Helicobacter pylori infection and chronic gastritis; use of the Updated Sydney System in histopathological evaluation of gastritis

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Research note

Keywords: Dyspeptic Patients, Helicobacter pylori, Gastritis and updated Sydney system

DOI: https://doi.org/10.21203/rs.2.14435/v1

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Abstract

Objective Helicobacter pylori is a major cause for chronic gastritis and further it is associated with development of peptic ulcer disease and gastric cancer. Therefore, the objective of this study was to classify gastritis according to the updated Sydney system guidelines and find the association of H. pylori with each of graded variable. Number of 152 dyspeptic patients who underwent upper gastro-intestinal endoscopy at a Teaching Hospital were enrolled. Of the 2 biopsies collected one was used for PCR to detect H. pylori. The other biopsy was fixed in formalin followed by paraffin embedding and stained with H&E stain. Gastritis was classified microscopically according to the updated Sydney system. Results: Gastritis was reported over a wide age group ranging from 18-84 years with a mean age of 51 years. Based on histological findings, 12% of patients were diagnosed as H. pylori associated chronic active gastritis. There was no significant association between each graded variable and H. pylori positivity. Of the 152 dyspeptic patients 34 were positive by PCR for H. pylori infection. All the dyspeptic patients with H. pylori infection had chronic active gastritis, suggesting an etiologic role of the bacterium in the histologic lesion.

Background

*Helicobacter pylori* is a Gram-negative, microaerophilic bacteria which colonizes the gastric epithelium inducing inflammation of the gastric mucosa [1, 2]. It is a major etiological agent for chronic active gastritis and associated with gastric adenocarcinoma and mucosa associated lymphatic tissue lymphoma (MALToma) [2, 3].

*H. pylori* has been classified as a class I carcinogen for humans by the International Agency for Research on Cancer (IARC) monograph committee in 1994. Prevalence of *H. pylori* infection is an enigma in Sri Lanka ranging from 3 to 70% [4,5,6]. Further resistance to clarithromycin is a problem [7] which results in eradication failure with triple therapy [6, 8].

Sequence of inflammatory responses are induced in response to colonization of *H. pylori* and these responses coupled to cellular damage initiates a histological cascade (Normal mucosa > Chronic active gastritis > Gastric atrophy > Intestinal metaplasia > Dysplasia > Gastric cancer) towards the cancer [9].

The Sydney system has been introduced to grade and classify chronic gastritis in 1990. It has been updated in 1994 to provide a framework for a standardized description of chronic gastritis. In this updated version, five histological variables namely chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia and *Helicobacter pylori* density are graded on a simple four point scale (absent or normal, mild, moderate and marked or severe abnormality) [10].

The aims of our study were to classify gastritis according to the updated Sydney system with graded variables and find association of *H. pylori* with each of graded variables, as histo-pathological assessment of the gastric mucosa is known to be good predictor of cancer risk in *H. pylori* positive patient.
Methods

Hundred and fifty two dyspeptic patients who underwent upper gastro intestinal endoscopy at Endoscopy unit at Colombo South Teaching Hospital, Sri Lanka were enrolled in this study. Ethical approval for the study was obtained from the Ethical Review Committee of University of Sri Jayewardenepura (723/13).

Two biopsy specimens were collected from the antrum during endoscopy of each patient after obtaining their written informed consent. Laboratory investigations were carried out at the Department of Microbiology and Department of Pathology, Faculty of Medical Sciences, University of Sri Jayewardenapura, Sri Lanka.

One biopsy was used for PCR targeting the \( glmM \) gene to identify \( H. pylori \) infection. DNA extraction from gastric biopsies and PCR was performed as mentioned in Ubhayawardana et al. 2015 [6].

Histological Investigations

The other specimen was fixed in 10% formalin followed by paraffin embedding, sectioning and stained with H & E stain. \( H. pylori \) infection was diagnosed based on the typical appearance of the bacterium along the mucus layer covering the gastric mucous membrane.

Histopathological changes were examined and gastritis was classified microscopically according to the modified Sydney system [10]. Five main histological changes in gastric mucosa were graded (chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia and \( H. pylori \) density) by the same investigator (consultant histopathologist).

Results

The age of the study population ranged from 18-84 years with a mean age of 51 years. Majority of patients, 43% belonged to the age group above 55 years followed by 34% cases in 40-55 years age group and 23% in 18-39 age group. \( H. pylori \) infection was identified in 12% (18/152) by histology and in 22% (34/152) by PCR assay targeting \( glmM \) gene. Based on histological findings, 12% (18/152) of patients were diagnosed as \( H. pylori \) associated chronic active gastritis, 82% (124/152) and 6% (10/152) of patients were diagnosed as having mild and moderate nonspecific chronic gastritis respectively (Figure 1).

In the study, Mononuclear infiltration (Inflammation) was present in all 152 biopsies (100%) with mild inflammation in 80% (122/152) while moderate and severe inflammation was noted 17% (26/152) and
3% (4/152) patients respectively. Polymorphonuclear cell infiltration (neutrophil activity) was observed in 11% (17/152) of the biopsy specimens. Neutrophilic activity was mild, moderate and marked in 8% (12/152), 2% (3/152) and 1% (2/152) of patients respectively. Overall 4% (6/152) of the patients had gastric atrophy, of which 4 (66%) patients belonged to the >55 years age group and 1 (16.5%) each in 40-55 years and 18-39 years age group. Interestingly intestinal metaplasia was not seen in the study.

