

Evaluation of Chronic Gastritis in Endoscopic Antral Biopsies Using the Up-dated Sydney System

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ABSTRACT

Objectives: To evaluate the histological parameters of chronic gastritis in endoscopic antral biopsies, to grade them according to the up-dated Sydney system and to compare the obtained results with those of others.

Methods: From the 1st of July 2018 to the end of December 2018, 100 endoscopic antral gastric biopsies were submitted to the Histopathology Unit in Al-Salam Teaching Hospital in Mosul, obtained from patients complaining of different clinical symptoms and referred for upper gastrointestinal endoscopy. Biopsies were assessed for the histological parameters of chronic gastritis and were also graded using the visual analogue scale of the up-dated Sydney system.

Results: The 100 biopsies belonged to 42 males and 58 females ranging from 9-85 years old with a mean of 42.7 years and a peak age incidence in the fourth decade. The commonest symptom was epigastric pain in (46%) of cases. Antral gastritis was the major endoscopic finding in (66%) of cases. All cases revealed mononuclear cell infiltration (100%), followed by neutrophilic activity (84%), glandular atrophy (22%), intestinal metaplasia (14%) and dysplasia (9%). *Helicobacter pylori* (*H. pylori*) was detected in (77%) of cases and a significant statistical association was found between *H. pylori* and each of: mononuclear cell infiltration ($P < 0.001$), neutrophilic activity ($P < 0.001$) and glandular atrophy ($P < 0.05$), while insignificant statistical association was observed between *H. pylori* and both intestinal metaplasia and dysplasia ($P > 0.05$).

Conclusion: Histopathological study of endoscopic antral gastric biopsy is of value in detection of *H. pylori* and various histological changes of chronic gastritis. A statistically significant association was found between *H. pylori* and each of: mononuclear cell infiltration, neutrophilic activity and glandular atrophy. Dysplasia is an important histological change in chronic gastritis that requires endoscopic follow up to rule out the possibility of gastric cancer, and it is advisable to be incorporated in the visual analogue scale of the up-dated Sydney system.

Keywords: chronic gastritis, antral biopsy, up-dated Sydney system.

تقييم التهاب المعدة المزمن في خزعات غار المعدة الناظورية باستخدام نظام سيدني المُحدَّث

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الخلاصة

الهدف من الدراسة: تهدف الدراسة إلى تقييم المعايير النسيجية لالتهاب المعدة المزمن من خلال استحصال خزعات ناظورية لغار المعدة، كما تهدف إلى تحديد درجات هذه المعايير وفقاً لنظام سيدني المُحدَّث، فضلاً عن مقارنة النتائج المستحصلة مع نتائج الدراسات السابقة.

الحالات والطرق: تم تقديم 100 خزعة نازظورية من غار المعدة من بداية شهر تموز 2018 إلى نهاية كانون الأول 2018 إلى وحدة النسيج المرضي في مستشفى السلام التعليمي في الموصل، وقد أخذت هذه الخزعات من مرضى يعانون من اعراض سريرية مختلفة وأحيلوا إلى تنظير الجهاز الهضمي العلوي. وقد تم تقييم الخزعات على وفق المعايير النسيجية لالتهاب المعدة المزمن وتحديد درجاتها باستعمال المقياس المماثل المرئي لنظام سيدني المُحدَّث.

النتائج: تعود الخزعات المائة إلى 42 ذكر و 58 انثى تتراوح اعمارهم بين 9- 85 سنة وبمتوسط عمر 42.7 سنة. أما الفئة العمرية الأكثر عرضة للإصابة فقد كانت في العقد الرابع. وكان العرض الأكثر شيوعاً يتمثل في ألم شرنوفي في 46% من الحالات، بينما كان التهاب المعدة الغاري النتيجة النازظورية الرئيسية في 66% من الحالات. اظهرت الحالات جميعها إرتشاح الخلايا احادية النواة (100%)، متبوعة بنشاط الخلايا المتعادلة (84%)، وضمور غددي (22%)، وتبدل معوي (14%) ونمو شاذ للنسيج في (9%) من الحالات. وتم اكتشاف الجرثومة الحلزونية البوابية في (77%) من الحالات والتوصل إلى وجود علاقة احصائية معنوية بين هذه الجرثومة وكل من إرتشاح الخلايا احادية النواة ($p < 0.001$) ونشاط الخلايا المتعادلة ($p < 0.001$) والضمور الغددي ($p < 0.05$) بينما لوحظ ارتباط احصائي غير معنوي بين الجرثومة الحلزونية البوابية وكل من التبدل المعوي والنمو الشاذ للنسيج ($p < 0.05$).

