

MORPHOLOGICAL SPECTRUM OF GASTRIC LESIONS - ENDOSCOPIC BIOPSY FINDINGS

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ABSTRACT

Objective: A retrospective study was carried out to determine the morphological spectrum of gastric lesions at Pathology Department of Army Medical College, Rawalpindi for the duration of 02 years.

Study Design: Descriptive Study.

Patients and Methods: The gastric mucosal biopsies of 787 patients received from Gastroenterology unit of Military Hospital Rawalpindi from January 2002 to December 2003, were studied by routine histopathology methods.

Results: A high frequency of gastric disease in males with a male to female ratio of 6:1 and an age range of 09 years to 85 years were observed. The clinical presentations mostly seen were abdominal pain, dyspepsia, vomiting, diarrhoea, decreased appetite and weight loss. On endoscopy the most frequently suspected lesions were gastritis 662(84.12%), stomach growth 45(5.72%), gastric ulcers 10(1.27%), while 70(8.89%) cases showed unremarkable mucosa. The histopathology revealed chronic non-specific gastritis 676(85.89%) followed by malignant tumours 45(5.72%), benign neoplasms 3(0.38%) and gastric ulcer 10(1.27%). A number of biopsies 53(6.73%) were unremarkable histologically.

Conclusion: The more prevalent lesions in this series were chronic active gastritis followed by tumours and gastric ulcers. H. pylori associated gastritis was seen in majority of the patients. Thus gastric biopsy is an essential tool for diagnosis and confirmation of clinically suspected cases.

Keywords: Gastritis, endoscopy, dyspepsia, gastric ulcer, gastric tumours

INTRODUCTION

The upper gastrointestinal flexible fiberoptic endoscope was first used in 1968 and proved to be a major break through in the diagnosis of oesophago-gastro-duodenal lesions [1]. The endoscopic biopsy not only permits exact diagnosis of specific entity but also provides an opportunity to see H. pylori status and plans for specific medical or surgical therapy [2,3]. Endoscopic screening may detect gastric mucosal lesions at an early stage especially atrophy, intestinal metaplasia and dysplasia so as to prevent progress of these lesions to invasive cancer [4,5].

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Diagnostic endoscopy is an invasive technique but has proved to be a simple, safe and well tolerated procedure [6]. In routine clinical practice, histology is often considered as the "gold standard" against which other tests are compared. Biopsy provides an excellent opportunity for the clinician and histopathologist to correlate the clinical data, endoscopic findings and pathological lesions. Using 2.8 mm channel endoscope reduces the risks of sampling error and taking multiple biopsy samples from antrum and corpus parts of gastric mucosa. The false negative histology results could be due to sampling error and recent or concurrent therapy with drugs while false positive histology can occur if the equipment is not properly cleaned [7,8].

Helicobacter pylori (*H. pylori*) was identified by Warren and Marshall [9] in 1983 in gastric antral mucosa, which is associated with chronic gastritis, peptic ulcer [10], non-ulcer dyspepsia, gastric carcinoma and B-cell mucosa associated lymphoid tissue (MALT) lymphoma [11-14]. This has gained even more importance since *H. Pylori* has also been classified as group 1 carcinogen by the World Health Organization (WHO) due to its role in the aetiology of gastrointestinal cancers [15,16].

This study was planned to determine the spectrum of gastric lesions, which can be diagnosed with this technique.

MATERIALS AND METHODS

Seven hundred and eighty seven consecutive endoscopic gastric biopsies received during January 2002 to December 2003, were studied in the department of Pathology, Army Medical College, Rawalpindi. This is a descriptive and retrospective study. The specimens were mostly received from the Gastroenterological unit of Military Hospital, Rawalpindi. The patients were both serving/ retired military personnel as well as civilians living in Rawalpindi and its suburbs. The relevant clinical information and demographic data was obtained from the laboratory request form. The gastrointestinal symptoms included abdominal pain, dyspepsia, vomiting, diarrhoea and weight loss. Patients of all ages and both sexes having undergone gastric biopsy were included in the study.

