Vol. 15, No. 4
ORIGINAL PAPER

MEDICINE

MEDICAL CHANNEL
OCTOBER - DECEMBER 2009

HISTOPATHOLOGIC SPECTRUM OF UPPER GASTROINTESTINAL ENDOSCOPIES

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ABSTRACT

OBJECTIVE: *To see the frequency of different endoscopy findings, Histologically classify chronic gastritis into H.pylori positive and H. pylori negative gastritis according to Sydney system and to see the frequency of esophagitis and duodenitis in H. pylori positive and H. pylori negative gastritis.*
DESIGN: *Retrospective Cross sectional study*
PLACE AND DURATION OF THE STUDY*: Endoscopy unit of medical unit one Civil Hospital Karachi,Jan 2006-Dec 2007*
MATERIAL AND METHOD*: A retrospective analysis of 1046 consecutive gross endoscopy findings and biopsies was done. All biopsies were done to investigate the different endoscopy lesions and also cause and type of gastritis. In every patient with gastritis on gross appearance three antral biopsies and in some corpus biopsy were taken and patients having any suspicious lesions were also biopsied. Biopsy specimens for gastritis were stained with Hematoxylin and Eosin and Gemisa staining, and analyzed according to Sydney classification by one single pathologist .*
RESULTS*: 1046 upper gastrointestinal biopsies were analyzed. Commonest Gross endoscopy findings was Gastritis in 83.4%. Histologically H pylori positive Gastritis in 37.3% and H pylori negative Gastritis in 53.2%*
According to Sydney classification inflammation was found more in H. Pylori negative gastritis ie 30.7% as compared to H. Pylori positive gastritis ie 5.3% (P value =0.001). whereas activity with neutrophil infiltration was found more in H. pylori positive gastritis i.e. 33.8% as compared to 19.8% in H. pylori negative gastritis (p value=0.001). On the other hand atrophy and intestinal metaplasia was not much different in two groups With H. Pylori positive gastritis ,duodenal ulcer was more common.
CONCLUSION*: Gastritis is the most frequent endoscopic finding. . Duodenal ulcer is more common as compared to gastric ulcer in our population and also more frequently seen in H Pylori positive cases.*
Active inflammation was more frequent in H pylori positive patients but the degree of atrophy and intestinal metaplasia did not differ in H. pylori positive and negative patients.
Regardless of the presence of H pylori ,quantifying the grade of gastritis with activity is important since this is related to the development of gastric cancer.

KEY WORD: Endoscopies, Histopathological spectrum

INTRODUCTION:

Upper gastrointestinal (GI) endoscopy is an established mode of investigation and treatment of a wide range of upper gastrointestinal conditions. In most cases it is the first line of investigation, comparing favourably with upper gastrointestinal radiographical studies and even giving better results. It is the best form of investigation for upper gastrointestinal bleeding because of its better diagnostic yield especially for superficial lesions such as oesophagitis, gastritis, duodenitis, Mallory Weiss tear etc. It also offers the opportunity for biopsy of lesions for histology in malignant disease, and histology, culture and urease test in Helicobacter pylori infection. It is also free from the possibility of exposure to ionizing radiation.[1] Upper gastrointestinal endoscopy is regarded as the investigation of choice in patients with upper gastrointestinal disorders which often present with dyspepsia.[2]. Helicobacter pylori (H. pylori), infection has been linked to acute and chronic gastritis, non-ulcer-dyspepsia, peptic ulcer, gastric adenocarcinoma and gastric non-Hodgkin's lymphoma of mucosa-associated lymphoid tissue (MALT). The

epithelial changes in H. pylori colonized gastric mucosa are easy to recognize in routine Haematoxylin & Eosin stained sections and are so distinctive that they can serve as a helpful histological indicator for the presence of H. pylori in gastric biopsies.[3] Chronic gastritis is a multifactorial disorder thought to be influenced by bacterial and host genetic factors. Histopathological examination is the mainstay of diagnosis, however features like the presence of Helicobacter pylori are difficult to evaluate on biopsy.[4] According to Gur G et al 2 biopsies for urease testing and 1 biopsy for histopathology obtained from the antrum or corpus of the stomach were sufficient to obtain the highest statistically significant diagnostic sensitivity[5] Following the discovery of Helicobacter pylori in 1983 and in an attempt to remove confusion in the diagnosis of various forms of gastritis the Sydney classification was introduced in 1990 and updated in Houston, Texas in 1994. The histological division of this classification utilizes graded variables. These include chronic inflammation, polymorphonuclear neutrophil activity, glandular atrophy, intestinal metaplasia and Helicobacter pylori density [6]

