

**Title:** Histopathological Spectrum of Upper-Gastrointestinal Lesions on Endoscopic Biopsies

**Running title:** Histopathological spectrum of upper GI lesions

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## Abstract

**Background:** Upper gastrointestinal (GI) lesions are significant contributors to morbidity, with endoscopy serving as a crucial minimally invasive tool for their visualization and biopsy. This study explores the demographic patterns of upper GI lesions by age, sex, and biopsy site, comparing the prevalence of neoplastic and non-neoplastic lesions across the esophagus, stomach, and duodenum, while underscoring the importance of early detection and management.

**Method:** This cross sectional retrospective study conducted at a tertiary care center in Gujarat, India, July 2019 to October 2021. A total of 104 upper GI tract biopsies were included and were categorized based on age, sex, site, endoscopic findings and histomorphology. Histopathological analysis involved routine processing, staining and microscopic examination by histopathologist.

**Result:** Out of 104 endoscopic biopsies, the majority were from the 46-55 age group, followed by 66-75, with a male to female ratio of 1.7:1. Oesophageal biopsies were most common (48%). Non-neoplastic lesions (52.8%) were predominant, with duodenitis (48%) and celiac disease (33.3%) most frequent. Neoplastic lesions (47.1%) were prevalent in the esophagus (36.5%), primarily squamous cell carcinoma. Gastric biopsies showed benign lesions like gastritis more than malignant, with adenocarcinoma most common. Endoscopic findings included thickening, scalloping, nodularity, polyps, or fragile growths, emphasizing the diversity of upper GI tract lesions and the need for early detection and treatment.

**Conclusion:** The study emphasizes biopsies' crucial role in promptly diagnosing esophageal malignancies and identifying premalignant conditions like Barrett's esophagus for timely intervention. It reaffirms the pivotal role of endoscopic biopsy in clinical management, stressing the necessity of a multidisciplinary approach.

**Keywords:** Histopathology, Upper Gastrointestinal tract, Endoscopy, Biopsies

## Introduction

Upper gastrointestinal (GI) lesions significantly contribute to global morbidity, ranging from benign inflammatory conditions to malignant neoplasms.(1) This study examines the demographic distribution of upper GI lesions by age, sex, and biopsy site, focusing on the esophagus, stomach, and duodenum. It compares the prevalence of neoplastic and non-neoplastic lesions, emphasizing the importance of premalignant conditions like Barrett's esophagus(In that columnar cells replace squamous mucosa after ulceration, arising from gastric migration or stem cell changes) and malignancies such as esophageal squamous cell carcinoma and gastric adenocarcinoma.(2) Common inflammatory conditions, including esophagitis (Eosinophilic esophagitis involves  $\geq 15$  eosinophils per field, while infectious esophagitis arises from various pathogens), gastritis (Acute gastritis involves inflammation; chronic gastritis includes autoimmune or H. pylori-associated glandular atrophy and metaplasia.) and duodenitis (Duodenitis is graded by neutrophil and plasma cell infiltration, villous height, and gastric metaplasia), are also analyzed alongside rarer findings like celiac disease and neuroendocrine tumors.(3) Early detection, especially of premalignant and malignant lesions, is essential for timely intervention and management. Endoscopy plays a pivotal role as a minimally invasive method for visualizing and biopsying lesions in the upper GI tract.

## Methods

This study, conducted at a Gujarat, India tertiary care center from July 2019 to October 2021, analyzed 104 upper GI endoscopic biopsies from patients with upper GI symptoms, excluding lesions of the mouth and pharynx, distal duodenal biopsies, and inadequately preserved specimens. Most esophageal and gastric biopsies were from thickened, friable, or ulcerated areas in the middle and lower esophagus. Duodenal biopsies were from the second part (D2) showing scalloping or nodularity. Tissues were processed, stained, and analyzed microscopically. Special stains were used to confirm H. pylori and other lesions. Malignant lesions were classified per WHO guidelines, and duodenal biopsies for suspected celiac disease were graded using Modified Marsh Oberhuber classification.

