Original Research Article

Histomorphological Spectrum of Endoscopic Biopsies in Upper Gastrointestinal Lesions

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Abstract

Background: Patients presenting with gastrointestinal (GI) symptoms are very common in clinical practice, and aetiologies range from congenital, inflammatory and neoplastic causes. Histopathological diagnosis provided from endoscopic biopsies provide us with a clear picture of the underlying lesion which mostly have such obscure clinical presentations. Upper gastrointestinal endoscopic biopsies are performed not only for the diagnosis of the disease but also for monitoring its course, determining its extent and responses to therapy and for early detection of complications. Therefore, accurate diagnosis facilitates a prompt and efficacious treatment outcome. **Methods**: In this 2-year retrospective study of upper gastrointestinal endoscopy (UGE) biopsies, A total of 55 patients were evaluated, two biopsies were deemed inadequate, and hence excluded from the study. The remaining cases were evaluated along with relevant clinical history and endoscopy findings. **Results**: Out of the 53 patients, 37 (69.8%) were male and 16 (30.1%) were female. Most of the malignant cases were diagnosed in the 4th and 5th decade. The study included 32 biopsies (60.3%) from the duodenum, 16 biopsies (30.1%) from the stomach and 5 biopsies (9.4%) from the esophagus. Nine cases (17%) were diagnosed as neoplastic; of which eight were Adenocarcinomas and one case of Squamous cell carcinoma (SCC). The non-neoplastic category comprised of 44 cases (83%). **Conclusions**: UGE is an effective investigative modality to assess patients with upper gastrointestinal symptoms, and to obtain representative biopsies to come to a concrete diagnosis to initiate effective management. Histopathology is therefore the gold standard for the diagnosis of endoscopically detected lesions of the GI tract.

Keywords: Upper Gastrointestinal tract, Endoscopic Biopsy, Histopathology, Neoplastic Lesions, Inflammatory lesions

Introduction

The upper gastrointestinal (UGI) tract extents from esophagus to duodenum (second part), and with the advent of endoscopy of upper digestive tract the diagnostic yield has been increased over the years. The diseases of upper gastrointestinal tract are highly prevalent in population and patients present with varied symptoms such as dysphagia, pain while eating, nausea, vomiting, dyspepsia, & loss of weight[1- 2]. The disease burden is known to affect the quality of life, which has effect on health care cost. The endoscopic biopsy is a powerful diagnostic tool which can be used for diagnosis of upper It can be incorporated easily in routine diagnostic protocols. The definitive diagnosis of upper gastrointestinal disorders is possible on histopathological evaluation and it provides clear picture of underlying disease which mostly have obscure clinical presentations[3-6]. This study aims to capitulate an effective approach in assessing endoscopic biopsies received in routine diagnostic practice, to first and foremost distinguish between nonneoplastic & neoplastic condition, and to determine the nature of inflammatory pattern.

Material and Methods

This 2-year prospective study was conducted in the Department of Pathology, at a teaching Hospital, from July 2019 to June 2021. A total 53 UGI endoscopic biopsies were evaluated. The copy of the endoscopic report, mentioning the site of the biopsy, a macroscopic description of the lesion if possible and the essential clinical information such as age, immune status, duration of symptoms and treatment if any were acquired before assessment. All the biopsy

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samples were fixed in 10% buffered formalin, followed by conventional tissue processing, cut at 3-4-micron thick sections, stained with Haematoxylin and Eosin. A biopsy devoid of mucosa was deemed inadequate for assessment, with the exclusion of atypical cells being identified. Periodic Acid Schiff (PAS) stain and Acid-Fast stains were performed wherever necessary. May Grunwald giemsa stain was used for H. Pylori. All tumors were classified according to the WHO classification system (2019).

