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Histopathological spectrum of lesions of upper gastrointestinal tract – A study of endoscopic biopsies

Biren Jitendra Parikh[1], Anuradha Harish Chilani[2], Riya Chetankumar Nayak[3], Kartavya Jatin Mistry[4], Priya Pravinbhai Gediya[5], Khushi Biren Parikh[6]

[1]Associate Professor, [2]Senior Resident, [3,4,5]2nd Year Postgraduate Resident, Department of Pathology, Narendra Modi Medical College and Sheth L.G. General Hospital, [6]Intern Doctor, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India

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ABSTRACT

Background: Gastrointestinal (GI) disorders are one of the most commonly encountered health problems in routine clinical practice. Dietary, environmental, geographic, and genetic factors are some of the key reasons contributing to the prevalence of these diseases. A wide spectrum of lesions is observed on histopathological examination of the upper GI tract (GIT). **Aims and Objective:** The study was carried out to determine the histopathological spectrum of upper GIT lesions and to compare the lesions with demographic and clinical data. **Materials and Methods:** The study was conducted on all consecutive upper GI endoscopic biopsies received in the Department of Pathology, Narendra Modi Medical College, Ahmedabad during the period from August 2020 to October 2022. **Results:** Non-neoplastic lesions were observed in 91.3% of all upper GI biopsies. Among these, gastric lesions (63.3%) were the most common followed by duodenal lesions (21.3%) and esophageal lesions (6.6%). The most commonly observed non-neoplastic lesions from the esophagus, stomach, and duodenum were reflux esophagitis with its consequence Barrett's esophagus, chronic gastritis, and chronic duodenitis, respectively. Neoplastic lesions were observed in 8.7% of all upper GI biopsies; out of which 4% were esophageal, 3.3% were gastric and 1.3% were duodenal. The most commonly observed neoplastic lesions from the esophagus, stomach, and duodenum were squamous cell carcinoma of the esophagus, adenocarcinoma of the stomach, and adenocarcinoma of duodenum, respectively. **Conclusion:** Endoscopic biopsy examination followed by histopathologic assessment is a convenient procedure and current gold standard for the accurate diagnosis of patients with upper GIT lesions.

Key words: Histopathology; Upper gastrointestinal; Endoscopic biopsies

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INTRODUCTION

The upper gastrointestinal tract (GIT) is composed of the esophagus, stomach, and small intestine (up to the second part of the duodenum). The tract consists of four layers with the innermost mucosa (barrier epithelium, lamina propria, and muscularis mucosa), submucosa, muscularis propria, and variable serosa or adventitia.[1]

Gastrointestinal (GI) disorders are one of the most commonly encountered health problems in routine clinical practice. Dietary, environmental, geographic, and genetic factors are some of the key reasons contributing to the prevalence of this condition.[2] There are several diagnostic investigations available for the evaluation of patients with upper GI symptoms where endoscopic examination with biopsy is performed as the initial diagnostic test.[3] The upper GI lesions can range from infectious diseases which can be treated medically to malignant lesions requiring surgical intervention and chemotherapeutic approach.[4]

The major indications for upper GIT endoscopic biopsy include evaluation of dyspepsia, odynophagia, dysplasia, peptic ulcer disease, infections, inflammatory

Address for Correspondence:
Dr. Kartavya Jatin Mistry, 2nd Year Postgraduate Resident Doctor, Department of Pathology, Narendra Modi Medical College and Sheth L.G. General Hospital, Maninagar, Ahmedabad, Gujarat, India. **Mobile:** +91-8238099332. **E-mail:** kmkartavyamistry@gmail.com

disorders, vascular disorders, mechanical conditions, toxic and physical reactions including radiation injury, and neoplasms.[5] Endoscopic biopsy examination followed by histopathological assessment is a convenient procedure and current gold standard for accurate objective assessment of patients with symptoms of upper GIT.[6]

Aims and objectives

The aim of this study is to determine the spectrum of histopathological lesions of biopsies from the upper GIT and to compare the lesions with demographic and clinical data.