## Results

Demographic and site wise distribution of upper GI lesions shows that maximum biopsies were obtained from the age group of 46-55 years followed by 66-75 years, with a male to female ratio 1.7:1. (Figure 1) Out of total 104 Endoscopic biopsy specimens maximum (50/104) were from Esophagus, followed by 27 each from the stomach and duodenum and biopsy was from the gastroesophageal junction.

Based on findings, the endoscopic biopsies were categorized into non-neoplastic and neoplastic and included 55 cases (52.8%) & 49 cases (47.1%) respectively. Among the non-neoplastic lesions, maximum cases 25 cases (24%) were from the duodenum. Among the neoplastic lesions, the highest number of cases were from the esophagus 38 cases (36.5%).

Results shows that maximum biopsies from the esophagus were obtained from the age group of 56-65 years, with a male to female ratio of 1.2:1. Out of total 50 total cases (n=12) 24% were non-neoplastic and (n=38)76% were neoplastic. There were an equal number of benign lesions in both the sexes, while malignant lesions were more common in males compared to

female patients with a male to female ratio 1.3:1. Out of total 12(24%) non-neoplastic cases, 11 (21.6%) cases were of esophagitis and one case of Barrett's esophagus. 38 (74.5%) cases of neoplastic lesions were obtained. Among the neoplastic cases all were malignant with squamous cell carcinoma most common (Figure 2). Out of 11 cases of esophagitis, maximum cases presented with erythematous changes on endoscopy. One case of Barrett's esophagus presented as an ulcerative lesion. Ulceration with the proliferative type of growth was commonly seen in squamous cell carcinomas whereas ulceration was not commonly associated with Adenocarcinoma. Adenocarcinoma usually presented as a proliferative lesion with or without ulceration.

Maximum biopsies from the stomach were obtained from the age group of 66-75 years, with a male to female ratio 1.7:1. Out of total 27 total cases (n=18), benign lesions were more common accounting for 66.7% while 33.3% were malignant. Benign as well as malignant lesions were more common in male patients. Most common benign lesion was gastritis (Figure 2) 48.1% which peaked in 66-75 years of age and adenocarcinoma (Figure 2) was the most common malignant lesion, which peaked in 46-55 years of age. Out of 13 cases of gastritis 09 cases were presented as an erythematous change on endoscopy. Maximum cases (06 cases) of adenocarcinoma presented as an ulcero-proliferative growth on endoscopy while hyperplastic polyp presented as polypoidal growth on endoscopy (Table 2).

Maximum biopsies of the duodenum were received from 46-55 years age group patients with a male to female ratio 3.5:1. Out of 27 biopsies, the majority of the lesions were 25 cases (92.6%) benign and 02 cases (7.4%) were neoplastic. Duodenitis (48%, 13/25) was the most common benign lesion encountered followed by 33.3% cases of celiac disease (Figure 2), hyperplastic polyp (7.4%) and a single case of tropical sprue. There were 2 cases of malignant duodenal lesions, were seen in elderly male (56-75 years) patients. One patient was of adenocarcinoma (Figure 2) and one was of well-differentiated neuroendocrine neoplasm.

Maximum cases of duodenitis (29.6%) presented as erythematous change on endoscopy. Half of the cases of celiac disease presented as nodular growth and half of the cases were presented as atrophy or scalloping on endoscopy. Both cases of hyperplastic polyp were presented as a polypoidal growth on endoscopy (Table 3).

## Discussion

Upper GI lesions are major causes of morbidity. Endoscopy visualizes and biopsies mucosal lesions, being minimally invasive and outpatient.(4)

In the present study, the majority of samples are of the oesophagus comprising 48.5% followed by an equal number of cases from the stomach and duodenum each comprising 25.7%, a study done by Sharma S et al also show the majority of samples were from the esophagus, whereas other studies Qureshi NA et al,(5) Vidyavathi K et al,(6) Sandhya et al(7), Rashmi K et al(8), Hussain SI et al(2), Abilash SC et al(9), show a majority of biopsies were from the stomach.

