] The dynamics of *H. pylori* infection in developed and developing countries are very different, and data are not comparable.[4] In the developed world, only a minority of children are infected during childhood, but the prevalence of infection rises in proportion to age with an apparent birth-cohort effect.[5-7] In most developing countries, the majority of children are infected with *H. pylori* by the age of 10-years and chronic infection continues during adult life.[6-8] Acquisition of *H. pylori* infection at the end of childhood or later might be associated with peptic ulceration, while infection during early childhood results in chronic *H. pylori* gastritis.[6-8] There is now evidence

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that chronic *H. pylori* gastritis may be associated with increased risk of malignant transformation of gastric tissue, such as mucosa-associated lymphoid tissue (MALT) gastric lymphoma and gastric carcinoma.[9,10] Recent evidence indicates that gastric cancer usually develops in persons infected with *H. pylori* but not in uninfected persons; the risk being increased in those with histologic findings of severe gastric atrophy, corpus-predominant gastritis, or intestinal metaplasia.[11]

The aim of the present study was to investigate the prevalence of *H. pylori* infection among a large group of dyspeptic patients, its correlation with symptoms and endoscopic findings and any socioeconomic and environmental risk factors.

Methods. This study was conducted between September 1997 and October 1998 in one Endoscopy Unit, Sana'a city, Yemen. Subjects were drawn from consecutive patients with chronic dyspepsia. Only those willing to participate in the study and who gave informed consent were enrolled. Ethical clearance was also obtained. Pregnant and lactating women were excluded, as were patients with esophageal or gastric tumors and cirrhosis. In addition, those who were receiving antisecretory drugs; for example H_2-receptor antagonists (H_2RA), proton pump inhibitors (PPI), antibiotics, nonsteroidal anti-inflammatory drugs (NSAID), corticosteroids or bismuth-containing drugs during the preceding 4 weeks were excluded. Urbanization status was categorized as urban (urban life setting since early childhood), rural (rural life since childhood) and urbanizing (moved from rural to urban life setting). Social class was categorized as mentioned elsewhere[12] into 5 classes: professional's (I), managerial (II), non-manual skilled (IIIN), manual skilled (IIIM), partially skilled (IV) and unskilled (V).

Endoscopic examination. Endoscopic examination was conducted using Olympus GIF QW endoscopes (Olympus Tokyo, Japan), and the presence of lesions in the esophageal and gastroduodenal mucosa was noted. Endoscopic differentiation was made between erosions and true ulcers. Erosions were defined as breaks in the mucosa <5 mm in diameter with no appreciable depth.[13] An ulcer was defined as a circumscribed break in the mucosa >5 mm in diameter with an exudates and appreciable depth.[14]

Biopsy-specimens Biopsy specimens were collected at the time of endoscopic examination using biopsy forceps (FB- 19K, Olympus Tokyo, Japan). Two biopsy specimens were obtained one from the antrum 2-3 cm from the pylorus, and the second from the body midway between the antral-body junction and cardia.

Rapid urease test. The collected tissue specimens were used for the rapid urease test, one in each slide, using the Campylobacter-like Organism (CLO) test (Delta-West Limited, Bentley Western, Australia). The diagnosis of *H. pylori* infection was based on a positive CLO test in at least one slide. Patients were diagnosed as *H. pylori* negative if both slides were negative. This test consists of a sealed plastic slide holding a mounted agar gel pellet containing urea, phenol red (pH indicator) buffers and bacteriostatic agents. The color of the gel changes to pink if the pH rises above 6.0. This color change should only occur when urea in the gel is hydrolyzed in the presence of urease, to release ammonia.[15]

Patients enrolled in the study were interviewed prior to endoscopic examination according to a standardized questionnaire. A database was established in the computer and included age, sex, childhood origin (town/village), current address (town/village), job, soci-economic status and social class (based on occupation of head of household), number of persons per household (adults and children under 14 years), water supply (well outside, own supply piped, municipal piped), boiled water for drinking (yes/no), uncooked vegetable eaten including qat leaves (yes/no), and smoking habits (yes/no). Patients were also questioned

Table 1 - Baseline characteristic of 275 dyspeptic patients screened for *Helicobacter Pylori* infection at the time of entry to the study.

