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

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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 CagA+ 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 serum was 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 (OR), (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.

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%). Spechler showed that H. pylori did not affect the pathogenesis of GORD [11]. In 2001, Warburton-Timms et al [12] demonstrated that CagA+ 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.
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.

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