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***Helicobacter pylori* Protection Against Reflux Esophagitis**

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Abstract

Background and Aim—Negative association has been reported between presence of *Helicobacter pylori* and developing gastroesophageal reflux disease (GERD) and its complications. The aim of this study was to determine whether *H. pylori* (HP) can be protective against GERD in an African American (AA) population.

Methods—From 2004 to 2007, we studied 2,020 cases; esophagitis (58), gastritis (1,558), both esophagitis and gastritis (363) and a normal control group (41). We collected their pathology and endoscopy unit reports. HP status was determined based on staining of gastric biopsy.

Results—HP data was available for 79 % (1,611) of the cases. The frequency of HP positivity in gastritis patients was 40 % (506), in esophagitis patients 4 % and in normal controls 34 % (11), while HP was positive in 34 % of the patients with both esophagitis and gastritis. After adjusting for effects of age and sex, odds ratio of HP was 0.06 (95 % CI 0.01–0.59; *P*value = 0.01) for the esophagitis group versus the normal group.

Conclusions—Our results show *H. pylori* has a significant negative association with esophagitis in AAs which may point to a protective role of *H. pylori* in the pathogenesis of esophagitis. In addition, *H. pylori* may be the reason for the low GERD complications in AAs.

Keywords

H. pylori; Reflux esophagitis; African Americans

Introduction

Since its discovery in the early 1980s [1], *Helicobacter pylori* has been the subject of substantial research which has resulted in revealing its role in the causation of several upper gastrointestinal diseases, including gastritis, peptic ulcer disease, gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma [1–5]. These findings have resulted in an aggressive approach to eliminate *H. pylori*. Antibiotics usage and improvement in sanitation over the past few decades have reduced *H. pylori* colonization in the stomach [6], and this may have indeed been a major reason for declines in gastric duodenal ulcers and noncardia gastric adenocarcinoma [7–11]. However, *H. pylori* may have some beneficial effects too, including protection against gastroesophageal reflux disease (GERD), Barrett's esophagus, and esophageal adenocarcinoma [8, 11–17]. It has been proposed that *H. pylori* eradication may cause reflux esophagitis [18–20] and aggravation of GERD symptoms [21].

Although Western countries, overall, have high prevalence rates of GERD [22], different ethnic groups living in these countries, such as Asians and African Americans, may have substantially lower prevalence rates of the disease. The prevalence of *H. pylori* has been reported to be higher in African Americans in comparison to white Americans [23], and at the same time African Americans have lower rates of GERD and its complications, e.g., Barrett's esophagus, than white Americans [22, 24, 25]. Higher prevalence of *H. pylori* in African Americans may be the reason for lower prevalence of GERD and Barrett's. Despite these lower rates, African Americans are experiencing a dramatic increase in esophageal adenocarcinoma [26, 27], which may be due to declining prevalence of *H. pylori* infection in all populations, including African Americans [28].

The large majority of studies of *H. pylori* in relation to GERD, Barrett's esophagus, and esophageal adenocarcinoma have been conducted in White populations, and there are relatively few studies in other groups. We conducted this study to examine the relationship between *H. pylori* and GERD in African Americans.

Materials and Methods

Patients and Data Collection

All cases and controls were selected from the Howard University Hospital, Washington, DC, a hospital that serves mainly the African American population. All patients were self-defined as African Americans. In all, 2,020 patients who had undergone esophagogastroendoscopy from January 2004 through December 2007 were selected for this study. All medical, laboratory, endoscopy, and pathology reports were reviewed. The following data were obtained from patient records: age at diagnosis, gender, race, date of diagnosis, histology, anatomical site of sample, and diagnosis. Cases were those who were diagnosed as having esophagitis, gastritis, or both. The gastritis group included both acute and chronic gastritis diagnosis. Those with esophageal or gastric cancer were excluded from the study. Controls were those who were reported to be normal on endoscopy and pathology, who did not have esophagitis or gastritis in endoscopy or pathology examination. The definition was independent of *H. pylori* status. In fact, *H. pylori* were more common in controls than in cases. In addition, this population does not represent asymptomatic normal population and those patients who had upper GI symptoms underwent the endoscopy. However, cases and controls are comparable in that they are all patients in the Howard Hospital. We excluded ulcer patients. We considered pathology proven gastritis for stratifying the patients. Presence of *H. pylori* in the samples from stomach was assessed using either silver staining or immunohistochemistry of biopsy samples. This study was approved by the Howard University Institutional Review Board (IRB).

Statistical Analysis

Numerical data was expressed as mean $\pm$ standard deviation (SD). Student's *t* test or one-way analysis of variance was used for comparison of means. Non-parametric tests were used for numerical data that didn't follow normal distribution. Categorical variables are compared using the χ^2 test. Age, sex and *H. pylori* infection were included in the multivariate logistic regression analysis to predict their independent effect on esophagitis. *P* values <0.05 were considered significant. Statistical analysis was performed using the SPSS 16.0 software package (IBM Corp., Somers, NY, USA).

Results

Clinico-Pathological Feature of Esophagitis Patients

Over the period of study, 2,020 patients [mean age (SD); 55.9 (16.1) years, age range 15–101; women: 1,219 (60.6 %)] were recruited (Table 1). Fifty-eight of the patients had esophagitis, 1,558 had gastritis, 363 had both esophagitis and gastritis, and 41 were normal controls.

H. pylori-Positive Individuals Had a Lower Risk of Esophagitis

Helicobacter pylori data were available for 79 % (1,611) of the study participants, among whom 38.3 % ($n = 617$) were positive for *H. pylori*. The frequency of *H. pylori* positivity in gastritis patients was 40 % ($n = 506$), 3.8 % ($n = 1$) in esophagitis patients, 34 % ($n = 99$) in patients with both esophagitis and gastritis, and 34 % ($n = 11$) in normal subjects (*P* value = 0.001).

