

ORIGINAL RESEARCH

Histopathological Spectrum of Endoscopic Biopsies In Patients With Upper Gastrointestinal Symptoms: An Experience From Eastern India.

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ABSTRACT

Objectives: To assess the histopathological spectrum of upper gastrointestinal biopsies among patients with various upper GI symptoms and their association with H. pylori, alcohol and smoking.

Material and method: The present study was a cross-sectional study, carried out on patients of Ispat General Hospital from December 2014 to Nov 2015. Endoscopic biopsy was taken and followed by histopathological evaluation.

Results: Out of total 100 biopsies, 64 were gastric biopsies, 20 duodenal biopsies and 16 esophageal biopsies. 56% male, 44% female. Common age group more than 58 years (38%). 56% smokers, 44% nonsmokers and 57% alcoholic. Out of 16 esophageal biopsy, 9 diagnosed as squamous cell carcinoma, 4 esophagitis, 3 GERD. Out of 64 gastric biopsies, 33 diagnosed as chronic gastritis (33), hyperplastic polyp (7), ulcer (1), adenocarcinoma (23). 69.70% cases of chronic gastritis were positive for H. pylori. Percentage of diffuse type of adenocarcinoma stomach was 69.5%. Out of 20 duodenal biopsies, 5 diagnosed as Adenomatous polyp followed by duodenal adenocarcinoma (4) and ampullary adenocarcinoma (1). Non-neoplastic lesion of duodenum included hyperplastic polyp (5) followed by duodenitis (4) and brunner gland hyperplasia (1).

Conclusion: We tried to highlight the importance of routine endoscopic biopsies in patients with upper gastrointestinal symptoms and stain for H. pylori should be routinely done for all cases of chronic nonspecific gastritis. Clinicians should be aware of increasing incidence of GERD and diffuse type of adenocarcinoma stomach in eastern zone.

INTRODUCTION

Upper gastrointestinal (GI) symptoms are frequently encountered in clinical practice (1). Clinicians traditionally have relied on pathologists to seek definitive answers to clinical queries. With the advent of modern endoscopic procedures, advanced endoscopes and better tools for tissue acquisition, the importance of establishing a definite tissue diagnosis for clinical correlation has increased (2). Furthermore, with the availability of minimally invasive therapeutic modalities like radio frequency ablation (RFA), endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), it has become imperative to diagnose benign, premalignant and malignant conditions early to treat them with curative intent (3,4). This is only possible by an accurate histopathological evaluation of the tissue biopsies acquired during upper GI endoscopy.

H. pylori is a spiral gram-negative bacterium that infects the gastric mucosa and initiates a chronic inflammatory cascade (5). While many patients with *H. pylori* infestation remain asymptomatic, a substantial proportion may subsequently develop benign diseases like peptic ulcer disease or even malignant neoplasms, including both gastric adenocarcinoma and lymphoma (6–8). *H. pylori* is endemic in this part of the world; while some studies have shown that high anti-*H. pylori* IgG titers are associated with gastric cancer, data are still scarce on the association of *H. pylori* with various upper GI pathologies (9,10).

Smoking and alcohol consumption has traditionally been considered risk factors for carcinogenesis (11). They increase the risk of esophageal and gastric cancer and synergize the risk of esophagitis, Barrett's esophagus, gastric and duodenal ulcer, and duodenitis (12). In the last decade or so, the consumption of alcohol and prevalence of smoking has increased many folds in the younger age group, which has probably also led to a paradigm shift in the demographic profile of upper digestive tract cancers, leading to a relatively younger age group now developing these malignancies (13,14).

OBJECTIVES

We undertook this study intending to assess (i) the histopathological spectrum of upper gastrointestinal biopsies among patients with various upper GI symptoms, (ii) their demographic and clinical profile, (iii) their association with *H. pylori*, and (iv) their association with conventional risk factors like alcohol and smoking.