Demographic data related to age and sex in the present study shows trends almost similar to other reported studies Qureshi et al(5), UK, Frank et al(10), USA, Vidyavathi K et al(6), India (Kolar), Rashmi K et al(8), Bangalore, Hussain et al SI(2), Kerala, Abilash SC et al(9), Srinagar, with male predominance whereas Piyaporn et al(11), have female preponderance. The present study shows the highest number of upper GI endoscopic biopsies between the 5<sup>th</sup> and 6<sup>th</sup> decade of life similar to other studies which also show preponderance between 40-60 years of age. The

reason for this finding is that males are comparatively more exposed to environmental pollutants as compared to females and are more indulged in habits of smoking and tobacco consumption as compared to females(12).

The present study shows a mild predominance of (52.4%) non-neoplastic lesions of the Upper Gastrointestinal tract shows similarity with other studies like Qureshi NA et al(5), (17%), Rashmi K et al(8), (44%), Abilash SC et al(9),(22%) while other studies like Vidyavathi K(6), Hussain SI(2) show a predominance of neoplastic lesions.

Chronic Nonspecific oesophagitis (10.5%) was the commonest diagnosis similar to the study by Qureshi NA et al.(5), Rashmi K et al(8), Abilash SC et al(9). Abhilash SC et al.(9) and Sandhya et al(7) reported 1% and 1.5% cases of the Barrett's esophagus respectively. The ulceration is nearly always induced by gastroesophageal reflux and is said to occur in 10% of patients with this condition. The main complications of Barrett's esophagus are peptic ulcer, stricture, bleeding plus the development of dysplasia and adenocarcinoma (Table 4).

Dysplasia is found in Barrett's esophagus in the absence of carcinoma in 5-10% of the cases and association with carcinoma in 68-100% of the cases. Malignant lesions were more common accounting for 74.5% of the total esophageal biopsies (n=51) while 25.5% were non-neoplastic lesions. Similar findings were observed in studies done by Qureshi NA et al(5) and Hussain SI et al(2).

The American College of Gastroenterology recommends 1-year endoscopy for Barrett's mucosa, 6-months for low-grade dysplasia, then yearly. High-grade dysplasia patients need expert confirmation, repeat endoscopy within 3 months, and biopsies to exclude carcinoma from flat mucosa(2). Esophageal Squamous dysplasia predicts Esophageal squamous cell carcinoma. Found in  $\geq 25\%$  adults above 35 years, it parallels carcinoma rates.(13) Squamous cell carcinoma (71%) was the most common histological type in malignant lesions which is comparable to various studies(9,14,15) ranging from 66% to 100%. 52.6 % of patients with esophageal carcinoma were in 56-75 years. These observations are similar to studies done by Abhilash SC et al(9) and Qureshi et al.(5) Esophageal cancer ranks eighth in incidence and 6<sup>th</sup> in mortality globally.(16) Sonja et al(17) state In the West, adenocarcinoma is rising, while squamous cell carcinoma remains predominant elsewhere. Parkin et al(16) state 80% of esophageal carcinomas are in developing countries, mostly esophageal squamous cell carcinoma. In India, it's the third/fourth leading cancer in men and women respectively.(18)

In this study, overall inflammatory lesions were more prevalent in stomach biopsies, with chronic non-specific gastritis being the most common diagnosis.

Memon F et al(19) and Gumber R et al(15) also showed similar trends. Gastritis with intestinal metaplasia or dysplasia is a significant histological finding, indicating a premalignant disease. In 11.1 % of cases, intestinal metaplasia/dysplasia was seen along with gastritis. A similar observation was also made by Abhilash SC et al(9) and Rashmi K et al[10]. Only 8.5% of gastric biopsies were diagnosed as a malignancy on histology, adenocarcinoma being the histological type. Memon F et al,(19) and Abhilash SC et al(9) also reported a lower prevalence of malignancy with frequencies of 5% and 7.5% respectively.

Non-specific duodenitis was the most common lesion encountered in the duodenum. Duodenum has a rich rapidly regenerating epithelial lining which can easily be affected by any inflammatory insult.(19) Inflammatory lesions are more common in the duodenum was also

shown by studies done by Abhilash SC et al (9) Qureshi NA et al (5), Hussain SI et al (2), Rashmi K et al (8), and Sandhya et al (7).

