Occupational Exposure to *Helicobacter pylori* for the Endoscopy Professional: A Sera Epidemiological Study

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Objectives: The purpose of this prospective study was to determine if medical and nursing staff in the United States who are regularly involved in endoscopic procedures are at an increased risk of acquiring Helicobacter pylori infection. Methods: One hundred and twenty-two gastroendoscopists and endoscopy nurses attending an advanced gastroendoscopy course (17 women, 105 men) completed a questionnaire consisting of past medical and professional history. Serum from each subject was collected and tested using a validated ELISA assay (sensitivity 99%, specificity 96%). H. pylori prevalence in the experimental group was compared to that of 510 blood donors. Results: In all age groups, H. pylori positivity was significantly higher among the study subjects compared with controls. Caucasian subjects, when matched to controls for age, race, and level of education, had significantly higher rates of H. pylori positivity. Foreignborn subjects, when compared to US-born subjects, also had higher rates of H. pylori positivity. There was no statistical difference of H. pylori positivity with respect to gender, years involved in endoscopy, or number of endoscopies performed monthly. Conclusion: H. pylori infection is more common in gastroendoscopists and endoscopy nurses than the general population and should be viewed as an occupational hazard.

INTRODUCTION

There is a strong association of *Helicobacter pylori* with gastroduodenal pathology, such as duodenal ulcers, type B gastritis, gastric ulcers, and gastric carcinomas (1–6). Although the exact mode of transmission has not been fully elucidated, there is mounting evidence that person-to-person transmission is the primary route of infection. Ramsey *et al* (7) reported an outbreak of epidemic gastritis with hypochlorhydria in 17 of 37 healthy volunteers participating in studies of acid secretion. An infectious cause was postulated, but no viral or bacterial pathogen was isolated at first.

The use of a common pH electrode with reinfusion of gastric juice may have been responsible for the transmission of an infectious agent. On retrospective examination of the biopsy specimens, Helicobacter pylori organisms were found (8). Gledhill et al (9) also noted epidemic hypochlorhydria in 4 out of 6 healthy subjects during a study of acid secretion. Similar to Ramsey's study, Gledhill et al used a common pH electrode with gastric reinfusion technique. Gledhill et al, however, could not isolate an infectious agent. Berkowicz et al (10) further supported the person-to-person transmission concept by testing inmates from an institution for the mentally retarded for H. pylori infection. The intimate contact among the inmates was the likely reason for their significantly increased incidence of H. pylori infections detected by serum ELISA tests. Finally, Mitchell et al (11) found an increased incidence of antibodies to H. pylori among families of children infected with C. pylori.

H. pylori infection rates among all patients undergoing endoscopy can range as high as 50% (12). Because Helicobacter pylori can be isolated from gastric secretions of such patients (12), medical and nursing staff involved in endoscopic procedures may have an increased risk for exposure and subsequent infection by this organism. Studies performed outside of the United States have shown conflicting results about the infection rate of H. pylori among endoscopy personnel. Two U.S. studies of H. pylori infection among small numbers of endoscopy personnel did not show a statistical difference in the infection rates compared to controls (13, 14).

The purpose of this prospective study was to determine if gastroendoscopists and endoscopic nurses in the United States are at an increased risk of acquiring *H. pylori* infection. If such an increased risk were to exist, it may pose a health hazard and call for more stringent guidelines for prevention of *H. pylori* transmission.

MATERIALS AND METHODS

Subjects

A total of 134 gastroendoscopists and endoscopy nurses attending an advanced therapeutic endoscopy course in Mi-

ami, Florida volunteered to participate in this study. The participants completed a medical and professional history questionnaire before giving their blood specimens. The questionnaire included the following items: age, sex, race, place of birth, previous diagnosis of peptic ulcer disease, known H. pylori infection, medications used for any current GI condition, GI symptomatology, such as abdominal pain, nausea, vomiting, and dyspepsia, number of yr performing or assisting in endoscopy, and, finally, the average number of upper endoscopies performed each month. Blood specimens were obtained from each participant for detection of IgG to H. pylori antigen by ELISA method, a very sensitive and specific test (15-20). Of the 134 participants, nine were excluded for equivocal ELISA results, and three were excluded for nonreadable labels, thus bringing the final total to 122 participants. Among the final 122 participants, there were 105 men and 17 women, with a mean age of 41 years and a range of 24-65 yr of age. There were 111 gastroendoscopists and 11 endoscopy nurses comprised of Caucasians (80%), Blacks (4%), Hispanics (6%), Asians (4%), and others (6%), all of whom were in the higher education level (college or higher).