After adjusting for effects of age and sex, *H. pylori* preserved its protective effect on developing esophagitis when comparing the esophagitis group versus normal subjects (OR 0.06, 95 % CI 0.01–0.59; *P* value = 0.01) (Table 2). Similar analyses showed no significant differences in *H. pylori* positivity comparing the gastritis or gastritis–esophagitis groups to normal subjects (Table 2).

Discussion

Our study showed that approximately 38 % of African Americans presenting to Howard University Hospital carried *H. pylori* in their stomach. But this proportion was much smaller in patients with esophagitis than in normal people (3.8 vs. 34.4 %). The mean age of patients with esophagitis (54 years) and gastritis (56 years) was less than normal subjects (58 years), but this is unlikely to be the reason for the difference because most people acquire *H. pylori* before the age of 20 [5]. Esophagitis patients were more likely to be males while gastritis patients were more likely to be females but this is unlikely to be the reason for the difference either, because *H. pylori* is nearly equally distributed among men and women. Indeed, after controlling the effect of age and gender in regression analysis, *H. pylori* remained a statistically significant protective factor for esophagitis in comparison to normal subjects [27]. However, *H. pylori* was not significantly associated with other pathologies compared to normal individuals.

Helicobacter pylori prevalence has a wide range based on geographic and ethnic characteristics. Since *H. pylori* has been proposed as a main factor for change in incidence of stomach cancer and also GERD, knowing its prevalence in each ethnicity is worthwhile. Smith et al. [23] studied the presence of *H. pylori* in different ethnicities and its effect on gastrointestinal diseases. Reviewing 248 upper endoscopies retrospectively, they found that the prevalence of *H. pylori* infection in Hispanics, and African Americans was 40 and 28 %, respectively. They also reported a possible protective role for *H. pylori* against the development of GERD and Barrett's esophagus. Our study shows that *H. pylori* is seen in 38.3 % of African Americans which is quite lower than the numbers reported for whites (42.5 and 49.5 %) [29, 30]. To our knowledge, the present study has the largest study sample size among those reporting on the prevalence of *H. pylori* infection in African Americans. However, since the prevalence is reported among those referred to Hospital, it cannot be extrapolated to African Americans in the general population.

Our results show that prevalence of *H. pylori* in the esophagitis group was much lower than normal subjects (3.8 vs. 34.4 %), and its presence can inversely affect the esophagitis development which is consistent with previous studies [23, 31–33]. The protective effect of *H. pylori* can be explained by its negative effect on gastric acid secretion [34] and also production of ghrelin, a hormone from the stomach [35]. Ghrelin stimulates appetite which can result in obesity—a well known risk factor for developing erosive esophagitis [35–37].

Most of the study subjects were female (60 %), and in all subgroups female sex made the dominant group, except for the esophagitis group which was predominantly composed of males. Previous studies have shown that male gender could be a risk factor for development of esophagitis [32, 38]. We were not able to find any association between *H. pylori* infection and gender.

The strength of the present study is its large number of African American patients, one of the minority groups with high risk of gastrointestinal diseases. The other important aspect of this study is using histologic testing to determine the *H. pylori* status. Some limitations of the present study are due to its retrospective design. Also, low number of subjects in the control group is another limitation.

In summary, *H. pylori* was seen in at least 38 % of African Americans referred to a major hospital, and it was associated with a reduced risk of esophagitis. Whether its eradication in patients with gastritis and/or esophagitis would harm African American patients needs to be clarified in prospective double-blind controlled clinical trials. In addition, higher prevalence of *H. pylori* may be the reason for the low GERD complications in African Americans, such as Barrett's esophagus and adenocarcinoma of the esophagus.

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Table 1

Characteristics of study participants

Characteristic	No. (%)	Mean age, years (SD)	Women, no. (%)
Total	2,020 (100)	55.9 (16.1)	1,219 (60.6)
Esophagitis	58 (2.9)	54.4 (16.9)	30 (51.7)
Gastritis	1,558 (77.1)	56.5 (16.2)	583 (37.5)
Esophagitis and gastritis	363 (18.0)	53.5 (15.4)	162 (44.8)
Normal	41 (2.0)	57.9 (14.2)	18 (45.0)
<i>P</i> value		0.01	0.01

Table 2Age, gender and *H. pylori* status as predictors of disease development

Predictor	Unadjusted odds ratio (95 % CI)	P value	Multivariate adjusted odds ratio (95 % CI)	P value
Esophagitis versus normal				
Male (vs. female)	1.35 (0.60–3.05)	0.46	1.82 (0.55–6.04)	0.32
Age (years)	0.98 (0.96–1.01)	0.30	0.97 (0.93–1.01)	0.15
<i>H. pylori</i> (present vs. absent)	0.08 (0.01–0.64)	0.01	0.06 (0.01–0.59)	0.01
Gastritis versus normal				
Male (vs. female)	0.73 (0.39–1.38)	0.33	0.83 (0.40–1.71)	0.61
Age (years)	0.99 (0.97–1.01)	0.60	0.99 (0.97–1.01)	0.32
<i>H. pylori</i> (present vs. absent)	1.27 (0.61–2.66)	0.52	1.37 (0.64–2.95)	0.41
Esophagitis and gastritis versus normal				
Male (vs. female)	0.99 (0.51–1.90)	0.97	1.08 (0.50–2.32)	0.83
Age (years)	0.98 (0.96–1.00)	0.09	0.97 (0.95–1.00)	0.06
<i>H. pylori</i> (present vs. absent)	1.0 (0.46–2.15)	1.0	1.11 (0.50–2.46)	0.80