Original Article

The relationship between helicobacter pylori infection and gastro-esophageal reflux disease

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Abstract

Background: Gastro-esophageal reflux disease   is a common condition, affecting 25%-40% of the population. Increasing attention has been paid to the relationship between *Helicobacter pylori* infection and reflux esophagitis.   **Aim:** The aim of this study was to investigate the association between C*agA+ H. pylori* and endoscopically proven gastro-esophageal reflux disease. **Patients and Methods:**   The study group included 60 hospital patients with gastro-esophageal reflux disease between 2007 and 2009 as compared with 30 healthy patients from a control group that was age and sex matched. *Helicobacter pylori* CagA+ was identified by an immunological test (Immunochromatography test) (ACON, USA). **Results**:   *Helicobacter pylori CagA+* was present in 42/60 (70%) of the patients with gastro-esophageal reflux disease and in 11/30 (36.6%) patients in the control group (p=0.002). The Odds ratio = 0.8004 with 95% Confidence Interval = from 0.3188 to 2.0094. The relative risk=1.35 that indicates an association between *Helicobacter pylori* and disease. **Conclusions:** The presence of *Helicobacter pylori* is significantly increased in patients with gastro-esophageal reflux disease as compared with the control group.

Keywords: Gastro-esophageal reflux disease, Helicobacter pylori, CagA+.

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Introduction

Gastro-esophageal reflux disease (GORD) results from abnormal esophageal acid exposure. Therefore, acid secretion is a necessary requirement for disease development. In the presence of atrophic pan gastritis, acid production is decreased and the esophagus is less likely to be exposed to acid reflux [1].   The effects of *Helicobacter pylori* (*H. pylori*) infection on the pathogenesis of GORD have been studied in many reports. Infection with *H. pylori* produces an increase in basal and stimulated gastric acid output through the secretion of gastrin, somatostatin, and inflammatory mediators [2], which is a possible cause of GORD [3]. Colonization of gastric mucosa by *H. pylori* may result in hypochlorhydria in patients with diffuse gastritis and gastric atrophy [4] and who seem to be at less risk of developing GORD [5]. Therefore, association between *H. pylori* infection and development of either hypochlorhydria or hyperacid secretion depends on the inflammatory response of the gastric mucosa. Thus, the effect of *H. pylori* infection on the development of GORD is contradictory and is an intricate relationship [6].

Another study found that *H. pylori* eradication did not aggravate the course of GORD [7] .

The reciprocal influence of *H. pylori* and GORD occurs concomitantly [8] and their relationship has been apparent as nearly none to a protective role of *H. pylori* against GORD development. Therefore, both conditions coexist in a considerable number of patients and the association varies according to the background prevalence of the infection in the populations studied. Thus, the role of *H. pylori* in the development of GORD has not been established [9] .

The main aim of this study was to investigate the relationship between C*agA+ H. pylori* and endoscopically proven gastro-esophageal reflux disease .

Patients and Methods

The study group included 60 patients who had been endoscopically diagnosed with gastro-esophageal reflux disease. These patients had a history of heartburn and dyspepsia at least three times a week for a period of more

than three months and had been referred for gastrointestinal endoscopy at Al-Kindi Hospital, Baghdad, between 2007 and 2009.

The exclusion criteria included patients with a history of upper gastrointestinal (GI) surgery, malignancy, esophageal varices, and antibiotics or bismuth consumption during the last six months It also included patients using H2 blockers, proton pump inhibitors (PPIs), alcohol, or non-steroidal anti-inflammatory drugs (NSAIDs) during the last four weeks. The control group was comprised of 30 healthy volunteers without any symptom of upper GI diseases.

The GORD group and control groups were sex and age matched. Written informed consent was obtained for all upper endoscopy and biopsy procedures. The study was approved by the Ethics Committee of the Al-Kindi Teaching Hospital and University of Health and Al-Kindi College of Medicine-Baghdad University.

Serological Tests
Blood samples (5 mL) were drawn into plain vacutainers from the antecubital veins of patients. The blood was allowed to clot for 30 minutes and centrifuged at 2000g for 15 minutes for clear separation of serum. Separated serums were stored at −20°C until analyzed. CagA antibodies Immunoglobulin G (IgG) for *H. pylori* were determined using an immunological test (immunochromatography test) (ACON, USA). Endoscopy was performed on the GORD patients and histopathological study was conducted on biopsy specimens that had been obtained from the gastric mucosa to confirm the diagnosis and presence of *H. pylori* in atrophic gastritis patients.

Statistical Analysis
Data were analyzed using descriptive statistics (frequencies for tables, mean and standard deviation) and inferential statistics (Chi- square test). Odds ratio (OD), (95% confidence interval (CI) and relative risk (RR) were calculated to evaluate the association between *H. pylori* and GORD. All of these were performed using MiniTab statistical software program 13.20. A P-value of ≤ 0.05 was considered significant.

