

Histomorphological study of duodenum with special reference to RUT (Rapid Urease Test) negative dyspepsia in a rural care setting

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Abstract

Introduction: In our institute duodenal biopsies are taken in patients having either, unexplained anemia, weight loss, recurrent loose stool, abdominal pain, dyspepsia or suspected malabsorption. In the present study we have evaluated histomorphological features of duodenal biopsies in patients presented with specifically Rapid Urease Test (RUT) negative dyspepsia. **Materials and Methods:** A retrospective observational study was conducted and data of duodenal biopsies were collected from January 2017 to December 2018. Histopathology slides of duodenal biopsies were reevaluated. We have correlated clinical and endoscopic findings with various histomorphological parameters. **Results:** We have included total 99 cases. Demographic profile of our study population shows wide age range (9 years to 74 years) with mean age 39.8 years and Male: Female ratio 1.1:1. Dyspepsia was the common presenting symptoms (64.6% cases) and malabsorption was suspected in 29 cases. 28.3% cases show villous architectural abnormalities which correlate significantly with endoscopic findings of duodenal nodularity. Moderate to severe lamina propria lymphoplasmacytic infiltration seen in 58.56% cases and correlates significantly with dyspeptic symptoms. Duodenal biopsy was diagnostic in 3% cases. **Conclusion:** Diagnostic yield of duodenal biopsy is low but informative with proper clinical background.

Keywords: Duodenal biopsy, Dyspepsia, Malabsorption

Introduction

Endoscopist takes duodenal biopsy during upper GI endoscopy in context of various symptomatology like suspected malabsorption, evaluation of chronic and intermittent diarrhea, iron deficiency anemia evaluation, diagnosis and monitoring of gluten sensitive enteropathy and diagnosis of neoplasia & dyspepsia [1, 2]

Malabsorption is defined as chronic or intermittent diarrhea lasting for more than 4 weeks with diminished absorption of one or more nutrients. Physicians diagnosed malabsorption when any of the following features were present: diarrhea, steatorrhea, weight loss, edema and or clinical features suggestive of nutritional deficiency [3]. Dyspepsia refers to presence of one or more of the following symptoms like postprandial fullness, early satiation, epigastric pain or epigastric burning sensation [4].

Functional dyspepsia found in majority of patients undergoing endoscopy; Helicobacter Pylori causes a small percentage of cases [5].

The present study assessed the histomorphological change according to symptomatology and various etiologies in the study population. Aim of our study is to correlate morphological changes with various symptoms specifically dyspepsia.

Material and Methods

Study Design: Retrospective observational study

Duration of study: 2 years (January 2017 to December 2018)

Place of study: A tertiary care center serving rural population.

Method of data collection: Data of all duodenal biopsy cases were collected from the register. Hematoxylin & Eosin stained slides of duodenal biopsy cases were retrieved from the archive and reviewed.

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Special stains like Giemsa stain, Periodic Acid Schiff stain was performed from retained block as required. We have included cases of all age and sex whose clinical data and duodenal biopsy slides were available.

Exclusion criteria: we have excluded cases having incomplete clinical profile, poorly oriented biopsy in histopathology slides, and rapid urease test positive cases.

Data analysis: Cases were evaluated on the basis of their clinical profile (like age, sex), clinical presentations, endoscopic findings and histopathological features. We have reviewed the histopathology slides stained with Hematoxylin & Eosin for features like villous architecture, villous crypt ratio, lamina propria inflammation, IEL (Intraepithelial

lymphocytes) at villous tip, presence of neutrophil and eosinophils in lamina propria and presence of microorganism. We have done the subjective grading of lamina propria inflammation to mild, moderate and severe grade. We have counted intraepithelial lymphocytes in 100 enterocytes of 5 villous tips.

Ethical consideration and permission: We have taken permission from Institutional Ethics Committee before conducting this study.

Statistical Analysis: We analyzed the collected data statistically in suitable software. We have correlated the clinical symptoms with the histomorphological features. Chi square test was applied to find out significance of difference and P value <0.05 was considered as significant.

Results

Age and Sex Distribution: Age range is 9 years to 74 years of present study population with mean age 39.8 years. Majority (40.4%) cases are from the age range of 21 – 40 years. There is slight male predominance with Male: Female ratio 1.1:1 (Table 1)

Table-1: Age and sex distribution (n = 99)

Age	Sex		Total
	Male	Female	
<= 20 years	8	8	16
21 – 40 years	15	25	40
41 – 60 years	19	10	29
> 60 years	10	4	14
Total	52	47	99

Clinical Presentation: Dyspepsia (64.6%) was the most common presenting symptoms followed by recurrent abdominal pain (36.4%), recurrent loose stool (16%), altered bowel habit and anemia (Table 2). Multiple symptoms are present in fair number of cases. Malabsorption was suspected in 29 (29.3%) cases.