MATERIALS AND METHODS

The present descriptive and observational study was undertaken in the Department of Pathology, Narendra Modi Medical College, Ahmedabad, during the period from August 2020 to October 2022. The study population consisted of all the patients who underwent upper GI endoscopic biopsies and whose specimens were received in the pathology department of the institute. Brief demographic and clinical data were noted from the case records, which included the age and sex of the patient, relevant habits, other investigative findings, and provisional clinical diagnosis. The endoscopic biopsy specimens were fixed in 10% formalin, processed by paraffin embedding technique, and stained with hematoxylin and eosin stain (H and E). If required additional sections were stained with Periodic Acid–Schiff stain and Giemsa stain to look for the presence of *Helicobacter pylori*. The sections were examined and a histopathological diagnosis was rendered. Tumors of the esophagus and duodenum were classified as per the recent WHO classification system,[7] while gastric tumors were classified according to Lauren classification. The data were expressed using parameters such as range, ratio, mean, median, and proportion.

Inclusion criteria

All endoscopic biopsies from the esophagus, stomach, and up to the second part of the duodenum were included in the study.

Exclusion criteria

All biopsies below the second part of the duodenum, biopsies of the oral cavity as well as oropharyngeal lesions, inadequate biopsy, and autolyzed tissue were excluded from the study.

RESULTS

The present study was done on a total of 150 upper GI endoscopic biopsies performed in patients.

The maximum number of cases was observed in the 5th decade with the mean and median age of patients being 44 (±15.75 SD) and 45 years, respectively. Slight male preponderance was observed with the male: female ratio of 1.05:1 (Figure 1).

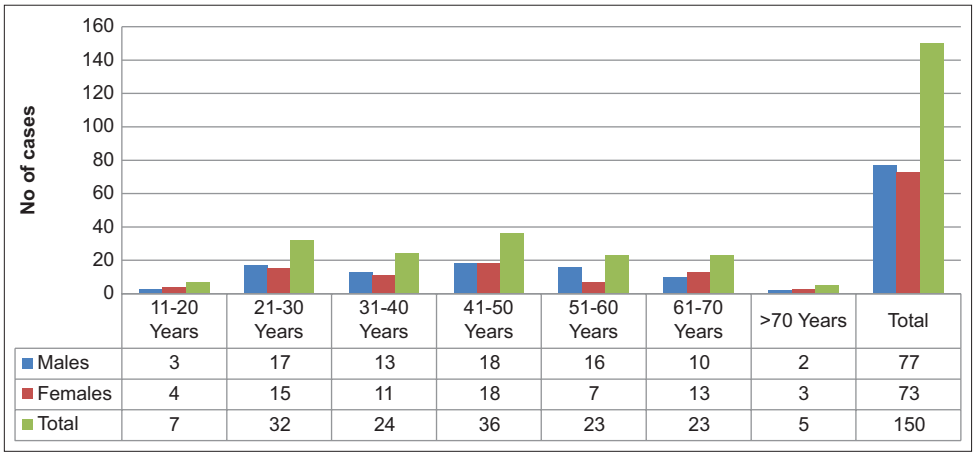
Out of 150 upper GI endoscopic biopsies, the majority specimens comprised of gastric biopsies (100, 66.6%) followed by biopsies from duodenum (34, 22.6%) and esophagus (16, 10.6%). Non-neoplastic lesions were more common (91.3%) compared to the neoplastic ones (8.7%). Figure 2 and Table 1 depict the relative frequency of various non-neoplastic and neoplastic lesions.

Among the non-neoplastic lesions of the esophagus, reflux esophagitis was the most common lesion. All cases of Barrett's Esophagus showed the associated findings of reflux esophagitis with a typical longstanding history of reflux with heartburn and all cases were chronic smokers and/or tobacco consumers in one or other forms.

