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Full Length Research Paper

Heliclobacter pylori associated chronic gastritis: Endoscopic and pathological findings, comparative study

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Helicobacter pylori **have been established as a major etiologic factor in the pathogenesis of chronic gastritis, peptic ulcer disease and in the development of gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue lymphoma. This study was conducted on 100 patients. All underwent upper endoscopy, and antral and corpus, and duodenal biopsies were taken. Findings of endoscopic gastritis were observed in 83 patients (p <0.001). Histologically mononuclear inflammatory cellular infiltrates were seen in 95 cases, majority of them showed grade 1 gastritis (64), whereas grade 2 and grade 3 gastritis found in 16 and 15 biopsies. The relationship between endoscopic and histological findings was significant (p <0.001).** ***H. pylori*** **colonization was found in the majority of the biopsies (92) (p <0.001). This study concluded that accurate endoscopic and histopathological examination of gastritis according to the Sydney grading system is valuable indicator of** ***H. pylori*** **infection. Endoscopical abnormalities suggesting gastritis were significantly correlated with the histopathologic findings. Finally, chronic active gastritis with lymphoid follicles was significantly correlated with** ***H. pylori*** **infection (p <0.001).**

Key words: Chronic gastritis, *Helicobacter pylori*, endoscopic and histological grading.

INTRODUCTION

Helicobacter pylori (H. pylori) infection has been established as a major cause of chronic gastritis, which affects approximately 50% of the world's population, and is important in the pathogenesis of other gastro-intestinal diseases as peptic ulcer disease (PUD), gastric adeno-carcinoma and gastric lymphoma (Rotimi et al., 2000; Rugge et al., 2011; Sokwala et al., 2012). Studies reported that the prevalence ranges from less than 15% in some populations to virtually 100%, depending on socio-economic status and country development (Malaty, 2007; Carrasco and Corvalan, 2013).

National Institute of Health Consensus Development Conference (1994) concluded that infected patients with *H. pylori* should receive antimicrobial therapy, as the risk of ulcer recurrence and associated complications do not diminish unless *H. pylori* infection is cured (Versalovic, 2003). Chronic inflammation plays an important role in the development of various cancers, particularly in

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digestive organs, including *H. pylori*-associated gastric cancer (GC) (Uemura et al., 2001). In the same view GC is an important leading cause of cancer-related death particularly in Europe, so understanding the pathogenesis of *H. pylori*-induced GC may improve risk stratification for prevention and therapy (Parkin et al., 2005; Wen and Moss, 2009). In addition to the above, *H. pylori* is well recognized as a class 1 carcinogen because its long-term colonization can provoke chronic inflammation and mucosal atrophy, which can further lead to malignant transformation (Lee et al., 2012).

Assessing gastritis involves clinical examination, endoscopic and histopathological examination (Rugge, 2007; Lauwers et al., 2010). Sydney grading system of chronic gastritis and its updated Houston version (1996) is the commonly-used nomenclature for gastritis and still remains inconsistent. Sydney system categorized gastritis according to intensity of mononuclear inflammatory cellular infiltrates, polymorph activity, atrophy, intestinal metaplasia and *H. pylori* density into mild, moderate and severe categories (Dixon et al., 1996; Dixon et al., 1997). Non-standard histology reporting formats are still widely used for gastritis and even specialists are often frustrated by histological definitions that make it difficult to identify candidates for clinico/endoscopic surveillance (Rugge et al., 2011). Additionally, there is no simple validated test to quantify the density of *H. pylori* infection (Tummala et al., 2004). The aim of this work was to compare between endoscopic and pathological findings of *H. pylori* gastritis and to provide an unequivocal information about grading of gastritis according to the 1996 Sydney grading system.

MATERIALS AND METHODS

Patient selection

During 12-months period (August 2012 to July 2013), 100 patients were selected from all the patients that were seen in the surgery outpatient clinic; Arar Central Hospital, KSA and who were suffering from symptomatic dyspepsia. The patients were examined clinically, and various routine laboratory investigations were done including complete blood count (CBC), liver and renal function tests, and bleeding and coagulation assessment. Then the patients underwent for upper gastro-intestinal endoscopy. Patients were excluded if they had taken *H. pylori* eradication treatment as antibiotics, proton pump inhibitors or H2 antagonists in the 4 weeks before endoscopy.