MATERIALS AND METHODS

The present study was a cross-sectional study carried out on patients with symptoms of upper gastrointestinal disease who attended the outpatient department of Ispat General Hospital, Rourkela, Odisha, India, from December 2014 to November 2015 after considering inclusion and exclusion criteria. The inclusion criteria were all biopsies done in adult patients of both sexes for various upper gastrointestinal symptoms with or without systemic symptoms. All cases of endoscopies where biopsies were not taken were excluded. The total number of upper GI biopsies done during the study period was 1425, and after considering exclusion criteria, the population size was 1000. Using sample size calculator by Raosoft Inc. (www.raosoft.com), after considering the margin of error of 9.78%, confidence level 96%, response distribution 50% in terms of the numbers selected above, the sample size came to 100.

Biopsies were taken during esophagogastroduodenoscopy (EGD) using a video endoscope (Olympus Optical Co Ltd., Tokyo, J). The biopsy tissue is placed on the filter paper for proper orientation, and then it is transferred to the bottle containing 10% neutral buffered formalin. After fixation, the biopsy specimen was processed in a fully automated tissue processor. Subsequently, tissue was embedded in paraffin with surface uppermost. 3 to 5

microns thick, 3-4 sections were taken perpendicular to the surface. Routine Hematoxylin and Eosin (H&E) and special stains like Periodic Acid Schiff (PAS) and Giemsa were done wherever indicated. Subsequently, a histopathological diagnosis was made.

RESULTS

Of 100 biopsies, 64 were gastric, 20 duodenal, and 16 were esophageal biopsies. Among 100 patients, 56% were males, with the majority (38%) were in the age group >58 years (Table 1). Of all the patients, 56% were smokers, and 57% consumed alcohol.

Table 1: Age- gender wise distribution of study subjects

Age Group	Gender				Total
	Male (56)		Female (44)		
18-28 Years	06	10.7%	04	09.1%	11
29-38 Years	07	12.5%	04	09.1%	10
39-48 Years	05	8.9%	12	27.3%	18
49-58 Years	13	23.2%	10	22.7%	23
> 58 Years	25	44.6%	14	31.8%	38
Total	56	100.0%	44	100.0%	100

Most patients presented with anorexia (42%) followed by dyspepsia (38%), weight loss (29%), pain (26%), vomiting (24%), hematemesis (17%), melena (13%), diarrhea (1%) (Table-2).

Table 2: Distribution of study subjects based on complaints

Complaints	Frequency	Percentage
Pain	26	26%
Hematemesis	17	17%
Vomiting	24	24%
Dyspepsia	38	38%
Diarrhoea	01	0 1%
Anorexia	42	42%
Mass Per Abdomen	00	00%
Weight Loss	29	29%
Malena	13	13%

Most patients on endoscopic appearance had an ulcer (65%) followed by the mass lesion (46%), erythema (2%), erosions (7%), polyp (15%) and gastropathy (2%) (Table-3).

Table 3: Distribution of study subjects based on endoscopic presentations

Endoscopic presentations	Frequency	Percentage %
Petechial Hemorrhages	00	00%
Erythema	02	02%
Erosions	07	07%
Polyp	15	15%
Ulcer	65	65%
Growth	46	46%
Gastropathy	02	02%

Out of total 16 esophageal biopsies, histopathology revealed neoplastic and non-neoplastic pathology in 9 and 7 biopsies, respectively. All neoplastic lesions were squamous cell carcinoma. (Figure 1). Non-neoplastic lesions consisted of esophagitis in four and GERD in three cases.