Of the histologically confirmed 18 patients, 16 (88%) patients had low *H. pylori* density, while 1 patient (6%) each had moderate and high density. Inflammation was seen in all the *H. pylori* positive patients, with mild inflammation in 39% (7/18) while 39% (7/18) and 22% (4/18) patients had moderate and severe inflammation respectively. Neutrophil activity was mild, moderate and severe in 39% (7/18), 22% (4/18) and 6% (1/18) of *H. pylori* positive patients respectively. Neutrophil activity was absent for rest of the *H. pylori* positive (6/18) patients. Among the *H. pylori* positive patients only 1 patient was found to have 6% mild glandular atrophy. There was no significant association between each graded variable and *H. pylori* positivity (Figure 2).

**Discussion**

The finding of a high incidence of chronic gastritis among dyspeptic patients in this population is a matter of concern; therefore information on histological features of the gastric mucosa is important. Grading of gastritis conveys information on severity of mononuclear infiltration (inflammation) and polymorphonuclear cell infiltration (activity). Glandular atrophy and Intestinal metaplasia indicate the chronicity of the disease. These variables are also associated with increased risk of gastric cancer [11]. In the present study, 4% cases showed gastric atrophy and most of the cases were in 6th and 8th decades of their life, which suggest that it progresses as age advances in chronic gastritis patients. A previous study has shown that the prevalence of atrophic gastritis increased with increasing age [12].

Mononuclear infiltrate was more intense than the neutrophilic infiltrate in most biopsies. Higher histological scores for polymorphonuclear infiltrate and mononuclear infiltrate were observed in *H. pylori* infected patients. It has been reported that *H. pylori* causes continuous gastric inflammation in virtually all infected persons [13]. In a previous study, more intense polymorphonuclear cell infiltration was reported in patients with *H. pylori* associated gastritis and it was associated with duodenitis than in infected patients without duodenitis [14].

Major histopathological features such as gastric atrophy, Intestinal metaplasia were absent even in the patients who were moderately or severely infected with *H. pylori*. Similar results have been reported in a previous study done in Brazil in 2009 [15]. Risk of gastric cancer for these *H. pylori* positive patients with
simple, non-atrophic gastritis may also be negligible since; intestinal metaplasia and atrophy are strongly associated with increased risk of gastric cancer.

*H. pylori* infection results in neutrophil activation and chronic gastritis; it has a role in the development of intestinal metaplasia [16]. However, early detection and eradication of *H. pylori* associated gastritis is important for patients in order to prevent the development of precancerous changes and gastric cancer.

Although, one of the most common causes for gastritis is colonization of gastric mucosa with *H. pylori*; cytomegalovirus infections, chronic idiopathic inflammatory and autoimmune disorders such as Crohn’s disease and pernicious anemia, and chemical damage due to alcohol abuse or nonsteroidal anti-inflammatory drug (NSAID) can be causes for gastritis in *H. pylori* negative dyspeptic patients [2]. In conclusion, all the dyspeptic patients with *H. pylori* infection had chronic active gastritis, supporting the etiologic role for the bacterium in the histologic lesion.

**Limitations**

In the study updated Sydney system was used for grading of gastritis. The updated Sydney system recommends gastric biopsies from five different sites; however, this was not possible in practice in this study because of the ethical issues. Further clinicians do not agree to collect that many biopsies due to post biopsy bleeding risk for patients. Other limitations related with histology include higher cost, longer turnaround time and dependence on the skills of the operator.

Another limitation in the study was the methods of staining used, because some authors reported that staining with alcian blue-periodic acid Schiff (PAS) enhances the detection of incomplete intestinal metaplasia due to the detection of sulphated mucos substances [17]. This is an important limitation as it could prevent the detection of incomplete intestinal metaplasia. In the present study, a consultant pathologist performed the histological investigations and issued the report independently. Based on the findings of the present study, it may be appropriate to conclude that for detection of *H. pylori* infection among symptomatic individuals it is necessary to use more than one diagnostic test as each test is associated with its own limitations. In this study, PCR has been shown to be a valuable method for detection of *H. pylori* in gastric biopsies.

**Declarations**

**Ethics approval and consent to participate**

Ethical approval for the study was obtained from the Ethical Review Committee of University of Sri Jayewardenepura (No. 723/13). Two biopsy specimens were collected from the antrum during endoscopy of each patient after obtaining their written informed consent.
Availability of data and material

The analyzed data used to support the findings of this study are included within the article. The data used during the study is available and will be provided by the corresponding author on reasonable request.

Funding

University Grants (ASP/06/RE/MED/2013/34 and ASP/06/RE/MED/2013/32) of University of Sri Jayewardenepura and a grant from State Pharmaceutical Corporation (SPC), Sri Lanka.

Acknowledgement

We would like to thank the patients who participated in the study and the nursing staff at Endoscopy unit, Colombo South Teaching Hospital, Kalubowila, Sri Lanka.

This study was funded by two University Grants (ASP/06/RE/MED/2013/34 and ASP/06/RE/MED/2013/32) of University of Sri Jayewardenepura and a grant from State Pharmaceutical Corporation (SPC), Sri Lanka. All grants are acknowledged for the financial support provided.

Competing interests: None

Consent for publication

A letter will be sent indicating the consent of all authors regarding publication.

Author’s contributions:

Nushka Ubyawardana - Specimen Collection and processing, Data analysis and manuscript writing

Manjula Weerasekera - Proposal writing and analyzing results, Supervision of PCR technique

Kamani Samarasinghe – Histological examination and reporting
Sameera Pemalal – Histology specimen processing

Deepaka Weerasekera - Specimen Collection and editing and proof reading of manuscript

Chinthika Gunasekera – Data analysis and manuscript writing

Neluka Fernando – Proposal writing and editing and proof reading of manuscript

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**Figures**

Figure 1

Results of histological Assessment
Figure 2

Graded changes in gastric mucosa in H. pylori positive patients