Endoscopy

It was done under general anesthesia and 2 gastric (one from the gastric antrum, and one from the body), and one duodenal biopsies were obtained. At the same time the patients were examined for presence / absence of findings suggestive of endoscopic gastritis as erythema / hyperemia, atrophy, and mucosal nodularity according to the criteria of Sydney system (Dixon et al., 1996). Additionally, the patients were examined for presence or absence of gastric erosions and findings suggestive duodenitis as hyperemia or ulceration according to Garg et al. (2012). Also, the patients were evaluated for the anatomic location of gastritis that including three major locations; antrum, antrum predominant pangastritis and corpus predominant gastritis, and patients were considered endoscopically normal, if the gastric mucosa was pink, smooth and lustrous (Yesim et al., 2004).

Histopathology

The biopsies were collected, placed on filter paper, fixed in 10% formalin, and sent for preparation of formalin-fixed, paraffin-embedded blocks, then tissue sections with 3 micron thickness were obtained. One slide was stained by routine (H&E), and the other with Giemsa stain for histopathological examination (by 2 experienced pathologists) including detection of *H. pylori* in the gastric mucosa.

The biopsies were evaluated for the intensity of mononuclear inflammatory cellular infiltrates, inflammatory activity, glandular atrophy, metaplasia and dysplasia (Dixon et al., 1997). Additionally, cases of chronic gastritis were graded according to the grading system that was provided by Houston-updated Sydney system (Dixon et al., 1996), which was depended on the intensity of mononuclear inflammatory cellular infiltrates within the lamina propria into 4 scales as follows: absent inflammation (grade 0), mild (grade 1), moderate (grade 2) and severe (grade 3) (Dixon et al., 1996).

Statistical analysis

The statistical analysis was undertaken using SPSS computer software (SPSS version 16 Microsoft windows). Z test was used for the comparison between two proportions. Results were considered to be statistically significant at $p < 0.05$.

RESULTS

Clinicoendoscopical findings

Patients' age, ranged from 20 years to 80 years with average 47 years and 63 out of all patients were males and 37 were females. All patients complained of heart burn, and nausea with epigastric pain that did not respond to ordinary treatment. Upper endoscopy revealed 5% of the patients showed normal appearing gastric mucosa. Findings of endoscopic gastritis detected in 83 patients ($p < 0.001$), among them hyperemia seen in 54, erosion in 14, ulceration in 3, and nodularity in 12 patients. Regarding the anatomic location of endoscopic gastritis, antral type-gastritis found in 63 patients ($p < 0.001$), antrum predominant pangastritis in 13, and corpus predominant gastritis detected in seven patients. Also, findings of endoscopic duodenitis in the form of hyperemia and ulceration were seen in 12 patients.

Histopathological findings

In concern to histopathological evaluation of the prcessed antral and body type gastric biopsies mononuclear inflammatory cellular infiltrates detected in 95 cases ($p < 0.001$). In relation to the intensity of these infiltrates,

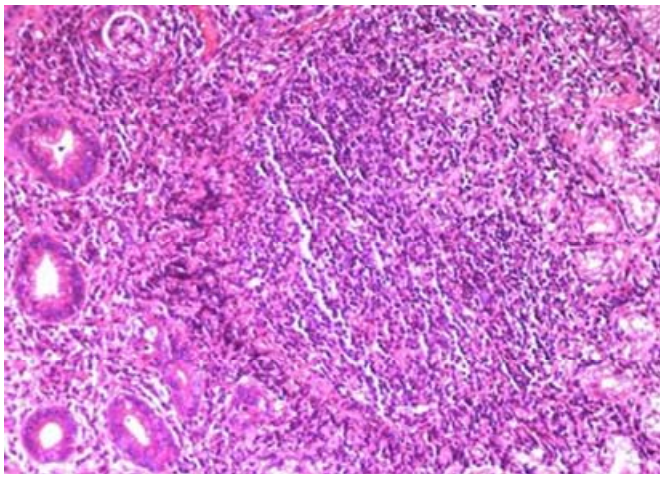

Figure 1. A case of G3 gastritis showing lymphoid follicle formation with severe mononuclear cellular infiltration in the lamina propria (H&E 200X).