Table-2: Distribution of Clinical Presentation

Clinical presentation	Number of cases	Percentage
Dyspepsia	64	64.6%
Recurrent abdominal pain	36	36.4%
Recurrent loose stool	16	16%
Altered bowel habit	4	4%
Anemia	3	3%

Endoscopic Findings: Endoscopic findings were available in 66 cases. Common findings were corpus predominant gastritis (29%), erosive duodenitis (19.7%), duodenal nodule (16.6%), erosive gastritis, antral gastritis etc. Other findings include pangastritis, fundal gastritis, duodenal ulcer, flattening of duodenal mucosa, polypoid lesion at duodenum, loose lower esophageal sphincter.

Site of Duodenal Biopsy: Data on site of duodenal biopsy was available in 52 cases and in majority (84%) the site was second part of duodenum. Only in few cases biopsy was taken from first part of duodenum (8%) or both first and second part of duodenum (4%) or junction of first and second part of duodenum (4%).

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Villous Architecture: Majority of cases (71.7%) villi are long and slender. Abnormal villous architecture are seen in 28 (out of 99) cases. Common villous architectural abnormalities are shortening of villous (39%), broad villi (27.5%) followed by villous atrophy (17%), focal villi fusion (17%), partial villi erosion (14%). Other findings include villi branching, damaged surface enterocytes etc. Overlapping features are also noted in few cases. (Image 1)

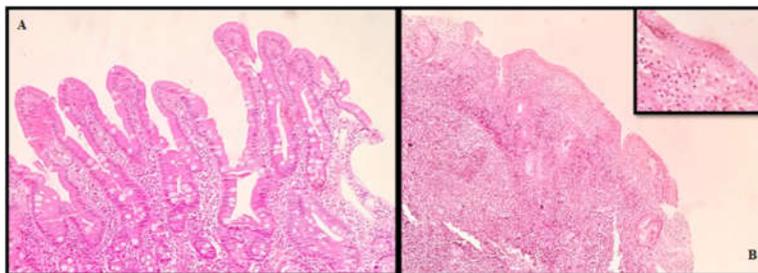


Image 1: (A) Normal duodenal biopsy showing long slender villi (100x magnification, H&E stain) (B) Duodenal biopsy showing severe

An endoscopic finding of duodenal nodularity correlates significantly (P Value <0.05) with villous architectural abnormality.

Villous abnormality in the form of shortening of villi, partial villous atrophy, villi erosion, fusion of villi seen in 8 out of 29 cases of suspected malabsorption but this is not statistically significant (P Value 0.92)

Lamina Propria Inflammation: Lympho-plasmacytic infiltration at lamina propria was graded as mild moderate and severe (subjective grading). Moderate and severe inflammation accounts for around 58.56% cases. Rest of the cases has mild inflammation or normal findings (Diagram 1). Neutrophilic infiltration noted in 7% cases and eosinophils present in 4% cases at lamina propria.

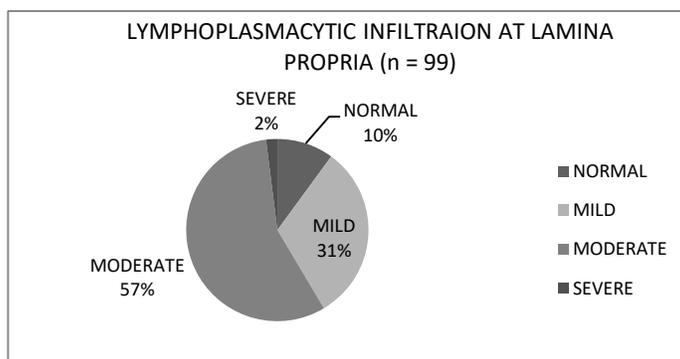


Diagram-1: Lympho-Plasmacytic Infiltration at Lamina Propria

We have correlated lamina propria inflammation with dyspepsia and there is significant moderate or severe lamina propria inflammation in patients with dyspepsia (P value < 0.05).

