Original article

Benign effects of Helicobacter pylori in gastric mucosa among symptomatic Sudanese patients

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Abstract:

Introduction:

Infection with Helicobacter pylori is a worldwide problem. It plays an important role in gastric malignancies. The pathogenesis of gastric malignancies involves multistep progression changes in gastric mucosa and the Helicobacter pylori infections is the first step in most of cases.

Aim:

The aims of this study were to clarify the benign changes in gastric mucosa after Helicobacter pylori infection; to evaluate the endoscopic and histological patterns of infection and to correlate endoscopic finding with histopathological parameters.

Materials and Methods:

A descriptive, retrospective study was done in Soba University Hospital between January 2009 - February 2013. Paraffin-embedded blocks, Giemsa and Haematoxylin and Eosin-stained slides, were obtained from 50 cases of Helicobacter pylori-associated chronic gastritis and examined under light microscopy. The clinical information and endoscopy findings were obtained from the records. The data was analyzed using Statistical Package for Social Sciences Software.

Results:

The most common affected age group was between 40-60 years. The prevalence of infection was equal in males and females. The commonest endoscopic finding was inflammation of gastric mucosa. Most patients presented with moderate degree of colonization; 62% of patients presented with a severe degree of chronic inflammation. There was a significant statistical correlation between the degree of Helicobacter pylori colonization and the degree of chronic inflammation ($p<0.05$). Most patients presented with severe degree of active gastritis. A significant correlation was found between the degree of chronic inflammation and degree of activity. The prevalence of lymphoid follicles in a single biopsy specimen from antral mucosa was 36%. The dysplasia was seen in 12%; eosinophilia 8%; atrophy 8% and intestinal metaplasia in 6% of the cases. No significant correlation was found between the endoscopic findings and histological findings.

Conclusion:

Helicobacter pylori infection causes chronic active gastritis and it has a role in the development of lymphoid follicles, intestinal metaplasia, atrophy and dysplasia.

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Introduction:

Infection with Helicobacter pylori (H. pylori) is common all over the world. It represents the most common cause of gastric cancer (5.5% of all cancers). It is implicated in the pathogenesis of a number of digestive tract disorders, such as chronic active gastritis, peptic ulceration, gastric cancer and mucosa-associated lymphoid tissue lymphoma [1].

The prevalence of infection ranges widely between developed and developing countries. In developing regions the infection rate is high and is approximately 80 % [2]. By contrast, the infection rate is as low as 10–20% in developed countries [3]. No sex predilection appears to exist for H. pylori infection [4, 5]. The mucous layer of the gastric mucosa is the primary site of H. pylori colonization and often contains large numbers of organisms. When in contact with epithelium, H. pylori organisms characteristically attach to, but do not penetrate, the surface mucous cells. However, in few cases some strains are capable of attacking the mucosa. These strains are regarded as carcinogenic strains [6].

In severe acute infection, grossly visible pseudomembranes and pus adherent to inflamed mucosa have been described [7]. In chronic H. pylori gastritis, epithelial degeneration is particularly prominent owing to intimate contact of the H. pylori organisms and persistence of infections [7]. There are no distinct endoscopic patterns of chronic H. pylori gastritis. Depending on the stage and type of gastritis, hyperemia, erosions, hypertrophy, and atrophy may coexist, in various combinations, in an individual patient [7]. The most common endoscopic finding was atrophy followed by nodularity then normal mucosa and finally erosion as revealed by a Japanese study [8].

Chronic H. pylori infections result in infiltrations of inflammatory cells like neutrophils, lymphocytes, macrophages and plasma cells [6]. Chronic active gastritis is the primary disorder that results from H. pylori colonization. H. pylori infects two thirds of the people in the world and it is regarded as one of the most common chronic inflammatory disorders of world's population [7]. H. pylori-induced ulcer disease, gastric cancer, and lymphoma are complications of this chronic inflammation [6].

Infiltration of tissues by eosinophils in H. pylori gastritis is a part of the inflammatory cells that play an important role in immune system. Its recruitment is mediated by H. pylori peptide (2–20), then eosinophil induce production of inflammatory mediators VEGF-A and TGF-β, that cause tissue remodeling and induce mucosal healing [9].

Within the stomach, H. pylori typically causes antral gastritis with high acid production, despite hypo-gastrinaemia; infection of the cardia occurs at somewhat lower rates. H. pylori are uncommon in oxyntic mucosa of the fundus and body except in heavy colonization [6]. In a subset of patients the gastritis progresses to involve the gastric body and fundus resulting in pan-gastritis. This pan-gastritis is associated with multifocal mucosal atrophy, reduced acid secretion, intestinal metaplasia, and increased risk of gastric adenocarcinoma [6].

The outcome of infections depend on specific strains of H. pylori: for example Cag A strains (carry chromosomal region known as the cytotoxin-gene associated pathogenicity island (*cag* A)) induce higher levels of cytokines IL-1, IL-6, IL-8, and TNF and may cause severe inflammation [10]. Cag A+ strains also induce gastric epithelial proliferation which is not accompanied by a parallel increase in apoptosis. This explains the heightened risk for gastric carcinoma that is associated with infection by Cag A+ strains of H. pylori [11].