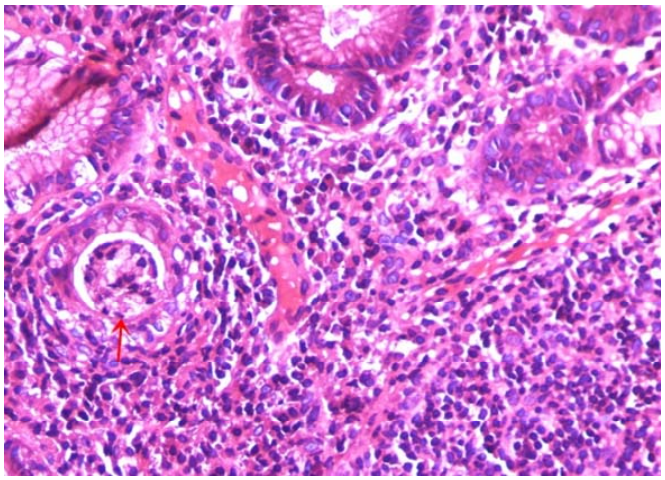

Figure 2. A case of G3 gastritis revealing active inflammation with neutrophils in the glandular lumen (arrow) and severe mononuclear cellular infiltration in the lamina propria (H&E 200X).

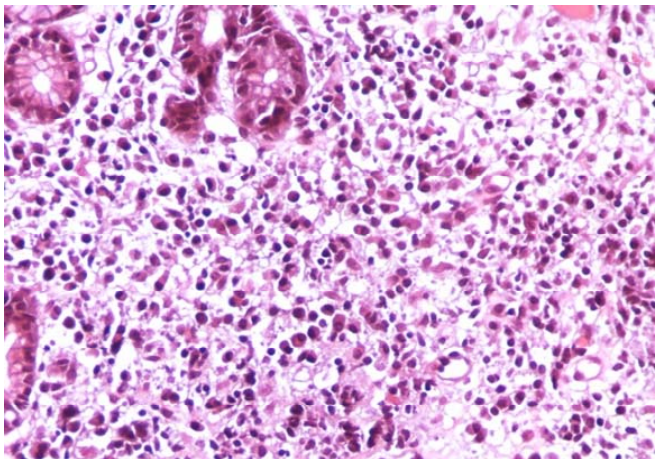

Figure 3. A case of G3 gastritis showing glandular atrophy with severe mononuclear cellular infiltration in the lamina propria (H&E 200X).

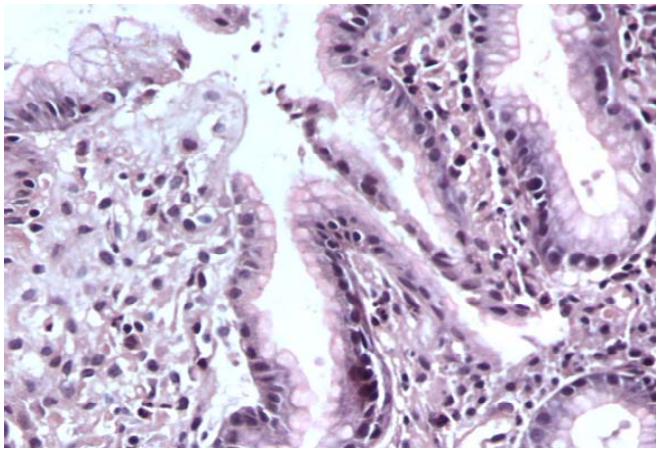

Figure 4. A case of G2 gastritis showing intestinal metaplasia with moderate mononuclear cellular infiltration in the lamina propria (H&E 200X).

