Original Article

Spectrum of Malabsorption in India – Tropical Sprue is Still the Leader

AK Dutta*, A Balekuduru**, A Chacko***

Abstract

Introduction: Two decades ago tropical sprue, Immunoproliferative Small Intestinal Disease (IPSID) and infections were common causes of malabsorption in India. It is possible that implementation of preventive health measures and improved sanitation may have changed the spectrum of disorders causing malabsorption. The aim of this study therefore was to assess the spectrum of malabsorption seen at our center during the past nine years.

Methodology: Patients seen at our center with malabsorption from January 2000 to December 2008 were included in this study. The etiological, clinical and investigation details were recorded on uniform structured data forms. The data obtained was retrospectively analyzed.

Results: Malabsorption was detected in124 patients during the study period. The mean age of patients was 31.9+16 years and 60.5% were males. Tropical sprue was the commonest etiology (29%) followed by celiac and Crohn's disease (15.3% each). Other important etiologies included parasitic infestations (9.7%) and immune deficiency disorders (5.6%). Intestinal tuberculosis was seen in only 2.4% patients.

Conclusions: We are witnessing a change in etiological spectrum of malabsorption . Celiac disease and inflammatory bowel disorders are emerging as important causes and ImmunoProliferative Small Intestinal Disease (IPSID) and intestinal tuberculosis are on the decline. Tropical Sprue however continues to be the commonest cause as in the past.

Introduction

Malabsorption syndromes (MAS) are important causes of morbidity and mortality in the tropics. Establishing the etiology of this challenging clinical entity requires judicious use of a wide array of tests. While in the developed countries non-infective causes predominate, tropical sprue and infective causes are common in developing countries like India.[1-3] During the last two decades, India has seen the emergence of celiac disease and inflammatory bowel disease.[4,5] Socioeconomic development and improvement in health and sanitation during this period might have reduced the incidence of chronic infective diarrhea and tropical sprue and changed the spectrum of malabsorption.[6,7] The aim of this study therefore is to provide an updated etiological spectrum of malabsorptive syndromes seen at our center during the past decade.

Patients and Methods

Patients seen at our center between January 2000 and December 2008 were screened retrospectively. Those with diarrhea of more than 1 month duration and abnormality in at least one of the following tests: i) Urine or blood xylose absorption test, ii) 72 hour stool fat excretion, iii) Serum vitamin B12 level were included in the study.

Absorption studies: After giving 5g xylose orally, amount excreted in urine during the next 5 hours (urine xylose test) or serum level after one hour (blood xylose test) was estimated. Excretion of less than 1g xylose in 5 hour urine sample or one hour serum level <0.55mM was considered abnormal.[8] Stool fat (72 hours) was estimated using Van de Kamer's technique. Patient was given diet containing 100g fat daily for 5 days and stool samples were collected from 3rd to 5th day. Fat malabsorption was diagnosed when 72hour stool fat was more than 18g/day.[9] Serum vitamin B12 less than 200 pg/ml was considered abnormal.

Clinical information, laboratory and treatment data were collected for all patients by a standardized review of medical charts using uniform structured data forms. Patients with malabsorption of two or more substances (abnormal urine/blood xylose test, reduced serum B12 level, increased 72 hour stool fat) in the absence of other causes of malabsorption were diagnosed to have tropical sprue.[10] Parasitosis was detected by microscopic examination of stained stool smears and occasionally on histology of duodenal mucosa. The diagnosis of celiac disease was established by modified ESPGAN criteria which require presence of duodenal mucosal biopsy changes and clinical response to gluten free diet.[11] Crohn's disease was diagnosed using a combination of endoscopic, radiological, histological features and response to treatment.[12] Intestinal tuberculosis (ITB) was diagnosed in presence of acid fast bacilli on mucosal biopsy or culture or presence of caseating granuloma on mucosal biopsy specimen.[13] The study was approved by institute review board and ethics committee.

The clinical and laboratory data are presented as mean value with standard deviation or median with range for continuous variables and as proportions for categorical variables. Comparison between categorical variables was done using Fisher's exact test and continuous variables were compared using Mann Whitney's U test. A two tailed p value of ≤0.05 was considered significant. Statistical analysis was done using SPSS 11.0 for windows .