Results

The study assessed endoscopic biopsies in the light of primarily ruling out inflammatory, premalignant and malignant processes. Two cases were devoid of mucosa and deemed inadequate were excluded from this study. Out of the 53 cases studied, 32 biopsies (60.3%) were from the duodenum, 16 biopsies (30.1%) were taken from the stomach and 5 biopsies (9.4%) from the esophagus [Table 1].

Table 1: Distribution of biopsies according to site and broad categories

	Esophagus	Stomach	Duodenum	Total
Neoplastic	2(3.7%)	0	7(13.2%)	9(17%)
Non- neoplastic	3(5.7%)	16(30.1%)	25(47.1%)	44(83%)
Total	5(9.4%)	16(30.1%)	32(60.3%)	53(100%)

In this study, 37 (69.8%) subjects were male, and 16 (30.1%) were female. The age group of this study ranged from, 17 years to 80 years, clustering of cases were seen in the 4th and 5th decade [Graph no-1].

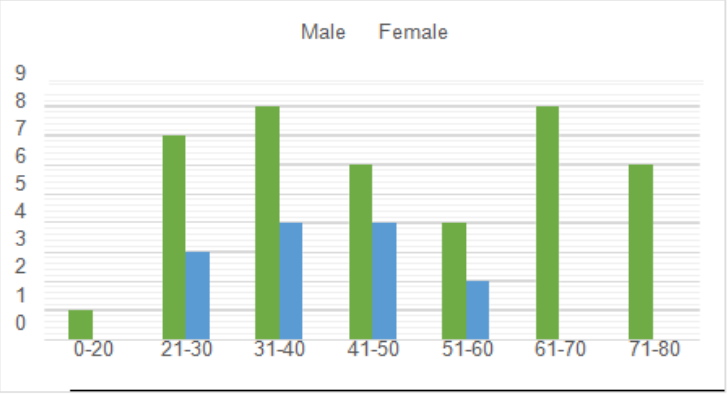

Fig 1: Distribution of age with Gender

In the non-neoplastic category, a total of 44 cases were diagnosed, eight (18.18%) cases with an acute inflammatory pattern, 32 (72.72%) cases as chronic inflammatory pattern and 4(9.09%) cases with an eosinophilic pattern.Esophageal pathological lesions presented primarily with dysphagia, odynophagia followed by abdominal pain associated with food intake and hematemesis. Out of the five esophageal biopsies, three cases (60%) were diagnosed as non-neoplastic and two cases (40%) were neoplastic. Among the nonneoplastic lesions two cases were chronic nonspecific esophagitis & one of them showed mild dysplasia. Single case of CMV esophagitis in a 51-year-old female, RVD positive with grossly punched out shallow ulcers was diagnosed, showing viral cytopathic changes of the stromal and endothelial cells. Two neoplastic lesions on histopathology were, one case of well differentiated squamous cell carcinoma (SCC) [Figure 1], wherein endoscopically a friable mass lesion was seen at the mid portion of the esophagus. Another case of adenocarcinoma was diagnosed at the gastro esophageal junction (GE), endoscopically seen as an ulcer proliferative lesion. Both ulcer proliferative mass lesions on endoscopy were diagnosed as Carcinomas. [Table 2a]

Table 2a: Correlation of endoscopic and histopathological findings of esophageal lesions.

Endoscopic Findings	Histopathological Findings			Total
	Esophagitis	Dysplasia	Carcinoma	
Edema	2	-	-	2
Erythema	1	1	-	2
Ulcers	1	-	-	1
Ulcero-proliferative lesion	-	-	2	2

A total of 16 cases of gastric biopsies were exclusively diagnosed as non-neoplastic lesions. We observed the most common symptoms related to gastric lesions were abdominal pain associated with food intake followed by non- bilious vomiting, pallor (lab investigations diagnosed anemia) and melena. Three cases were part of an anemia workup of patients, all showed chronic inflammatory pathology on microscopy, of which one was confirmed as Pernicious Anemia with anti-parietal antibodies positive. The remaining two cases, follow up was inconclusive. One case of chronic gastritis was positive for Helicobacter pylori organism which were of helical shaped [Figure 2b]. Even though, three lesions were suspicious for malignancy on endoscopy findings, all were diagnosed as inflammatory. Gastric neoplastic lesions were not seen in this study [Table 2b].