Among all the non-neoplastic lesions of upper GI biopsies, chronic gastritis was the most common lesion. Among all cases of chronic gastritis patients, five cases (5.6%) were noticed to be of *H. pylori* diffuse antral gastritis, and one case (1.1%) was found to be of chronic atrophic gastritis. The remaining cases of chronic gastritis (83 cases) were categorized as "non-specific". In all cases of *H. pylori* chronic gastritis, intestinal metaplasia was found. In the case of chronic atrophic gastritis, associated intestinal metaplasia with low-grade dysplasia was observed. Hematology parameters of a patient with chronic atrophic gastritis were in favor of megaloblastic anemia. All cases of hyperplastic polyps revealed associated findings of chronic gastritis.

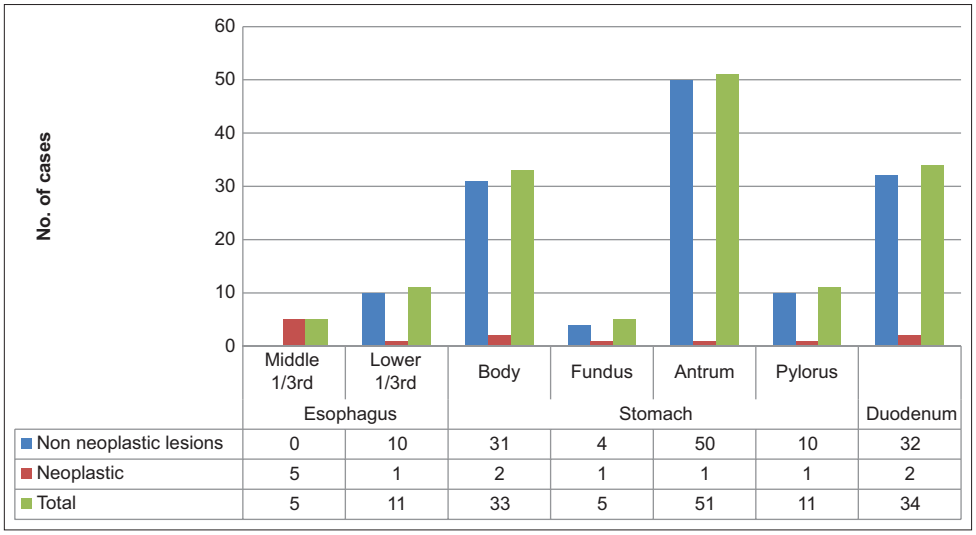
Chronic non-specific duodenitis was the main lesion found among the non-neoplastic duodenal lesions. In one case, the possible diagnosis of celiac disease was suggested on a duodenal biopsy which was classified as Type 2 (updated version of the original Marsh classification). However, further workup with serology tests, follow-up biopsy, and clinical pathological correlation was recommended to confirm the diagnosis. Two cases of peptic ulcer were noted in the duodenum with evidence of pyloric gland metaplasia in one of them.

Among the neoplastic lesions of the esophagus, squamous cell carcinoma (SCC) was more frequent than adenocarcinoma. All five cases of esophageal SCC were from the middle third of the esophagus while a case of adenocarcinoma was reported from the cardio-esophageal junction. All patients of esophageal SCC were chronic smokers and a striking male dominance was noted for



	11-20 Years	21-30 Years	31-40 Years	41-50 Years	51-60 Years	61-70 Years	>70 Years	Total
Males	3	17	13	18	16	10	2	77
Females	4	15	11	18	7	13	3	73
Total	7	32	24	36	23	23	5	150

Figure 1: Age and sex distribution



	Middle 1/3rd	Lower 1/3rd	Body	Fundus	Antrum	Pylorus	Duodenum
	Esophagus		Stomach				
Non neoplastic lesions	0	10	31	4	50	10	32
Neoplastic	5	1	2	1	1	1	2
Total	5	11	33	5	51	11	34