Characteristics	n (%)
Sex	
Male	162 (59)
Female	113 (41)
Age groups	
≤20	20 (7)
21-30	60 (22)
31-40	105 (38)
≥40 (41-75)	90 (33)
Qat chewers	
(Uncooked green leaves)	155 (56)
Current smokers	70 (25)
Social class (based on occupation of head of household)	
I + II	77 (28)
IIIN + III M	102 (37)
IV + V	96 (35)
Severity of dyspeptic symptoms	
Mild	143 (52)
Moderate	103 (37)
Severe	29 (11)
Endoscopic diagnosis	
Duodenal ulcer	43 (16)
Errosive duodenitis	42 (15)
Antral erosions (gastritis)	113 (41)
Macroesophagitis	37 (13)
No gross abnormality	40 (15)
Positive H.pylori infection (CLOtest % (95% CI)	226 (82.2%; 95% CI: 78 to 87%)

CLOtest - Campylobacter-like Organism
I - professionals, II - managerial, IIIN - non-manual skilled, III M - manual skilled, IV - partially skilled, V - skilled

Table 2 - Univariate analysis of the prevalence of *H.pylori* infection by categories of independant variable of 275 patients who presented with dyspepsia (*).

Variables and categories	Frequency of positive cases (%)	n of positive cases/total n of patients	Univariate RR (95% CI)	p-value
Sex				
Male	(88)	142/**162**	1.54 (1.1 to 2.2)	0.007
Female	(74)	84/**113**	0.63 (0.5 to 0.84)	
Age (years)†				
≤20 years	(65)	13/**20**	0.78 (0.56 to 1.08)	
21-30 years	(78)	47/**60**	0.94 (0.81 to 1.09)	
31-40 years	(81)	85/**105**	0.98 (0.87 to 1.10)	
>40 (41-75)	(90)	81/**90**	1.95 (1.05 to 3.61)	0.028
Urbanization status†				
Rural	(75)	43/**57**	0.67 (0.4 to 1.12)	
Urbanizing	(84)	104/**124**	1.13 (0.78 to 1.62)	0.23
Urban	(84)	79/**94**	1.14 (0.72 to 1.8)	
Social class † (based on occupation of head of household)		65/**77**	1.2 (0.7 to 2.0)	
I + II	(84)	81/**102**	0.84 (0.6 to 1.2)	0.9
IIIN + III M	(79)	80/**96**	1.1 (0.7 to 1.7)	
IV + V	(83)			
Family size (Number of persons per household)				
≥6	(86)	169/**197**	1.3 (1.0 to 1.69)	0.021
<6	(73)	57/**78**	0.59 (0.4 to 0.87)	
Number of children under 14 years old per household				
≥5	(95)	72/**76**	3.9 (1.5 to 10.0)	0.001
<5	(77)	154/**199**	0.74 (0.7 to 0.84)	
Water supply				
Well outside or own supply piped	(73)	48/**66**	0.58 (0.37 to 0.9)	0.034
Municipal, piped	(85)	178/**209**	1.24 (1.0 to 1.56)	
Boiled water for drinking				
Yes	(87)	95/**109**	1.1 (0.99 to 1.23)	0.112
No	(79)	131/**166**	0.8 (0.66 to 1.0)	
Chewing qat leaves >3 days per week (Uncooked green leaves)				
Yes	(88)	137/**155**	1.65 (1.13 to 2.42)	0.004
No	(74)	89/**120**	0.6 (0.8 to 1.0)	
Currently smoking				
Yes	(87)	61/**70**	1.5 (0.8 to 2.8)	0.3
No	(81)	165/**205**	0.9 (0.8 to 1.0)	
Severity of dyspepia				
Mild	(84)	120/**143**	1.13 (0.82 to 1.56)	0.5
Moderate/Severe	(80)	106/**132**	1.0 (0.7 to 1.4)	
Endoscopy diagnosis				
Duodenal uler and erosive duodenitis	(91)	77/**85**	2.1 (1.1 to 4.0)	0.023
Isolated antral erosions	(77)	62/**81**	1.76 (1.11 to 2.8)	0.018
Other endoscopic abnormalities	(80)	87/**109**	0.86 (0.6 to 1.22)	0.503

* patients were screened by Urease Campylobacter-like Organism(CLO) test of gastric biopsies during endoscopy
RR - relative risk, † x2 test for trend, CI - confidence intervals
I - professionals, II - managerial, IIIN - non-manual skilled, III M - manual skilled, IV - partially skilled, V - skilled

in a standardized manner regarding 5 predefined symptoms:[16,17] day or night time epigastric pain, nausea or vomiting, heartburn, early satiety, and postprandial discomfort defined as fullness, belching, distension or regurgitation occurring after a meal. The severity of each symptom was scored as: 0=absent; 1=mild awareness (recalled on direct questioning); 2=moderate (present but not impairing activity); 3=severe (interfering with daily work and life). Frequencies of symptoms were scored as: 0=absent (less than once per month); 1=rarely (once or less per week); 2-occasional (2-3 days per week); 3=often (more than 3 days per week). Global symptoms index (GSI)= (severity score x frequency score), for each symptom (0-9) and for total symptom score (0-225). Dyspepsia was defined as the presence of at least 2 symptoms of the 5-symptom complex, with moderate to severe intensity (severity score sum >6) and a duration of more than 6 months. It was graded according to the GSI for total symptom score into mild (<49), moderate (49-100), and severe (>100).