Chronic nonspecific gastritis five (31.25%) [Figure 2a] was the most frequent histopathological finding among the non-neoplastic lesions presented as erythema or edema grossly on endoscopy and chronic peptic ulcer were eight (50%), followed by two (12.5%) cases of acute gastritis/acute erosive gastritis & one case (6.25%) of eosinophilic gastritis.

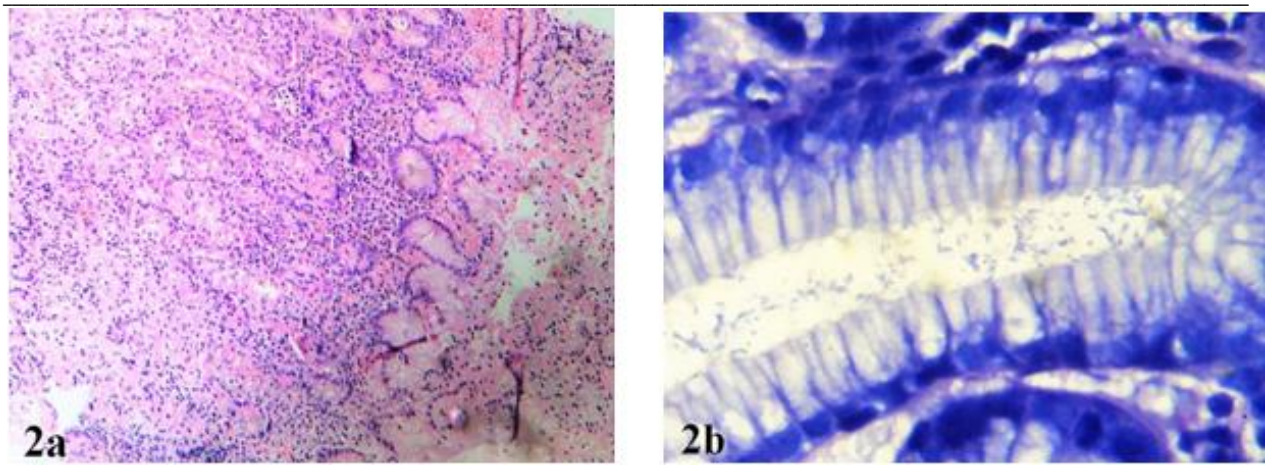

Figure 2a: Chronic gastritis showing marked mononuclear cell infiltrate in lamina propria (H&E, X40); 2b: Mucosal glands of chronic gastritis showing heavy colonization of H Pylori (May Grunwald Giemsa Stain, x1000)

Table 2b: Correlation between endoscopic and histopathological findings of Stomach lesions

Endoscopic Findings	Histopathological Findings			Total
	Gastritis	Dysplasia	Carcinoma	
Edema	4	-	-	4
Erythema	4		-	4
Ulcers	8	-	-	8
Polypoidal growth/ Suspicious for malignancy	3	-	-	3
Varices	1	-	-	1
Ulcero-proliferative lesion	-	-	-	0

In the duodenal biopsies, 25 cases (78.12%) were non neoplastic, and seven cases (21.87%) were neoplastic. The initial workup for duodenal pathologies revealed patients presenting mostly commonly with pain in abdomen associated with hunger, followed by loose stools, pallor (lab investigations diagnosed anemia) and obstructive jaundice. Three patients presented with obstructive jaundice, who investigated radiologically showed a mass lesion at the ampullary location of the duodenum, these biopsies were diagnosed on histomorphology as adenocarcinoma. Out of 25(78.12%) nonneoplastic duodenal endoscopic biopsies 15(60%) cases were diagnosed as chronic nonspecific duodenitis [Figure 3a] out of which one showed gastric foveolar metaplasia [Figure-3b], followed by five (20%) were duodenal ulcer on histology; three (12%) were eosinophilic duodenitis and one (4%) case each of Cryptosporidium Parpum duodenitis [Figure 3c] & duodenal adenoma.