Vac A strains of H. pylori are responsible for augmentation of inflammation and persistence of infections by suppression of immune response. This is achieved by blocking proliferation of T cells by inducing T cell arrest in G1/S phase and interferes with T cell receptor signals [12]. Vac A strains are responsible for gastric cancer also. This is carried out through loss of balance between apoptosis and cell proliferation resulting in precancerous lesions such as gastric atrophy, intestinal metaplasia, and dysplasia [13].

As a result of long term inflammation in the gastric mucosa, the gastric epithelia exhibit different degrees of dysplasia. The incidence of dysplasia in asymptomatic patients with first degree relative gastric carcinoma was 15% and with patients without family history of gastric carcinoma was 13% according to study done in Iran [14].

The updated Sydney System is a modern method in classification of gastritis, aiming for systematic diagnostic reports that meet clinical needs. This system classifies the degree of H. pylori colonization, chronic inflammation, activity to mild moderate sever groups which have pathological and clinical significance [15] .

The aims of this study are to clarify the pathological lesions in gastric mucosa after H. pylori infection; to study the endoscopic and histological patterns of infection and correlate endoscopic findings with histopathological parameters. The common age group affected and sex predilection were also determined.

Materials and methods:

After Soba University Hospital approved our study and the consent was taken from the patients (parent consent taken from patients less than 18 years), data were collected from pathology lab and endoscopy department. The patient's data were collected from the patients request forms into a predesigned questionnaire. No patient's personal information was included.

Inclusion criteria: all Sudanese patients undergoing endoscopic biopsy at Soba Hospital with full record information between January 2009-February 2013 were included in our study.

Exclusion criteria: Non- Sudanese patients and patients with incomplete data records.

Histological slides were stained with Hematoxylin and Eosin stain (H&E stain) and Giemsa stain. Then slides were reviewed to confirm the presence of H. pylori and determine the degree of inflammation, activity, incidence of atrophy, intestinal metaplasia, lymphoid follicles and oesinophilia.

The histological grade of the degree of gastric mucosal inflammation, activity and H. pylori colonization were evaluated according to updated Sydney System. The scores were defined as: 0 for absent, 1 for mild, 2 for moderate, and 3 for marked (or severe).

Endoscopic findings were correlated with histological features.

The findings were analyzed by statistical Package for Social Science (SPSS) analytical system. Determination of Spearman's correlation coefficient was also made, and $P < 0.05$ was considered to be statistically significant.

Results:

A total of 50 Sudanese patients with H. pylori-associated chronic gastritis aged from 11 to 84 years at Soba University Hospital during the period from January 2009-February 2013 were enrolled in the study. The mean age was 47.78 years, with 25(50%) males and 25(50%) female (Figure 1).

Most patients (58%) presented with moderatate degree of colonization followed by severe degree of colonization in 28%, then mild degree of colonization present in 14% as per the criteria of the Sydney System. 62% of patients presented with severe degree of chronic inflammation, followed by moderate degree of chronic inflammations (28% of the cases) then mild degree present in 10% of the cases as per the criteria of the Sydney System. There was a significant statistical correlation between the degree of H. pylori colonization and the degree of chronic inflammation ($p<0.05$).

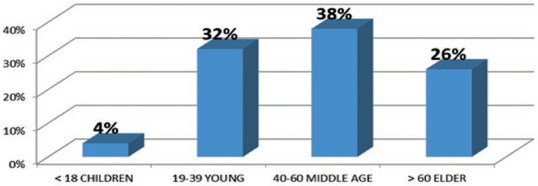

Figure-1. Age Distribution of H.pylori gastritis (n=50)

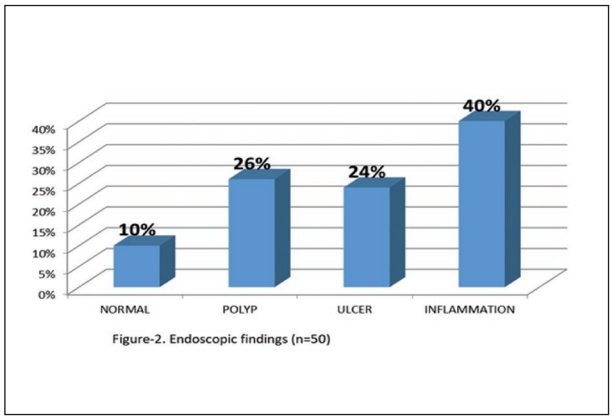

Figure-2. Endoscopic findings (n=50)