Results

One hundred and twenty four patients with chronic diarrhea

*Assistant Professor, **Senior Resident, ***Professor, Department of Gastrointestinal Sciences, Christian Medical College & Hospital, Vellore 632 004
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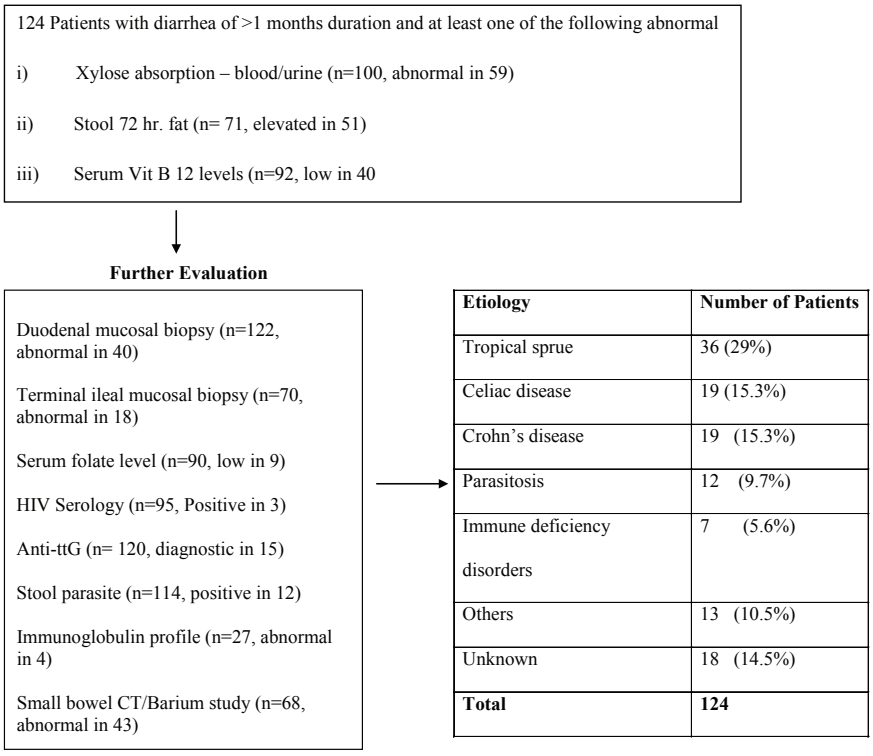

Etiology	Number of Patients
Tropical sprue	36 (29%)
Celiac disease	19 (15.3%)
Crohn's disease	19 (15.3%)
Parasitosis	12 (9.7%)
Immune deficiency disorders	7 (5.6%)
Others	13 (10.5%)
Unknown	18 (14.5%)
Total	**124**

Fig. 1 : Etiological profile of malabsorption disorders

Table 1 : Demographic and blood investigations of patients with tropical sprue, celiac disease and Crohn's disease

	Tropical sprue (n=36)	Celiac disease (n=19)	Crohn's disease (n=19)	p (Tropical sprue vs Celiac disease)	p (Tropical sprue vs Crohn's disease)
Age (Years)	33.5 (4-76)	13 (4-41)	32 (10-53)	0.001	0.47
Sex (%Males)	13 (36.1%)	8 (42.1%)	9 (47.4%)	0.44	0.3
Hemoglobin (g%)	10.7 (4.3-16)	11 (4.9-15.7)	9.7 (4.6-15.1)	0.97	0.37
Albumin (g%)	3.8 (1.7-4.8)	3.8 (1- 4.7)	2.9 (1.1 – 4.7)	0.35	0.002

due to malabsorption were seen during the nine year study period. Nineteen of them were in pediatric age group (<15 years of age). Their mean age was 31.9±16 years and 60.5% were males. Seventy two percent of patients (89 of 124) belonged to eastern part of India reflecting the geographic distribution of patients seeking health care at our institution. Stool fat (72 hours) was estimated in 71 patients and it was abnormal in 51 (71.8%). Abnormality on blood or urine xylose absorption test was detected in 59% of the 100 patients (60 urine xylose, 34 blood xylose and 6 had both) who underwent this test. In the 92 patients who had estimation of vitamin B12, low levels were seen in 40 (43.4%) patients. Mean hemoglobin was 10.6± 2.8g% and median albumin 3.7g/dL (range 1- 4.8g/dL). Hypoalbuminemia was noted in 50 patients (40.3%).

After confirming the presence of malabsorption, further investigations to establish the etiology were performed based on clinician's judgement. These included upper gastrointestinal endoscopy with duodenal mucosal biopsy, colonoscopy with multiple segmental biopsies (including terminal ileum), IgG anti-tTG (using human substrate), HIV serology, immunoglobulin profile, serum folate levels and stool examination for parasites. Fig. 1 shows the number of patients who underwent these investigations and the number in whom it was abnormal. Anti- tTG was positive in 15 of the 19 celiacs. It was also positive in 8 patients with other malabsorptive disorders. Duodenal mucosal biopsy was abnormal in 40 patients – villous atrophy of varying grades in 20, increased intraepithelial lymphocytes in 14, parasites in 3, lymphangiectasia in 2, and granuloma in 1. Of the 36 patients with tropical sprue, 8 had villous atrophy on duodenal biopsy. Terminal ileal biopsy showed chronic ileitis in 11 patients with Crohn's disease and one of these also had granuloma. Small bowel imaging using CT abdomen or barium meal follow through was performed in 68 patients. Abnormalities were detected in 43 patients which were generally non-specific. Thickening of mucosal folds was seen in 24 patients, dilated small bowel loops in 12, flocculation of barium in 5 and strictures in 2 of them.