METHODS

After signing an informed consent form, blood specimens were obtained from each participant by standard venipuncture technique. Each blood specimen was labelled, spun down to collect the serum, and stored in -70° F until frozen and then transported to Dr. B.J. Marshall at the University of Virginia, Charlottesville, Virginia.

ELISA technique

The serum assay used for the study was a validated ELISA assay, PyloriScreen (sensitivity 98.8%, specificity 95.9%), supplied by New Horizons Diagnostics (Columbia, MD). This enzyme-linked immunoassay qualitatively detects circulating IgG to *Helicobacter pylori* in human serum or plasma. In this ELISA test, antigens prepared from *H. pylori* are attached to the surface of the test wells, and the patient's serum or plasma is diluted and placed in the wells. Enzyme conjugated anti-human IgG is placed in the well, which binds to any patient IgG bound to the antigen. Excess conjugate is removed from the well and substrate is added. Enzyme in the antibody conjugate bound to the well will "develop" the substrate-causing appearance of a colored product. The amount of the colored product in the well is read by a microplate spectrophotometer set at 450 nm.

This absorbance value or optical density (O.D.) reading is then compared to control and standard values. Every absorbance value from sample sera is corrected for background by subtracting from it the absorbance value obtained from the blank wells. In the PyloriScreen test, the corrected absorbance value of a patient's serum is compared to the corrected absorbance value of the calibrator serum. If the ratio of the sample's corrected absorbance value compared

Table 1

Positive Helicobacter pylori Exposure: Age Classification

	Control group $n = 510$	Experimental group $n = 122$
<45 years old*	10% (37/370)	49% (43/88)
≥45 years old*	25% (35/140)	65% (35/140)

p = < 0.0001.

to that of the calibrator serum is less than 0.85, it is considered "negative" for antibody to *H. pylori*. If the same ratio is greater than 1.15, the sample is considered "positive" for antibody to *H. pylori*. Any ratio value falling between 0.85 and 1.15 is considered "equivocal." Nine of the initial 134 participants had "equivocal" results and thus were excluded from the statistical analysis.

PyloriScreen has been evaluated in clinical settings compared to the reference methods of histopathology, tissue culture, rapid urease test, and ¹⁴C breath test, revealing a sensitivity rate of 98.8% and a specificity rate of 95.9%. (21)

Control group

H. pylori prevalence in our group was compared with that of 510 healthy blood donors (mean, 41 yr; range, 20–77 yr) from Charlottesville, Virginia (22). The control group was racially similar to our study population with 97% (495/510) Caucasian and 3% (15/510) Black subjects. Statistical analysis was performed with both the entire control group and a highly matched control group from the original blood donors in terms of age, race, and level of education (college level or higher).

Statistical analysis

Statistical analysis included χ^2 test of independence and the Z-test, a test of difference between proportions using normal approximations.

RESULTS

Gastroenterologists/endoscopy nurses and control group

The percentage of *H. pylori* positivity in the entire experimental group, 53% (65/122), differed significantly from that of the control group, 14% (72/510) (p < 0.0001).

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The experimental group (n = 122) and control group (n = 510) were also compared according to age stratification. For those less than 45 yr of age in the experimental group, 49% (43/88) were *H. pylori* positive compared with 10% (37/370) in the control group (p < 0.0001) (Table 1).

For those equal to or greater than 45 yr of age, 65% (22/34) were positive for *H. pylori* in the experimental group compared with 25% (35/140) in the control group (p < 0.0001) (Table 1).

