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Diagnostic utility of endoscopic duodenal biopsies and histopathological finding in upper gastrointestinal diseases: A 2-year analysis

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ABSTRACT

Background: Diseases of gastrointestinal (GI) tract present wit myriad signs and symptoms. Appropriate management of these diseases involves proper evaluation. Upper GI endoscopies are becoming increasingly popular because it helps in first localizing the lesion and then biopsy specimens can be obtained from affected area. Duodenal biopsy followed by histopathological examination may clinch the diagnosis in majority of the cases. **Aims and Objectives:** The aim of the study was to find out diagnostic utility of endoscopic duodenal biopsies and histopathological finding in the upper GI diseases. (1) To analyze duodenal endoscopic biopsy samples obtained from patients presenting with the upper GI symptoms. (2) To correlate endoscopic and histopathological findings in studied cases. **Materials and Methods:** A retrospective and prospective observational study was carried out at the private histopathology center over a period of 2 years. All the patients underwent upper GI endoscopy with duodenal biopsies using flexible endoscope. Histopathology of the samples obtained from endoscopic duodenal biopsies in patients presenting with the upper GI symptoms were analyzed. The endoscopic findings such as mass lesion or ulcerative lesion were correlated with histopathological findings. **Results:** Out of these 704 biopsies, 303 (43.04%) were esophageal biopsies, 220 [31.25%] were gastric, and 181 [25.71%] were duodenal biopsies. There were 129 (71.27%) males and 52 (28.73%) females with a M: F ratio of 2.5: 1. The mean age of the cases was found to be 54.7 ± 12.32 years. Out of 181 biopsies which were performed in this study, 100 (55.25%) lesions were found to be having neoplastic etiology whereas 81 (44.75%) lesions were found to have non-neoplastic etiology. Among patients who were found to have duodenal growth on endoscopy well differentiated adenocarcinoma (15.47%) followed by moderately differentiated adenocarcinoma (6.63%) were the common pathologies. In cases of non-neoplastic etiology, non-specific duodenitis was most common pathology (17.13%). **Conclusion:** Endoscopic biopsy followed by histopathological examination is cornerstone of the management of patients presenting with intractable upper GI symptomatology.

Key words: Endoscopy; Biopsy; Histopathological examination; Adenocarcinoma; Duodenitis

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INTRODUCTION

With advances in the field of gastrointestinal (GI) medicine, diagnostic endoscopy is becoming increasingly common and has become an integral part of evaluation of various GI pathologies.[1] Although advances in medical imaging have made it easier to make non-invasive diagnosis in many GI pathologies in many cases histopathological examination is the only gold-standard test, which can conclusively diagnose pathological condition affecting GI tract. Diagnostic endoscopy and biopsy of the affected area are the standard part of management of patients with various GI pathologies.[2] Various indications for duodenal biopsy include malabsorption syndromes, unexplained iron deficiency anemia, Initial diagnosis and then follow-up of gluten sensitive enteropathy, intractable diarrhea particularly

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in cases of acquired immunodeficiency syndrome, presence of occult blood in stool and suspected benign as well as malignant lesions of duodenum.[3] In some cases such as in patients of eosinophilic gastroenteritis duodenal biopsy can be part of endoscopic biopsies which are taken from multiple sites including from esophagus, stomach, and duodenum. The contraindication to duodenal biopsies includes suspected or actual perforation, active variceal bleeding, and patients having severe thrombocytopenia. The relative contraindications include patients on antiplatelets and anticoagulant drugs.[4] In expert hands this procedure is usually uneventful however in soe cases complications such as injury to gastroduodenal artery causing bleeding and consequently presenting as hematemesis or melena can be seen. In rare cases, particularly in older individuals, substantial hemorrhage may cause hemodynamic instability such as hypotension requiring ICU admission and appropriate management.[5]

In the lesions of duodenum, the GI symptomatology tends to be non-specific, and endoscopy plays an important role in patient management. Endoscopy and acquisition of biopsy with histopathological analysis are essential in the diagnosis and treatment of various GI pathologies. The histopathology diagnosis needs correlation with clinical features, endoscopy findings and radiology.[6]