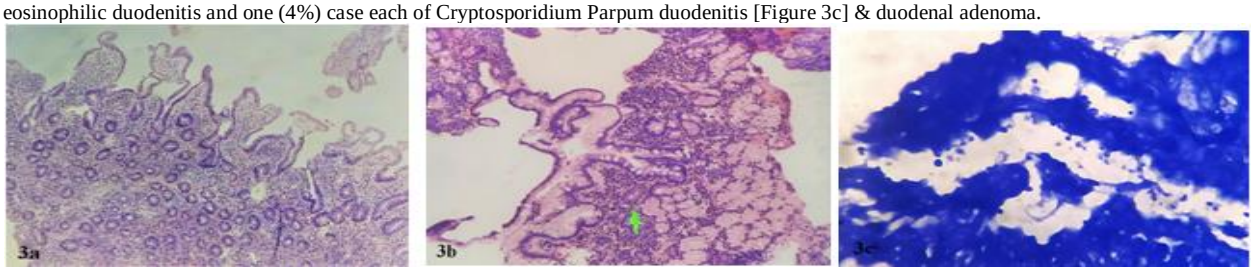

Figure 3a: Microphotograph of Chronic nonspecific duodenitis showing diffuse mononuclear infiltrate in lamina propria (H&E x40); 3b: Microphotograph of Chronic nonspecific duodenitis showing gastric (H&E x200); 3c: Numerous spherical organisms of Cryptosporidium Parvum lining the surface epithelium of duodenum (Giemsa Stain x1000)

Out of the seven carcinoma cases, five were seen as an ulcer proliferative lesion on endoscopy and two were seen as polypoidal lesions suspicious for malignancy on endoscopy which was confirmed on histopathology as adenocarcinoma [Figure 4] periampullary region (Table 2c). Majority of the cases diagnosed as malignant were in their seventh decade of life.

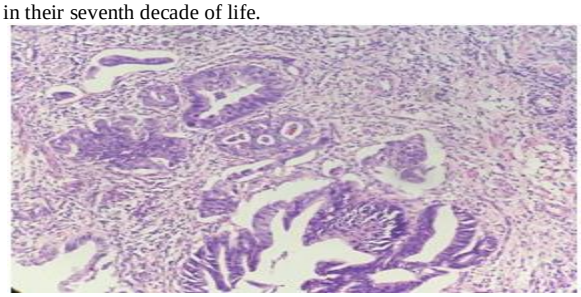

Fig 4: Microphotograph of well differentiated adenocarcinoma of duodenum (H&E, x400)

Table 2c: Correlation between endoscopic and histopathological findings of Duodenal lesions

Endoscopic Findings	Histopathological Findings			Total
	Duodenitis	Dysplasia	Carcinoma	
Edema	7	-	-	7
Erythema	6		-	6
Ulcers	5	-	-	5
Polypoidal growth/ Suspicious for malignancy	4	-	2	6
Stricture	2	-	-	2
Ulcer proliferative growth	-	-	5	5

Table 3 gives a general overview of the cases discussed in this study according to site & histological subtyping. The lesions in esophagus, stomach & duodenum varied with predominance of non-neoplastic pathology.