Figure 2: Site-wise distribution of neoplastic and non-neoplastic lesions

esophageal SCC (4/5 cases, 80%). Out of 5 cases of SCC, 4 cases were moderately differentiated while one case was well differentiated. Esophageal adenocarcinoma was moderately differentiated and showed associated evidence of Barrett's esophagus in adjacent mucosa. The most common presenting clinical features in patients with esophageal carcinoma were dysphagia, odynophagia, and progressive weight loss irrespective of the type of carcinoma, and all esophageal carcinomas were noted between the 5th and 6th decade.

In the stomach, the only neoplastic lesion found in the study was adenocarcinoma. Out of five cases of it, four cases were of signet ring cell type (diffuse gastric carcinoma) and one case was of moderately differentiated intestinal type adenocarcinoma. The age group for the patients with signet ring cell carcinoma varied between the 3rd and 5th decades and an equal gender distribution was noted among the patients. An intestinal type of adenocarcinoma was noted in the 5th decade in a male patient.

In duodenal biopsies, one case of adenomatous polyp and one case of moderately differentiated adenocarcinoma were observed among the neoplastic lesions. Both were male patients and fell within the 5th-decade of age group.

DISCUSSION

Endoscopy provides a unique opportunity to visualize the mucosal surface of the GI tract. In the context of a specific clinical picture, endoscopic images may be all that is required to make a specific diagnosis or provide sound clinical management. However, more often than not, endoscopists need to sample tissue. Examination by a qualified pathologist of specimens obtained at endoscopy is a routine and critical part of managing patients with disorders of the alimentary tract.[8]

The most common indications for upper GIT endoscopy are dyspepsia, dysphagia and odynophagia,

gastroesophageal reflux disease (GERD), persistent nausea and vomiting, occult GI bleeding, and surveillance for malignancy.[9] Malignant tumors of the upper GIT usually have a long natural history and may present at a fairly advanced stage. The incidence of GI malignancies increases with age which has led to increased number of endoscopies as well as biopsies to detect the cases at the earliest stage. Even the slightest clinical suspicion in middle and old age warrants an endoscopic biopsy and histopathological analysis.

In the present study, a total of 150 endoscopic biopsies from upper GIT were examined histopathologically. Table 2 depicts the comparative analyses of the present study with other studies taking into consideration – age and gender distribution of patients as well as the site distribution of endoscopic biopsies.

In most of the studies, the upper GI biopsy was performed in the patients after 3rd decade and a typical male preponderance was noted in the study population. Gastric biopsies formed the dominant group of samples in most of the studies which resembles the present study. However, in the present study, the duodenal biopsy was the next common site to be sampled after the gastric biopsy samples, which is in contrast with most other studies, which revealed the esophageal site as the next common site to be sampled after the gastric location.

Table 3 depicts the histopathological spectrum observed in upper GIT biopsies in different studies. In the present study, non-neoplastic lesions outnumbered the neoplastic ones, which is in concordance with various studies.[11-13,15,18] However, the studies of Bhargavi et al., Nazrin et al., and Dutta et al., showed neoplastic lesions to be the