The patients were prepared for gastric endoscopic examination by Olympus CLE-10 gastrocope. The tissue was fixed in 10% formaldehyde, routinely processed in an automatic tissue processor (Model RH-12 EP Sakura, Japan) for 17 hours and then embedded in paraffin wax. Three to five sections of 4 micron thickness were cut on rotary microtome (Model 1512 Leitz, England) and routinely stained with Haematoxylin and Eosin (H&E) and Toluidine blue stain in ultra histodyer (Model RSH 100-11 Sakura, Japan). The tissue blocks

were serially sectioned. In selected cases Periodic-acid Schiff (PAS) staining was also performed to detect signet ring cancer cells. The tumours were classified according to the WHO classification of gastric tumours.

All these biopsies were graded morphologically according to updated Sydney system emphasizing the importance of combining topographical, morphological and etiological aspects together for making clinical diagnosis of chronic gastritis, whereas revised Sydney System in Houston (1994) divided chronic gastritis into atrophic and other special forms of gastritis [17].

Majority of the biopsies were taken from antral part of gastric mucosa and revealed activity by the presence of polymorph neutrophils in the lamina propria, in the intraepithelial sites or both. *Helicobacter pylori* were mostly identified in the antral biopsies and correlated with the activity in the antral glands. Two pathologists examined the sections independently and final histological diagnosis was made in the light of clinical and endoscopic findings [18,19].

STATISTICAL ANALYSIS

SPSS version 10.0 was used to analyze the data. Percentages were calculated to describe the data.

RESULTS

Gastric mucosal biopsies of 787 patients were studied between 2002 to 2003 at the Pathology Department. The age of patients varied from 09 to an age of 85 years. The majority of the patients belonged to 5th and 6th decades (fig. 1)). Out of 787 gastric biopsies, 677(86%) were from male patients and 110(14%) from female. Male to female ratio was 6 : 1.

The majority of the patients were biopsied for either gastritis or tumours of stomach. In a few cases the clinical diagnoses was dyspepsia, pernicious anaemia, gastric / duodenal ulcer or chronic diarrhoea. The specimens varied from 1 to 4 tiny fragments of antral / body parts of the stomach tissue

(average 2-3), each not more than 2 to 3 mm in diameter. Only three specimens were declared inadequate for histological opinion.

The endoscopy showed preponderance of gastritis (84.12%), followed by gastric tumours (5.72%), gastric ulcers (1.27%) and normal appearing mucosa (8.89%). Histologically, majority of cases showed chronic non-specific gastritis followed by tumours and ulcers. More definite categorization of the various morphological lesions is depicted in (tables-1&2) whereas H. pylori association in various gastric lesions is shown in (table-3).

In 53 (6.73%) cases., no pathological findings were seen, therefore, these were reported as unremarkable gastric tissue Out of 676 cases of chronic nonspecific gastritis, 401 (59.32%) cases revealed mild inflammation, 172(25.44%) biopsy specimens showed moderate inflammation and severe degree of inflammation was noted in 103 (15.24%) patients. In 472 cases of chronic active inflammation, mild, moderate and severe activity (presence of neutrophils) was noted in 268(56.80%), 128(27.10%) and 76 (16.1%) respectively.

Various degrees of dysplastic changes in cases of chronic non-specific gastritis are shown in (fig. 2). Out of 472 cases, 47(10%) H. pylori associated chronic active gastritis also revealed atrophic and intestinal (Goblet Cell) metaplastic changes.

DISCUSSION

Biopsy sampling of the gastric mucosa at diagnostic endoscopy provides a useful information which helps in the diagnosis of various lesions [1,3]. Good clinical and endoscopic information is a fundamental part of "adequacy" and this strongly affects how a biopsy should be read. However, the precise diagnosis becomes more certain on histopathological examination. The most common indications for gastric biopsy are; to detect various types of gastritis along with evidence of Helicobacter pylori status, gastric ulcers and different tumours [4 - 6,20].

Demographic data related to age, sex and the clinical presentation in our cases showed trends similar to other reported studies [21,24,27,38]. Majority of the cases (>95%) in this series revealed lesions in the antral part of gastric mucosa. In our biopsy specimens, material was technically adequate and it is comparable to other studies [18,20].