Table 3: Distribution according to Site of biopsy (n=53)

Diagnosis	Site of the Biopsy			Total
	Esophagus	Stomach	Duodenum	
Adenocarcinoma	1(1.8%)	0(0.0%)	7(13.2%)	8(15%)
SCC	1(1.8%)	0(0.0%)	0(0.0%)	1(1.8%)
Inflammatory lesion	1(1.8%)	8(15.09%)	19(35.8%)	27(50.9%)
Ulcer	1(1.8%)	8(15.09%)	5(9.4%)	14(26.4%)
Dysplasia	1(1.8%)	0(0.0%)	0(0.0%)	2(3.7%)
Adenoma/ Papilloma	0(0.0%)	0(0.0%)	1(1.8%)	1(1.8%)
Total	5(9.4%)	16(30.1%)	32(60.3%)	53(100%)

Discussion

Upper Gastrointestinal tract lesions vary from inflammatory, metaplastic, dysplastic to malignant and diagnosing this lesion correctly is crucial for providing the treatment and management to patient. The endoscopic biopsy offers a great chance to diagnose the upper gastrointestinal lesions but as the biopsy is very tiny there are limitations in diagnostic interpretations. This can be overcome by taking multiple biopsies from abnormal mucosa which will increase the chances of accurate diagnosis and reduce the errors in interpretation.

The present study reiterates the concept that distinguishing neoplasia from an inflammatory process in a GI biopsy is usually straightforward unless tissue sampled showed equivocal atypical cells obscured by dense inflammation, or reactive atypia. An understanding of the basic histology of the anatomical sites is essentially crucial to understand if the mucosa is indeed undergoing metaplasia [Table 4].

Table 4: Types of metaplasia as per site

Anatomical Site	Normal Epithelium	Metaplasia
Esophagus	Non keratinizing Stratified squamous, glycogenic acanthosis	Intestinal metaplasia (GE junction), Pancreatic Acinar metaplasia
Gastric	The surface/pit epithelium is foveolar type mucinous throughout the stomach regardless the region. **Cardiac and Antrum** Composed predominantly of mucinous glands Typically have abundant stroma compared to fundus and body.	a. Intestinal metaplasia b. Pancreatic acinar metaplasia Pyloric pseudometaplasia of gastric body mucosa
Mucins- Neutral PAS- Positive Alcian blue (AB) at pH 2.5 -Negative	**Fundus and body** Contain specialized tightly packed oxyntic glands, comprising of two cell types: Parietal cells- eosinophilic looking cells with a centrally placed nucleus. Chief cells- basophilic looking cells with a basally located nucleus	Mucins- Acidic PAS- Positive Alcian blue (AB) at pH 2.5 -Negative
Duodenum	Mucosa comprises of villi and crypts. Normal villi to crypt ratio 3-5:1. Villi are lined by absorptive cells with a brush border interspersed with goblet cells. Crypts along with the above two cells contain Paneth cells, neuroendocrine cells. Submucosal Brunner glands The lamina propria normally shows mixed mononuclear cells.	Gastric foveolar metaplasia

We aim to understand the dominant pattern of primary inflammation in the nonneoplastic cases. '**Acute inflammatory pattern'** defined by neutrophilic infiltrate in the lamina propria and/or epithelium, with minimal architectural distortion[7,8]. In this study 8 cases showed acute inflammatory pattern, some of which were accompanied by ulcerations or mucosal erosions.

'Chronic inflammatory pattern' is characterized by mucosal, glandular and surface architecture distortion with the dominant presence of chronic inflammatory cells. Intraepithelial lymphocytosis is a nonspecific finding with a diverse differential diagnosis including early celiac disease[8,9]. This study had 32 cases of chronic inflammatory pattern

'Eosinophilic pattern' is diagnosed abnormal eosinophilic infiltrate in the mucosa and lamina propria and cut- offs for counts vary depending on the site; exceeding >30 or 40 eosinophils/HPF is considered abnormal. Intraepithelial eosinophils and eosinophil crypt abscesses formation might be seen[8-12]. In our study four cases had eosinophilic pattern.

'Metaplastic pattern' is characterized by replacement of native mucosa with another differentiated cell type. Different types of metaplasia as per site as discussed above in Table 4.