After a biopsy specimen is obtained by duodenal biopsy its histopathological examination is the most crucial part of management as the report of histopathological examination will be deciding further management of the concerned patient.[7] Ideally a duodenal biopsy specimen should have at least 5 consecutive villi so as to be able to appreciate the villous architecture and its distortion if any. Various pathologies which can be diagnosed on histopathological examination of biopsy specimen include villous atrophy, crypt cell proliferation, crypt hyperplasia, thickening of mucosa, various benign and malignant lesions and colonization of lamina propria by organisms such as cryptococcus and invasion of epithelial cells by cytomegalovirus.[8] One of the important findings which may be seen in duodenal biopsy includes duodenal gastric metaplasia which may be secondary to gastric acid or due to H Pylori infection. The other pathologies which may be commonly encountered include chronic non-specific duodenitis, eosinophilic duodenitis, Chron's disease, gluten sensitive enteropathy, and various hyperplastic, hypoplastic, destructive, and infiltrative lesions.[9]

However, it must be kept in mind that the endoscopic biopsy is an invasive procedure as well as have a considerable cost. Its neither in the interest of patients nor in the interest of treating physician or surgeon to undertake endoscopic biopsies followed by histopathological examination of the specimen for non-specific purposes and there is a need to rationalize the indications for undertaking these endoscopic biopsies.[10]

This study aims to analyze the demographics of duodenal lesions, their endoscopic findings with correlation of endoscopy and histopathology.

Aims and objectives

The aim of the study was to find out diagnostic utility of endoscopic duodenal biopsies and histopathological finding in upper GI diseases. (1) To analyze duodenal endoscopic biopsy samples obtained from patients presenting with upper GI symptoms. (2) To correlate endoscopic and histopathological findings in studied cases.

MATERIALS AND METHODS

A retrospective and prospective observational study was carried out at the private histopathology center over a period of 2 years from January 2020 to December 2021 which included all the duodenal endoscopic biopsy samples received in the pathology department. Keeping power (1-Beta error) at 80% and confidence interval (1-alpha error) at 95%, the minimum sample size required, as calculated on the basis of pilot studies, was 120 patients; therefore, we included 181 (more than minimum required number of cases) specimens in this study. Demographic data such as age and gender of the patients was noted from case papers. Clinical details such as major presenting complaints, duration of illness and course of illness over a period of time was noted. If imaging has been done then the reports such as that of ultrasound, computerized tomography and magnetic resonance imaging were reviewed. Any history of major surgery in the past or any history of systemic illness was noted, drug history was noted from clinical records. If any biopsy was done previously then its findings were noted. All the patients underwent upper GI endoscopy with duodenal biopsies using flexible endoscope. All biopsies were performed by gastroenterologists of endoscopic surgeons who had considerable experience of performing such biopsies. The endoscopic biopsy samples were put on a filter paper for proper orientation and immediately immersed in 10% neutral buffered formalin.

Five-micron thick sections were prepared and slides were made. Each slide was stained with Hematoxylin and Eosin stain and microscopic examination was done. Additional sections were stained with Giemsa stain to find out H.Pylori infection. Alcain blue staining was done to find out intestinal metaplasia and Per-iodic acid schiff stain was done wherever necessary. Lesions were diagnosed as per the World Health Organization classification of GI tumor and tumor like conditions. The gross appearance

of affected site was noted down from notes taken during endoscopy and distribution of duodenal lesions depending on its endoscopic findings and histopathological features were noted.

While doing histopathological examination villous height as well as architecture was analyzed. Villous to crypt (V: C) ratio was noted. Pathological findings such as Presence of crypt hyperplasia, abnormalities of Surface enterocytes, Brush borders presence of pathologies such as Gastric metaplasia as well as chronic duodenitis was looked for. The presence of microorganisms such as *Giardia*, Mycobacterium avium intracellular, cytomegalovirus, and Cryptococcus neoformans was looked for and if present was noted down. A careful histopathological examination was done to diagnose benign or malignant pathologies.

The SSPS 21.0 software was used for statistical purposes and $P<0.05$ was taken as statistically significant.