In this study, 33.3% had celiac disease. Marsh-Oberhuber criteria, based on small bowel biopsies, is used for grading (20). Increased intraepithelial T lymphocytes suggest celiac disease even without villous atrophy (3). In this study Type III (66.6%) was most common, while Type I (11.1%) was least. In contrast, Memon F (19) found 76.1% with suspected celiac disease, with mild cases more prevalent. Difficulty identifying IELs due to small biopsies may explain fewer Type I cases. Duodenum had the fewest malignant cases (1.9%), consistent with other studies by Rashmi K et al (8), Somani et al (21), and Khandige S et al (22).

## **Conclusion**

This study highlights endoscopic patterns correlated with histopathology for early detection and treatment. It provides valuable insights into the demographic distribution, lesion types, and comparisons with other studies, aiding in understanding regional trends and advancing diagnostic approaches. Histopathology is crucial in assessing upper GI lesions from endoscopic biopsies, distinguishing between non-neoplastic, premalignant, and neoplastic conditions, especially in Barrett's esophagus. Esophageal biopsies were common, with malignancy in 47.6%, predominantly in the esophagus, especially in those aged 50-60. Gastric and duodenal lesions are often benign, but suspicion and timely histopathological study aid early management. Accurate diagnosis improves patient outcomes, while understanding lesion demographics tailors management. The synergy between endoscopy and histopathology enhances diagnostic precision, guiding optimal clinical decisions and improving care.

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## **Availability of data**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## **Funding sources**

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## **Ethical statement**

The study was approved by the Institutional Ethics Committee. (GCSMC/EC/Dissertation/APPROVE/2019/0091)

## **Conflicts of interest**

None declared.

### Author contributions

All the authors have participated in one or more parts of the present study; Anupama Ishwar Dayal conducted the test; Tejas Atulbhai Contractor and Himali Parsotambhai Thakkar performed the data analysis and wrote the manuscript; Sandesh Omprakash Agrawal and Hani Kamleshbhai Patel collected the data.

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**Table 1.** Comparison of endoscopic findings with histopathology on non-neoplastic and neoplastic lesion of oesophagus and gastro-oesophageal junction

Lesion		Endoscopic Findings							
Non neoplastic	Histological types	Ulcerative %	Proliferative %	Ulceroproliferative %	Polypoidal %	Stricture %	Erythematous %	Nodular %	Total %
	Esophagitis	00	00	00	00	01 (2%)	09 (18%)	01 (2%)	11 (22%)
	BE	01 (2%)	00	00	00	00	00	00	01 (2%)
	Dysplasia	00	00	00	00	00	00	00	00
Neoplastic	SCC	09 (18%)	10 (20%)	07 (14%)	01 (2%)	00	00	00	27 (54%)
	Adeno Ca	00	03 (6%)	04 (8%)	01 (2%)	00	00	00	08 (16%)
	Signet Ring Adeno Ca	01 (2%)	00	01 (2%)	00	00	00	00	02 (4%)
	Basaloid Sq. Ca	00	01 (2%)	00	00	00	00	00	01 (2%)
Total		11 (22%)	14 (28%)	12 (24%)	02 (4%)	01 (2%)	09 (18%)	01 (2%)	50 (100%)

**Abbreviation:** BE: Barret's Esophagus; Adeno Ca: Adenocarcinoma; SCC: Squamous Cell Carcinoma

**Table 2.** Comparison of endoscopic findings with histopathology findings of gastric lesions

Endoscopic Finding	Lesions					Total
	Gastritis (%)	Gastric ulcer (%)	Dysplasia (%)	Hyperplastic polyp (%)	Adeno ca (%)	
Ulcerative	01 (3.7%)	01 (3.7%)	02 (7.4%)	00	01 (3.7%)	05 (18.5%)
Proliferative	01 (3.7%)	00	01 (3.7%)	00	02 (7.4%)	04 (14.8%)
Ulceroproliferative	00	00	00	00	06 (22.2%)	06 (22.2%)
Polypoidal	00	00	00	01 (3.7%)	00	01 (3.7%)
Multiple Polypoidal	00	00	00	00	00	00
Nodular	00	00	00	00	00	00
Erythematous	09 (33.3%)	00	00	00	00	09 (33.3%)
Edematous	02 (7.4%)	00	00	00	00	02 (7.4%)
Total	13 (48.1)	1 (3.7%)	3 (11.1%)	1 (3.7%)	09 (33.3%)	27 (100%)