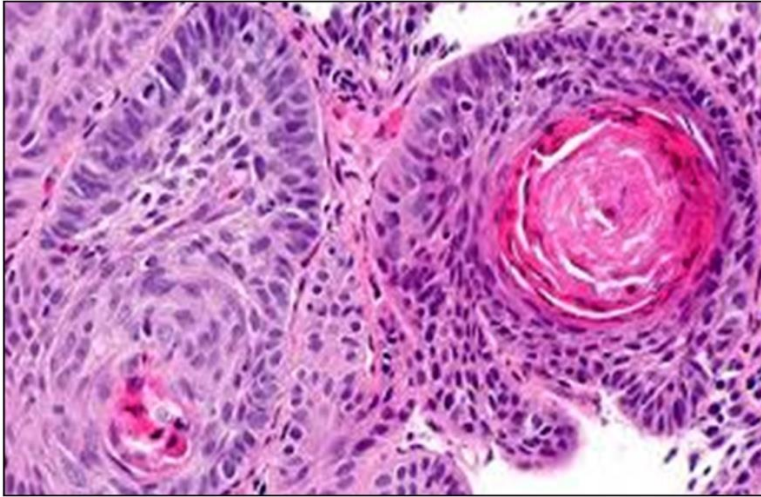


Fig.1: Squamous cell carcinoma (40X)

Out of total 64 gastric biopsies, neoplastic and non-neoplastic pathologies were seen in 23 and 41 biopsies, respectively. Non-neoplastic lesions consisted of chronic gastritis in 33, ulcer in 1 and hyperplastic polyp in 7 biopsies. All neoplastic lesions were adenocarcinoma. Out of total 20 duodenal biopsies, neoplastic and non-neoplastic pathologies were seen in 10 biopsies each. The most common neoplastic lesion was adenomatous polyp in five biopsies, followed by duodenal adenocarcinoma in four and ampullary adenocarcinoma in one biopsy. Among non-neoplastic lesions, the most common was Hyperplastic polyp in five biopsies, followed by duodenitis in four and Brunner gland hyperplasia in one biopsy (Table-4).

Table 4: Distribution of histopathological lesions in the esophagus, stomach and duodenum

Histopathological Diagnosis	Site of biopsy			Total
	Esophagus	Stomach	Duodenum	
Squamous cell carcinoma	09	0	0	09
Esophagitis	04	NA	NA	04
GERD	03	NA	NA	03
Adenocarcinoma	0	23	05	28
Adenomatous polyp	0	0	05	05
Chronic Gastritis	NA	33	NA	33
Ulcer	0	01	0	01
Hyperplastic polyp	0	07	05	12
Duodenitis	NA	NA	04	04
Brunner gland hyperplasia	NA	NA	01	01

GERD- Gastroesophageal reflux disease, NA- Not applicable.

The most common non-neoplastic pathology, chronic gastritis (figure 2), was detected in 33 of 41 gastric biopsies; 56% were males. Chronic gastritis was most common in the age group

of more than 58 years (31.25%). In the present study, 82.35% of gastric biopsies were from the antrum and 15.15% from the body (Table-5).

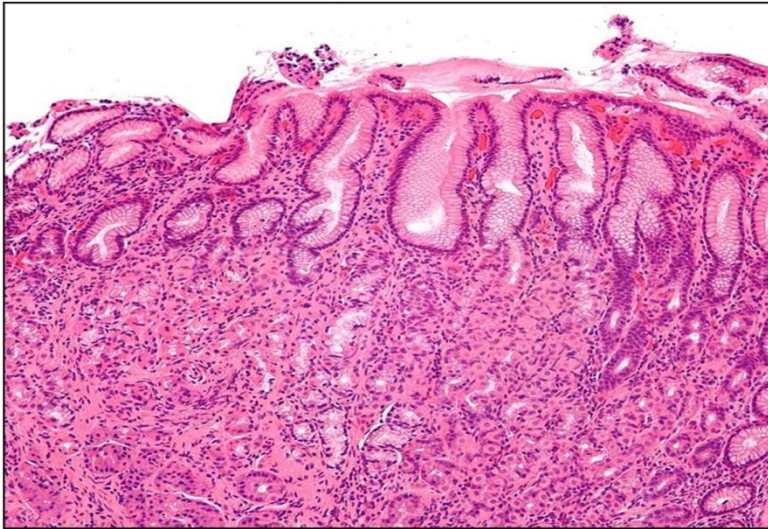


Fig2: Antral biopsy showing chronic gastritis with mononuclear inflammatory infiltrate (10x)