absent inflammation (G0) observed in 5 cases, grade 1 gastritis (G1) in 64 ($p < 0.001$), grade 2 gastritis (G2) in 16, and grade 3 gastritis (G3) found in 15 cases ($p < 0.001$). In addition to the above, lymphoid follicles with germinal center formation were seen in 6 cases (Figure 1), whereas active inflammation with neutrophilic infiltration were identified in 10 cases (Figure 2). Also, 7 cases showed mucosal glandular atrophy (Figure 3), one case revealed intestinal metaplastic changes (Figure 4), and another one revealed dysplastic changes (Figure 5). *H. pylori* colonization found in 92 cases (Figure 6) ($p < 0.001$), one among them was gastric adenocarcinoma develops on top of *H. pylori*-induced chronic gastritis. Eight cases were free from *H. pylori* infection. Among *H. pylori* infected cases, findings of endoscopic gastritis were seen in 83 patients, and the ratio between endoscopic findings and histopathological positivity of *H. pylori* was 90.2%, as well as *H. pylori* seen in the majority of patients with endoscopic findings of duodenitis (91.7%) ($p < 0.005$) .

Regarding all the parameters of endoscopy and histopathology, there is insignificant correlation between grade 1 gastritis (G1) and endoscopic hyperemia ($p > 0.001$), yet the latter revealed significant relation with *H. pylori* colonization, as well as *H. pylori* colonization reveals a significant correlation with endoscopic duodenitis ($p < 0.001$) (Table 1). Histologically, *H. pylori*, mononuclear inflammatory cellular infiltrates, lymphoid follicles and inflammatory activity observed among most

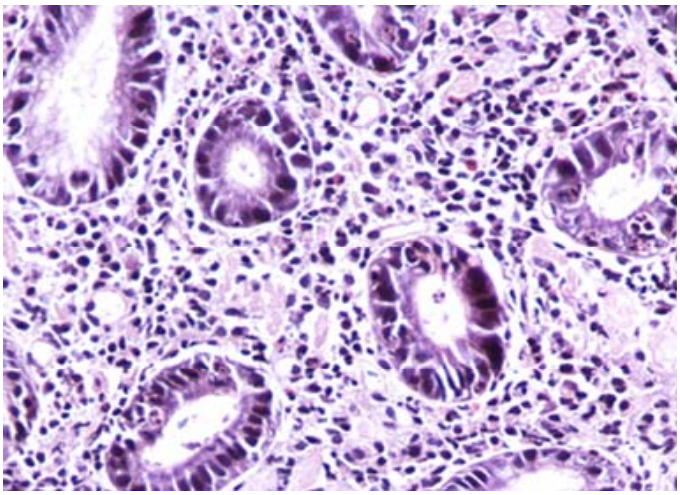

Figure 5. A case of G2 gastritis revealing dysplastic changes with moderate mononuclear cellular infiltration in the lamina propria (H&E 200X).

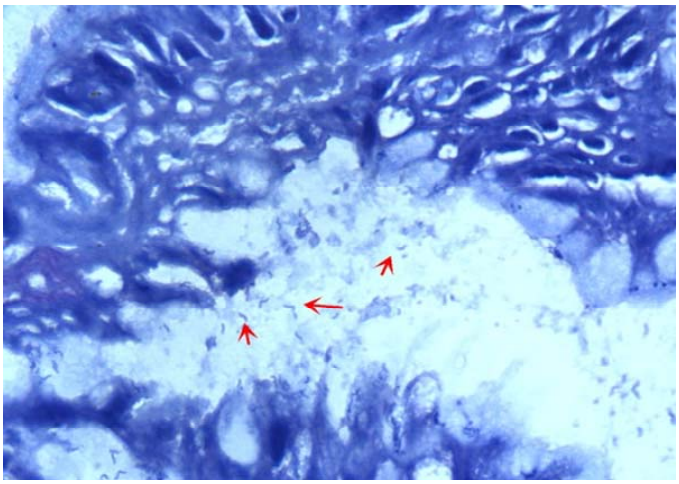

Figure 6. A case of G2 gastritis showing severe *Helicobacter pylori* colonization within the superficial mucus overlying the foveolar epithelial cells (arrows) (giemsa stain 400X).

of the studied cases (95%) with ($p < 0.001$).

