Duodenal biopsy in malabsorption- A clinicopathological study

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Abstract

Aims: To study the morphologic spectrum of duodenal biopsy specimens in malabsorption, to correlate the histology with clinical, endoscopic and serological investigations and to assess various aetiologies of malabsorption.

Material and Methods: Duodenal biopsies of 50 patients presenting with symptoms of malabsorption were analysed over a period of one year. The clinical details of patients, including their routine blood investigations, serology for Serum tissue transglutaminase (IgA t TG) and Upper gastrointestinal (UGI) endoscopic findings were noted. The villous architecture, villous to crypt ratio (V: C ratio), crypt examination and Intraepithelial lymphocytes were counted. Other findings like presence of parasites, dilated lymphatics, granulomas were also noted down.

Results and conclusions: The mean age of presentation was 32.5 years, with a mild female preponderance. Endoscopic mucosal abnormalities were found in 42% of cases and microscopic villous atrophy in 46% of cases. Increase in IELs was found in 48% of cases. Celiac disease was the leading cause (28%) of malabsorption whereas Tropical sprue accounted for only 4% of cases. Not a single case of tuberculosis was encountered.

Keyword: Duodenal biopsu, Malabsorption, Celiac diseases, Intraepithelial lymphocytes, Rillous architecture

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Introduction

Malabsorption is defined as diminished absorption of one or more dietary nutrients. Patients with malabsorption present with a wide spectrum of clinical features like weight loss, diarrhoea, abdominal pain, anaemia, multivitamin deficiency etc. The clinical consequences and expression of malabsorption are extremely variable.[1]

Important causes of malabsorption are gluten-sensitive enteropathy, autoimmune enteropathy, infections like tropical sprue, bacterial overgrowth/blind loop; protein allergy (milk, soy), eosinophilic gastroenteritis, primary intestinal lymphangiectasia, chronic granulomatous disease; infiltrative diseases like amyloidosis; inherited disorders like microvillous inclusion disease, abetalipoproteinemia and neoplastic disorders like Waldenstrom's macroglobulinemia and lymphoma.

Small intestinal mucosal biopsy examination remains one of the most important steps in evaluating patients with malabsorption. Duodenum being the most accessible site is commonly used for biopsy. Multiple biopsies obtained from the second part of duodenum has the advantage of not only increasing the accuracy and reducing false negative findings, but also has value in the study of spectrum of morphologic abnormalities of small bowel mucosa. Abnormal mucosal architectural pattern varies from mild to moderate villus shortening to flat mucosa and increased intraepithelial lymphocytes.[2]

We aimed to study the morphologic spectrum of duodenal mucosal biopsies in malabsorption, to correlate the histology with clinical, endoscopic and serological investigations and to assess various aetiologies of malabsorption.

Material and Methods

Endoscopic guided duodenal biopsies of 50 patients presenting with symptoms of malabsorption were analysed over a period of one year in a tertiary care hospital. Patients presenting with complaints of chronic diarrhoea of small bowel type for >1month or those with short stature (after ruling out endocrinal disorder) or iron deficiency anaemia not responding to oral iron therapy were included in the study. Patients who gave history of chronic NSAIDS or long term antibiotic use and those with history of major gastrointestinal surgery were excluded from the study.

The clinical details of patients, including their routine blood investigations, serology for Serum tissue transglutaminase (IgA t TG) and upper gastrointestinal (UGI) endoscopic findings were noted.

A detailed microscopic examination of the duodenal biopsies was carried out and areas where at least 3 villi appeared well oriented were selected for examination. The villous architecture, villous to crypt ratio (V: C ratio) and crypt examination was done. Intraepithelial lymphocytes (IELs) were counted in 100 enterocytes and were graded into normal (0-20 per 100 epithelial cells), borderline increase (21-30 per 100

epithelial cells), significant increase (>31 per 100 epithelial cells). The presence of parasites, dilated lymphatics and granulomas were also looked for.

Results

The age of presentation ranged from 3.5 years to 62 years, with a mean age of 32.5 years.