Table 5: Relation between site and chronic gastritis (histopathological)

Relation between site and gastritis (histopathological)		
site	Chronic Gastritis	Percentage
antrum	28	84.85%
fundus	0	0.00%
body	5	15.15%
pylorus	0	0.00%
cardia	0	0.00%
total	33	100%

Out of 33 cases of chronic gastritis, *H. pylori* was positive in 23 patients (69.70%). Thereby, chronic gastritis was antral predominant and was intimately associated with *H. pylori* positivity in most of the cases (Figure 3). Adenocarcinoma of the stomach was more common in 49- 58 years, with 65% in males.

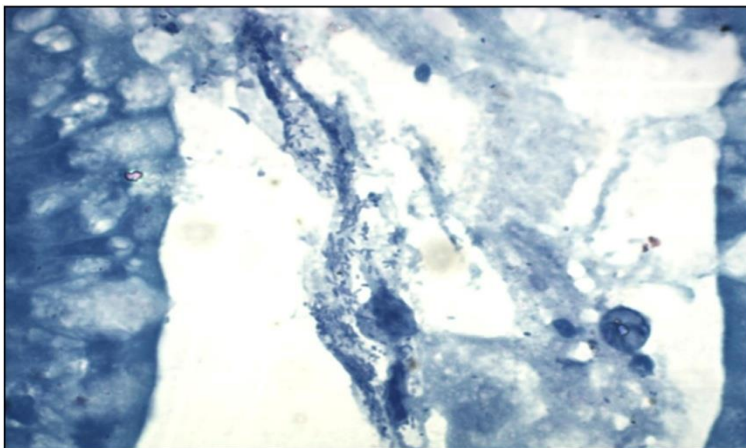


Fig. 3: H. Pylori in antral biopsy (modified geimsa stain 100x)

Both neoplastic and non-neoplastic lesions of the stomach were significantly more in age >40yrs than in the younger age group (<40yrs). Our study showed that smoking and alcohol consumption predisposed to neoplastic and non-neoplastic lesions of the stomach and duodenum. Out of 23 patients developing neoplastic lesions of the stomach, 14 patients had a history of alcohol consumption, and 14 patients had a history of smoking. Among 41 patients with non-neoplastic lesions of the stomach, 12 patients had a history of alcohol consumption, and 13 had a smoking history. Both alcohol consumption and smoking were significantly associated with both neoplastic and non-neoplastic lesions of the stomach ($p < 0.05$) (Table-6, 7).

Table 6: Statistical relation of alcohol with neoplastic and non neoplastic lesion of stomach

Alcohol	Neoplastic lesion of stomach	Non neoplastic lesion of stomach	Total
Yes	14	12	26
No	9	29	38

p value 0.0181(significant)

Table 7: Statistical relation of smoking with neoplastic and non neoplastic lesion of stomach

Smoking	Neoplastic lesion of stomach	Non neoplastic lesion of stomach	Total
Yes	14	13	27
No	9	28	37

P value 0.0348 (significant)

Out of the ten patients developing neoplastic lesions of the duodenum, all patients had a history of alcohol consumption, and none had a history of smoking. Among ten patients with non-neoplastic lesions, six patients had a history of alcohol consumption, and 6 had a smoking history. Smoking was significantly associated with the duodenum's neoplastic and non-neoplastic lesions ($p < 0.05$) (Table-8, 9).