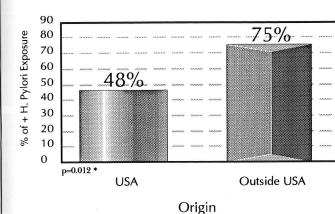


Fig. 1. Country of origin classification in experimental group.

Gender

Prevalence of *H. pylori* infection was not statistically significant between males and females in the experimental group. The *H. pylori* infection rate for males was 54% (57/105) and for females was 47% (8/17) (p = 0.5795).

Country of origin

For subjects in the experimental group, the *H. pylori* infection rate among foreign born participants (n = 27) was 75% (18/24), whereas U.S. born participants (n = 95) had an infection rate of 48% (47/98) (p = 0.012; Figure 1).

Gastroendoscopists and endoscopy nurses

The *H. pylori* infection rate did not differ between gastroendoscopists and endoscopy nurses. Gastroendoscopists had an infection rate of 52% (58/111) compared to the infection rate of 55% (6/11) among endoscopy nurses.

Race

The experimental group was predominantly comprised of Caucasians (n = 97) with limited contributions from other racial groups: Blacks (n = 5), Asians (n = 6), Hispanics (n = 7), and others (n = 7). In order to use matched pairs for statistical purposes (experimental group *versus* control group) in terms of race as well as age and level of education (college level or higher), Caucasian subjects were used.

The other racial groups lacked sufficient numbers of subjects and controls for any meaningful statistical comparison. Moreover, because foreign countries of origin significantly affected H. pylori positivity rates, only U.S. born Caucasian subjects (n = 88 from the experimental group and n = 260 from the control group, (mean, 40 yr; range, 20-68 yr)) were used. Among the experimental group of Caucasian subjects who were less than 40 yr of age, 37% (17/46) were H. pylori positive compared with 7% (6/87) in the control group (p < 0.0001). For those equal to or greater than the age of 40, 52% (22/42) were H. pylori positive compared with 10% (17/173) in the control group (p < 0.0001). When combining both age groups, H. pylori positivity was 44% (39/88) among the Caucasian experimental

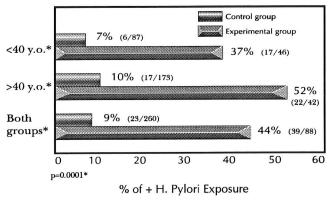


Fig. 2. Comparison of positive H. pylori exposure in matched pairs.

subjects compared with 9% (23/260) in the control group (p < 0.0001, Figure 2).

Raw data regarding other racial groups for *H. pylori* positivity was 80% (4/5) for Black subjects, 33% (2/6) for Asian subjects, and 57% (4/7) for Hispanic subjects. Statistical analysis was not performed in these subjects because of inadequate sample size.

Exposure time

Years involved with endoscopy. Participants in our experimental group were asked to report the number of yr spent as a gastroendoscopist or endoscopy nurse on the initial questionnaire. The number of yr involved in endoscopy was further analyzed in four distinct time period groups. The group classified as having less than 10 yr of endoscopic exposure had a 43% H. pylori infection rate. For the 10-14- yr group, the H. pylori infection rate was 59%. For the 15-19-yr group, the H. pylori infection rate was 45%. Finally, the greater than 20-yr group had an infection rate of 54%. There was no statistical difference in H. pylori infection rates among the four subclassification groups (p = 0.2465).

Number of upper endoscopies performed each month. Participants in the experimental group were also asked to report the number of upper endoscopies performed each month. They were to choose from three different subclassifications: 10-20 per month, 21-40 per month, or more than 40 per month. The highest *H. pylori* infection rate (68%) occurred within the 10-20 per month group. The 21-40 per month group was next with a 64% *H. pylori* infection rate. Finally, the more than 40 per month group had an infection rate of only 47%. However, the *H. pylori* infection rates between the three subclassification groups was not statistically significant (p = 0.2083).

Previous ulcer history and GI symptomatology. Nine participants (7.4%) in the experimental group reported a previous history of peptic ulcer disease (eight duodenal ulcers, one gastric ulcer). Seven of these nine participants had *H. pylori* positivity by ELISA testing (77.7%).