MATERIAL AND METHODS

A retrospective analysis of 1046 consecutive gross endoscopy findings and biopsies was done. Biopsy specimens were of 578 male and 468 female patients whose ages ranged from 20 to 86 years. All biopsies were done to investigate the different endoscopy lesions and also cause and type of gastritis, and to plan the patients treatment. In every patient three antral biopsies and in some corpus biopsy were taken. Eight hundred and seventy six biopsies were obtained from the antral region, Thirty three from the gastric corpus region, Eighty seven from duodenal region and Sixty from oesophageal region.

Biopsy specimens were cut into histological sections and stained with Hematoxylin and Eosin (H-E) and Gemisa staining, and analyzed by one single pathologist .

The following parameters were evaluated for gastritis: 1.Infiltration by polymorphonuclear cells in the corium and epithelium labeled as chronic active gastritis according to the Sydney system; 2. presence of lymphoid follicles labeled as chronic gastritis with inflammation; 3. presence of intestinal metaplasia; 4. presence of atrophic gastritis.5.presence or absence of H.pylori.

STATISTICAL ANALYSIS:

Results were analyzed by SPSS version-15. Frequencies were calculated in percentages. Chi square test was used to see the relationship between the categorical data and p-value less than 0.05 was taken as significant.

Table-1 Gross Endoscopy Findings:

Oesophagus	Stomach	Duodenum
Oesophagitis 27.6% (289/1046)	Gastritis 83.4% (872/1046)	Duodenitis 21.6% (226/1046)
Ca Oesophagus 4.7% (49/1046)	Gastric erosions 7.9% (83/1046)	Duodenal ulcer 9%(94/1046)
Oesophageal ulcer 4.3% (47/1046)	Gastric ulcer 3.8% (40/1046)	
Oesophageal candidiasis 0.9% (7/1046)	Gastric carcinoma 1.9% (20/1046)	

· Most cases had more than one finding

Table-2 Gastritis according to Sydney classification

Type of Gastritis	H.Pylori +	H. Pylori -	P- value
chronic active gastritis polymorph infiltration	33.8%	19.8%	0.001
chronic inflammatory gastritis	5.3%	30.7%	0.001
intestinal metaplasia	2.3%	4.1%	0.25
gastric atrophy	1%	5.2%	0.57

Table-3 Different Oesophageal and Gastric Carcinomas

Oesophagus	Stomach
Squamous Cell Carcinoma 2.4% (25/1046)	Adenocarcinoma in 0.8% (8/1046)
Undifferentiated Carcinoma in 1.1% (12/1046)	Undifferentiated in 0.9% (9/1046),
Adenocarcinoma 0.2% (2/1046)	Dysplasia in 0.1% (1/1046).
Dysplastic in 1% (10/1046)	Lymphoproliferative in 0.2% (2/1046).

RESULTS:

Two thousand two hundred and twenty six upper gastrointestinal endoscopy were performed during the year 2006-2007. About 1046 upper gastrointestinal biopsies were performed. Out of which 55.3% (n=578) were of male patients whereas 44.7% (n=468) were of female patients.

Gross endoscopy findings are described in Table 1

Antral biopsies were taken in 83.7% (876/1046), corpus biopsies in 3.2% (33/1046). Histopathologically H.Pylori positive gastritis in 37.3% (391/1046).H.Pylori negative gastritis in 53.2% (567/1046).

According to Sydney classification as described inTable-2 inflammation was found more in H. Pylori negative gastritis ie 30.7% as compared to H. Pylori positive gastritis ie 5.3% (P value =0.001). whereas activity with neutrophil infiltration was found more in H. pylori positive gastritis i.e. 33.8% as compared to 19.8% in H. pylori negative gastritis (p value=0.001).On the other hand atrophy and intestinal metaplasia was not much different in two groups

Different types of oesophageal and gastric carcinomas are described in Table-3

With H.Pylori positive gastritis,duodenal ulcer was seen in 15.6% whereas 7.2% of H.pylori negative gastritis had duodenal ulcers. On the other hand duodenitis was present in 26.6% and 20.4% respectively in H.pylori positive and H.pylori negative gastritis. Oesophagitis was found in 29.8% and 20.4% of H.pylori positive and negative gastritis respectively.