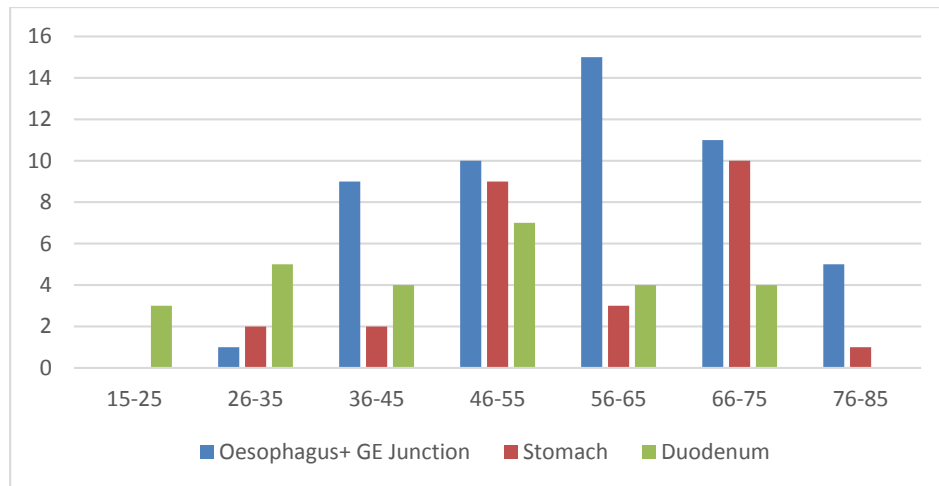
**Abbreviation:** Adeno Ca: Adenocarcinoma

**Table 3.** Comparison of endoscopic findings with histopathology findings of duodenal lesion

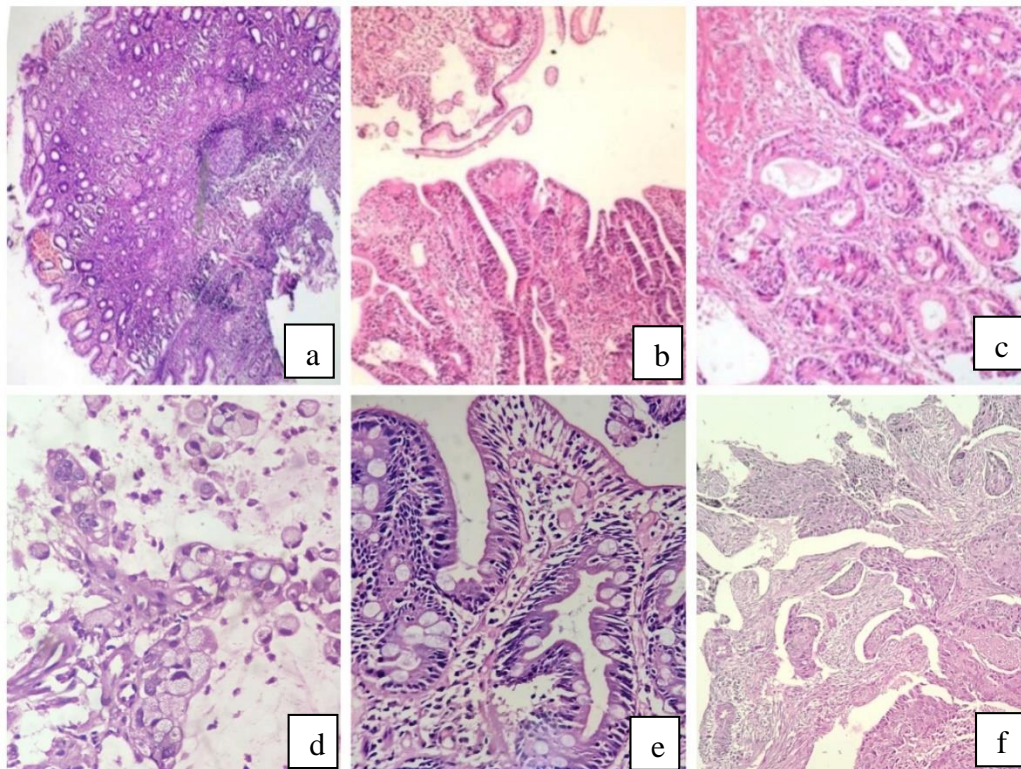
Endoscopic findings	Duodenitis (%)	Celiac disease (%)	Tropical sprue (%)	Hyperplastic polyp (%)	Malignancy (%)	Total (%)
Ulcerative	04 (14.8%)	01 (3.7%)	00	00	00	05 (18.5%)
Ulceroproliferative	00	00	00	00	01 (3.7%)	01 (3.7%)
Proliferative	00	00	00	00	01 (3.7%)	01 (3.7%)
Polypoidal	01 (3.7%)	00	00	02 (7.4%)	00	03 (11.1%)
Nodular	00	04 (14.8%)	00	00	00	04 (14.8%)
Erythematous	08 (29.6%)	00	01 (3.7%)	00	00	09 (33.3%)
Scalloping, atrophy	00	04 (14.8%)	00	00	00	04 (14.8%)
Total	13 (48.1%)	09 (33.3%)	01 (3.7%)	02 (7.4%)	02 (7.4%)	27 (100%)