الاستنتاج: تعد الدراسة النسيجية المرضية للخزعة النازظورية لغار المعدة ذات قيمة في اكتشاف الجرثومة الحلزونية البوابية والتغيرات النسيجية المختلفة لالتهاب المعدة المزمن.

تم التوصل إلى ارتباط مهم احصائياً بين الجرثومة الحلزونية البوابية وكل من إرتشاح الخلايا احادية النواة ونشاط الخلايا المتعادلة والضمور الغددي.

يُعد النمو الشاذ للنسيج تغيراً نسيجياً مهماً في التهاب المعدة المزمن يتطلب متابعة نازظورية لاستبعاد احتمالية حدوث سرطان المعدة، ويُصحح أن يتم احتوائه في المقياس المماثل المرئي لنظام سيدني المُحدَّث.

الكلمات المفتاحية: التهاب المعدة المزمن، خزعة غار المعدة، نظام سيدني المُحدَّث.

INTRODUCTION

Inflammation of gastric mucosa is the simple definition of gastritis¹, and chronic gastritis is recognized by chronic inflammatory cell infiltration of the gastric mucosa, mainly plasma cells and lymphocytes (sometimes with lymphoid follicle formation), leading to eventual atrophy of the glandular epithelium and intestinal metaplasia which is strongly related to increased risk of gastric carcinoma².

There are many etiological factors of chronic gastritis, however the most common cause is infection with the bacillus *Helicobacter pylori*³⁻⁵. which most often presents as antral gastritis and gastric biopsy generally demonstrates *H. pylori* as spiral-shaped or curved bacilli, concentrating within the superficial mucus of the surface epithelium and neck region of the glands⁶.

Gastritis was classified in different ways, however to avoid confusion, a system was proposed in 1991 for microscopic reporting of gastritis referred to as "The Sydney System" which included a spectrum of morphological, topographical and possible etiological factors of gastritis⁷. The value of this system lies in grading of different histological parameters of chronic

gastritis including: *H. pylori* density, mononuclear cell infiltration (as a sign of chronic inflammation), neutrophilic infiltration (as a sign of activity), glandular atrophy and intestinal metaplasia, using the visual analogue scale of the up-dated Sydney system⁸.

AIMS OF THE STUDY

To evaluate various histological parameters of chronic gastritis in endoscopic antral biopsies, to grade them according to the up-dated Sydney system, and to compare the obtained results with those of others.

MATERIAL AND METHODS

Over the period from the 1st of July 2018 to the end of December 2018, 100 endoscopic biopsy specimens were obtained from gastric antrum of patients complaining of different clinical symptoms referred for upper gastrointestinal endoscopy at Al-Salam Teaching Hospital in Mosul. The clinical data concerning the presenting symptoms of patients were obtained from the submitted request forms.

Each biopsy specimen consisted of 2-3 tissue fragments, fixed in 10% formalin, processed according to the standard histopathology techniques and stained with the routine hematoxylin-eosin stain, in addition to modified Giemsa stain for a proper demonstration of *H. pylori*⁹.

Sections were assessed for the histological parameters of chronic gastritis, together with grading of these parameters using the visual analogue scale of the up-dated Sydney system presented in **Figure 1**.

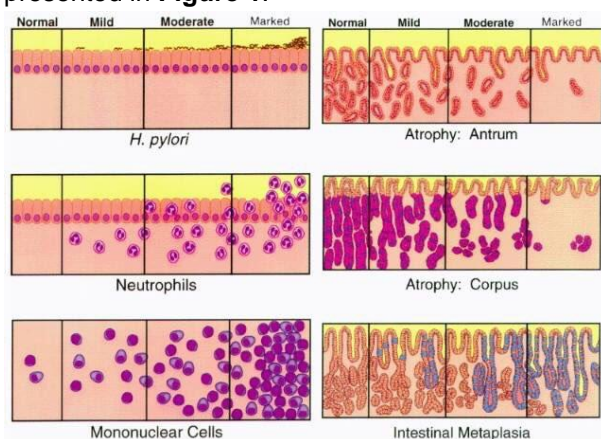


Figure 1: Visual analogue scale for grading of chronic gastritis: The Up-dated Sydney System⁸.

Results were statistically analyzed using Z-test of one proportion in which P-value<0.05 was regarded as a significant result.

RESULTS

The 100 endoscopic antral gastric biopsies were analyzed as follows:

Distribution According to Age and Sex

Patients were distributed over a wide age range from 9 to 85 years, with a mean of 42.7 years and a peak age incidence in the fourth decade.

There were 42 males and 58 females with a male to female ratio of 1: 1.3. **Figure 2**.

Clinical Symptoms

The main complaint was epigastric pain in 46 (46%) cases, followed by dyspepsia in 17(17%) cases, nausea and vomiting in 16 (16%) cases and upper GIT bleeding in 10 (10%) cases. The rest was presented with weight loss in 7(7%) cases and anemia in 4(4%) cases.