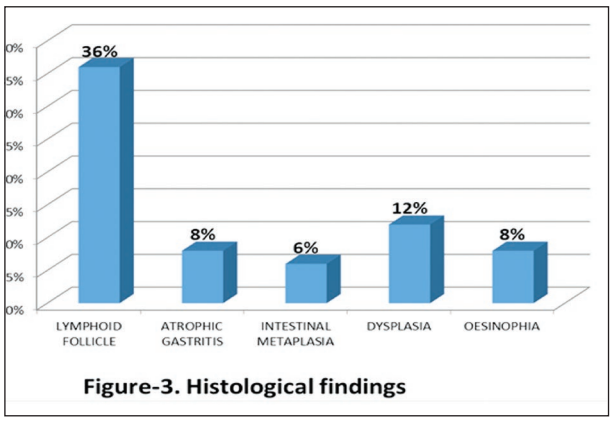

Figure-3. Histological findings

Most patients presented with severe degree of active gastritis (44%) followed by moderate degree of activity in 22% of cases then mild degree of activity in 18% of cases and only 16% of cases did not show active gastritis as per the criteria of the Sydney System. A significant correlation was found between the degree of chronic inflammation and degree of activity (Figure 2). The prevalence of lymphoid follicles in a single biopsy specimen from antral mucosa was 36%. Four cases (8%) of eosinophilia in gastric tissue were found; two of them showed severe degree of chronic inflammation. In our study the dysplasia was seen in 12% of cases; atrophy was noted in only 8% of cases and intestinal metaplasia in 6% of the cases (Figure 3).

No significant correlation was found between the presence of active gastritis and intestinal metaplasia or atrophic gastritis (P=0.921, P=0.118, respectively). No significant correlation was found between the endoscopic findings and histological findings.

Discussion:

H. pylori are the most important causes of chronic non-neoplastic diseases of the stomach, which are precursors for both gastric adenocarcinoma and gastric lymphoma. In this research we studied the benign effects of Helicobacter pylori infection on the gastric mucosa.

This study showed the prevalence of H. pylori infection in symptomatic patients was identical in both sexes; this is similar to studies done in Sudan and Senegal [4,5] .

This study is based on histological detection of H. pylori. The most common age group affected by H. pylori chronic gastritis ranged between 40-60 years. This is similar to a study done in India [16].

Regarding the degree of chronic inflammation, most patients presented with severe degree of chronic inflammations, followed by moderate, then mild degree as per the criteria of the Sydney System, in contrast to a similar study done in Duhok (Iraq) which found that most patients presented with moderate degree of chronic inflammation [17]. The degree of chronic inflammations results from different strains of H. pylori as proved by a study done in Japan [10].

Our results demonstrate that there is correlation between the degree of H. pylori colonizations and degree of chronic inflammations. This is similar to a studies done in Niger and Kenya [18,19]. Most cases presented with severe chronic active gastritis; the degree of activity can be explained by different strains of H. pylori. As reported, cag A strains cause release of IL-8 resulting in neutrophil recruitment[20].

This study showed that the most common endoscopic finding in H. pylori infection was gastritis followed by polyp, then the ulcer; and normal mucosa present in 10 % of the cases (Figure 2). This is in contrast to a similar study done in Japan [8]. The difference in endoscopic findings can be explained by the different strains of H. pylori in different areas.

This study revealed that a significant correlation was found between the degree of chronic inflammations and the degree of activity (P<0.000). This is similar to a study done in Kenya [19]. Mucosal lymphoid follicles represent primarily an immune response to H. pylori. In the present study the

prevalence of lymphoid follicles in a single biopsy specimens from antral mucosa was 36%; this is in contrast to similar study done in West Germany in Bayreuth Hospital where mucosal lymphoid follicles were found in 54% of the cases [21]. In another study done in Kenya, it was noted that lymphoid follicles were evident in 11% of the cases [19]. However, if multiple samples were obtained from gastric mucosa, the lymphoid follicles are found in almost all H. pylori-infected patients, and their presence in the gastric mucosa is highly specific for H. pylori-associated gastritis as reported in the United States from the Texas study [22].

In the current study, four cases (8%) of eosinophilia in gastric tissue were found; two of them showed severe degree of chronic inflammations and the other two cases showed moderate degree of chronic inflammations i.e. none of them showed mild degree of inflammation. In spite of that, no significant correlation was found with the degree of chronic inflammation and oesinophilia. It may be due to the limited number of our cases, in contrast to the results of a similar study done in Kenya where they found significant positive correlation between the gastric tissue eosinophils density and the degree of chronic inflammation [19].

This study revealed that atrophy was minimal and represents only 8% of cases; intestinal metaplasia was presented in 6% of cases. Dysplasia was seen in 12% of cases. This is near to a study done in Iran, where they found H. pylori-associated dysplasia in asymptomatic patients with first degree relatives gastric carcinoma was 15% and with patients without family history of gastric carcinoma was 13% [14].

No significant correlation was found with the endoscopic findings and histological findings. This is similar to the Baghdad (Iraq) study [23].

Limitations:

This study faced some limitations like incomplete data records giving rise to a small number of cases. Single endoscopic biopsy impaired full application of updated Sydney system

Conclusions:

The most common endoscopic finding in H. pylori infection was inflammation of gastric mucosa. H. pylori infection results in chronic active gastritis and it had a role in the development of lymphoid follicles, intestinal metaplasia, mucosal atrophy and dysplasia.. No correlation was found between the endoscopic findings and histological findings.

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