Statistical methods. Data were collected in a personal computer and statistical analysis was conducted using statistical package for Social Science (SPSS Inc., Chicago, Illinois; version 9.00, 1999); Epi-Info version 6.02, 1994 (CDC, Atlanta, Georgia and World Health Organization, Geneva); and Confidence Interval Analysis (CIA) software package; version 1.0, 1989 (Grander MJ, Winter PD, Grander SB). Continuous variables were expressed as means (±SD) and 2-tailed t-test was used for calculating statistical significance. Chi-square test was used to analyze categorical variables and for trend analysis. Two by 2 tables were used to calculate univariate relative risk. Multivariate analysis was computed using statistical package for social sciences. Ninety-five percent confidence intervals (CI) were computed to indicate precision of sample estimate, the variability of the characteristics being studied, and the degree of confidence required. A p-value of <0.05 was taken as statistically significant.

Results. Baseline characteristics of the study population are given in **Table 1**. In total 275 patients were included, 162 men (59%) and 113 women (41%). The age range was (16-75 years) and mean age (±SD) 37.5 (±12) years. Out of 275 subjects who presented with dyspeptic symptoms (41%) had antral gastritis and (16%) had duodenal ulcer. The prevalence of *H. pylori* infection based on rapid urease test in gastric biopsies was 82.2% (95 CI: 78%-87%).

Univariate analysis of risk factors associated with the presence of *H. pylori* infection at the time of entry to the study is presented in **Table 2**. Out of 12 variables tested, significant association was observed with male sex (RR 1.54; 95% CI 1.1-2.2), age over 40 years (RR=1.95; 95% CI: 1.05-3.61), overcrowding in the household [≥6 persons per household] (RR=1.3; 95% CI: 1.0-1.69), the presence of ≥5 children under 14 years per household (RR=3.9; 95% CI: 1.5-10), municipal water supply, piped and stored in cistern (RR=1.24; 95% CI: 1.0-1.56), the consumption of uncooked green vegetables, particularly chewing the fresh leaves of qat (RR=1.65; 95% CI: 1.13-2.42) and the presence of a duodenal ulcer or erosive duodenitis at endoscopic examination (RR=2.1; 95% CI: 1.1-4.0), and isolated antral erosions (RR=1.76; 95% CI: 1.11-2.8). The prevalence of *H. pylori* infection in the age group 41-75 years was 90% (95% CI: 82%-95.3%) and the age group 16-30 years 75% (95% CI: 64.1 to 84%). The observed difference between these 2 proportions was 15% (95% CI for this difference 3.7%-26.3%; P=0.0168). Trend analysis elicited a significant increase in prevalence of *H. pylori* with age (X^2 trend=7.794; P=0.0052) but not with social class categories. However, subjects from combined manual social class categories (III M+IV+V) in an urban setting were more likely to be infected with *H. pylori* than those from higher social class categories (I+II+III N) in the same setting [RR=2.49; 95% CI: 1.18-5.25; P=0.008]. Moreover, increased childhood household density (≥5 per household) in an urban setting was more likely to be associated with *H. pylori* infection in subjects from combined manual social class categories (III M+IV+V) as compared to those from higher social class categories (I+II+III N) in the same setting. (RR=1.65; 95% CI: 1.17-2.33; P=0.0123).

On multivariate stepwise logistic regression analysis, out of the seven significant variables in univariate analysis, 3 variables only retained their independent association with *H. pylori* infection as shown in **Table 3**. These variables were age >40 years (odds ration (OR)=2.2; 95% CI: 1.03-4.64; P=0.043), the presence of ≥5 children under 14 years old per household (OR=6.62; 95% CI: 2.245-19.5; P=0.001), and duodenal ulcer disease (OR= 3.7; 95% CI: 1.38 to 10.0; P=0.009). The remaining 4 variables failed to retain their statistical significance in the multivariate model.