Majority of the patients who underwent biopsy were having complaints of dyspepsia along with clinical diagnosis of pernicious anaemia, gastric / duodenal ulcer, chronic diarrhoea or evidence of gastric outlet obstruction. Our study cases on endoscopic examination were having 65.05% antral gastritis followed by 13.97% pangastritis. No specific symptoms could be attributed to H. pylori infection, as there was no difference in symptomatology between H. pylori positive and H. pylori negative patients. These results are in conformity to a previous study [21]. Endoscopic appearance of gastric mucosa in 70 cases was normal. Fifty three (75.71%) of 70 cases revealed unremarkable gastric mucosa on histological examination. Whereas 17 biopsies showed mild chronic nonspecific inactive gastritis, not associated with H. pylori infection. Therefore in few cases no correlation between endoscopic findings and histologic gastritis was found which is also consistent with previous studies [22,23].

Histologically 85.89% cases revealed chronic active gastritis and chronic inactive gastritis and H. pylori positivity was seen in 70% of cases in our study. Similar results have been seen in a study by Schultz et al [24], which showed 87% cases having chronic active gastritis, and 87.7% gastric biopsies were positive for H. Pylori. In other series over all infectivity of H. pylori was 83% in adult population undergoing GI endoscopy for various reasons [25,26]. However another study revealed frequency of 46.23% and 77.78% H. pylori infection in gastritis patients who presented with non-ulcer dyspepsia and duodenal ulcer respectively [27].

A study by Fareed [28], had shown similar results narrating that high density of

H. pylori in the antrum was due to its alkaline pH and a direct association of neutrophilic activity with H. pylori density. In another study 57% antral mucosal biopsy specimens showed positivity for H. pylori microorganisms [29]. Majority of our cases (70.26%) also showed H. pylori infection and correlated with the presence of neutrophils and lymphocytes in the lamina propria. It shows the causative role of H. pylori in peptic ulcer disease and non-ulcer dyspepsia in Pakistan as also suggested by other studies [27-29].

H. pylori negative chronic gastritis patients could be due to effects of drug therapy or failure to see H. pylori in the tissue specimens. Out of 472 cases, 47(10%) H. pylori associated lesions showed chronic atrophic changes and intestinal metaplasia, which is comparable to other studies revealing similar changes in 12 to 16 % of their cases [30, 31].

The histopathological findings in gastric biopsies did not correlate with the patients who were clinically diagnosed as pernicious anaemia. This is in contrast to a study done by Sari [32], which showed chronic atrophic gastritis and intestinal metaplasia in 26.6% patients each and dysplasia in 10% cases.

In our study, gastric biopsy revealed malignant tumours in 45(5.71%) cases which were clinically also suspected of gastric tumours. A diagnostic yield of over 95% has been claimed for endoscopic gastric biopsy undertaken for a suspected neoplasm especially in the advanced stages [33,34]. Helicobacter pylori has been found in 30/45 cases (62.50%) in this study where as other series revealed one-third of patients having gastric cancer were associated with H. pylori infection [15,35-37]. The other morphological features observed in gastric adenocarcinoma cases included atrophic changes in glands, intestinal (goblet cells) metaplasia and dysplasia along with evidence of H. pylori

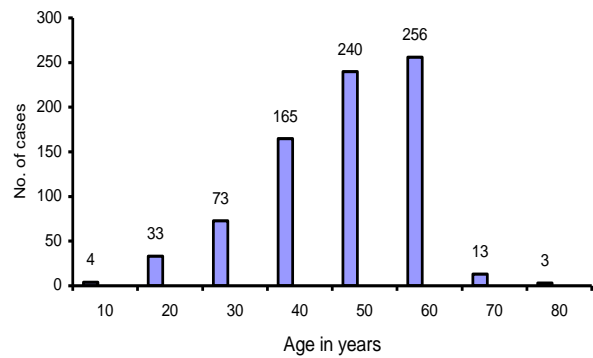


Fig. 1: Age wise distribution of the study cases (n=787)