Endoscopic Results

Information regarding endoscopic findings was available in all cases including: isolated antral gastritis in 66 (66%) cases, pangastritis in 13(13%) cases and gastritis limited to antrum and corpus in 11 (11%) cases. Moreover antral gastritis was found to be associated with GU in 6(6%) cases and with DU in 4(4%) cases.

Histological Findings

The obtained results regarding various histological parameters found in tissue sections together with grading of these parameters according to the up-dated Sydney system are summarized in **Table 1** and as follows.

1- *Helicobacter pylori*: It was demonstrated in 77(77%) cases out of 100, including 30 males and 47 females with a male to female ratio of 1: 1.5, and distributed among varying age groups with a higher rate of distribution in those 60 years and over. **Figure 3**.

H. pylori was found in mild density in 39(50.6%) cases, moderate in 31(40.3%) cases while severe density was recorded in 7(9.1%) cases only. **Figure 4**.

2-Mononuclear cell infiltration: Chronic inflammation represented by mononuclear cell infiltration was detected in all the 100(100%) cases **Figure 5**, with varying degrees where 17(17%) cases showing mild infiltrate, 56(56%) cases moderate and 27(27%) cases were characterized by severe mononuclear cell infiltration, of which 4 cases have also demonstrated lymphoid follicles with germinal centers formation. **Figure 6**.

3-Neutrophilic activity:Active inflammation represented by neutrophilic infiltration was detected in 84(84%) cases **Figure 7**, and was graded as mild, moderate and severe in 31(36.9%), 35(41.7%) and 18(21.4%) cases respectively.

4- Glandular atrophy:It was observed in 22(22%) cases **Figure 8**, and was mild in 8 (36.4%) cases, moderate in 11(50%) cases, while only 3(13.6%) cases have showed severe atrophic changes.

5- Intestinal metaplasia:It was found in only 14 (14%) cases **Figure 9**, out of which 7(50%) cases were mild, 4 (28.6%) cases moderate and severe in 3(21.4%) cases.

6- Dysplasia:Besides the above, dysplasia was another histological finding observed in 9(9%)

cases **Figure 10** , and graded as mild in 5(55.6%) cases, moderate in 2(22.2%) cases and severe in the last 2(22.2%) cases.

Correlation between histological parameters and *H. pylori*: Among the 100 cases that showed mononuclear cellinfiltration, *H. pylori* was detected in 77 (77%) cases, while undetected in 23 (23%) cases. Moreover all the 27 cases with severe mononuclear cell infiltration including those with lymphoid follicles formation were shown to be positive for *H. pylori*.

Concerning the 84 cases with neutrophilic infiltration, *H. pylori* was positive in 77 (91.7%) cases of them, while 7 (8.3%) cases that showed neutrophilic activity were negative for *H. pylori*.

In relation to glandular atrophy which was seen in 22cases,*H. pylori* was observed in 17(77.3%)

cases, however it was not observed in the rest 5(22.7%) cases.

Out of the 14 cases in which intestinal metaplasia was noticed, 10(71.4%) cases displayed *H. pylori*, while the remaining 4 (28.6%) cases did not.

Regarding the 9 cases of dysplasia, *H. pylori* was found in 6 (66.7%) cases, while it was not found in the other 3 (33.3%) cases.

Statistically, results were very highly significant regarding the association of *H. pylori* with both mononuclear cell infiltration and neutrophilic activity with P-value = 0.000. The result was also significant in relation to *H. pylori* and glandular atrophy with P-value = 0.011. However results were statistically not significant regarding the association of *H. pylori* with both intestinal metaplasia (P = 0.109) and dysplasia (P= 0.317). **Table 2** .