Results

The results of this study revealed that male patients constituted 66.6% of the studied group and this was not significantly different from the control group as shown in Table 1. There was no significant difference in mean age allocation and smoking between the GORD patients and control group (Tables 2 and 3). The youngest age of the patients in the GORD group was 19 years and the oldest age was 84 years. In the control group, the youngest age was 20 years and the oldest age was 76 years.

There is a significant increase in *H. pylori* infection (p=0.002) in GORD patients when compared with the control group. The Odds ratio (OD)= 0.8004 with 95%

CI= from 0.3188 to 2.0094. The relative risk = 1.35, which indicates an association between *H. pylori* and GORD as shown in Table 4.

Table 1 Sex disparity between GORD patients and control group

Sex	GORD patients		Control group		*P* value
	No.	%	No.	%	
Male	40	66.6	15	50	Not significant
Female	20	33.3	15	50	0.126
Total	60		30		

Table 2 Age distribution between GORD patients and control group

Age in years	GORD patients No. 60	Control group No. 30	*P* value
Mean	45.67	44	
SD	15.54	15.22	
Minimum	19	20	Not significant
Maximum	84	76	P=0.876

Table 3 Relationship of smoking between GORD patients and control group

Smoker	GORD patients (No. 60)		Control group (No. 30)		*P* value
	No.	%	No.	%	
Yes	25	41.6	19	63.3	Not significant
No	20	33.3	8	26.6	0.108
Ex-smoker	15	25.0	3	10.0	

Discussion

The aim of this study was to investigate the relationship between *cagA+ H. pylori* and endoscopically proven GORD. We found no significant difference in age, sex and smoking between the two groups. There was a significant (P=0.002) increase in *CagA+ H. pylori* in GORD disease (70%). Another study found that the prevalence of *H pylori* infection in patients with gastro-esophageal reflux disease was 38.2% (range 20.0%-82.0%) [10]. Spechler showed that *H. pylori* did not affect the pathogenesis of GORD [11]. In 2001, Warburton-Timms et al [12] demonstrated that C*agA+ H. pylori* were found in 81% of patients with a normal esophagus, in 70% with mild esophagitis, in 69% with moderate esophagitis, and in 46% with severe esophagitis. This heterogeneity between the studies may be due to the geographical location of the studies due to the difference in the prevalence of *H. pylori* in the Far East, North America and Western Europe. For example, a study from South America showed a higher prevalence of GORD with *H. pylori* that is in agreement with our study [13]. Other studies reported higher percentages of GORD with *H. pylori* by Gisbert et al. in 2001 [14] (57%) and in 1996 by Liston et al. [15] (76%) that was in accordance with our results. This gives the impression that *H. pylori* in patients with gastro-esophageal reflux disease is lower in countries where the prevalence of *H. pylori* in the general population is high. The cause may be related to many factors, such as study design, selection of cases and controls, severity of disease activity, dietary, genetic factors and method of testing for *H. pylori*.

Table 4 Helicobacter pylori in GORD patients compared with control group

H. pylori CagA+	GORD patients		Control group		P value	Odd ratio	Relative risk
	No.	%	No.	%			
H. pylori Positive	42	70	11	36.6	0.002	0.8004 95% CI: 0.3188 to 2.0094	1.35
H. pylori Negative	18	30	19	63.3			
Total	60		30				

The relationship between *H. pylori* and GORD was assessed by Odds ratio that describes the strength of association between the two [16]. In our study, Odds ratio was 0.8004 with 95% CI= from 0.3188 to 2.0094 and relative risk= 1.35, which indicates an association between *H. pylori* and GORD. Other studies illustrated the range of Odds ratio from 0.16 [17] to 1.58 [13], while others demonstrated similar results to this study [18,19]. This heterogeneity among results may be due to the location of the studies.

As mentioned previously, *H. pylori* in patients with gastro-esophageal reflux disease from the Far East differs from Western Europe and North America. In 2010, Roman and Pandolfino [20] mentioned that environmental factors had an effect. The severity of *H. pylori* gastritis (Hp gastritis) had an effect on GORD development. *H. pylori* with predominant antral gastritis is responsible for increased gastric acid secretion and thus promotes GORD. Conversely, *H. pylori* with diffuse gastritis induces gastric atrophy. In this particular case, *H. pylori* eradication may restore acid secretion and lead to a more scathing refluxate in patients with predisposing conditions for GORD.

Conclusion

In this study, the presence of *Helicobacter pylori* was significantly increased in patients with gastro-esophageal reflux disease.

Acknowledgement

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