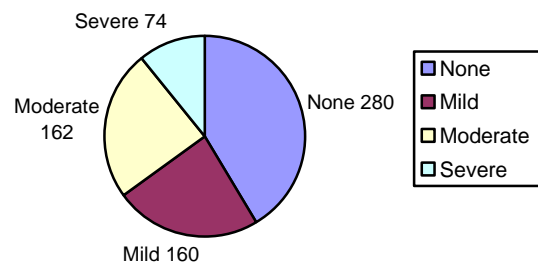


Fig. 2: Grades of dysplastic changes in chronic active gastritis (n=676)

Table-1: Pattern of non-neoplastic lesions in gastric biopsies (n=686)

Types of Lesions	No. of Cases	%age
Chronic nonspecific active gastritis	472	68.80
Chronic inactive gastritis	204	29.73
Gastric ulcer	10	1.47

Table-2: Spectrum of benign and malignant tumours in endoscopic gastric biopsies (n=48)

Types of Tumour	No. of Cases	%age
Malignant tumours		
Adenocarcinoma	42	87.51
Gastrointestinal stromal tumour (GIST)	02	4.16
Non-Hodgkin Lymphoma (Diffuse large cell type)	01	2.08
Benign tumours		
Leiomyoma (GIST)	01	2.08
Gastric adenomatous polyps	02	4.16

Table-3: H. pylori positivity in study cases (n=787)

Type of Lesions	No. of cases	H. Pylori +ve Cases	%age
Chronic nonspecific active gastritis	472	400	84.74
Chronic inactive gastritis	204	75	36.76
Tumours	48	30	62.50
Gastric Ulcers	10	4	40.0
Unremarkable cases	53	0	-

infection [15,38]. Similar changes have been documented in our study cases.

One case of primary malignant lymphoma of stomach was detected in this series, which also revealed changes in adjoining mucosal tissue such as chronic atrophic gastritis, intestinal metaplasia and marked dysplastic changes with prominent lymphoid follicles. These observations correlate to other studies [39-41].

In our series, 3 cases of gastrointestinal stromal tumours (GIST) were diagnosed. Two were labeled as malignant tumours, whereas one of 45 clinically suspected tumours proved to be a case of gastric leiomyoma on histopathological examination and it is comparable to other studies in which gastric leiomyoma mimicked a carcinoma [42,43].

CONCLUSION

To conclude the fiberoptic diagnostic gastric endoscopy is relatively less invasive, cost effective and provides good diagnostic yield in confirming various gastric lesions. In this study, chronic active gastritis was the commonest lesion noted in the endoscopic antral biopsies. Majority of the cases were associated with *H. pylori* infection, which reveals its high prevalence in Pakistan. Malignant tumors as a group were next frequently seen pathological entity.