GI symptomatology was noted by 14 participants (11.5%); nine were *H. pylori* positive (64.28%). Among

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participants who reported taking medications related to any GI condition, the H. pylori infection rate was 38.5% (10/26). The most common medications used were H_2 -receptor antagonists, followed by omeprazole and antacids.

DISCUSSION

In 1983, Warren and Marshall (23) were the first investigators who observed and appreciated the potential significance of finding curved bacilli on the gastric epithelium of patients with active chronic gastritis. This gram-negative, microaerophilic organism was initially named Campylobacter pyloridis but was subsequently reclassified as Helicobacter pylori. Marshall fulfilled Koch's postulates by ingesting H. pylori and subsequently developing histologically proven gastritis accompanied by a mild self-limited illness (24). Since the initial identification of H. pylori, exhaustive efforts have been made to better understand the organism's epidemiological pattern, the pathogenesis for disease, and the rationale for treatment. It is now widely accepted that H. pylori infection in the United States occurs more frequently in lower socioeconomic groups, minority groups (especially Blacks and Hispanics), and the elderly (25). With its epidemiological pattern resembling that of hepatitis A and polio, the primary mode of transmission is believed to be through person-to-person contact via the fecal-oral route (25).

There have been reports of *H. pylori* being transmitted by endoscopes and pH probes (7, 9, 26, 27). Because *H. pylori* can be isolated in gastric secretions, any person in contact with such secretions is theoretically at increased risk of being infected. Gastroendoscopists and endoscopy personnel who have almost daily contact with patients undergoing endoscopic evaluations are potentially at a very high risk of infection.

Previous studies that have been conducted to answer the question of *H. pylori* infection among endoscopy staff have yielded conflicting results. Morris *et al* (12), in a 1986 New Zealand study, evaluated the rate of *H. pylori* infection as detected by ELISA tests among 21 gastroenterologists, 11 clinic nurses, and four registrars. Overall, nine of 36 total subjects (25%) had positive serology for *H. pylori*. When comparing the rate of *H. pylori* infection with 261 local nonpatient control population (37% positive), there was no statistical difference in the rate of *H. pylori* infection. There was also no relationship of *H. pylori* infection with age, length of time of involvement in gastroendoscopic procedures, and number of procedures performed per month.

In 1987, Rawles *et al* (13), in a study from the United States, enrolled 22 physicians and 16 nurses to detect H. *pylori* infection by using ELISA tests. Twenty-four endoscopy patients as well as 20 blood donor controls were also tested for H. *pylori*. Prevalence of positive serology in the endoscopy personnel, endoscopy patients, and controls were 32%, 46%, and 10%, respectively. The difference between the endoscopy patients and controls was significant (p =

0.02). Although there was a 3–4-fold higher prevalence of H. pylori infection among the endoscopy personnel compared to controls, this was not statistically significant (p = 0.13).

Reiff et al (28), in a 1989 European study, investigated endoscopy staff (n = 45), dental staff (n = 58), orphanage children (n = 24), psychiatric patients (n = 58), and family contacts of H. pylori infected patients (n = 55) for prevalence of IgG and IgA antibody response to H. pylori using immunoblot tests. Among the endoscopy staff, family contacts, and psychiatric patients, there was no significant difference in the total antibody or IgG response compared with controls.

Mitchell *et al* (29), in an Australian study, measured the incidence of *H. pylori* infection by ELISA tests among 33 gastroenterologists, 68 gastroenterology nurses, and 35 general practitioners. Fifty-one percent of gastroenterologists, 19% of gastroenterology nurses, 28% of general practitioners, and 21.5% of blood donor controls were positive for *H. pylori*. The prevalence of *H. pylori* infection was significant among the gastroenterologists group when compared with controls (p < 0.01) but not between the gastroenterology nurses and general practitioners groups. In addition, there was no statistical difference between the general practitioners and control group nor did the prevalence of *H. pylori* infection differ in relation to the number of yr worked in the field among all the groups.