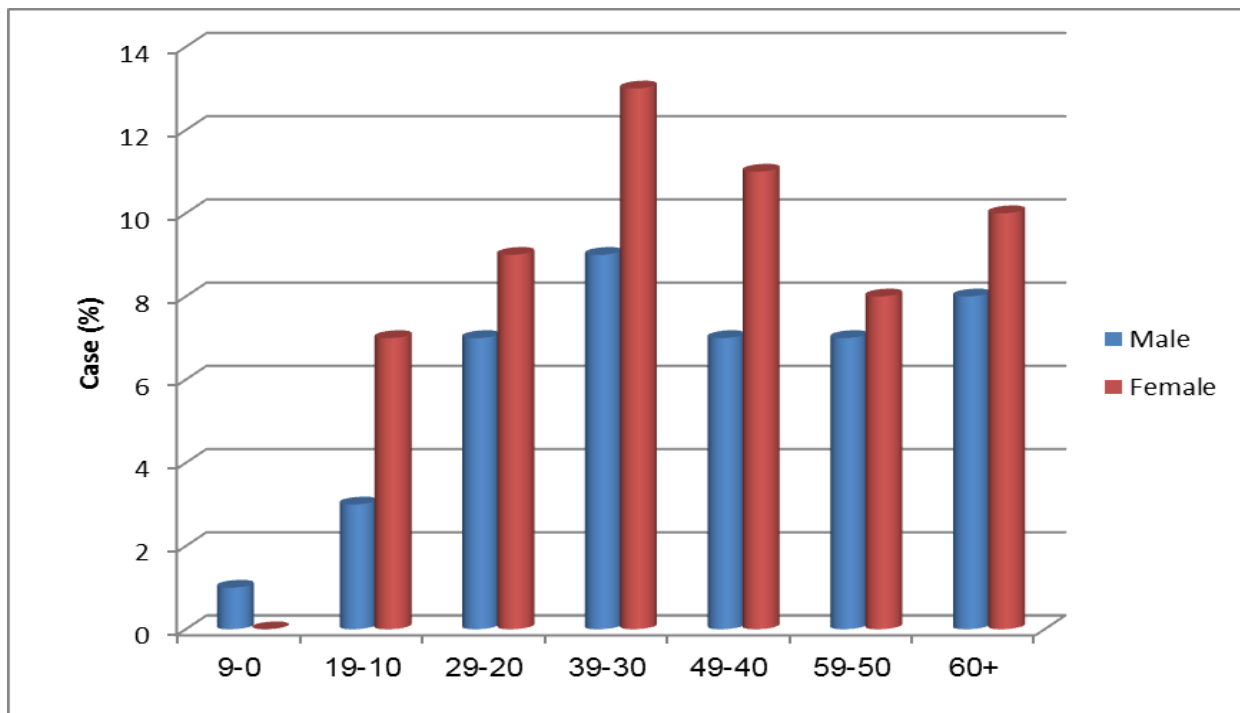


Figure 2: Distribution of patients according to age and sex

Table 1: Grading of histological parameters of chronic gastritis.

Parameters	No. of cases	Mild n(%)	Moderate n(%)	Severe n(%)
<i>H. pylori</i>	77	39(50.6%)	31(40.3%)	7(9.1%)
Mononuclear cell infiltration	100	17(17%)	56(56%)	27(27%)
Neutrophilic activity	84	31(36.9%)	35(41.7%)	18(21.4%)
Glandular atrophy	22	8(36.4%)	11(50%)	3(13.6%)
Intestinal metaplasia	14	7(50%)	4(28.6%)	3(21.4%)
Dysplasia	9	5(55.6%)	2(22.2%)	2(22.2%)