Table 8: Statistical relation of alcohol with neoplastic and non neoplastic lesion of duodenum

Alcohol	Neoplastic lesion of duodenum	Non neoplastic lesion of duodenum	Total
Yes	10	6	16
No	0	4	4

p value 0.086687307(not significant)

Table 9: Statistical relation of smoking with neoplastic and non neoplastic lesion of duodenum

Smoking	Neoplastic lesion of duodenum	Non neoplastic lesion of duodenum	Total
Yes	0	6	6
No	10	4	14

p value 0.010835913(significant)

DISCUSSION

The current study shows (i) In the esophagus, squamous cell carcinoma is the most common neoplastic pathology while esophagitis and GERD are the most common non-neoplastic lesions identified; in stomach adenocarcinoma among neoplastic and chronic gastritis among non-neoplastic lesions are most common; similarly in duodenum adenomatous polyp among neoplastic and hyperplastic polyp and duodenitis among non-neoplastic etiologies were most common (ii) Most patients with both neoplastic and non-neoplastic pathologies present most commonly with anorexia, dyspepsia and other non-specific symptoms with alarm features (iii) *H. pylori* has an intimate association with the development of gastritis (iv) Both smoking and alcohol are significant risk factors associated with the development of both neoplastic and non-neoplastic lesions in esophagus, stomach and duodenum.

Upper Gastrointestinal tract diseases are one of the most encountered pathologies in clinical practice. Endoscopic biopsy and histopathological evaluation are undertaken in patients with alarm symptoms for a definitive diagnosis.

This study compared the clinical symptoms and findings observed during the histopathological examination of patients with previous data obtained by various studies. The present study analyzed 100 upper gastrointestinal biopsies, including 64 gastric biopsies, 20 duodenal biopsies and 16 esophageal biopsies.

Males undergoing upper GI endoscopy were more than the number of females; similar findings were found in the previous studies by Gulia et al. and Sheikh et al. (15,16). In all these studies, males outnumbered females, possibly due to the increased prevalence of smoking and alcohol use in this population. Like previous studies, anorexia was the most commonly reported symptom in patients undergoing upper GI endoscopy. In our study, anorexia was reported in 42% of patients, similar to the study done by Ravikumar et al. (34%) and Spiller et al. (39%). (17,18)

In the present study, the most common site of biopsy noted was the stomach (64%), since most of the study population was of older age group and older adults have an increased risk of gastritis because the stomach lining tends to thin with age and because older adults are more likely to have *H. pylori* infection (19). Results of this study correlated well with the studies done by Islam et al. (66.36%) and by Sheikh et al. (64.8%) (16,20).

From various studies, it has been seen that esophageal cancer ranks as the 7th most frequent cancer (21). The most common lesion in the esophageal biopsies in the present study was squamous cell carcinoma (56%). More than 90% of esophageal tumors are squamous cell carcinoma or adenocarcinoma, while other types like melanoma, lymphoma, stromal, and neuroendocrine tumors are rarely seen (22). Similar findings were seen in a study done by Memon et al., where it was 78.6% squamous cell carcinoma and by Islam et al., 81.25% squamous cell carcinoma (20,23).

The most common histological pattern noted in gastroduodenal biopsies was chronic gastritis followed by adenocarcinoma, which may have been due to excessive alcohol consumption, presence of *H. pylori* bacteria and immune dysregulation (24). The result of this study well correlates with the study done by Gulia et al. and Memon et al. (15,23). GERD was observed more in the present study (3%) as compared to incidence (1.54%) found by Gulia et al. (15). The high incidence of GERD is possibly due to people eating more spicy foods and foods with high-fat content. Other triggers include alcohol, smoking, large meals, and lying down too soon after eating (22).

H. pylori was noted in 69.7% of cases of chronic gastritis, which is similar to that noticed by Jemilohun et al. (63.5%) and Sáez TJ et al. (59.8%) (25,26). The high incidence of *H. pylori* infection maybe because people belong to low socioeconomic status and overcrowded areas

with poor hygiene practices(27). The most common site affected by gastritis was the antrum (82.3%). Results are in harmony with studies done by Villako et al.(64%) and by Gotthard et al. (65%) (28,29).