Finally, the most recent study conducted in the United States by Kahlon *et al* (14) included 50 subjects (30 physicians and 20 nurses/technicians) who underwent ELISA testing for *H. pylori* antigen. *H. pylori* antibody was present in nine (18%) subjects, indeterminate in two (4%) subjects and absent in 39 (68%) subjects. The authors concluded that there was a relatively low incidence of *H. pylori* antibody prevalence among this health care population.

Our data clearly showed a statistically significant difference in the rate of H. pylori antibody positivity among endoscopy personnel compared to blood donor controls in all age groups. The prevalence of H. pylori infection in the experimental group was 53% (65/122) compared with that of the control group, 14% (72/510) (p < 0.0001). Our trial included the largest number of endoscopy personnel to date. Gastroenterologists and nurses enrolled in the study were from many different geographic areas in the U.S. Twentyseven states were represented by the participants, with the largest group from Florida (n = 30). Even with the wide variation in location, the rate of *H. pylori* antibody positivity was significantly elevated across every age group when compared to matched controls. Interesting to note, there was no statistical relationship between H. pylori positivity and the number of yr performing endoscopy and the number of endoscopies performed every month. One can speculate that only a minimal number of exposures to secretions containing H. pylori may be required for transmission of infection. The discrepancy in the results from various other studies from the United States and abroad may be due to several ted ige ily va-

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nomic status. None of the previous studies described in detail the demographics of the control group and how it was matched. We tried to select the most accurately matched control group for the predominantly U.S.-born Caucasian subjects. Unfortunately, a sufficient control group was lacking for the other racial groups and foreign-born subjects. Third, the country of origin can significantly affect the rate of *H. pylori* positivity. Among the other two United States studies, there was no mention about the presence or absence of foreign-born endoscopy personnel enrolled in their studies. Our study found a much higher rate of H. pylori positivity among foreign-born endoscopy personnel (75%) compared with those born in the United States (48%). We excluded foreign-born subjects for the matched pairs so as not to bolster the H. pylori positivity rate for the experimental group. Even with their exclusion, the rate of H. pylori positivity among the U.S.-born Caucasian subjects

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different factors. First, the rate of H. pylori infections found

among endoscopy patients may vary widely between the study locations. Only one study tested endoscopy patients

during the trial, revealing a significantly higher rate of H.

pylori infections compared to controls (13). Thus, it is not

known if endoscopy personnel working in a region with

very high H. pylori infection rates have, in turn, higher risk

of being infected with H. pylori. Second, the selection of a

poorly matched control group can alter study outcome.

Ideally, the control group should be matched in terms of age,

sex, race, place of birth, geographic location, and socioeco-

was significantly higher than the control group (44% (39/

88) vs 9% (23/260), respectively). Fourth, the socioeco-

nomic level during childhood probably plays a major role

for obtaining *H. pylori* infections. In Third World countries,

a significant rate of H. pylori acquisition seems to occur

during early childhood (30, 31). The observation of higher

H. pylori positive rates among the elderly may not be due to

increased exposure time. This observation may actually

reflect an age-cohort phenomenon (32) whereby the older

generation obtained their H. pylori infection during child-

hood before the era of modern sanitation. People born after

the period of improved sanitary conditions are probably not

among U.S. gastroenterologists and endoscopy nurses is

significantly higher than the control population. Such a high

infection rate may pose a serious public health problem and

should call for more strict precautionary guidelines for en-

doscopic procedures. With increasing evidence of H. pylori-

associated gastric cancers and even gastric lymphomas (33–

36), endoscopy personnel should consider ELISA testing

and then possible treatment for H. pylori. Future studies

regarding the transmissibility of H. pylori to gastroenterol-

ogists should address all of the above factors that may

erroneously affect the outcome of such studies. Promising

new technology (37) in isolating the exact strains of H.

pylori by methods such as repetitive sequence DNA (rep-

PCR), restriction of PCR products (AFLP), and randomly

Our data suggest that the rate of H. pylori infection

at the same risk of obtaining H. pylori infections.

amplified polymorphic DNA (RAPD) will most likely prove once and for all the precise routes of transmission for this ubiquitous organism.

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