Original article:

Clinical and etiological spectrum of chronic diarrhoea

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ABSTRACT

Background: Chronic diarrhoea has a prevalence of around 4%. It impacts the patient's health mentally, socially and financially. The differential diagnosis of chronic diarrhea is humongous, and taking relevant history is time consuming. An accurate diagnosis is fundamental for administering effective therapy which is available for majority of the conditions that cause chronic diarrhoea. This study is aimed at ascertaining the causes of chronic diarrhoea and the prevalence of malabsorption among patients with chronic diarrhoea.

Methods: Patients above the age of 18 presenting with chronic diarrhoea studied for etiology and malabsorption. A total of 30 patients who fulfilled the selection criteria were examined clinically and evaluated by laboratory and imaging tests.

Results: Among the 30 patients of chronic diarrhoea studied 20 were males and 10 were females. The most common cause was IBS (60%), followed by Crohn's disease (13.33%). The prevalence of malabsorption was 26.7%; with the most common cause was IBS (50%) followed by Crohn's disease (25%). A male preponderance was observed in both chronic diarrhoea and malabsorption. Statistically significant association was found between malabsorption and high serum SGOT, serum ferritin levels (p value<0.05).

Conclusion: The commonest cause of chronic diarrhea is colonic in origin. In our study population, IBS; a functional gut disorder is the commonest cause of chronic diarrhea. The inflammation of the gastrointestinal tract ranks the second cause in the list of etiology of chronic diarrhea. Iron deficiency anemia and carbohydrate malabsorption were prevalent in these patients with chronic diarrhea.

Keywords: Chronic diarrhoea, D- Xylose, IBS, malabsorption,

INTRODUCTION

Chronic diarrhoea is a common clinical problem. Prevalence of chronic diarrhoea in the general population ranges between 3-5%.[1] Medical advice is often sought for unless weight loss, rectal bleeding, fecal incontinence or abdominal pain. A correct diagnosis helps in effective therapy and improves the quality of life of the patient. More common mechanisms of diarrhea are; reduced absorption of the water from the intestine. This happens in the setting of slow rate of absorption. The other mechanism is due to nutrient content in the bowel which interferes with water absorption and keeps it in the lumen bound to carbohydrates. Multiple studies have established tropical sprue as the most common causes of diarrhea with malabsorption in tropical courtiers. Celiac disease is being increasingly diagnosed in India. Malabsorption syndrome is a common condition in India because of the tropical climate and the generally poor socioeconomic condition of the vast population. Hot and humid climate is especially conducive for the development of chronic infection and subsequent inflammation of the gut leading to reduced absorption of the

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dietary contents. Poor dietary hygiene due to poor socioeconomic condition exacerbates such a condition. In tropical countries, tropical sprue and parasitic infestations are the usual causes of chronic diarrhea. With improvement in the socioeconomic and sanitary conditions in the country coupled with the increasing use of antibiotics, frequency of malabsorption due to infectious causes might have declined. Celiac disease is being reported with increasing frequency as the responsible factor for malabsorption between both adults and children. Patients who have celiac disease might develop secondary small intestinal bacterial overgrowth that might temporarily respond to treatment with antibiotics. Such a condition leads to a difficult diagnosis. Therefore, it is necessary to determine demographic, clinical and laboratory parameters which help to differentiate among the various causes of diarrhea and malabsorption especially in tropical countries. Hence the present study was done at our tertiary care centre to identify the various etiologies of chronic diarrhoea, and the prevalence of malabsorption in patients with chronic diarrhoea.

METHODS

Patients above the age of 18 years excluding pregnant females; presenting with diarrhoea lasting for more than 4 weeks, were hospitalsed. Department of General Medicine undertook the study during the period from September 2017 to August 2019. The study design was cross-sectional observational study. Total of 30 patients presenting with chronic diarrhoea were assessed by clinical, hematological, biochemical, radiological, endoscopic and histo-pathologic means to identify the cause of diarrhoea and if malabsorption was present in them.

INCLUSION CRITERIA

a) Age more than 18 years

b) Diarrhoea lasting for more than 4 weeks

EXCLUSION CRITERIA

a) Pregnancy

The ethical clearance was obtained from the Institutional Ethical committee.