Discussion. This prospective clinical study was conducted on consecutive patients who presented with chronic dyspepsia. The prevalence of *H. pylori* infection based on the rapid urease test on gastric biopsies, was 82.2% (95% CI: 78%-87%). Such a high prevalence rate is consistent with what is found in other developing countries, where exposure to *H. pylori* occurs early in childhood, and the cumulative infection rate is high. This status may be resulting from poor sanitation and hygiene and lack of clean water.[18,19]

The presence of *H. pylori* colonization of gastric mucosa of our dyspeptic patients was detected by using the rapid urease (CLO) test. This gel urease test is currently the tissue-based gold standard for the diagnosis of *H.pylori* from gastric biopsy. It provides a simple and convenient method for in-vitro detection of urease enzyme produced by the bacteria in gastric mucosal samples.[15] There is now an extensive evidence that this test has a more than 90% sensitivity and more than 98% specificity.[20-23] In order to maximize specificity of the

CLO test and to avoid false positive results we conducted early reading (hourly for 6 hours) and omitted the late (24 hours) reading.[20,22] To increase the sensitivity of the test, 2 biopsy specimens were examined separately, and both were incubated at 37°C.[20] Given the characteristics of the method used; the prevalence of *H. pylori* in our study was 82.2%. Comparable high prevalence rates of *H. pylori* in gastric biopsies have been reported by El-Guneid et al[24], Yemen (93%); Britt et al,[25] Kuwait (96.6%); Khan et al,[26] Kingdom of Saudi Arabia (82.1%); and Kang et al,[27] Singapore (73%). In striking contrast, lower prevalence rates have been reported by Marshall and Warren,[28] Australia (58%), and by Shousha et al,[29] United Kingdom (46%). Increasing prevalence of *H. pylori* colonization of gastric mucosa of our dyspeptic patients was observed with male sex, age over 40 years, large family size (≥6 persones per household), many children under 14 years (≥5 per household), municipal water supply, regular chewing of qat leaves, and gastroduodenitis or duodenal ulcer, or both.

Most population-based studies[18] have found seroprevalence of *H. pylori* infection similar in asymptomatic males and females as in the EUROGAST Study Group.[30] However, in dyspeptic patients like ours men were found to be more likely positive for *H. pylori* than women.[27] The increasing prevalence with age is a well-known feature of the epidemiology of *H. pylori* infection.[30] Although this is a clinical study of dyspeptic patients, yet there was a significant difference in prevalence of *H. pylori* infection between the age group 41-75 years (90%) and age group 16-30 years (75%). This difference might be attributed to a birth-cohort effect as the older age group were born at a time when the risk of infection during childhood was higher than in those born later. Urbanization and the crowded living conditions of expanding cities might result in a decline in hygiene for large sections of the population. This phenomenon may be associated with a concomitant rise in exposure and prevalence of *H. pylori* infection.[5] In the urban setting in this study, *H. pylori* infection was more likely associated with combined manual social class categories (III M+IV+V) than in higher social classes categories (I+II+III N). Social class may act as a proxy measure for conditions and practices within the household that increase the likelihood of transmission of the organism from infected to uninfected subjects.[31] It is agreed that lower socio-economic status is associated with a higher prevalence of *H. pylori* infection. This relationship has been found worldwide.[32] Seroprevalence studies from western societies indicated increased prevalence of *H. pylori* among lower manual social class categories[33,34] Such increased prevalence of *H. pylori* in manual social class categories was noticed in this study in the urban setting only. The association between *H. pylori* infection and the current household conditions has been the subject of many studies. As in this study, several household conditions were observed to have a significant positive association with *H. pylori* infection such as the number of children per household (if 5 or more) and household density (number of persons per household).[1,18,31,34] Environmental sources such as food and water seem unlikely vehicles for *H. pylori* infection in a developed world.[18] However, reports from developing countries including this study indicate that the use of municipal water rather than community wells were more likely associated with *H. pylori* infection.[35,36] In addition, we found like others that there was an association between *H. pylori* infection and the consumption of uncooked vegetables and food from street vendors[4,18,35] and that a history of smoking was not associated with an increased risk of *H. pylori* infection.[18]

In this study, there was no obvious relationship between *H. pylori* infection and the severity of dyspepsia which was carefully assessed by means of a predesigned rating scale.[16,17] This bias might have been resulted from the questionable reliability of subject histories.[16] However, the reported association in our study between *H. pylori* infection and the endoscopic finding of gastroduodenal erosions or duodenal ulcer, or both has been extensively documented in the literature.[15,26,28,37,38] The limitation of the present study was the use of a single method for detection of *H. pylori* as we did not have access to histopathology.

In conclusion, the prevalence of *H. pylori* infection was high in our dyspeptic patients. Subjects from combined manual social class categories in urban setting were more likely to be infected than those from higher social class categories in the same setting. Advancing age (>40 years), increased childhood household density and duodenal ulcer disease was significantly associated with *H. pylori* infection.

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