Table 1: Frequency of different lesions reported on upper GI biopsies

Lesions	Location	Histopathological diagnoses	Number	Percent
Non-neoplastic lesions (137 cases, 91.3%)	Esophagus (10 cases, 6.6%)	Reflux esophagitis	5	3.3
		Eosinophilic esophagitis	1	0.6
		Barrett's esophagus	3	2
		Candida esophagitis	1	0.6
	Stomach (95, 63.3%)	Chronic non-specific gastritis	83	55.3
		Chronic *Helicobacter pylori* gastritis	5	3.3
		Chronic atrophic gastritis	1	0.6
		Acute erosive hemorrhagic gastritis	1	0.6
		Eosinophilic gastritis	1	0.6
		Hyperplastic polyp	3	2
		Fundic gland polyp	1	0.6
	Duodenum (32, 21.3%)	Chronic non-specific duodenitis	29	19.3
		Duodenal peptic ulcer/Peptic duodenitis	2	1.3
		Celiac disease	1	0.6
Neoplastic lesions (13 cases, 8.7%)	Esophagus (06, 4%)	SCC	5	3.3
		Adenocarcinoma	1	0.6
	Stomach (05, 3.3%)	Signet ring carcinoma (Diffuse gastric carcinoma)	4	2.6
		Intestinal type adenocarcinoma	1	0.6
	Duodenum (02, 1.3%)	Adenocarcinoma	1	0.6
		Adenomatous polyp	1	0.6
Total			150	100

SCC: Squamous cell carcinoma

Table 2: Comparative analyses of age and gender distribution of patients and site of endoscopic biopsies

Study	Age		M:F ratio	Site of biopsy (%)		
	Peak age group	Mean age		Esophagus	Stomach	Duodenum
Present	41–50	44	1.05:1	10.6	66.6	22.6
Dutta et al.[10]	51–60	53.08	2.33:1	10	80	10
Eslavath and Kalyan[11]	31–50	-	1.9:1	31.3	50	18.7
Bhargavi et al.[12]	-	-	-	22.6	60.4	17
Bhat et al. [13]	-	56.63	1.5:1	24	55	10
Nazrin et al.[14]	-	53.2	1.6:1	39.2	45.1	11.1
Theresa et al.[15]	31–40		1.34:1	14.5	74.3	11.2
Rani et al.[16]				30	46	24
Sharma et al.[17]	5th–6th decade	-	-	49.5	32	15.5
Krishnappa et al.[18]	51–60	-	2.03:1	25	68	7

Table 3: Relative frequencies of various lesions in different studies

Study→		Present study	A	B	C	D	E	F	G	H
Lesions ↓										
Non-neoplastic lesions (%)	Reflux esophagitis	3.3	-	15	6.6	1.5	2.9	7.8	2	-
	Eosinophilic esophagitis	0.6	-	-	-	-	-	-	-	-
	Barrett's esophagus	2	-	5.6	3.7	1	-	1.9	-	-
	Candida esophagitis	0.6	1.6	-	-	-		0.6	-	-
	Chronic non-specific gastritis	55.3	23.3	33.1	-	24	20	30.3	11	29
	Chronic *H. pylori* gastritis	3.3	5	-	-	13	-	13.8	9	3
	Chronic atrophic gastritis	0.6	-	1.2	-			14.4	-	2
	Acute erosive hemorrhagic gastritis	0.6	-	4.3	-	-	3.7	5.2	-	2
	Eosinophilic gastritis	0.6	-	-	-	-		1.9	-	-
	Hyperplastic polyp stomach	2	1.6	5	-	7		2.6	4	-
	Fundic gland polyp stomach	0.6	1.6		-	-		-	8	-
	Chronic non-specific duodenitis	19.3	5	12.5	12.2	3	7.4	5.2		-
	Duodenal peptic ulcer/Peptic duodenitis	1.3	3.3	6.2	-	1	1.4	3.9		-
	Celiac disease	0.6	-	-	2.8	1.5		-		-
Neoplastic lesions (%)	SCC esophagus	3.3	6.67	2.5	10.37	17.5	28.8	2.6	24	11
	Adenocarcinoma	0.6	1.6	0.6	1.8	-	4.4	-	5	-
	Signet ring carcinoma stomach (Diffuse gastric carcinoma)	2.6	36.6	6.2	-	14	18.5	3.9	7	-
	Intestinal type adenocarcinoma stomach	0.6	3.3	-	-	-	-	-	5	-
	Adenocarcinoma duodenum	0.6	-	-	0.9	1	0.7	-	-	-
	Adenomatous polyp duodenum	0.6	-	-	-	1.5	1.4	-	-	-

A: Dutta et al. [10], B: Eslavath and Kalyan[11], C: Bhargavi et al.[12], D: Bhat et al.[13], E: Nazrin et al.[14], F: Theresa et al.[15], G: Rani et al.[16], H: Krishnappa et al.[18]

predominant group over the non-neoplastic lesions. A wide variation in frequencies between non-neoplastic and neoplastic upper GI lesions in different studies could be due to wide variability in risk factors exposure in the different study population.