Procedure: All the participants were also informed about the study procedure and the information required from them for the study. A voluntary informed written consent was taken from the participant those who consented were included in the study. A strict confidentiality was maintained about the personal details of the participants and information related to the study. Consent form was available in English, Hindi as well as in Marathi. In case of illiterate participants/relatives' consent was taken in presence of witness. Any third-party person not directly attached to the study was taken as witness. The patients were put through standard hematological and serum biochemical tests of Hemogram with MCV and ESR, blood glucose,

HbA1c, LFT, RFT, CRP, S. Amylase, S. Lipase, S. Ferritin, S. Electrolytes (sodium and potassium), S. calcium and S. Phosphate. While the hemogram provided evidence of anemia; MCV and S. ferritin were indicative of B12 deficiency and iron deficiency respectively. ESR and CRP provided evidential proof of inflammation. S. amylase and lipase provided clue to any pancreatic etiology of chronic diarrhea. Stool investigations were done which included stool routine microscopy with occult blood testing, stool staining with Sudan III stain for fat globules and stool culture/sensitivity. Stool investigations provide us objective evidence of the type of diarrhoea (mucoid/ watery/ infective/ secretory) and if there is any blood in stools (colitis or upper GI blood loss with occult blood).

Malabsorption is evidenced with presence of fat globules in the stool. 25 gram Urinary D-Xylose testing was done for carbohydrate malabsorption.

D-xylose more than 4.5 gm in 24 hours urine was considered positive test. Radiological investigations included ultrasound of abdomen and pelvis for screening of any abdominal pathology and contrast enhanced CT scan of abdomen and pelvis/enterography was done wherever indicated. Upper Gastrointestinal endoscopy was done with biopsies taken from first and second part of the duodenum as indicative of any small bowel pathology. Colonoscopy was also done with biopsies from the margins of any ulcerations of edematous part of colon as well as random biopsies were taken.

STATISTICAL ANALYSIS

Microsoft Excel 2010 was used to compile the collected data and analyzed using SPSS (Statistical Programme for Social Sciences) software version 23. ANOVA, and Fisher's exact tests were applied wherever applicable. All tests were two-tailed with a 95% CI (confidence level, $P < 0.05$) considered as statistically significant. The study findings were discussed and compared with the other relevant studies after taking into consideration the materials, study design, and results. Conclusions were drawn based on the study results.

RESULTS

This study was conducted among 30 cases of chronic diarrhoea and was evaluated for the various causes of chronic diarrhoea and malabsorption. Following tables and graphs shows observations of the study.
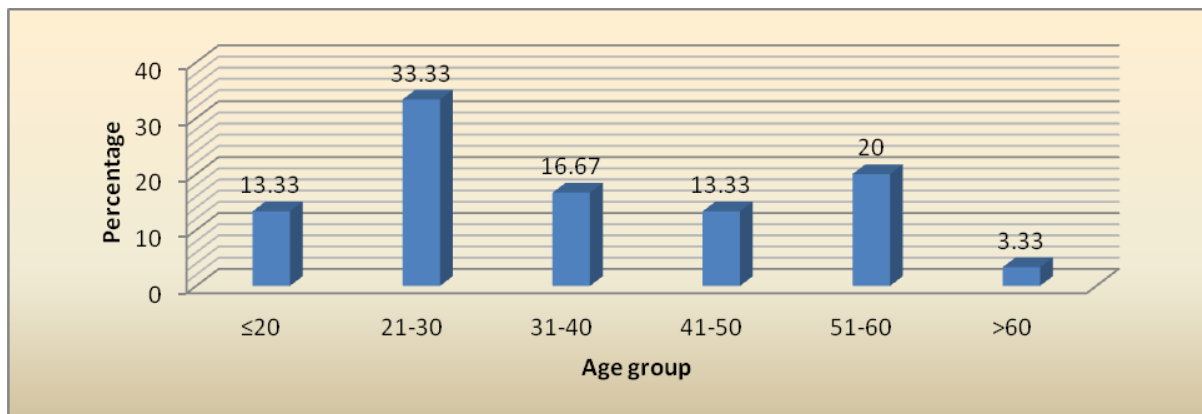

Figure 1) Age Group Distribution

The maximum numbers of patients were in the age group of 12-30 years (33.33%), followed by in 51-60 years (20%). The mean age among the distribution of patients was 36.7 ±13.34 years.

