THE ROLE OF HELICOBACTER PYLORI IN THE PATHOGENESIS OF LOWER ESOPHAGEAL DISEASES

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ABSTRACT

Background: *Helicobacter pylori* causes chronic gastritis with variable activity and topographic distribution. Patient age at acquisition, expression of gastritis, strain virulence, host factors and environmental factors determine the outcome of infection. Well-established consequences are peptic ulcer disease (PUD) and gastric neoplasia. However, the interrelation between H. pylori infection and GERD is complex and poorly understood.

Patients and methods: The study was conducted on 30 patients presenting to the Endoscopy Unit of Kasr-Elaini Hospital, Cairo University, with upper gastro-intestinal symptoms (e.g. heartburn, epigastric pain and regurgitation of acidic contents into the mouth) and in whom upper endoscopy revealed signs of reflux esohagitis. Grading of reflux oesophagitis was done according to the Los Angeles (LA) classification system. Biopsies were obtained from the antrum, body, cardia and the lower esophagus above the Z-line and were examined histopathologically according to the Updated Sydney classification system. Clinical, endoscopic and histopthological data were collected, tabulated and statistically analyzed.

Results: Of the examined group, 12 patients (40%) proved to be H. pylori positive and 18 patients (60%) proved to be H. pylori negative. Prevalence of carditis increased with the H. pylori positive status more than H. pylori negative (91.7% versus 72.2% respectively) as well as severity of it (16.6% versus 5% respectively). Columnar-lined oesophagus (CLO) was present in 2 patients (16.7%) of the H. pylori positive group and 2 patients (11.1%) of the H. pylori negative group. However, these results did not reach the statistical significance.

Conclusions: It was concluded that there is no statistically significant correlation between H. pylori status and reflux esophagitis. The prevalence and severity of carditis is more likely to be associated with H. pylori other than reflux esophagitis. There is no correlation between H. pylori status and the presence of Barrett's esophagus.

Key words: *Helicobacter pylori* – Reflux esophagitis – Carditis - Barrett's esophagus.

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- **ACG**: American College of Gastroenterology
- **AIDS**: Acquired Immune Deficiency Syndrome
- **B7-H1**: (programmed death-1 ligand 1), a member of B7 family of proteins associated with T cell inhibition.
- **BabA2**: Blood group antigen-binding adhesion
- **BAO**: Basal Acid Output
- **CagA**: Cytotoxin-associated gene A
- **CD**: Cluster of Differentiation
- **CI**: Confidence interval
- **CIM**: Cardial intestinal metaplasia
- **CLO**: Columnar lined oesophagus
- **CO2**: Carbon Dioxide
- **DLBCL**: Diffuse large B-cell lymphoma
- **DNA**: DeoxyriboNucleic Acid
- **DU**: Duodenal ulcer
- **DupA**: Duodenal ulcer promoting gene A
- **EGF**: Epidermal Growth factor
- **EGJ**: Esophagogastric junction
- **ESD**: Endoscopic suturing device
- **EMR**: Endoscopic mucosal resection
- **FDA**: Food and Drug Administration
- **GERD**: Gastro-esophageal reflux disease
- **GI**: Gastrointestinal

- **HCL**: Hydrochloric Acid
- **HP**: Helicobacter pylori
- **HpSA**: H. pylori stool antigen test
- **H2RA**: Histamine (2) receptor antagonists
- **IARC**: International Agency for Research on Cancer
- **ICAM 1**: Intercellular adhesion molecule 1
- **IceA**: Induced by contact with epithelium
- **IFNγ**: Interferon Gamma
- **Ig A**: Immunoglobulin A
- **Ig G**: Immunoglobulin G
- **IL**: Interleukin
- **Kd**: Kilodalton
- **LA**: Los Angeles
- **LASER**: Light Amplification by Stimulated Emission of Radiation
- **LES**: Lower esophgeal Sphincter
- **MALT**: Mucosa-associated lymphoid tissue
- **MHC**: Major histocompatibility complex
- **mRNA**: Messenger RiboNucleic Acid.
- **NERD**: Nonerosive reflux disease
- **NF-kB**: Nuclear factor kappa B
- **NIH**: National Institute of Health
- **NSAIDs**: Nonsteroidal anti-inflammatory drugs
- **OipA**: Outer inflammatory protein A
- **OR**: Odds Ratio
- **OTC**: Over The Counter

- **PAO**: Peak Acid Output
- **PCR**: Polymerase Chain Reaction
- **PPI**: Proton pump inhibitor
- **REAL**: Revised European American Lymphoma
- **rRNA**: Ribosomal RiboNucleic Acid
- **RUT**: Rapid Urease Testing
- **TGFa**: Transforming growth factor alpha
- **TGFb**: Transforming growth factor beta
- **Th**: T- helper cell
- **tLESRs**: Transient Lower Oesophageal Sphincter Relaxations
- **TNFa**: Tumor necrosis factor alpha
- **UBT**: Urea Breath Testing
- **VacA**: Vacuolating cytotoxin A

Introduction

The role of Helicobacter pylori (H. pylori) in inducing peptic ulcer disease, chronic gastritis, gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma has been well established ***(Inadomi et al., 1998)***.