Reflux esophagitis and its sequelae Barrett's esophagus were commonly observed in various studies among the non-neoplastic lesions of the esophagus. Risk factors that contribute to the development of esophageal reflux include age over 50, body mass index above 30, smoking, anxiety, depression, and decreased physical activity. Medications that regulate the lower esophageal sphincter pressure, including nitrates, calcium channel blocker agents, and anticholinergics play a role. Recently, non-alcoholic fatty liver disease has been reported to increase the risk of developing reflux esophagitis.[19] The prevalence of Barrett's esophagus is 10–15% in patients who are undergoing endoscopy for GERD.[20] In the present study, all cases of Barrett's esophagus revealed associated evidence of reflux esophagitis, and all patients had habits of smoking/tobacco consumption.

Chronic non-specific gastritis was the most common non-neoplastic lesion encountered in most of the studies. *H. pylori* gastritis has been the topic of extensive research for the past few decades. *H. pylori* gastritis was commonly noted lesion in various studies.[10,13,15,16,18] Varied frequencies of *H. pylori* gastritis might be due to variables such as geographic area, age, race, ethnicity, and socioeconomic status. Rates appear to be higher in developing than in developed countries and they seem to be decreasing with improvements in hygiene practices and due to the availability of good antibiotics and antacids. Sometimes routine H and E stains may not be well suited to locate *H. pylori* in the tissue section and its detection may be missed. Hence, in every gastritis case, it should be a regular practice to perform the special stain for better appreciation of *H. pylori* organisms. In our experience, the Giemsa stain is one of the most satisfactory stains to visualize the organisms in the tissue section because of its simplicity and better yield due to good contrast. All cases of chronic atrophic gastritis should be thoroughly assessed for hematological parameters to rule out pernicious anemia. In the present study, we found the same association which provides indirect evidence of autoimmune etiology. Although antibody tests could not be performed in this patient, the gastric biopsy findings with concurrent megaloblastic anemia were in favor of an autoimmune etiology in the said case. In the present study, the association of atrophic chronic gastritis and intestinal metaplasia with dysplasia was noted. Chronic atrophic gastritis and intestinal metaplasia are thought to be important precursor conditions for the development of gastric carcinoma. In most cases, the gastric non-neoplastic polyps are incidental findings. The hyperplastic polyp is the second most common gastric polyp after the fundic gland polyp (FGP). In this study, all cases diagnosed as hyperplastic gastric polyps showed evidence of concurrent chronic non-specific gastritis. This strongly suggests a possible inflammatory nature of hyperplasic gastric polyps. However, the term inflammatory polyp is

a common misnomer for this polyp and that should be discouraged because it can be confused with inflammatory fibroid polyp, which is managed much differently. Examination of the surrounding mucosa is necessary in evaluating the underlying pathology (for example, *H. pylori*, autoimmune gastritis, or reactive gastropathy) in each case of hyperplastic polyp. In the present study, a patient of gastric FGP was a regular user of proton pump inhibitor (PPI). The incidence of FGPs has escalated substantially with the extensive use of PPIs. Conversely, following the decreasing rate of *H. pylori* infection, hyperplastic polyps have become less frequently observed in North America.[21]

In the duodenum, chronic non-specific duodenitis was the most common non-neoplastic lesion in various studies (Table 3). Gastric and duodenal peptic ulcers were observed with varied frequencies in different studies. In the present study, we reported two cases of duodenal peptic ulcer disease.