In the present study, gastric carcinoma was more common in males than females (1.27:1). This correlates with the study done by Rampazzo et al.with the male: female ratio of 2:1 and Koea JB et al.,which reported it to be is 1.45:1 (30,31). In this study, gastric carcinoma is more common in males than females because the male gender is a risk factor; males are more exposed to fumes, dust, and smoking habits. Most of the study population are elderly males, who are more susceptible to *H. pylori* infection; it also triggers gastric cancer (32).Out of 23 gastric carcinoma cases, the most common type of carcinoma in the gastric biopsies in the present study was diffuse adenocarcinoma (69.5%). But in a study done by Rampazzo et al.in 2012, out of 335 adenocarcinoma cases (40.9%) was a diffuse type (30). A study was done by Mohammad A et al. found that out of 10 adenocarcinoma cases, the diffuse type was (40%). This suggests an increasing incidence of diffuse adenocarcinoma of the stomach (33). In the present study, the incidence of diffuse-type more common than intestinal type may be due to genetic susceptibility of individuals of this area and family history of inheritance of mutated gene; however, confirmation of this needs further study. A literature search showed that gastric cancer in eastern India is higher than in the rest of the country (32).

The most common neoplastic lesion is an adenomatous polyp, followed by duodenal adenocarcinoma and ampullary adenocarcinoma. The hyperplastic polyp is the most common non-neoplastic lesion, followed by duodenitis and Brunner gland hyperplasia. The present study had 20 duodenal biopsies, of which ten were non-neoplastic and ten neoplastic.

In the present study, 25% were malignant, including adenocarcinoma of the duodenum and ampullary carcinoma, and 75% were benign cases, similar to the study done by Tadashi Terada and SK Islam et al. (20,34).

In the present study, among all non-neoplastic lesions, 25% were Hyperplastic polyp, 20% were duodenitis, and 5% were Brunner gland hyperplasia. The commonest benign lesion seen is a hyperplastic polyp, similar to SK Islam et al. 2014, but in a study done by Terada, the commonest benign lesion was duodenitis (20,34).

Sjodahl K et al., in a study of 251 gastric cancers among 69,962 cohort members, showed that the risk of developing gastric cancer was almost twice as high in daily smokers as in never smokers; also, combined use of cigarettes and alcohol increased the risk of gastric cancer, compared to nonusers (35). The results in our study are in sync with these results; additionally, our study establishes that not just neoplastic but alcohol and smoking significantly predispose to non-neoplastic lesions as well.

Chuang et al., in their study on 9275 patients undergoing upper GI endoscopies, showed that upper digestive tract cancers are commoner in individuals with smoking or alcohol addiction; our results are also in sync with these findings (12). The authors also showed that smoking, alcohol, and other risk factors like betel quid chewing have an addictive effect on carcinogenesis with a 2.12-fold risk of duodenitis and 1.29-fold risk of duodenal ulcers, apart from increasing the risk of gastric and esophageal lesions. In our study, most neoplastic and non-neoplastic lesions developed in alcohol users and smokers. It underscores the importance of deaddiction as a simple measure in preventing carcinogenesis of the digestive tract apart from preventing non-neoplastic lesions and significant morbidity and mortality.

CONCLUSION

Upper GI endoscopy should be accompanied by relevant biopsies in patients with upper gastrointestinal symptoms with alarm features. Biopsies should be taken from normal-appearing mucosa on endoscopy for patients suffering from dyspepsia, and staining for *H. pylori* should be routinely done for all cases of chronic non-specific gastritis. Clinicians

should be aware of the increasing incidence of GERD due to food habits and lifestyle changes. Clinicians should also be sensitized about the growing incidence of the diffuse type of adenocarcinoma of the stomach in eastern zone, which has a prognostic significance. Reiteration that conventional risk factors like smoking and alcohol predispose to neoplastic and non-neoplastic pathologies also underlines the importance of initiating more aggressive community awareness programs to educate individuals, especially in the younger age group.

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