Inclusion criteria

All endoscopic biopsies examined during study period were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

1. Cases in whom there was missing clinical or procedural data
2. Biopsies taken from oral cavity or biopsies taken from any part of GI tract other than duodenum.

RESULTS

A total of 704 upper GI endoscopic biopsies were done in the study duration. Out of these 704 biopsies 303 (43.04%) were esophageal biopsies, 220 [31.25%] were gastric, and 181 [25.71%] were duodenal biopsies (Figure 1). Only cases who have undergone duodenal biopsies were included in this study.

Out of 181 patients undergoing duodenal biopsies, there were 129 (71.27%) males and 52 (28.73%) females with a M: F ratio of 2.5: 1. The analysis of age group of the studied cases showed that the most common affected age group was between 61 and 70 years (25.41%) followed by 51–60 years (20.44%) and 41–50 years (19.89%). The youngest patient was 8-year-old male child while the oldest patient was 84-year-old male. The mean age of the cases was found to be 54.7±12.32 years (Table 1).

Depending on the endoscopic and clinical findings the lesions were classified into different categories. Amongst patients who were found to have duodenal growth on endoscopy well differentiated adenocarcinoma (15.47%) followed by moderately differentiated adenocarcinoma (6.63%) were the common pathologies. Among patients having ulcerative lesions duodenitis (11.60%) was the most common pathology whereas neuroendocrine tumor (7.18%) was the most common pathology seen in patients who had been found to have polyps on endoscopy. Immunohistochemistry was done in 21 cases of neuroendocrine tumors and all the tumors showed variable positivity for synaptophysin and chromogranin. The tumors were graded depending on Ki76 index in to grade 1 (85.71%), grade 2 (9.52%) and grade 3 (4.76%). Well differentiated adenocarcinoma presented with stenotic lesions in two patients (1.10%) (Figures 2-4) (Table 2).

Out of 181 biopsies which were performed in this study, 100 (55.25%) lesions were found to be having neoplastic etiology whereas 81 (44.75%) lesions were found to have non-neoplastic etiology. Amongst the cases with neoplastic etiology well differentiated adenocarcinoma (15.47%) was the most common single neoplastic pathology in studied cases followed by neuroendocrine tumors (11.60%). IN cases of non-neoplastic etiology non-specific duodenitis were most common pathology (17.13%) (Table 3).

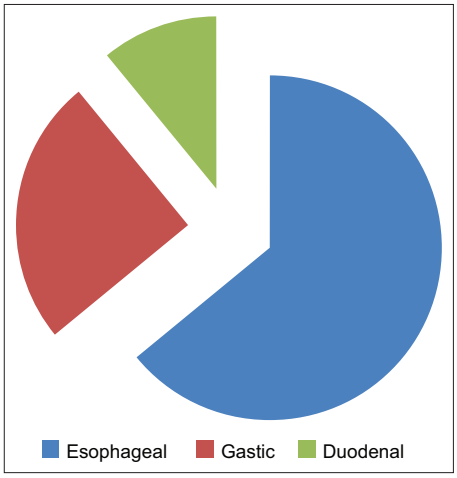

Figure 1: Location of upper GI biopsies in studied cases

Table 1: Age distribution of the studied cases

Age in years	Number of cases	Percentage
1 to 10	1	0.55
11 to 20	8	4.42
21 to 30	10	5.52
31 to 40	17	9.39
41 to 50	36	19.89
51 to 60	37	20.44
61 to 70	46	25.41
71 to 80	21	11.60
Above 80	5	2.76
Total	181	100