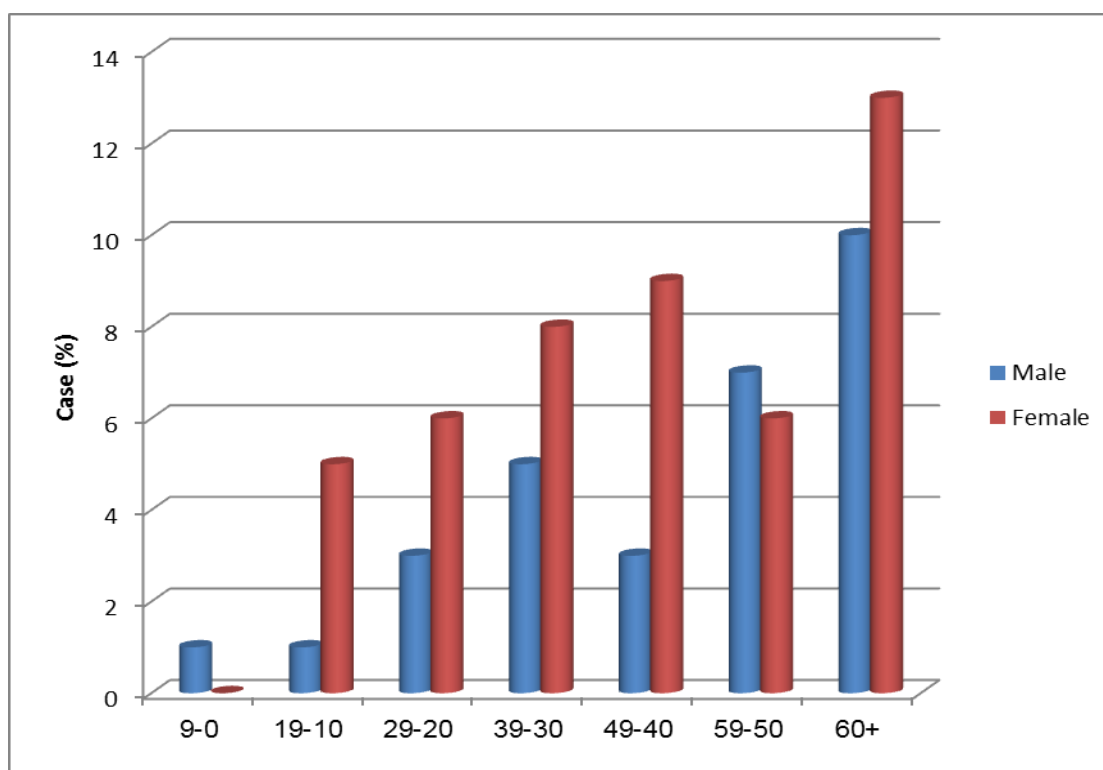


Figure 3: Distribution of *H. pylori* positive patients according to age and sex

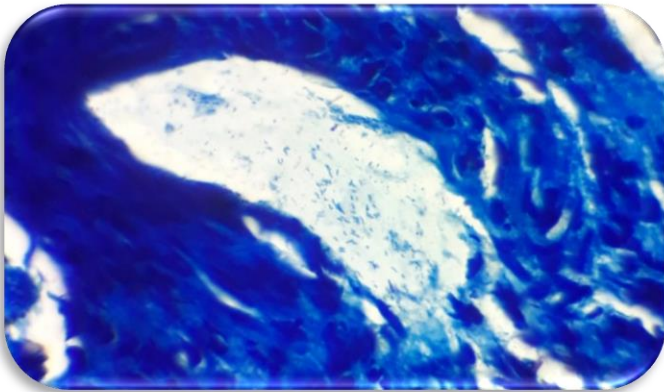


Figure 4: Antral gland demonstrating severe density of *Helicobacter pylori* (Giemsa stain X1000)

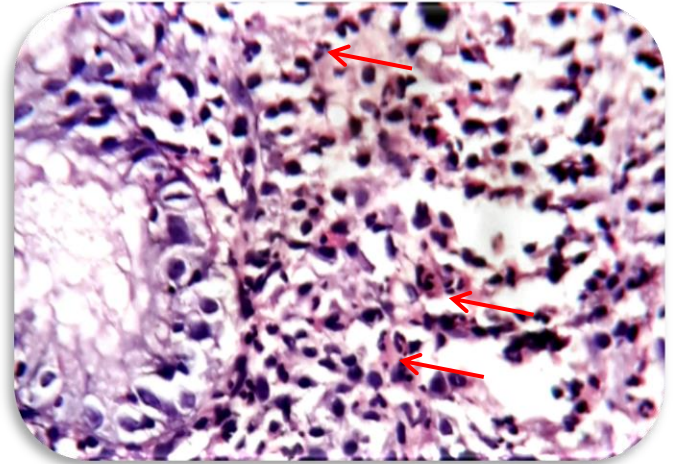


Figure 7: Antral mucosa with active inflammation (moderate grade of neutrophilic infiltration), (H&E X400).

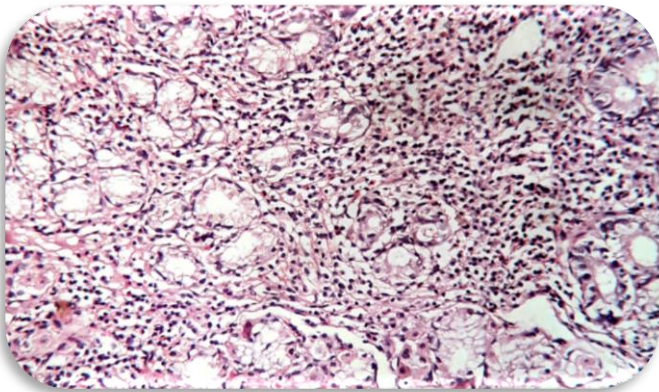


Figure 5: Chronic inflammation of the antral mucosa (severe grade of mononuclear cell infiltration), (H&E X100)

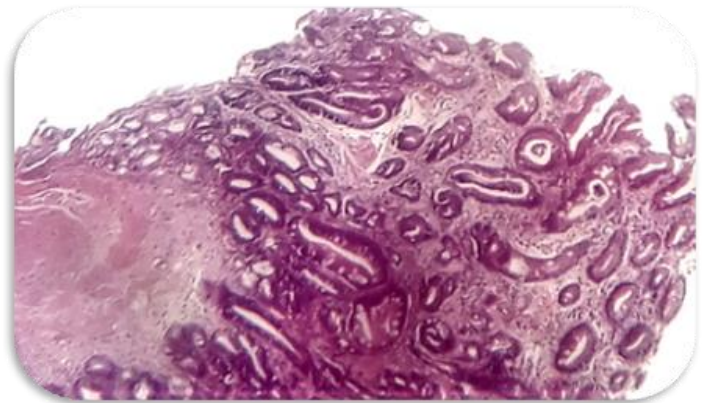


Figure 8: Moderate glandular atrophy of the antral mucosa (H&E X40)