Table 1: Gender distribution of patients with chronic diarrhea and malabsorption:

Gender	Chronic diarrhea		Malabsorption	
	Number	Percentage	Number	Percentage
Male	20	66.67	05	62.50
Female	10	33.33	03	37.50
Total	30	100	08	100

Among 30 patients of chronic diarrhea, males (20 cases; 66.67%) outnumbered females (10 cases; 33.33%) and male to female ratio was 2:1; similarly in malabsorption patients males (5 cases; 62.50%) outnumbered females (3 cases; 37.50%) and male to female ratio was 1.67:1.

Table 2 : Etiology of chronic diarrhea and Malabsorption among patients:

Etiology	Chronic Diarrhoea		Malabsorption	
	Number	Percentage	Number	Percentage
IBS	18	60.00	04	50.00
Crohn's disease	04	13.33	02	25.00
Intestinal TB	03	10.00	01	12.50
Ulcerative colitis	03	10.00	00	00
B cell lymphoma	01	03.33	01	12.50
Eosinophilic enteritis	01	03.33	00	00
Total	30	100	08	100

Among 30 patients majority of patients had IBS (60%), followed by Crohn's disease (13.3%), Intestinal TB (10%), Ulcerative colitis (10%), B cell lymphoma (3.33%) and Eosinophilic enteritis (3.33%) as etiology of chronic diarrhea among patients.

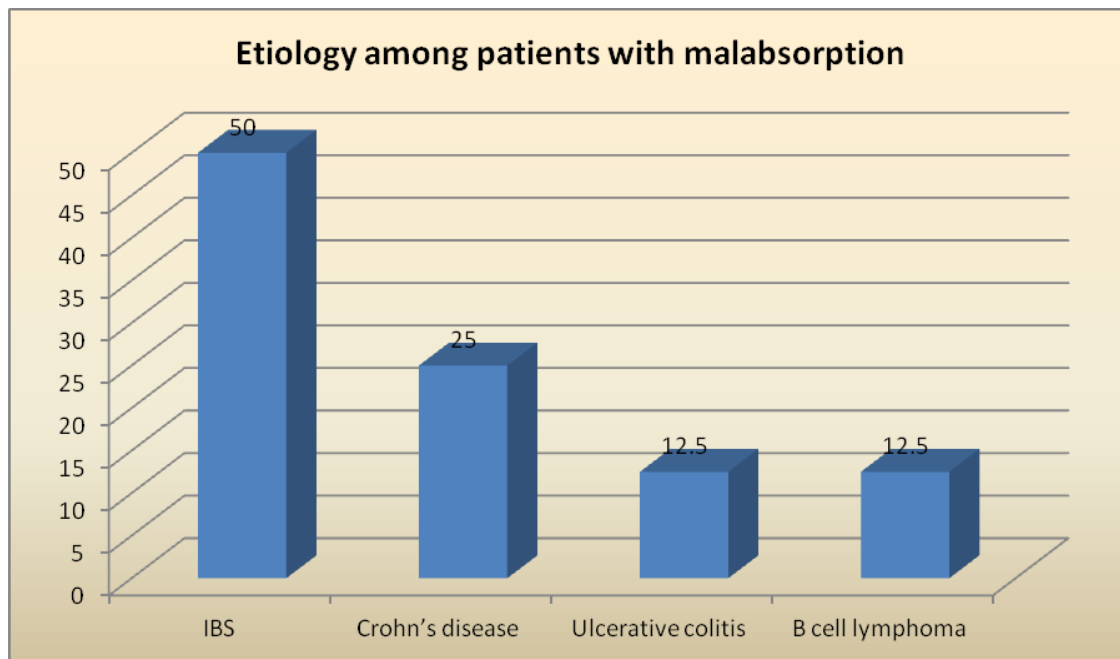**Figure 2: Etiology among patients with malabsorption:**

Table 3 : Comparison of investigations in patients with and without malabsorption:

Variable	Malabsorption		P value
	Present (n=8)	**Absent (n=22)**	
Hemoglobin (g/dl)	10.51 ±2.02	10.94 ±1.85	0.59
TLC(per cmm)	5.26 ±0.71	5.03 ±0.18	0.16
Platelet count (x10^9/l)	2.95 ±0.39	2.51 ±0.65	0.06
MCV (*fl)*	83.06±8.41	83.63 ±8.18	0.87
ESR (mm/hr)	26.01 ±15.48	25.54 ±15.95	0.94
CRP (mg/L)	9.78 ±2.51	6.21 ±2.23	0.21
Urinary D Xylose (mg/L)	24.21 ±3.19	20.43 ±7.81	0.19
Serum bilirubin	1.11 ±0.32	1.19 ±0.27	0.49

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SGPT(IU/L)	37.13±5.43	37.00 ±7.03	0.96
SGOT(IU/L)	33.88 ±4.12	28.22 ±7.13	0.04*
ALP(IU/L)	40.13 ±9.06	35.72 ±9.58	0.27
Urea(mg/dL)	14.37 ±5.37	13.45 ±3.83	0.61
Serum creatinine(mg/dL)	0.65 ±0.31	0.56 ±0.26	0.43
S. Amylase(IU/L)	35.88 ±7.42	36.68 ±7.65	0.81
S. Lipase(IU/L)	24.00 ±4.79	23.59 ±3.89	0.83
Sodium(mEq/L)	143.25 ±5.47	142.63 ±5.04	0.71
Potassium(mEq/L)	3.95 ±0.52	4.24 ±0.45	0.14
Calcium(mg/dL)	8.69 ±0.54	8.75 ±0.61	0.66
Serum Ferritin(ng/ml)	90.37 ±47.41	131.22 ±73.68	0.04*
Total proteins(gm/dL)	5.43 ±0.80	5.38 ±0.39	0.81
Serum albumin(gm/dL)	2.80 ±0.69	3.15 ±0.42	0.11

It was observed that SGOT and Serum ferritin showed statistically significant association in patients with and without malabsorption (P<0.05) while serum bilirubin, SGPT, ALP, blood urea and electrolytes showed no statistically significant association in patients with and without malabsorption. (p>0.05)

Table 4 : Urinary D Xylose test among patients with chronic diarrhea:

Urinary D Xylose test	Number	Percentage
Positive	08	26.67
Negative	22	73.33
Total	30	100

Among 30 patients of chronic diarrhea, 8 (26.67%) patients showed Urinary D Xylose test positive.

Table 5 : Stool analysis among patients with chronic diarrhea:

Parameters		Number	Percentage
Stool R/M	Normal	20	66.67
	Abnormal (Pus/RBC/Mucus/parasites)	10	33.33
Stool OB	Positive	09	30.00
	Negative	21	70.00
Stool Sudan III stain	Positive	00	00
	Negative	30	100

Table 6: Diagnostic test results among patients with chronic diarrhea:

Diagnostic test and results		Number	Percentage
USG abdomen	Normal	21	70.00
	Abnormal	09	30.00
Biopsy (Stomach/duodenum)	Normal	23	76.67
	Abnormal	07	23.33
Colonoscopy	Normal	18	60.00
	Abnormal	12	40.00
CE-CT abdomen & pelvis	Normal	18	60.00
	Abnormal	12	40.00

USG abdomen was abnormal in 9 (30%) patients. The abnormal USG findings were thick walled small bowel loop, mesenteric lymphadenopathy, colon wall thickening. Among 30 patients of chronic diarrhea, 7 (23.33%) patients showed abnormal biopsy. The abnormal biopsy findings were villous atrophy and H. Pylori bacteria presence. The colonoscopy was abnormal in 12 (40%) patients with findings of colitis, ulceration and edema of the ileo-cecal junction. The CE-CT abdomen was abnormal in 12 (40%) patients with findings of wall thickening, lymphadenopathy and mural thickening.