**Table 4.** Comparison of upper gi lesions with other studies

Lesion	Qureshi NA et al, (5)UK, 2007, n=913	Sandhya et al,(7) Puducherry, 2012, n = 192	Rashmi K et al, (8) Bangalore, 2013, n=100	Hussain SI,(2) Kerala 2015 n=132	Abilash SC,(9) Srinagar 2016 n=200	Memon F et al(19), UK 2015, n=433	Present study n=105
Esophageal lesions							
Esophagitis	182 (19.9%)	3 (1.54%)	14(14%)	1 (0.8%)	14 (7%)	-	11 (10.5%)
Barrett's Esophagitis	126 (13.8%)	3 (1.54%)	-	4 (3%)	2 (1%)	-	1 (0.9%)
Esophagial Malignancy	74 (8.1%)	2 (1.03%)	11 (11%)	45 (34%)	17 (8.5%)	-	38 (36.2%)
Gastric lesions							
Gastritis	462 (50.6%)	-	28 (28%)	42 (31.8%)	55 (27.5%)	120 (54%)	13 (12.4%)
Gastric Ulcers	-	-	8(8%)	3 (2.3%)	10 (5%)	4(1.8%)	1(0.9%)
Polyp	-	-	-	-	14 (7%)	-	1(0.9%)
Gastric Dysplasia	-	-	1(1%)	-	5 (2.5%)	-	3(2.8%)
Gastric Malignancy	20 (2.2%)	-	27 (27%)	30 (22.7%)	15 (7.5%)	11 (4.9%)	9 (8.5%)
Duodenal lesions							
Duodenitis	12 (1.3)	6 (3.1%)	4 (4%)	7 (5.3%)	44 (22%)	-	13 (12.3%)
Duodenal Carcinoma	-	-	2 (2%)	-	-	-	2 (1.9%)



**Figure1.** Demographic and site wise distribution of upper GI lesions



**Figure2.** histomicrograph of upper GI tract lesion

a: Stomach: Chronic Gastritis With Follicle Formation H and E X100

b: Duodenum: Adenocarcinoma Well -Differentiated H and E X 100

c: Stomach: Adenocarcinoma Well Differentiated H and E X100

d: Signet ring adenocarcinoma H and E X10

e: Duodenum: Celiac Sprue With Villous Atrophy & Intra Epithelial Lymphocytes H and E X400

f: Esophagus: Squamous Cell Carcinoma Moderately H and E X 100

Source: GCS medical college hospital and research center, Ahmedabad, Gujarat