H. pylori has been reported to have a significant association with a variety of extra-gastric diseases including cardiovascular, cerebrovascular, hepatologic, skin and joint diseases. However, definite proof with sound scientific evidence has not been provided for most of these associations ***(Gasbarrini et al., 2004)***.

The vast majority of pathologies in the esophagus, stomach and duodenum are related to either H. pylori infection or gastro-esophageal reflux disease (GERD). Both conditions affect a large proportion of the population and they may occur either concomitantly or independently. The question of whether the two conditions are mutually exclusive, synergistic or simply independent is an issue that has been raised several years ago and is still a matter of ongoing debate ***(Labenz and Malfertheiner, 1997)***.

Some studies suggested that H. pylori conferred protection from GERD and that its eradication, as in the treatment of duodenal ulcer, was associated with an increased risk of erosive esophagitis. A post hoc analysis of eight double-blind prospective trials revealed that eradication of H. pylori in patients with duodenal ulcer was not associated with the development of erosive esophagitis, new symptomatic GERD or

worsening of symptoms in patients with pre-existing GERD ***(Laine and Sugg, 2002)***.

The strong argument for the protective role of H. pylori against GERD came from epidemiological studies. A low prevalence of H. pylori infection in patients affected by GERD in the magnitude of 5-10% when compared with a control population has been reported by some authors ***(Cremonini et al., 2003)***.

The protective potential of H. pylori has further been emphasized in studies that discovered more virulent strains to be less prevalent or even absent in severe forms of GERD. Cag A positive strains were suspected to protect from Barrett's adenocarcinoma ***(Vaezi et al., 2000)***. These early observations were not confirmed in a large United States (US) population ***(Wu et al., 2003).***

By extending the analysis beyond Cag A to other H. pylori virulence factors (Vac As1, Ice A1), some authors reported a decreased prevalence of these factors in patients with GERD or with more severe forms of GERD ***(Arents et al., 2001)***, while others did not ***(Leodolter et al., 2003).***

Aim of the work

To determine the role of H. pylori in the pathogenesis of lower esophageal diseases and to identify those patients in whom H. pylori is a friend/foe of the esophagus to permit the development of clinical guidelines on a sound scientific basis.

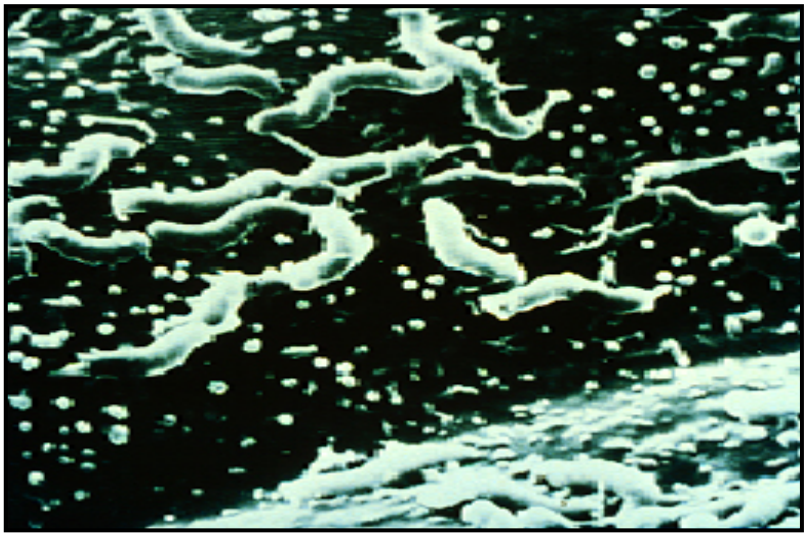
CHAPTER 1: *HELICOBACTER PYLORI*

Gastric organisms were first observed more than 100 years ago and their association with gastritis has been recognized since the 1970s. The true implication of these microbes was not fully realized, however, until 1982 when Marshall and Warren identified and subsequently cultured the gastric bacterium, *Campylobacter pyloridis*, later reclassified as *Helicobacter pylori* (H. pylori) ***(Marshall and Warren, 1984)***.

-MICROBIOLOGY:

H. pylori is a spiral shaped, microaerophilic, gram negative bacterium measuring approximately 3.5 microns in length and 0.5 microns in width.

Figure (I): Electron microscopic picture for H. pylori**.**



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