Table-3: Duodenal Biopsy Interpretation

Duodenal biopsy interpretation	No. of cases	Percentage
Normal	30	30.30%
Normal villi with moderate lympho-plasmacytic infiltration at lamina propria	33	33.33%
Non-specific duodenitis	21	21.21%
Brunners gland hyperplasia	5	5.05%
Crohn's disease	1	1.01%
Celiac disease	1	1.01%
Non-hodgkins lymphoma	1	1.01%
Others	7	7.07%
Total	99	100%

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Intraepithelial Lymphocytes: Intraepithelial lymphocytes (IEL) range from 2 to 25 in present study with mean IEL 5.5.

Duodenal Biopsy Interpretation: Duodenal biopsy was diagnostic in 3 cases (3.33%). 21 cases show features of nonspecific duodenitis and 5 cases show brunner's gland hyperplasia. 30 cases were normal and rest of the cases show non-specific findings (Table 3)

Discussion

The issue of performing a routine duodenal biopsy is controversial [1] and justifiable to cost benefit ratio. However many studies have shown the unsuspected duodenal pathology in routine duodenal biopsies [6, 7]

In present study, the commonest clinical presentation of duodenal biopsy cases were dyspepsia, recurrent abdominal pain, loose stool etc. which is quite similar to study conducted in Mayo clinic where chronic dyspepsia (46%) and diarrhea (35%) were the commonest indication for duodenal biopsy.(8)In Burger et al study also the common indications were dyspepsia, anemia, weight loss, diarrhea etc [9]

In our study population, mean age for undergoing upper gastrointestinal endoscopy with duodenal biopsy was 39.8 years and Male: Female ratio was 1.1:1. These findings are similar to another study conducted in India by Basavaraj et al [10] where mean age was 38.25 with slight male predominance, but study from Mayo clinic and Burger et al study have mean age slightly higher (50 years 54.6 years respectively) with female predominance [8, 9]. However Stanghellini V et al demonstrated that *Helicobacter pylori* (H pylori) negative dyspeptic patients are younger when compared to H pylori positive cases with male predominance [11]

As per diagnostic yield was concern, duodenal biopsy was diagnostic in 3 cases. We reported one case of celiac disease (confirmed with transglutaminase positivity). Apart from this, two clinically suspected cases of Non-Hodgkin's Lymphoma and Crohn's disease were confirmed by duodenal biopsy histopathology.

A regional difference in celiac disease is attributed to genetic, dietary and immunological factors; most of the cases were from states of North India possibly due to high wheat consumption [12, 13]. However, A study from south India with 101 patients of malabsorption, reported prevalence of celiac disease was 15.8%. (14) Major histopathological features of untreated celiac disease in duodenal biopsies are intraepithelial lymphocytosis, increased number of inflammatory cells at lamina propria and villous atrophy [15]. However diagnostic yield of routine duodenal biopsy for celiac disease was low as reported by Castro F et al, Stoven SA et al [8, 16].

In present study, villi architecture was normal in 71 (71.7%) cases. Earlier studies by Balasubramanian P et al (14) reported normal villi architecture in 40.6% cases. Endoscopic duodenal nodularity was found in 16.6% cases in our study which are quite similar to study conducted by Castro F et al [16].

In present study, endoscopic duodenal nodularity correlates significantly with villous architectural abnormality. Zukerman GR et al study also found villous blunting and thickening in several duodenal biopsies taken in endoscopic nodular duodenitis cases [17]. Another study conducted among children (6 – 17 years) from India show presence of villous atrophy in 47% cases of duodenal nodularity [18].

In our study moderate to severe lamina propria lymphoplasmacytic infiltration was found in 58.56% cases and correlate significantly (P value < 0.05%) with dyspeptic symptoms. According to Collins et al study also *Helicobacter Pylori* negative dyspepsia (non-ulcer dyspepsia) cases have higher mononuclear cell counts compare to control group [19].

Li et al study in patients with nodular duodenitis demonstrated significant chronic inflammation in H pylori negative cases compared to control [20]. Moderate to severe lamina propria lympho-plasmacytic cell infiltration seen in variety of conditions including celiac disease, peptic duodenitis, non-specific duodenitis, drug and infection [21].

New insights have been come in pathogenesis and significance of duodenal inflammation in dyspepsia (functional). Recent studies indicated “gut brain microbial axis” [22] and persistent of duodenal inflammation in post infection [23] as potential role in dyspepsia.

Conclusion

In proper clinical setting duodenal biopsies are informative and in selected situation also diagnostic. A significant lamina propria lympho-plasmacytic infiltration seen among patient presented with rapid urease test negative dyspepsia may actually strengthening “gut brain microbial axis” hypothesis and need further study in this area.

Findings: Nil; **Conflict of Interest:** None initiated
Permission from IRB: Yes

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