Mean age=54.7±12.32 years

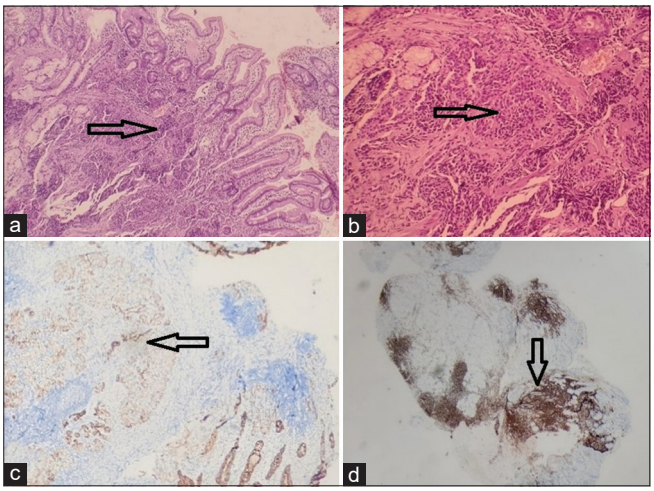

Figure 2: (a) Duodenal mucosa with tumour composed of insular and trabecular pattern invading the muscularis mucosa (b) Tumor cells are small, monotonous having moderate finely granular cytoplasm, small nucleoli, salt and pepper chromatin (c) Immunohistochemistry showing positivity for cytokeratin (d) Immunohistochemistry showing positivity for synaptophysin and chromogranin

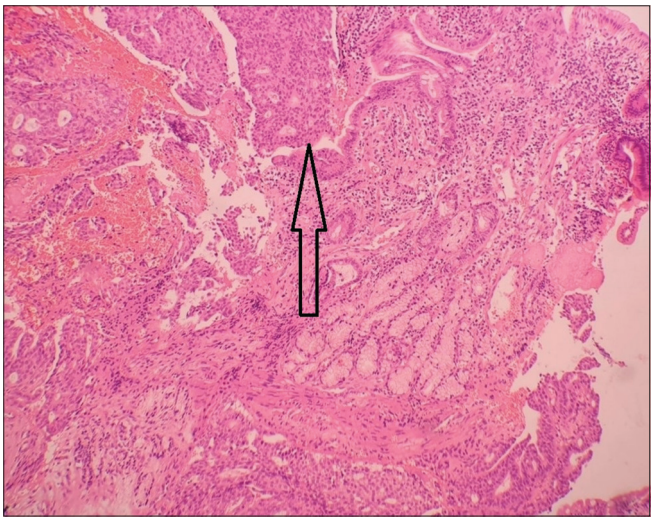

Figure 3: Duodenum with well differentiated adenocarcinoma having cribriform and glandular pattern infiltrating the muscularis mucosa

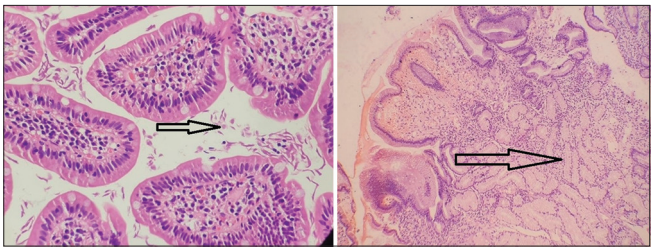

Figure 4: Giardia trophozoites seen along the surface of foveolar epithelial cells (Left), Hyperplastic lobules of Brunner glands extending from the submucosa into the lamina propria s/o Brunner gland hyperplasia (right)

DISCUSSION

Duodenal endoscopy is done as a part of work up of patients presenting with upper GI symptomatology. The lesions responsible for upper GI symptomatology are myriad and may consist of inflammatory, hamartomatous, benign, or malignant lesions.[11] Endoscopy, when combined with biopsy is minimally invasive, easy, and cost-effective procedure in the diagnosis of the upper

Table 2: Distribution of duodenal lesions depending on its endoscopic findings and histopathological features