There was a slight female preponderance with male: female ratio being 1:1.18

A majority (84%) of patients presented with classical symptoms of malabsorption like chronic diarrhoea of small bowel type, steatorrhoea, weight loss and abdominal pain. Rest of the 16% patients had atypical presentations like refractory iron deficiency anaemia, short stature, severe hypoproteinaemia and seizure disorder.

Investigations revealed anaemia in 28 patients (mean Haemoglobin of 9.2 gm/dl), hypoalbuminemia in 6 patients and steatorrhea in 39 patients. IgA t TG levels were performed in 17 cases, of which 14 cases showed significantly, raised levels ranging from 15 IU/ml to 480 IU/ml.

UGI endoscopy was normal in 29 cases (58%) and the remaining 21 cases (42%) showed mucosal abnormalities in the form of granular mucosa, fissuring and decreased mucosal folds.

Microscopic examination:

Table 1 shows that 40% of the cases revealed normal villous architecture, 46% of cases showed villous atrophy of varying degrees (Mild atrophy-18%, Moderate atrophy-24% and severe atrophy- 4%) and in 14% of cases villous architecture could not be judged due to its poor orientation.

Table 1: Villous architecture - Histological evaluation

Villous architecture	No. of cases	Percentage (%)
Normal villi	20	40
Mild villous atrophy	9	18
Moderate villous atrophy	12	24
Severe villous atrophy	2	4
Poorly oriented biopsy	7	14
Total	50	

Table 2 highlights that a majority (52%) of cases showed normal IELs. Significant increase in IELs was found in 38% of cases and borderline increase in 10% of cases. Significant increase in IELs was mostly associated with villous atrophy and normal IELs with normal villous architecture.

Table 2: Villous architecture and IELs- Histological evaluation

Villous architecture	Normal IELs	Borderline increase in IELs	Significant increase in IELs
Normal	17	1	2
Mild atrophy	2	2	5
Moderate atrophy	1	2	9
Severe atrophy	0	0	2
Poorly oriented biopsy	6	0	1
Total	26 (52%)	5(10%)	19(38%)

Table 3 reveals that 29 cases showed normal endoscopic mucosal appearance, of which 18 cases showed normal villous architecture, 6 cases showed villous atrophy and 5 biopsies were poorly oriented. In the remaining 21 cases showing endoscopic mucosal abnormality in the form of granular mucosa, decreased folds and fissuring, a majority (17 cases) showed villous atrophy, 2 cases showed normal villous architecture and 2 biopsies were poorly oriented. Endoscopic – histologic correlation was found in 35 out of 43 well oriented biopsies (81.4%).

Table 3: Comparison of endoscopic and histologic findings

Histologic changes	Endoscopic mucosal appearances				
	Normal	Granular mucosa	Decreased folds	Fissuring	Total
Normal villi	18	1	1	0	20
Mild atrophy	5	1	1	2	9
Moderate atrophy	1	2	3	6	12
Severe atrophy	0	0	1	1	2
Poorly oriented	5	1	0	1	7
Total	29	5	6	10	50

Table 4 shows that in 20 cases, the underlying aetiology of malabsorption was demonstrated, of which celiac disease was the leading cause (n=14), followed by Tropical sprue (2 cases), Cryptosporidiosis (2 cases), Giardiasis (1 case) and Primary lymphangiectasia (1 case). In the remaining 30 cases, no definite cause for underlying malabsorption was demonstrated on histology.