A general comprehensive overview of upper GI biopsies (Table 5), gives a simple systematic approach to biopsy specimen, which can be put into practice while reporting.

Table 5: Systematic Approach to Upper Gastrointestinal Biopsies

1. Biopsy mucosa is representative of site mentioned in requisition form.
2. Rule out neoplastic process
Spot the dominant inflammation pattern: define the type-neutrophilic, chronic, eosinophilic, granulomatous.
4. Identify sub patterns of inflammation, mixed patterns
5. Etiological clues: infections (Special stains), medication induced(PPI's)
6. Indicators of prognosis and cancer risk: Atrophy, Metaplasia

Esophageal Biopsies

In our study, out of five esophageal biopsies, three cases (60%) were diagnosed as non-neoplastic and two cases (40%) were neoplastic , which is comparable with study done by R. Krishnappa et al (2013) which showed out of total 25 patients with esophageal lesions, non-neoplastic (56%) lesions were more compared to the neoplastic lesions (44%), however study done by Anjana M.L et al.(2021) revealed commonly encountered esophageal lesion in upper GI biopsies were neoplastic lesions (80%) and nonneoplastic lesions were (20%)[13,14].

The present study report showed that the common nonneoplastic lesion was chronic nonspecific esophagitis [three cases (60%)]. A study conducted by Rosy Khandelia et al (2017) and Margaret TJ. et al (2019) had similar finding of Chronic nonspecific esophagitis as commonest non neoplastic lesion[15,16].

A single case of viral esophagitis with cytopathic changes of Cytomegalovirus was included in this study, which highlights that endoscopic biopsy directed at the base of the ulcer increases the diagnostic yield as observed in this case. Although there are not a stipulated minimum number of biopsies, obtaining three samples has a sensitivity of at least 80%[13,17]. The qualitative research of CMV by polymerase chain reaction (PCR) has a higher sensitivity and can assist in confirmation of histopathological diagnosis, although it does not distinguish a latent infection from a clinically significant one[13,17].

In the present study, both patients of esophageal cancer presented in the 7th decade and endoscopically both showed a visible friable mass at the lower half of the esophagus, one diagnosed as Squamous cell carcinoma (SCC) and one adenocarcinoma at the gastresophageal (GE) junction. These findings are comparable to R. Krishnappa et al (2013) however studies of Rani et al (2018) and Nazrin M et al (2019) showed predominance of SCC in the esophagus[13,18,19].

Gastric Biopsies

Out of 16 cases of gastric biopsies, all were exclusively non neoplastic (100%), this observation correlated well with study done by Bilal A. Sheikh et al (2015) in which out of 93 biopsies from stomach, 68 (73.11%) revealed nonneoplastic lesions and study done by Vanktesh V et al (2019) revealed, out of the total 103 biopsies from stomach, 91(88.34%) were non neoplastic and 12 (11.65%) were neoplastic[20, 1].Chronic nonspecific gastritis, five cases (31.25%) was the most frequent histological diagnosis among these gastric non-neoplastic lesions which presented as erythema patch endoscopically, which is similar to the study done by Hirachand et al (35.16%) and Anjana ML et al (52.8%)[21,14]. Three of cases as part of anemia work up were diagnosed as chronic gastritis which is comparable with study done by Hela Elloumi et al (2016), out of 177 patients, chronic gastritis was found in 149 cases (84%)[22].Present study had low incidence of H Pylori chronic gastritis (6.25%), which is in contrast with study done by Sharma et al (2015), where H. pylori was identified in 45 (50.56%) cases of chronic gastritis on gastric mucosal biopsies, reason behind this discrepancy may be that the chronic cases of H. pylori gastritis have low yield on biopsy and also multiple biopsies are needed for demonstration of organism[23].