The etiological spectrum of MAS in our patients is shown in Fig. 1. Tropical sprue was the commonest etiology (29%) followed by celiac disease and Crohn's disease (15.3% each). Twenty seven percent of our patients from east India had tropical sprue while 36.4% south Indian patients had this condition (p=0.37). Parasitic infections were seen in 12 patients – giardiasis in7, strongyloidiasis in 4 and cryptosporidiosis in 1. Immune deficiency disorders were seen in 7 patients – AIDS in 3, IgA deficiency in2, agammaglobulinemia in 1 and CVID in 1. Other causes included intestinal tuberculosis in 3, diabetic diarrhea in 2, chronic pancreatitis in 2, eosinophilic gastroenteritis in 2, intestinal lymphangiectasia in 2 and collagen vascular disorder in 2. In 5 patients no cause could be ascertained and 13 patients had incomplete evaluation.

Comparison of age, sex and blood investigations between patients with tropical sprue and celiac disease as well as tropical sprue and Crohn's disease is shown in Table 1. Patients with celiac disease were younger than those with tropical sprue (p=0.001). Hypoalbuminemia was commoner in patients with Crohn's disease compared with tropical sprue (p=0.002).

Discussion

In this paper we report one of the largest series of MAS from India. An interesting observation of this study is that tropical sprue continues to be the commonest etiology of MAS in spite of emergence of celiac and Crohn's disease. There has been one study from northern India (Lucknow – 99 patients) and one from western India (Mumbai – 50 patients) describing the etiological profile of MAS.[3,6] Similar to our observation, tropical sprue was the commonest etiology in Lucknow study (39%). In contrast, celiac disease (26%) and intestinal tuberculosis (26%) were the two most common causes of MAS in Mumbai study. One possible explanation for the high prevalence of tropical sprue in our study compared to western India may be presence of endemic and epidemic forms of the disease in south India in contrast to only endemic form of tropical sprue in the west of the country.[2] Another interesting observation is the absence of Immunoproliferative small intestinal disease (IPSID) as a cause of MAS in the present study. In 1998, our center had reported the largest series of IPSID patients (n=15) in India.[14] As intestinal microbes have been postulated as trigger factors for IPSID, improved sanitation and nutrition during the past decade may

be responsible for absence of this disease in our series or it may just be referral bias due to small number of patients.

Celiac disease as a cause of malabsorption has definitely gained prominence in the past two decades and so has been the case with inflammatory bowel disease.[4,5,15] These were the next two common causes of MAS in this study. Celiac disease has been predominantly reported from north India and is rare in south India due to consumption of rice as staple diet and difference in HLA type.[16] Of the 19 patients with celiac disease, only 2 were from south India. Although anti- tTG was positive in eight patients with other malabsorptive disorders, the possibility of concomitant celiac disease in these patients cannot be excluded. Crohn's disease of small intestine can cause malabsorption due to extensive small bowel disease or resection or bacterial overgrowth upstream of strictured segments. Crohn's disease was cause of MAS in 9% of the patients in Lucknow series while it was not seen in Mumbai series. The emergence of Crohn's disease in India has been postulated to be due to improved sanitation.[17]

Intestinal Tuberculosis (ITB) accounted for only 2.4% of our cases. The low prevalence of ITB in this study may be due to low prevalence of malabsorption in this disorder (20%) and widespread use of anti-tuberculous therapy empirically at primary and secondary health care centers.[3] There have been numerous reports associating parasitic agents with malabsorption.[18-19] Parasites were the primary etiological agent in 10% of our patients (absence of acquired or inherited immune deficiency). Four of the seven patients with immune deficiency also had intestinal parasitosis.

Pediatric patients have a different etiological profile of MAS with parasites and celiac disease dominating the list.[5,19] Similar observations emerged in our study as well. Among our 19 pediatric patients, 9 (47.4%) had celiac disease, 3 giardiasis, 3 Crohn's disease, 2 tropical sprue, 1 IgA deficiency and no cause was elucidated in one. In a report of 137 pediatric patients with malabsorption from north India, celiac disease was seen in 26%, intestinal parasites in 9% and none had tropical sprue.[5] In contrast, in another series of 47 children with chronic diarrhea from north India, tropical enteropathy responding to broad spectrum antibiotics was seen in 46.8% cases and celiac disease in 6.8%.[20] In a Nigerian study on 142 children with chronic diarrhea, enteropathogenic agents were identified in stools of 90 (63%) patients.[19] In 18 patients (14.5%) an etiology for MAS was not identified. One potential limitation of this study is that evaluation for bacterial overgrowth was not performed in all the patients with unknown etiology.

MAS due to various etiologies may differ in the age of presentation and the nature of abnormalities on blood investigations. We compared the demographic profile and blood investigations among the three common etiological subgroups of MAS. As celiac disease occurs mainly in children and young adults, these patients were younger than those with tropical sprue (Table 1). Crohn's disease patients had significantly lower albumin as compared with tropical sprue (Table 1). The cause of low albumin in Crohn's disease patients is multifactorial including gut loss, malabsorption, increased catabolism and inadequate intake.

In conclusion, patients with chronic diarrhoea and MAS continue to be an important group referred for management to a gastroenterology unit in tropical countries. Appropriate evaluation and therapy offers a chance of cure in most patients. While the prevalence of IBD and celiac disease is increasing and IPSID and ITB declining, tropical sprue continues to be the commonest etiology of MAS.

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