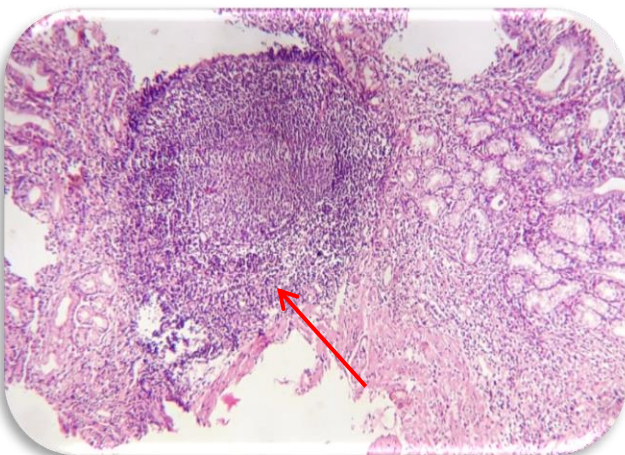


Figure 6: Lymphoid follicle formation in a severely inflamed antral mucosa (H&E X40)

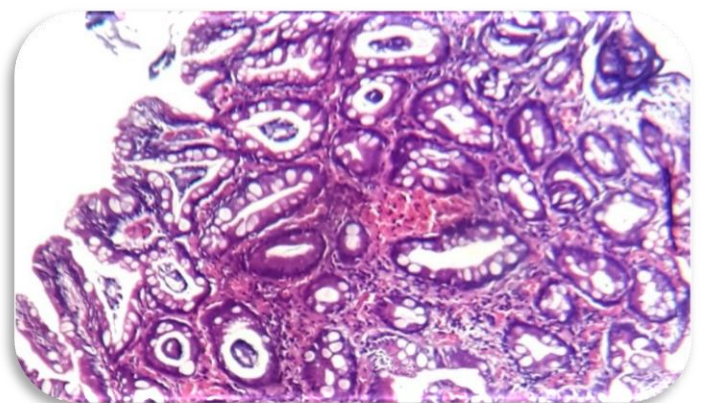


Figure 9:- Antral mucosa with severe intestinal metaplasia (H&E X100)

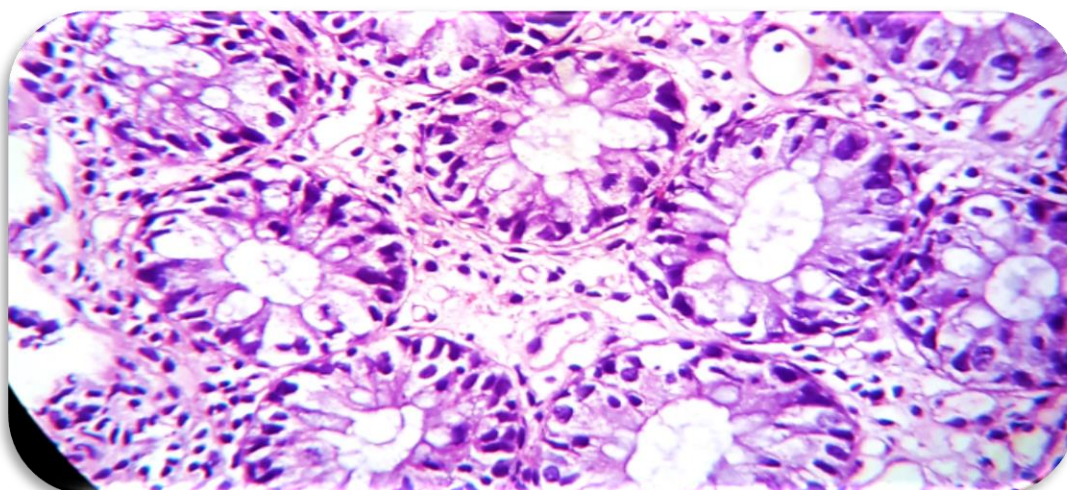


Figure 10: Antral glands with severe dysplastic changes (H&E X400).