REFERENCES

1. Blackstone MO. Endoscopic Interpretation. Normal and pathologic appearances of the Gastrointestinal tract. **Raven Press New York 1984; 1: 13-15.**
2. Sipponen P, Stolte M. Clinical impact of routine biopsies of the gastric antrum and body. **Endoscopy 1997; 29: 671-8.**
3. Sipponen P. Update on the pathologic approach to the diagnosis of gastritis, gastric atrophy and *Helicobacter pylori* and its sequelae. **J Clin Gastroenterol 2001; 32: 196-202.**
4. Suvakovic Z, Bramble MG, Jones R, Wilson G, Idle N, Ryott J, et al. Improving the detection rate of early gastric cancer requires more than open access gastroscopy: a five year study. **Gut 1997; 41 (3): 308 - 313.**
5. Barr H. Endoscopic screening for upper gastrointestinal malignancy. Westaby D, Lombard M. In: Therapeutic Gastrointestinal Endoscopy. **Martin Dunitz Ltd (UK) 2002; 54-56.**
6. Pasricha PJ - Gastrointestinal Endoscopy. Lee Goldman J, Claude Bennett. In. Cecil Textbook of Medicine **W B Saunders 2000; 21: 649-650.**
7. Duggan AE, Legan RPH. *Helicobacter Pylori*: Diagnosis and management. Bloom S. In; Practical **Gastroenterol 2002; 471 - 473.**
8. Silverstain MD, Petterson T, Talley NJ. Initial endoscopy or empirical therapy with or without testing for *Helicobacter pylori* for dyspepsia: a decision analysis. **Gastroenterol 1996; 110: 72 - 83.**
9. Warren JR, Marshall BJ. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. **Lancet 1983; 1: 1273 - 1275.**
10. Kazi JI, Jafarey NA, Alam SM et al. Association of *Helicobacter pylori* with acid peptic disease in Karachi, **J Pak Med Assoc 1990; 40: 240.**
11. Forman D, Webb P, Parsonnet J. *Helicobacter pylori* and gastric cancer. **Lancet 1995; 345: 1591-4.**
12. Bayer droffer E, Neubauer A, Rudolph B, Bayerdroffer E, Neubauer A, Rudolph B, Thiede C, Lehn N, Eidt S, et al. Regression of Primary gastric lymphoma of mucosa-associated lymphoid tissue after cure of *Helicobacter pylori* infection. **Lancet 1995; 345(8965): 1591 - 4.**
13. Price AB. The histological recognition of *Helicobacter pylori*. In Lee A, McGraud F (eds). *Helicobacter pylori*: techniques for clinical diagnosis and basic research. London: **W.B Saunders 1999; 33 - 49.**
14. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamagudi S, Yamakido M et al. *Helicobacter pylori* infection and the

- development of gastric cancer. **N Engl J Med** 2001; **345**: 784 - 9.
15. Versalovic J. Helicobacter pylori. Pathology and diagnostic strategies. **Am J Clin Pathol** 2003; **119**: 403 - 412.
 16. Madan E, Kemp J, Westblom TU, Subik M, Sexton S, Cook J, et al. Evaluations of staining methods for identifying Campylobacter pylori. **Am J Clin Path** 1988; **90**: 450.
 17. Dixon MF, Genta RM, Yardley JH, Correa P, et al. Classification and grading of gastritis. The updated Sydney system. **Am J Surg Path** 1996; **20**: 1161 - 81.
 18. Genta R, Graham D, Kihira K, Takimoto T, Saifuku K, et al. Comparison of biopsy sites for the histopathological diagnosis of H.pylori: A topographic study of H.pylori density and distribution. **Gastrontest Endosc** 1994; **40**: 342.
 19. Satoh K, Kimura K, Taniguchi Y, Kihira K, Takimoto T, Saifuku K et al. Biopsy sites suitable for the diagnosis of Helicobacter pylori infection and the assessment of the extent of atrophic gastritis. **Am J Gastroenterol** 1998; **93**: 569.
 20. Dominis M, Dzebro S, Gasparov S, Buljevac M, Colic-Cvrlje V, Banic M et al. Morphology of gastritis and Helicobacter pylori infection. **Lijec Vjesn** 2002; **124**: 36 - 42.
 21. Khaar HB, Umar M, Khurram M et al. Endoscopic and Histopathological Evaluation of 306 Dyspeptic patients. **Pak J Gastroenterol** 2003; **17**: 4 - 7.
 22. Rubin C. Are there three types of Helicobacter pylori gastritis? **Gastroenterol** 1997; **112**: 2108.
 23. Genta R, Hamner H. The significance of lymphoid follicles in the interpretation of gastric biopsy specimens. **Arch Pathol Lab Med** 1994; **118**: 740.
 24. Schultz M, Duarte I, Chianale J, Bravo R, Vergara MT, Lianos J et al. Frequency and histopathologic features of chronic gastritis in 300 patients without endoscopic lesions. **Rev Med Chil** 1996; **124**: 545 - 52.
 25. Qureshi H, Ahmed W, Syed S, Lodi TZ, Zuberi SJ et al. Helicobacter pylori clearance and its eradication in duodenal ulcer patients. **J Pak Med Assoc** 2004; **54**(8):63-4..
 26. Zaitoum AM. Histology compared with chemical testing for urease for rapid detection of Helicobacter pylori in gastric biopsy specimen. **J Clin Path** 1993; **46**: 684 - 85.
 27. Hussain S, Khattack JL. Clinical, Biochemical and Histopathological correlation of Helicobacter pylori infection in dyspepsia. **Pak J of Gastroenterol** 1994; **8**: 5-12.
 28. Fareed R, Abbas Z, Shah MA. Effect of Helicobacter pylori density on inflammatory activity in stomach. **J Pak Med Assoc** 2000; **50** (5) 148-51.
 29. Butt AK, Khan AA, Khan AA, Izhar M, Alam A, Shah S, Shafqat F et al. Correlation of Helicobacter pylori in Dental Plaque and Gastric mucosa of dyspeptic patients. **J Pak Med Assoc** 2002; **52**: 196 - 97.
 30. Satarkar RP, Sawant P, Nanivadekar S, Shroff C. Helicobacter pylori and intestinal metaplasia of gastric mucosa. **India J Gastroenterol** 1997; **16**: 16 - 7.
 31. Khan UF, Ashraf J, Qureshi S. Incidence of Intestinal Metaplasia in patients with Helicobacter positive gastritis. **J Rawal Med Coll** 2003; **19**: 12 - 4.
 32. Sari R, Ozen S, Aydogdu I, Yildirim B, Sevinc A. The pathological examination of gastric mucosa in patients with Helicobacter pylori-positive and negative pernicious anemia. **Helicobacter** 2000; **5**: 215 - 21.
 33. Yani H, Noguchi T, Mizumachi S, Tokiyama H, Nakamura H, Toda M, Okita