In present study gastric ulcers were eight cases (50%); our results are discordant with studies carried out by Krishnnapa Rashmi et al (2013) & Sk Md Jaynul Islam et al (2014) which had lower incidence of gastric ulcer i.e., eight cases (20%) & 11 cases (15.07%) respectively[13,24]. Incidence of two (12.5%) cases of Acute gastritis / Acute erosive gastritis found in our study is on higher side as compared with study done by Anjana M.L et al- three cases (2.8%) & Krishnappa rashmi et al- four cases (10%)[13,14].

Duodenal Biopsies

In this study, out of 32 cases, 25 cases (78.12%) were non neoplastic, and seven cases (21.87%) were neoplastic which is comparable with study done by Deepa Rani et al (2018) which had 20 cases (83.34%) nonneoplastic lesions and four cases (16.66%) neoplastic lesions out of 24 cases whereas in study done by Suvarna S et al, 25 cases were from duodenum which had 80% neoplastic and 20% non-neoplastic cases[18,25]. Two of the duodenal biopsies were suboptimal for assessment, as can be understood that this particular anatomical site the biopsies are smaller due to the difficulty in maneuvering of the scope and may be inadequate in up to 28% of the samples[26,27]. A well-oriented duodenal biopsy specimen should have at least 4–5 consecutive elongated, well-distended villi from the base to the tip[27].The most common diagnosis in our study was chronic nonspecific duodenitis or peptic duodenitis 19(76%), a condition associated with acid injury. Similar study done by Sneha Jawalkar et al (2015) showed that out of 49 cases of duodenal biopsies 85.7% cases were of chronic duodenitis, however Santhi Kiran et al, revealed lower incidence, 381 cases (9.52%) out of 719 deodenal biopsies[28,29].Included as part of an anemia workup we received a total five cases of duodenal biopsies, out of which four cases showed chronic inflammatory pathology with mucosal architectural distortion, & enterocyte damage which decreases the ability of the intestine to absorb iron[27,28]. One was diagnosed as malignancy, which emphasizes the notion, that multiple biopsies increase diagnostic yield even in a neoplastic scenario[24,25].

In present study five cases (20%) of duodenal ulcer were found, this incidence is less as compared to study done by Siddiqui et al (2020) which showed out of 114 duodenal biopsies, 29 cases (25.43%) were duodenal ulcers & study by Margaret TJ. et al (2019) showed six cases (35.29%) of duodenal ulcer out of 17 duodenal biopsies[30,16].Among the nonneoplastic lesions, our study had, three cases (12%) of eosinophilic duodenitis which is compatible with study done by Genta et al - 31 cases (8.37%)[31]. The study of Genta et al[31] indicates that eosinophilic duodenitis is associated with involvement of the other sites in the gastrointestinal tract. Most of the cases of eosinophilic duodenitis in this study were associated with eosinophilic enteritis. Seven of the histologically confirmed cases of malignancy (adenocarcinoma) were either reported as a mass, nodule or presented as mucosal thickening. This is in concordance with the findings of Prasad et al[32] and Somaniet al[33], who reported growth and mucosal thickening as most common endoscopic finding in malignant lesions.This study highlights the importance of histopathological examination of endoscopic biopsies for the diagnosis of upper gastrointestinal lesions. Endoscopic biopsies can not only provide valuable information concerning nonneoplasic or neoplastic nature of lesion & the primary inflammatory patterns, but also aid in identifying aetiological clues i.e., infections, medication effects (Proton pump inhibitors) or toxic ischemic effects.

Conclusion

UGE is an effective investigative modality to assess patients with upper gastrointestinal symptoms, and to obtain representative biopsies to come to a concrete diagnosis to initiate effective management. Endoscopic biopsy of upper gastrointestinal tract is helpful in diagnosing lesions but can also be used to monitor disease course and its complications. These are useful in judging the response to treatment and follow of patients with relapse.

Abbreviations

GI- Gastrointestinal
UGE- Gastrointestinal endoscopy
PAS - Periodic Acid Schiff stain

SCC- Squamous cell carcinoma
CMV- Cytomegalovirus

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