Table 2 : Association between *H. pylori* status and histological parameters of chronic gastritis

Parameters	No. of cases	<i>H. pylori</i>		P-value
		Positive	Negative	
Mononuclear cell infiltration	100	77(77%)	23(23%)	0.000*
Neutrophilic activity	84	77(91.7%)	7(8.3%)	0.000*
Glandular atrophy	22	17(77.3%)	5(22.7%)	0.011**
Intestinal metaplasia	14	10(71.4%)	4(28.6%)	0.109***
Dysplasia	9	6(66.7%)	3(33.3%)	0.317***

*: Very highly significant (p < 0.001)

** : Significant (p < 0.05)

***: Not significant (p > 0.05)

DISCUSSION

In the present study, chronic gastritis was noticed in a wide age group ranging from 9–85 years with a mean age of 42.7 years which is more or less consistent with other studies where

the mean age was 47 years,¹⁰⁻¹³ and 48 years in another one¹⁴. However chronic gastritis was reported in an older age group in another previous study with a mean of 65.8 years¹⁵.

In this study an increase in the rate of *H. pylori* infection with increasing age (60 years and

above) was observed which is in agreement with the results of other studies¹⁶⁻¹⁸. On the other hand 3 cases of chronic gastritis were recorded in children 10 years and below, 2 (66.6%) of them showed no evidence of *H. pylori*, which was inconsistent with a previous study that showed an increased rate of *H. pylori* infection in children¹⁹. Probably, the low number of children patients involved in this study has affected the proper assessment of *H. pylori* infection rate in this age group.

A predominance of females having chronic gastritis has been noticed in this study with a M:F ratio of 1:1.3 which is in line with the study of Maharjan et al, in which M:F ratio was 1:1.07¹⁵. On the contrary a higher M:F ratio was observed in many previous studies carried out by Chen et al,²⁰ Pruthi et al²¹ and Park et al,²² where they reported a M:F ratio of 1.8: 1, 2.3:1 and 2.8:1 respectively.

In the same respect, females were found to have a higher rate of *H. pylori* infection than males, which is comparable to the result of a previous study¹⁵. However, such a finding is not in line with the findings of others where males were found to have the higher rate of *H. pylori* infection^{11,14,21}.

In the current study, the clinical symptoms the patients complaining of were variable, on the top of the list was abdominal pain mainly epigastric (46%) followed by dyspepsia (17%). Such results are consistent with that of a previous study which recorded these symptoms in (92%) and (42.3%) of cases respectively¹⁵. On the contrary, dyspepsia was the commonest presenting clinical symptom (33.3%), followed by abdominal pain (22.2%) in the study carried out by Pruthi et al²¹.

Gastric antrum was the site of endoscopic biopsy in the present study, as well as in the studies conducted by Garg et al¹¹, Park et al²², and Dhakhwa et al²³. Antral gastritis was the commonest endoscopic finding in this series (66%), which is comparable to another study where antral gastritis represented the main form of gastritis.⁽¹⁰⁾ However other studies showed antral ulcer and erosion as the major endoscopic findings^{15,21}.

In this series, *H. pylori* was identified in (77%) of cases which is similar to the study conducted by Latif et al²⁴, as well as in parallel with the results

of Kalifehgholi et al²⁵, Kumar et al²⁶, and Abdul Jabbar²⁷, that showed *H. pylori* in 86.8%, 78% and 75.3% of cases respectively. However higher *H. pylori* positive results were observed in the studies conducted by Hassan et al¹⁰, and Pourakbari et al²⁸, which were 93.7% and 95% respectively. On the other hand, the result of this study is relatively high when compared with the results of Pruthi et al²¹, and Dhakhwa et al²³, that displayed *H. pylori* in only 47% and 44% of cases respectively. The variation in the results above may be attributed to biopsy sampling, where multiple biopsies may be needed to improve results¹⁵, in addition, the use of special stain (e.g Giemsa) and immunostain are helpful for better detection of *H. pylori*^{29,30}. However poor identification of *H. pylori* may be affected by a prior treatment with proton pump inhibitors or antimicrobial agents¹⁵. In this respect, another biopsy from the corpus is advisable to obtain positive results for *H. pylori*^{31,32}.

Mononuclear cell infiltration formed the major histological variable in the present study, since it was encountered in all cases (100%) which is similar to the studies conducted by others^{11,19,22,33}. More than half of cases (56%) showed moderate grade of mononuclear cell infiltration, while severe grade was found in (27%) of cases and the mild one was restricted to (17%) of cases only. These results were comparable to those of others^{19,22,33}. Moreover *H. pylori* was detected in (77%) of cases with mononuclear cell infiltration which is regarded statistically as a very highly significant result ($P < 0.001$) and that is consistent with a previous study¹⁵. In the same connection, as the grade of mononuclear cell infiltration was higher, the possibility of *H. pylori* detection was more and with increased density. This is consistent with the results of other studies^{11,19,34}, however it is inconsistent with the study of Udoh et al that found no association between the grade of mononuclear cell infiltration and density of *H. pylori*¹⁴. In addition, the 4 cases of those having severe mononuclear cell infiltration with lymphoid follicles formation also displayed *H. pylori* in all of them which is compatible with the study of Dhakhwa et al²³. However other studies found *H. pylori* in about half of the cases with lymphoid follicles^{21,35}. The importance of lymphoid follicles formation lies in being a characteristic feature of

chronic *H. pylori* infection and the absence of the organism in such cases is more in favour of being missed by the examiner, or the infection being eradicated⁸.