Table 4: Malabsorption- Etiology

	No. of cases	Percentage (%)
Celiac disease	14	28
Tropical sprue	2	4
Cryptosporidiasis	2	4
Giardiasis	1	2
Primary lymphangiectasia	1	2
Unknown	30	60

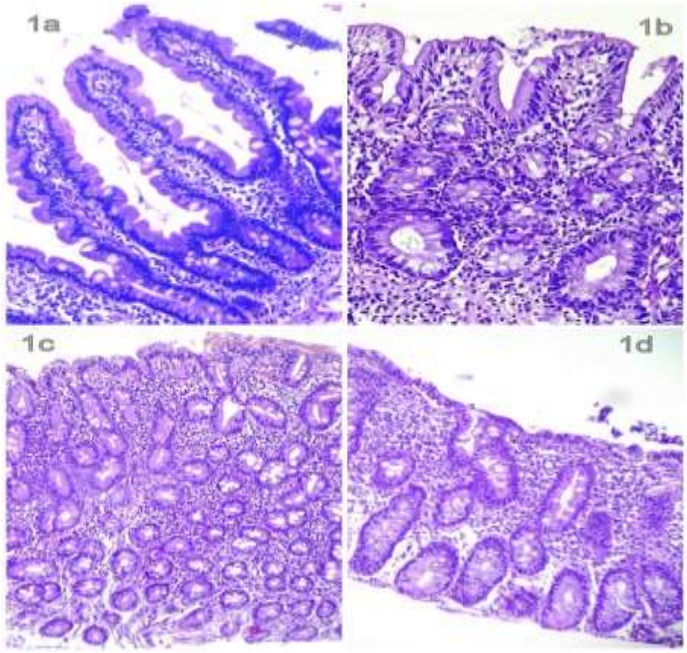

Fig.1a Normal duodenal mucosa showing well oriented villi (HE x 100)
Fig.1b Mild villous atrophy with borderline increase in IELs (HE x 100)
Fig.1c Moderate villous atrophy with significant increase in IELs (HE x 100)
Fig.1d Complete villous atrophy with significant increase in IELs, in a case of Celiac disease (HE x 100)

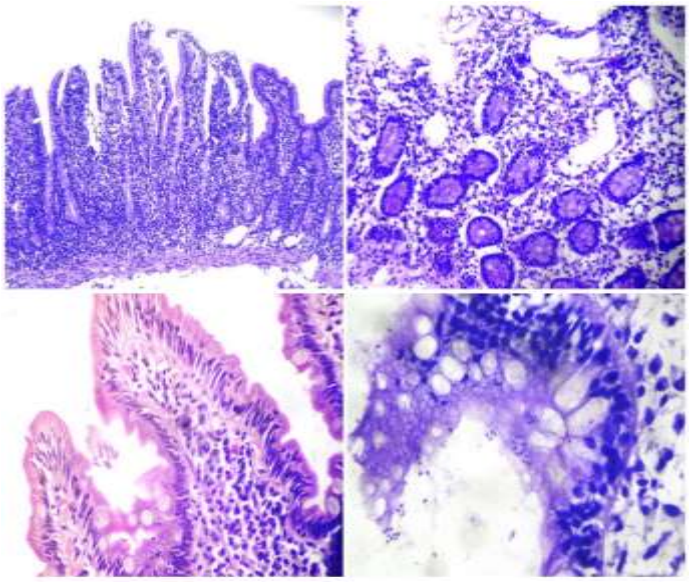

Fig. 2a Tropical sprue: Mild villous atrophy, Increased IELs more prevalent in the crypts than in the surface epithelium (HE x 100)
Fig. 2b Lymphangiectasia- dilated lymphatic channels located in the mucosa (HE x 100)

Fig. 2c Giardiasis, Pear shaped trophozites along the brush border of enterocytes (HE x 400)
Fig. 2d Cryptosporidiasis, 2 to 5 µm, spherical, basophilic bodies located at the apex of enterocyte (HE x 400)

Discussion

In the present study, the youngest patient was 3.5 years and oldest was 62 years, the mean age being 32 years. Our results are comparable with other studies in the literature where the mean age of patients was in the range of 34.3– 37.5 years.[3,4]

We found a slight female preponderance. This finding is in contrast to most of the studies in the literature where a male preponderance was found, with 60-62% of patients being males.[4,5]

Majority (84%) of our patients presented with classical symptoms of malabsorption, of which chronic diarrhoea was the most common complaint. It was associated with steatorrhea (n=39), weight loss (n=25) and abdominal pain (n=10). The remaining (16%) patients had atypical presentation, such as short stature, seizure disorder, iron deficiency anaemia refractory to oral iron therapy and severe hypoproteinaemia, which was similar to other studies in the literature.[3,6]