DISCUSSION:

The upper gastrointestinal flexible fibreoptic endoscope was first used in 1968 and proved to be a major break through in the diagnosis of oesophago-gastro-duodenal lesions. The endoscopy 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. Endoscopy 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 [7]

Good clinical and endoscopy 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 [8,9]

From 2006-2007 two thousand two hundred and twenty six endoscopies were done ,Usually biopsy was not done in normal mucosal appearance.1046 biopsies were performed. The most common endoscopy findings were gastritis including localized and pangastritis in 83.4% (872/1046), this was followed by oesophagitis in27.6% (289/1046), duodenitis in 21.6% (226/1046), duodenal ulcer 9% (94/1046) with various combination of lesions. This is similar to the results of Khalid Mehmood et al [10] where they found gastritis in 13.8%, oesophagitis in 11.1%. duodenal ulcer in 8.1%, duodenitis in 7% and gastric ulcer in 3.4%. Duodenal ulcer was more common than Gastric ulcer in our study and also in the above mentioned study . Whereas study in Nigeria by S K Mustapha. MT Bolori etal [2] showed oesophagitis in 227 (67%) of patients followed by gastritis including erosions 60% and duodenitis (27.9%) with considerable overlap in findings . They found more frequent gastric ulcer in 6.4% as compared to 4.8% duodenal ulcer .

On histopathology H pylori positive gastritis was seen in 37.3% (391/1046) and H pylori negative gastritis in 53.2% (567/ 1046). Previously we found equal frequency of H pylori positive and negative gastritis which was out of 306 patients, 47 % (n=144) were found to be H.pylori positive and 53 % (n=162) were H-pylori negative[11]. Study by Seed Afzal etal [7] showed majority of cases had H pylori positivity (70.2%) similarly Hamamatul Bushra Khan et al [12]also reported H pylori positive in 81% (n=248) subjects with dyspepsia and endoscopic and histopathologic evidence of gastritis. The less prevalence of H pylori in our patients may be due to the frequent use of H2 blockers , proton pump inhibitors and antibiotics . Nurdjanah etal [13] from Indonesia reported 21 (22.8%). H pylori positive patients out of 92 endoscopied and the high percentage tendency of H pylori positive in chronic atrophic gastritis with metaplasia, although most of the patients had superficial gastritis.

According to Sydney classification inflammation with activity demonstrated by polymorphonuclear cells more in H pylori positive cases as compared to H pylori negative gastritis. According to Mendonca et al [14] in H pylori positive cases the isolated finding with the higher specificity is the presence of polymorphonuclear cells in the stroma (activity) however, it has low sensitivity .

Different grades of inflammation intensity have already been observed in H. pylori infected and non-infected patients reporting that the diagnosis for this bacterial colonization cannot be based only on patterns of inflammation. et al [4]saw that the presence of H pylori is strongly associated with an acute and a chronic inflammatory infiltrate. The presence of neutrophils on biopsy is strongly associated with the presence of H pylori and with the density and the grade of the chronic inflammatory infiltrate. The chronic inflammatory response is an intermediary between the acute inflammatory process and glandular atrophy. The lymphocytic infiltrate is also a precursor lesion of the lymphoid follicles. The presence of mast cells does not appear to be related to any of the other inflammatory parameters. The presence of one feature is a strong indicator for the presence of other inflammatory features.

Atrophy and intestinal metaplasia was equally found in H pylori positive and H pylori negative gastritis in our study. Although Some studies have shown that intestinal metaplasia is less frequent in H. pylori non-infected patients [15,16,17] However, Gisele Alborghetti Na etal [18] found that 20.5% of biopsy specimens identified as H. pylori revealed intestinal metaplasia with no significant differences related to the concentration of bacteria ($P = 0.08$). 32.5% were cases without bacteria .This study showed no association between intestinal metaplasia and the presence of H. pylori. According to M E Craanen et al, their data did not prove a causal relationship between H Pylori infection and histogenesis of intestinal metaplasia, they suggested that HPylori plays an important role in the development of intestinal metaplasia in the gastric mucosa . whether H Pylori has to be present at all times during this process or is only necessary as a trigger needs further research .[19]