Endoscopic finding	Histopathological finding	n	%
Duodenal growth	Adenocarcinoma		
	Well differentiated	28	15.47
	Moderately differentiated	12	6.63
	Poorly differentiated	7	3.87
	Tubular/tubulo villous/ pancreatico-duodenal/pyloric gland adenoma	12	6.63
	Duodenitis	7	3.87
	Suspicious of malignancy	3	1.66
	Neuroendocrine tumor (NET)	4	2.21
	Brunner gland hyperplasia	1	0.55
	Gastrointestinal stromal tumor	1	0.55
	Unremarkable features	2	1.10
	Total	77	42.54
Ulcers	Duodenitis	21	11.60
	Well differentiated adenocarcinoma	11	6.08
	Early ischemia	1	0.55
	Gastric metaplasia	2	1.10
	Neuroendocrine tumors	1	0.55
	Suspicious of malignancy	1	0.55
	Tubular adenoma	1	0.55
	Total	38	20.99
Polyps	Neuroendocrine tumors	13	7.18
	Brunner gland hyperplasia	7	3.87
	Inflammatory polyp	2	1.10
	Tubular adenoma	2	1.10
	No specific lesion	1	0.55
	Total	25	13.81
Thickened duodenal fold	Duodenitis (4)	4	2.21
	Brunner gland hyperplasia (1)	1	0.55
	Ischemic enteritis (1)	1	0.55
	Gastric heterotopia (1)	1	0.55
	Total	7	3.87
Flattened mucosa	Celiac disease/autoimmune enteropathy/peptic duodenitis	10	5.52
	Peptic duodenitis/Drug hypersensitivity/Megaloblastic anemia (5)	5	2.76
	No specific lesion (4)	4	2.21
	Total	19	10.50
Nodularity	Neuroendocrine tumors	4	2.21
	Gastric heterotopia	2	1.10
	Brunner gland hyperplasia	1	0.55
	Nodular duodenitis	1	0.55
	Total	8	4.42
Stenosis	Well differentiated adenocarcinoma (2)	2	1.10
	Gastric heterotopia (1)	1	0.55
	Ischemic enteritis (1)	1	0.55
	Total	4	2.21
Erosions	Eosinophilic enteritis	1	0.55
	Non-specific duodenitis	1	0.55
	Telangiectasia	1	0.55
	Total	3	1.66

Table 3: Distribution of duodenal neoplastic lesions (total cases-100)

Neoplastic versus non-neoplastic lesions	Histopathology findings	No of patients	Percentage
Neoplastic lesion	Well differentiated adenocarcinoma	41	22.65
	Moderately differentiated adenocarcinoma	12	6.63
	Poorly differentiated adenocarcinoma/Mucinous carcinoma	8	4.42
	Neuroendocrine tumour	21	11.60
	Tubullovillous/tubular/pyloric gland/pancreatico-biliary type adenoma with low/high grade dysplasia	15	8.29
	Suspicious of malignancy	1	0.55
	GIST	1	0.55
	Dysplasia	1	0.55
	Total	100	55.25
Non neoplastic lesion	Non-specific duodenitis	31	17.13
	Brunner gland hyperplasia	11	6.08
	Celiac disease/autoimmune enteropathy/peptic duodenitis/IBD	10	5.52
	Unremarkable	8	4.42
	Gastric heterotopia	5	2.76
	Peptic duodenitis	5	2.76
	Acute inflammation with ulceration	3	1.66
	Ischemic enteritis	3	1.66
	Inflammatory polyp	2	1.10
	Eosinophilic enteritis	1	0.55
	Telangiectasia	1	0.55
	Giardiasis	1	0.55
	Total	81	44.75

GI lesions. In the present study, endoscopic duodenal biopsies were examined with histopathological analysis and correlated with their respective endoscopic features. A total of 181 endoscopic biopsies from duodenum were analyzed within this study period. Middle aged to elderly patients was more commonly affected and majority of the patients (118 patients) were falling in the age group of 41 to 61 years with mean age of 54.7 years. It showed male preponderance with male: female ratio of 2.5:1 as males are commonly exposed to more risk factors causing duodenal diseases.[12]

Nazrin et al., conducted a study to determine the spectrum of histopathological lesions of upper GI tract. For this purpose, the authors analyzed esophageal, gastroesophageal junction and duodenal biopsies of patients presenting with the upper GI symptoms. Among 15 cases of duodenal biopsies, 13 (86.67%) cases showed non-neoplastic lesions and 2 (13.33%) were neoplastic one of which was adenocarcinoma (6.67%).[13] The percentage (55.2%) of neoplastic lesions was more in our study as compared to these studies.