Among the neoplastic lesions, esophageal SCC was the most common lesion found in most of the studies including the present study (Table 3). However, the study done by Dutta et al., Eslavath and Kalyan revealed the signet ring carcinoma of the stomach to be the dominant neoplastic lesion. In the present study, all cases of SCC of the esophagus were from the middle 1/3rd of the esophagus. The same site predilection was also observed in other studies.[12,18] Esophageal SCC is more common in male patients. This might be due to the more prevalent habit (risk factor) of smoking and alcohol consumption in the male gender in population. Esophageal adenocarcinoma arises in the setting of Barrett's esophagus, and hence, it is found near the cardio-esophageal junction; a site where Barrett's esophagus arises. In the present study, we found an adjacent focus of Barrett's esophagus in a case of adenocarcinoma. Patients with Barrett's esophagus have a risk of esophageal adenocarcinoma 30–60 times more than that of the general population with an incidence rate of over 100 times that of the general population.[20]

Gastric signet ring cell carcinoma was more frequently observed in various series including the present study as compared to an intestinal type of gastric adenocarcinoma. This might be due to a decreasing trend of *H. pylori* gastritis, which is a proven risk factor for the intestinal type of gastric adenocarcinoma. Sometimes, signet ring carcinoma may be clinically silent for a long time as it usually produces a diffuse thickening of the stomach wall (leather bottle stomach) rather than a frank ulcerated or polyploid growth. This creates not only a late presentation of obstructive symptoms but also a missed diagnosis of malignancy merely on endoscopic examination. Hence, a biopsy of the thick appearing wall of the stomach during endoscopy is imperative for early detection of signet ring carcinoma. Gastric signet ring carcinoma was found at a slightly younger age than intestinal-type adenocarcinoma and no gender predilection was noted in the present study.

Duodenal neoplastic lesions were not as common as esophageal or gastric neoplasms. In most series, common duodenal neoplastic lesions noted were adenomatous polyp and adenocarcinoma.

Limitations of the study

This study is a single-center experience. Interobserver variations in the biopsy interpretation and variability in biopsy sampling may underscore the results. However, even with the limitations of this study, there are still significant inferences that can be made.

CONCLUSION

Biopsy sampling of upper GI mucosa during diagnostic endoscopy provides useful information. Histopathological findings may serve to correct a mistaken endoscopic finding and thus endoscopy is incomplete without biopsy. The present study states the importance of upper GI endoscopic biopsy in diagnosing various non-neoplastic and neoplastic lesions of GIT. Endoscopic biopsy of upper GIT provides a highly useful diagnostic tool for early detection of premalignant and malignant lesions. Histopathological examination in combination with clinical history, endoscopic findings, and special stains serves as the gold standard for arriving at a diagnosis and thus helps in the appropriate management of patients.

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ETHICAL APPROVAL

The present study was approved by Narendra Modi Medical College Institutional Review Board.

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Authors' Contributions:
BJP - Definition of intellectual content, prepared first draft of manuscript, manuscript preparation and submission of article; **AHC -** Interpretation of data for the article; **RCN -** Concept and design of article; **KJM -** Literature survey, manuscript editing, and proofreading; **PPG -** Data collection; **KBP -** Preparation of figures and manuscript editing.

Work attributed to:
Narendra Modi Medical College and Sheth L.G. General Hospital, Maninagar, Ahmedabad, Gujarat, India.

Orcid ID:
Biren Jitendra Parikh - https://orcid.org/0009-0008-4180-0481
Anuradha Harish Chilani - https://orcid.org/0009-0004-4175-8528
Riya Chetankumar Nayak - https://orcid.org/0009-0001-8635-1578
Kartavya Jatin Mistry - https://orcid.org/0009-0003-1640-5686
Priya Pravinbhai Gediya - https://orcid.org/0009-0008-1277-8422
Khushi Biren Parikh - https://orcid.org/0009-0002-9862-4411

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