Active inflammation represented by neutrophilic infiltration in the lamina propria or inside the glandular lumina was observed in (84%) of cases which is in line with the study conducted by Park et al, in which the result was (78.7%)²². However, the result in the present study outnumbered that observed in a previous one which showed only (33.6%) of cases having neutrophilic activity.⁽¹⁵⁾ On the other hand, neutrophilic infiltration was noticed in all *H. pylori* positive cases which is compatible with the study of Dhakhwa et al²³, while it was present in (40.7%) of *H. pylori* positive cases in the study of Maharjan et al¹⁵. Neutrophilic infiltration was shown to be a sensitive indicator for the presence of *H. pylori* and disappears following the treatment of infection³⁶.

In this study a very highly significant association was found between neutrophilic infiltration and the presence of *H. pylori* ($P < 0.001$). This is comparable to other studies in this concern^{11,23,37}. In the current study 7 (8.3%) cases were found to have neutrophilic infiltration, and they were negative for *H. pylori*. Here of the many possible etiological factors, Crohn's disease may be considered, in addition to drug or alcohol induced and bile reflux gastritis⁸.

Atrophic changes of the mucosa were found in (22%) of cases in the present study. This is relatively higher than that of Garg et al study which showed atrophy in (12.3%) of cases¹¹. Most of the cases of atrophy were seen in patients >50 years of age which is in agreement with other studies^{15,21,38}. Moreover 17 (77.3%) cases of atrophic gastritis were also positive for *H. pylori* that was more or less consistent with the result of Pruthi et al which was 62.5%²¹. Likewise a significant association was found between atrophy and the presence of *H. pylori* ($P < 0.05$), which is in contrast with the findings of others where the association was statistically insignificant^{11,15}.

Intestinal metaplasia was encountered in (14%) of cases which is consistent with Hassawi study which recorded this change in 15% of cases³⁹. However our result is higher than that recorded by Dhakhwa et al in which intestinal

metaplasia was found in only 5% of cases²³. On the other hand, a higher rate was found in the study of Al- Nuaimy et al in which 23% of cases showed intestinal metaplasia¹⁶. The latter may be attributed to the fact that the use of special stain for mucin could improve the diagnostic rate of intestinal metaplasia. In the same respect, biopsy taken from the area of incisura angularis is said to be of value concerning the detection of intestinal metaplasia which initially develops in this region⁴⁰. There was no significant statistical association between *H. pylori* and intestinal metaplasia ($P > 0.05$). This finding is in parallel to what has been discussed elsewhere^{15,23}.

Dysplasia was another important histological variable observed in this study. It has been mentioned to have resulted from exposure of gastric epithelium to free radicals damage and proliferative stimuli resulting from chronic inflammation which over time can lead to carcinoma⁶. This study revealed dysplasia in 9% of cases which is more or less consistent with the study of Hassan et al in which 6.4% of cases showed dysplastic changes¹⁰. However, the finding of this study is in disagreement with that of Al- Nuaimy et al where no dysplasia was recorded¹⁶, despite the fact that both studies were carried out in the same locality. One reason for this discrepancy may be the compromised immunity of people in our study due to the poor conditions they passed through in the previous years which rendered them vulnerable to *H. pylori* infection and chronic inflammation, that could induce this change.

Although *H. pylori* may no longer be detected in cases of dysplasia as mentioned by Dobrilla et al⁴¹, the organism has been identified in 6 (66.7%) out of the 9 cases of dysplasia in the present study. However this result is statistically insignificant as P -value was > 0.05 . Chronic atrophic gastritis associated with severe dysplasia requires periodic endoscopic follow up to rule out the possibility of gastric cancer, since the improvement of endoscopic techniques made possible the early detection of mucosal changes that predict malignancy⁴².

CONCLUSIONS

Histopathological study of endoscopic antral gastric biopsy is of value in detecting *H. pylori* and various histological changes of chronic gastritis.

– Statistically significant associations were found between *H. pylori* and each of : mononuclear cell infiltration, neutrophilic activity and glandular atrophy.

– Dysplasia is an important histological change in chronic gastritis that requires endoscopic follow up to rule out the possibility of gastric cancer, and it is advisable to be incorporated in the visual analogue scale of the up- dated Sydney system.

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