Japanese study showed that Glandular atrophy and intestinal metaplasia were found in more than half of H pylori positive patients but were remarkably low in H pylori negative patients. These results confirm the tight link between H pylori infection ,atrophic gastritis and intestinal metaplasia in the stomachs of Japanese. Ocassionally it was found in glandular atrophy and intestinal metaplasia tissues H pylori negative, while in the tissues without glandular atrophy or intestinal metaplasia it might be found H pylori positive. These findings suggest that most patients with intestinal metaplasia and glandular atrophy have been infected with H pylori at some stage. H pylori infection may provide the proper environment for atrophic gastritis and intestinal metaplasia to occur. At the final stage of the disease gastric atrophy with intestinal metaplasia is not a hospitable environment for H pylori and is associated with dramatic reduction or even disappearance of the organism.[20]

Also H. pylori infected Japanese patients showed severe atrophic and metaplastic gastritis in comparison with Nepalese. These results may be associated with the high incidence of gastric cancer in Japanese [21]

We found Atrophic gastritis and intestinal metaplasia more in patients >50years of age which is in accordance with previous studies. Atrophic gastritis is not a normal aging process, but instead is likely to be the result of H. pylori infection, while intestinal metaplasia is caused by both the aging process and H. pylori infection [22]

With H.Pylori positive gastritis .Duodenal ulcer was seen in 15.6% whereas 7.2% of H.pylori negative gastritis had duodenal ulcers. On the other hand duodenitis was present in 26.6% and 20.4% respectively in H.pylori positive and H.pylori negative gastritis. Oesophagitis was found in 29.8% and 20.4% of h.pylori positive and negative gastritis respectively. Previously we found The group of H.pylori +ve patients had isolated gastritis in 39.5%, gastroesophageal lesions in 22.9%, gastroduodenal lesions in 18.75% patients, and combination of lesions in oesophagus, stomach and duodenum in 18.75%. The group of H. pylori –ve patients had isolated gastritis in 42%, gastroesophageal lesions in 2I%, gastroduodenal lesions in 19 % and combinations of lesions in oesophagus, stomach and duodenum in 17.90%. Those results showed that the presence of H.pylori was not associated with increased frequency of any specific endoscopic lesion.[11]

The degree of oesophageal damage correlates positively with that in the duodenal mucosa, although the overall prevalence of erosive oesophagitis is not influenced by H. pylori [2 3]

CONCLUSION:

We conclude that grossly on endoscopy,

gastritis is the most frequent finding. Duodenal ulcer is more common as compared to gastric ulcer in our population and also more frequently seen in H Pylori positive cases.

H pylori negative gastritis was more frequent as compared to H. pylori positive gastritis. Active inflammation as seen by the presence polymorphonuclear cells was more frequent in H. pylori positive patients but the degree of atrophy and intestinal metaplasia did not differ. Although intestinal metaplasia was more in elderly patients. Regardless of the presence of H pylori ,quantifying the grade of gastritis with activity is important since this is related to the development of gastric cancer.

REFERENCES:

1. Aduful HK, Naaeder SB , Darko R et al. Upper Gastrointestinal Endoscopy at the Korle Bu Teaching Hospital, Accra, Ghana. Ghana Med J. 2007 March; 41: 12–16
2. Mustapha SK , Bolori MT, Ajayi NA et al. Endoscopic Findings And The Frequency Of Helicobacter Pylori Among Dyspeptic Patients In North-Eastern Nigeria. Highland Medical Research Journal 2007; 5: 78-81.
3. Kumar A, Bansal R, Kishore S et al. Histopathological changes in gastric mucosa colonized by H. pylori. Indian Journal of Pathology and Microbiology 2006; 49: 352-6.
4. Moorchung N, Srivastava AN, Gupta NK et al. The histopathology of chronic gastritis. Indian J Pathol Microbiol. 2007 Jan; 50: 18-24.
5. Gur G, Boyacioglu S, Demirhan B et al. The importance of increasing the number of gastric biopsies in the diagnosis of Helicobacter pylori. Hepato-gastroenterology Journal. 1998 Nov-Dec; 45 :2219-23.
6. Sylvester C. Nwokediuko, O. C. Okafor: Gastric Mucosa In Nonulcer Dyspepsia: A Histopathological Study Of Nigerian Patients. The Internet Journal of Gastroenterology. 2007; 5: 2.
7. Afzal S, Ahmad M , Mubarik A et al. Morphological spectrum of gastric lesions - endoscopic biopsy findings .pakistan armed forces medical journal . June 2006; 56:143-9.
8. Pasricha PJ, Lee Goldman J, Clande Bennett. Cecil Textbook of Medicine W B Saunders 2000; 21: 649-50.
9. Dominis M, Dzebro S, Gasparov S et al. Morphology of gastritis and Helicobacter pylori infection. Lijec Vjesn 2002; 124: 36 – 42.
10. Mahmood K, Saeedi M I, Mohammad R, Ziaud Din. Upper gastrointestinal Endoscopic findings in patients with dyspepsia J Postgrad Med Inst 2006 Mar; 20: 70-3.
11. Shaikh N A, Bhatty S, Kumari S, Akhtar S, Manzoor H, Aziz A , Altaf K. Endoscopic findings in Helicobacter pylori positive and negative patients with histologic gastritis Med Channel 2005 Mar; 11: 16-8.
12. Khaar H B, Umar M, Khurram M et al. Endoscopic and Histopathological Evaluation of 306 Dyspeptic Patients. Pak J Gastroenterol 2003 Mar; 17: 4-7.
13. Siti N, Bayupurnama, Putut. Histopathological pattern of gastric biopsies of helicobacter pylori positive patients in sardjito general hospital, yogyakarta, indonesia Journal of Gastroenterology and Hepatology. 2000 Dec; 15: 12, H11-H11(1).
14. Mendonça AL, Meneses AC, Chapadeiro E. Sensibilidade e especificidade de alterações histológicas da mucosa gástrica antral para o diagnóstico do Helicobacter pylori. J Bras Patol. 1999;35:125-32
15. Hui PK, Chan WI, Cheung PS, Chan JK, Ng CS. Pathologic changes of gastric mucosa colonized by Helicobacter pylori. Hum Pathol. 1992;23:548-56.
16. Rugge M, Di Mario F, Cassaro Met al. Pathology of the gastric antrum and body associated with Helicobacter pylori infection in non-ulcerous patients: is the bacterium a promoter of intestinal metaplasia? Histopathology. 1993;22:9-15.
17. Wang CC, Wu MS, Wang HH et al. Helicobacter pylori infection and age on the development of intestinal metaplasia - a multiple logistic regression analysis. Hepatogastroenterology. 1998; 45:2234-7
18. Alborghetti Nai G; Parizi A C G; Barbosa R L . Association between Helicobacter pylori concentration and the combining frequency of histopathological findings in gastric biopsies specimens. Arq.Gastroenterol. 2007 July/Sept; 44: 3.
19. Craanen M E, Dekker W , Blok P, Ferwerda J. Intestinal metaplasia and H Pylori: an endoscopic bioptic study the gastric antrum .Gut 1992 Jan 33: 16-20.
20. Zhang C, yamada N, Matsuhisa M W T, Mat Suku N. H pylori infection,glandular atrophy and intestinal metaplasia in superficial gastritis,gastric erosion,erosive gastritis,gastric ulcer and early gastric cancer. World J gastoenterol 2005 :11: 791-96.
21. Matsuhisa T, Miki M, Yamada N, Sharma SK, Shrestha BM Helicobacter pylori infection, glandular atrophy, intestinal metaplasia and topography of chronic active gastritis in the Nepalese and Japanese population: The age, gender and endoscopic diagnosis matched study. Kathmandu Univ Med J (KUMJ). 2007 Jul-Sep; 5 : 295-301.
22. Ohkuma K, Okada M, Murayama H et al. Association of Helicobacter pylori infection with atrophic gastritis and intestinal metaplasia. Journal of gastroenterology and hepatology. 2008 Jul; 15 :10; 1105-12
23. TAHA Ali S, Wilson A, Christopher J. M. Correlation between erosive oesophageal and gastro-duodenal diseases. The influence of aspirin, simple analgesics, and Helicobacter pylori. European journal of gastroenterology & hepatology 2002; 14: 1313-17.