- K et al. A blind comparison of the effectiveness of endoscopic ultrasonography and endoscopy in staging early gastric cancer. **Gut** 1999; **44**: 361.
34. Mori M, Sugimachi K. Clinicopathologic studies of gastric cancer. **Semin Surg Oncol** 1990; **6**: 19.
35. Bhasin DK, Kakkar N, Sharma BC, Joshi K, Sachdev A, Vaiphei K, Singh K et al. Helicobacter pylori in gastric cancer in India. **Trop Gastroenterol** 1999; **20**: 70 - 2.
36. Takeuchi K, Ohno Y, Tsuzuki Y, Audo T, Sekihara M, Hara T, Kuwano H et al. Helicobacter pylori infection and early gastric cancer. **J Clin Gastroenterol** 2003; **36**: 321 - 4.
37. Uemura N, Okamoto S, Yamamoto S. H. Pylori infection and the development of gastric cancer. **Keio J Med** 2002; **51**: 63 - 8.
38. Malekzadeh R, Sotoudeh M, Derakhshan MH, Mikaeli J, Yazdanbod A, Merat S et al. Prevalence of gastric precancerous lesions in Ardabil, a high incidence province for gastric adenocarcinoma in the northwest of Iran. **J Clin Pathol** 2004; **57**: 37 - 42.
39. Arista - Nasr J, Herrera - Goepfert R, Lazos - Ochoa M, Pichardo R. Histologic changes of the gastric mucosa associated with primary gastric lymphoma in endoscopic biopsy specimens. **Arch Pathol Lab Med** 2000; **124**: 1628 - 31.
40. Ahmad A, Govil Y, Frank BB. Gastric mucosa - associated lymphoid tissue lymphoma. **Am J Gastroenterol** 2003; **98**: 975 - 86.
41. Fischbach W, Dragosics B, Kolve-Goebeler M, Ohmann C, Greiner A, Yang Q et al. Primary gastric B- cell lymphoma: Results of a prospective multicenter study. **Gastroenterol** 2000; **119**: 1191.
42. Pasta V, Monti M, Martino G, Merlino G, Bianchini GP, Boccaccini F et al. Gastric Leiomyoma. Diagnostic and surgical problem. **G Chir** 1999; **20**: 413-8.
43. Cademartiri F, Luccichenti G, Lucidi V, Cusmano F, Pavone P. Stromal malignant cancer with leiomyoma - like presentation. A case report. **Radiol Med** 2001; **80**-81.