Most of the literature studies on malabsorption concentrate on the underlying aetiology. Very few studies analysed the overall duodenal villous architecture, IELs and their correlation. The results of present study were compared with literature (Table 5). Our results were comparable with those of Ghosal U et al[4], whereas Dutta A et al[5] found villous atrophy in 12.3% and increased IELs in only 8.6% of cases. The assessment of IELs has evolved since 1970s. The normal upper limit of IELs was set at 40 per 100 epithelial cells around 30 years ago.[7] Biagi F et al studied cases of celiac disease, they found the number of IELs in these cases to be in the range of 23 to 70 per 100 epithelial cells and proposed the upper limit of significant increase in IELs as 25 per 100 enterocytes.[8] Similarly, Veress B et al proposed the upper limit of IELs to be 20 per 100 enterocytes.[9]

In the present study 21 cases showed endoscopic mucosal abnormality, of these 17 cases showed villous atrophy of varying degree on histology. 2 biopsies were poorly oriented and only 2 showed normal villi. Thus, we found altered endoscopic mucosal appearances to be helpful in the diagnosis of histologic changes in the mucosa. Our results were comparable with the studies in the literature by Rondonotti E et al and Triester SL et al who demonstrated high sensitivity and specificity of endoscopic lesions in the diagnosis of altered mucosal architecture.[10,11]

Aetiology of malabsorption varies widely as per geographical location and age of patient.[2] While celiac disease, eosinophilic gastroenteritis, Crohn's disease, lymphangiectasia are frequent causes of malabsorption in western countries; tropical sprue, parasitic infections, intestinal tuberculosis, primary immunodeficiency syndrome are seen frequently in developing countries.[3]

With improvement in the socioeconomic status, antibiotic use, and changing dietary habits, relative incidence of each disorder is changing. Infectious diseases like tropical sprue, tuberculosis are becoming rarer and celiac disease is emerging as main cause of malabsorption both in children and adults.[3] Apart from this, owing to the awareness of atypical extra intestinal symptoms of celiac disease, availability of sensitive and specific serologic tests, use of duodenal biopsy and a high index of suspicion the incidence of celiac disease is rising. Occurrence of the so called typical presentation is now below 50%. Others present with atypical manifestations, such as short stature, refractory anaemia, or metabolic bone disease.[6] Within India, celiac disease was increasingly reported in northern and western India[3,12] whereas, tropical sprue is reported in south India. Thakur B et al[12] found intestinal tuberculosis (26%) as one of the leading causes of malabsorption.

The present study also found celiac disease as the leading known aetiology of malabsorption (14 cases-28%), of which 5 cases presented with atypical symptoms. In contrast, we found only 2 cases (4%) of tropical sprue. Cryptosporidiasis, Giardiasis and Primary lymphangiectasia were the other aetiologies. The incidence of these aetiologies was comparable with the literature studies.We did not find a single case of Tuberculosis and Crohn's disease as the underlying aetiology.

Table 5: Comparison of histological changes

Study	Total cases	Villous architecture		Intraepithelial lymphocytes		
		Villous atrophy n (%)	Normal architecture n (%)	Normal n (%)	Significantly Increased n (%)	Borderline increase n (%)
Dutta A et al[5]	162	20(12.3)	142(87.65)	138(85.2)	14(8.6)	-
Ghoshal U et al[4]	226	120(53.1)	106 (46.9)	100(44.2)	126(55.8)	-
Present study	50	23(46)	20 (40)	26 (52)	19 (38)	5 (10)

Summary and Conclusion

Duodenal biopsies in clinical cases of malabsorption revealed histologic abnormalities in the form of villous atrophy (46%) and increased IELs (48%). The leading aetiology was celiac disease (28%). In contrast, tropical sprue was seen in only 4% of cases and none showed tuberculosis, thus highlighting the changing pattern of malabsorption in developing country like India.

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