DISCUSSION

Despite its declining incidence, gastric cancer (GC) (especially the intestinal-type mainly associated with *H. pylori* infection) is still a highly lethal malignancy (Parkin et al., 2005) as well as primary prevention though *H. pylori* eradication is consistently recommended (Correa et al., 2000; Leung et al., 2004). Gastric mucosal atrophy is generally considered the "cancerization field" in which GC develops. Based on such a rationale, and incorporating the experience gained with the Sydney system (Dixon et al., 1996) and the international group (Operative Link on Gastritis Assessment) (OLGA) proposed an equivalent grading and staging systems for reporting gastric histology rank gastritis-induced cancer risk according to both the topography and the extent of glandular atrophy (Rugge et al., 2008; Rugge et al., 2010). The available clinicopathological classifications of gastritis are inconsistently used, possibly because most of them do not provide clinicians with immediate prognostic and therapeutic information. In addition, because they lack explicit ranking of severity, the descriptive labels of chronic gastritis carry the risk of being misinterpreted by general practitioners (Rugge et al., 2007).

In this study the endoscopical findings of gastritis revealed a significant relation with majority of patients showing hyperemia (54 patients) ($p < 0.001$), followed by erosion in 14, mucosal nodularity in 12, and ulceration in 3 patients ($p < 0.005$). There is a significant correlation between endoscopical findings and anatomic location of gastritis as antral type represents the major one ($p < 0.001$). Additionally, the endoscopical findings of gastritis and duodenitis revealed a significant relationship (83 and 12 patients, and $p < 0.001$). Histologically, 95 cases revealed mononuclear inflammatory cellular infiltrates, and 5 cases were G0. Among the former cases G1 gastritis observed in 64 cases, G2 in 16 cases and G3 in 15 cases. The relation between these grades of gastritis was significant ($p < 0.001$). Lymphoid follicles found in 6 cases ($p < 0.001$), inflammatory activity in 10 cases ($p < 0.001$), glandular atrophy in 7 cases, intestinal metaplasia and dysplasia each of them observed in one case ($p < 0.001$). The relationship between endoscopical findings, inflammatory infiltration and *H. pylori* colonization was significant ($p < 0.001$), whereas the relation between G0 gastritis and hyperemic gastric mucosa was insignificant ($p > 0.001$). Additionally there was a higher significant correlation between *H. pylori* colonization and hyperemia, as well as with gastric erosion, and duodenitis ($p < 0.001$). All grading of gastritis (G1, 2, and 3) showed *H. pylori* colonization, whereas G0 was negative, and 2 patients of endoscopically normal appearing gastric mucosa revealed *H. pylori* colonization. Our endoscopical findings are in agreement with a study revealed by the presence of erythema in 68% of patients, antral erosion in 7%, duodenal ulcer in 5% and normal gastric mucosa in 20% out of 300 patients (Garg et al., 2012). Calabrese et al. (1999) reported erythema in 44 and 43% of patients, respectively, and Yesim et al. (2004) found endoscopic gastritis in 54 out of 64 patients (84%), the majority showed endoscopic erythematous / exudative gastritis (81.3%).

In this study mononuclear inflammatory infiltrates detected in majority of biopsies (95/100), as well as various grades of gastritis were seen, whereas 5% of our cases were G0. Garg et al. (2012) found mononuclear inflammatory infiltrates in the majority of the cases (70%) with 20% of them were endoscopically normal, yet they showed chronic inflammation on histology. Our results

Table 1. Correlation between endoscopic and histopathological findings of all cases studied.