Among the 77 cases which showed duodenal growth on endoscopy, adenocarcinoma was diagnosed in 47 (61%) cases with 4 (5%) cases of neuroendocrine tumor and 12 (15%) cases of tubular, tubulovillous, or pyloric gland adenoma. With this finding it can be concluded that endoscopic presentation of growth at duodenum has a high probability of having malignant nature and it must be biopsied. Amongst the 38 cases presented with duodenal ulcers, there were 21 (55%) cases of duodenitis and 11 (29%) cases of adenocarcinoma. There were four cases of duodenal stenosis of which 50% were diagnosed as adenocarcinoma. Ghosn et al., conducted a study of 1428 patients presenting with dyspepsia who underwent gastroscopy with gastric and duodenal biopsies.[14] The authors found that age above 40 years was associated with increased likelihood of exhibiting abnormal gastric biopsy result. Gastritis and metaplasia were detected more frequently than glandular atrophy ($P<0.001$) with gastritis being present the most ($P<0.001$). The presence of *H. pylori* and the gastric biopsy results were not associated with any of the duodenal biopsy results. Cloyd et al., also reported similar findings in their study of endoscopic duodenal biopsies.[15]

In our study, non-specific duodenitis (37.8%) was the most common non-neoplastic lesion followed by Brunner gland hyperplasia (13.5%) along with celiac disease (11.7%) gastric heterotopia (6%), ischemic enteritis (4%), peptic duodenitis (6%), inflammatory polyp (2.2%), eosinophilic enteritis (1.1%), severe active duodenitis (3.3%), giardiasis (1.1%), and telangiectasia (1.1%). However, 12.3% cases showed typical features of celiac disease and 10% of the cases showed duodenal mucosa with no specific pathology. In the study conducted by Terada[16] among the benign duodenal lesions, nonspecific duodenitis (60%) predominated which in concordance with our study which showed 38% cases with nonspecific duodenitis. Though there is no specific etiology of non-specific duodenitis, the authors such as Kreuning et al., believe it to be a stage of duodenal ulcer disease.[17]

IN our study 19 cases of clinically suspected Celiac disease showed flattened duodenal mucosa of which only 10 cases (52%) showed classic histologic features of Celiac disease with 6 cases diagnosed as Marsh Type 1 and 4 cases with Marsh type 3. Rest of the cases which had shown flattened duodenal folds on endoscopy included peptic duodenitis, drug hypersensitivity and megaloblastic anemia. Vogelsang et al., conducted a prospective study to establish the diagnosis of celiac disease.[18] For this purpose duodenal biopsy specimens were analyzed in patients suspected to be having celiac disease. The authors analyzed biopsies from the descending duodenum and the duodenal bulb of 51 patients with suspected or diagnosed celiac disease. The diagnosis of celiac disease and classification of the histological changes were performed by one pathologist. In the two index cases, the diagnosis of celiac disease could only be established by taking the biopsies from the duodenal bulb, and not from the descending duodenum. In the retrospective analysis, the number of intraepithelial lymphocytes was on average higher, but not significantly, in the descending part of the duodenum. On the basis of these findings the authors concluded that in patients who have already been on a gluten-free diet in childhood and later abandoned their diet, an additional duodenal bulb biopsy should be done. Similar histopathological findings in patients of celiac disease were also reported by the authors such as Iacucci and Ghosh[19] and Freeman.[20]

Limitations of the study

Relatively small number of patients was the limitation of our study, a study with large number of specimens will further substantiate the findings of our study. Moreover, patients with dietary restrictions for celiac disease were also included in this study and in those cases typical features of celiac disease may be absent.

CONCLUSION

Endoscopic biopsies followed by histopathological examination are one of the important parts of workup of patients presenting with intractable upper GI symptomatology. An accurate histopathological diagnosis is essential in appropriate management of these patients.

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AAP- Concept and design of the study; interpreted the results, prepared first draft of manuscript and critical revision of the manuscript, statistically analyzed, and interpreted; reviewed the literature and manuscript preparation; **SM-** Design of the study, statistically analyzed and interpreted, preparation of manuscript and revision of the manuscript; **AS-** Concept and coordination of the overall study.

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