Histological feature	Endoscopical finding					
	Endoscopic gastritis No. 83				Duodenitis No. 12	Normal No. 5
	Hyperemia No.= 54	Erosions No.= 14	Ulcerations No.= 3	Nodularity No.= 12		
Infla. cells						
Go= 5	1	-	-	-	-	4
G1= 64	47	4	-	6	6	1
G2= 16	4	3	1	2	6	-
G3= 15	2	7	2	4	-	-
Activity= 10	2	3	2	3	-	-
Lymphoid F= 6	-	1	2	3	-	-
Atrophy= 7	-	2	2	2	1	-
Metaplasia= 1	-	-	-	1	-	-
H.P = 92	53	13	2	11	11	2

Infla, inflammatory; No., number of cases; F, follicles; H. P, *helicobacter pylori* colonization.

are in parallel with Khan et al. (1999) who found 32% of patients with chronic gastritis histologically had normal endoscopical findings, hence emphasizing the role of biopsy even in normal endoscopic cases.

The endoscopical finding of mucosal nodules may be not an essential diagnostic parameter as a study conducted by Nakashima et al. (2011) who reported lymphoid follicles were not present at the sites of endoscopically identifiable nodules and patients with endoscopically diagnosed nodules showed them in areas ranging from the gastric antrum to the gastric angulus, but histological features of them observed in areas extending from the antrum to the corpus. Additionally, a surprise mentioned by Matsushia and Aftab (2012) who found the scores of chronic inflammation, neutrophil activity, glandular atrophy and intestinal metaplasia were significantly lower with *H. pylori* positive Bangladeshis then in Japanese at all gastric sites, they linked this to a hypothesis that is related to *H. pylori* strains and these patients are typically infected with a Western-type of *H. pylori* (Vilaichone et al., 2004). Regarding the anatomic location of endoscopic gastritis in our study, antral type represents a higher percentage (63%) followed by antrum predominant pangastritis (13%) and corpus predominant that encompasses 7%. These findings are in agreement with Matsushia et al. (2007) who reported antral gastritis represented a higher percentage of endoscopic gastritis regardless age period of patients, yet our findings are in disagreement with Uemura et al. (2001) who reported corpus predominant gastritis represented a higher percentage in Japanese patients. So, the pathogenesis of *H. pylori*, anatomic location of gastritis may be changeable according to the *H. pylori* strains and residency.

In this study the sensitivity of endoscopical abnormalities for gastritis was 90.2%, a previous study performed on 100 patients found this sensitivity 91.7% (Al-Hamdani et al., 2001). In this study grade 1 gastritis (G1) found in 67.4%, G2 in 16.8%, and G3 in 15.8% and all of them revealed *H. pylori* colonization; this is in agreement with a study of (Rugge et al., 2007) who found G1 gastritis in 68%, G2 in 14%, and G3 in 12% of cases studied. Also, the same study discussed that duodenal ulcer found in 86% of patients is associated with gastritis. Histologically, *H. pylori* is detected in the majority of our biopsies (92%) including patients with hyperemia, erosion and nodularity. Patients with duodenitis showed *H. pylori* colonization in 91.7%. Inflammatory activity with neutrophils is found in 10 cases, and glandular atrophy in 7 cases, whereas intestinal metaplasia and dysplasia are each seen in one case. Most of these findings are in agreement with Garg et al. (2012) who observed *H. pylori* in patients with hyperemia and erosion in 37 and 57%, respectively and also found mononuclear inflammatory cellular infiltrates in all cases with the majority (70%) exhibiting mild inflammation (G1) while, 27% showed moderate inflammation (G2). Reported 33% of Garg et al. (2012) cases showed an activity which is not parallel to our findings and this may be attributable to the large number of his cases (300). The same previous author found glandular atrophy in 12.3% and intestinal metaplasia in 7% of cases that are near to our findings, as well as in accordance with findings observed by Atisook et al. (2003) and Hussein et al. (2009). In the current study *H. pylori* is found in 92% of all biopsies which is near to study done by Kumar et al. (2006) who showed positivity in 78%.

Conflict of Interests

The author(s) have not declared any conflict of interests.

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