DISCUSSION

We found that malabsorption was prevalent in 8 out of the 30 patients (26.7%) with the maximum numbers of patients seen in the age group of 12-30 years (33.3%) followed by in the age group of 51-60 years (20%). The mean age was 36.7 ±13.34 years. We noted that Pipaliya et al in their study of etiological spectrum of chronic diarrhea: malabsorption was observed in the mean age of 36.5±12.6 years, and 49% of the patients were found to be males[2]. Similarly, Ghoshal et al in their study on the spectrum of malabsorption syndrome in adults observed that out of 275 patient; the mean age of the patients was 37.5 ± 13.2 years with males 167 (61%)[3].In another study by Simadibrata M et al it was observed that small bowel diseases with chronic diarrhea in 78 patients, the age groups affected were 30-39 years and 50-59 years[4]. Among 30 patients in our study; the majority of patients were suffering from IBS (60%), followed by Crohn's disease (13.3%), Intestinal TB (10%), Ulcerative colitis (10%), B cell lymphoma (3.33%) and Eosinophilic enteritis (3.33%). Pipaliya et al in their study reported that the common etiology for malabsorption in chronic diarrhea was tropical sprue (48.3%), parasitic infections (12.3%) and tuberculosis (10.8%). Other causes included immunodeficiency (7.3%;), celiac disease (5.4%), Crohn's disease (5.4%), small intestinal bacterial overgrowth (5.4%), hyperthyroidism (1.9%), diabetic diarrhea (1.9%), systemic lupus erythematosus (1.4%), metastatic carcinoid (0.5%) and Burkitt's lymphoma (0.5%). Improved hygienic conditions and sanitary services have lead to a reduction in the prevalence of infectious etiology of malabsorption hence rise in non infectious causes of diarrhea is noted in India. In our study, the mean hemoglobin of the patients was 10.83 ±1.87 g/dl. The mean total leukocyte count of the patients was 5072.67 ±1575.41 per cmm in the patients with chronic diarrhea. The mean platelet count of the patients was 253 ±64 x10^9/l. The mean MCV was 83.48±8.10 fl and ESR was 25.67± 15.56 mm/hr. Among 30 patients of chronic diarrhea, 11 (36.67%) patients showed CRP test positive. Only 8 (26.67%) patients showed positive Urinary D Xylose test. Studies by Bertomeu A et al (1991) and Read NW et al (1990) suggested that initial abnormal screening tests such as a high erythrocyte sedimentation rate and anemia have a high specificity for the detection of organic disease with chronic diarrhea[5]. Goddard AF et al (2000) and Ackerman Z et al (1996) also found the presence of iron deficiency in chronic diarrhea as a sensitive indicator of small bowel enteropathy, particularly celiac disease however, this test lacks the specificity[6]. As per the guidelines of the British society of Gastroenterology, basic screening for malabsorption must include complete blood count, electrolytes & urea, liver function tests, vitamin B12, folate, calcium, ferritin, erythrocyte sedimentation rate, and C reactive protein. Faecal occult blood testing is primary intended for detection of blood loss in the gut as one of the causes of chronic diarrhea with blood loosing lesions, but its role in the evaluation of malabsorption is ill defined. It was observed in our study that USG abdomen was abnormal in 9 (30%) patients. The abnormal USG findings were thick walled small bowel loop, mesenteric lymphadenopathy; colon wall thickened etc. which suggest diseases of the

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gastrointestinal tract and other organs that could be responsible for chronic diarrhea. Among 30 patients of chronic diarrhea, 7 (23.33%) patients had villous atrophy in the duodenum and H. Pylori infection of the stomach, which could be play a role in chronic diarrhea and malabsorption. Ghoshal et al also reported abnormal duodenal biopsy in 226 (82%) patients with malabsorption syndrome 17 (7.5%) showing subtotal villous atrophy, 58 (25.7%) had partial villous atrophy and 45 (20%) had blunting of villi and one patient had normal villi. 217 cases (96%) had increased mononuclear infiltrate and 126 (55.8%) had increased intraepithelial lymphocytes. The colonoscopy helped to detect colitis, ulceration and edema of the ileo-cecal junction in 12 (40%) patients in our study. The contrast enhanced CT scan of the abdomen was abnormal in 12 (40%) patients in our study. The abnormal findings were wall thickening of intestinal wall, lymphadenopathy and mural narrowing. It was observed that among 30 patients of chronic diarrhea, 8 (26.67%) patients showed malabsorption. Among 8 patients majority of patients had IBS (50%), followed by Crohn's disease (25%), Ulcerative colitis (12.5%) and B cell lymphoma (12.5%) as etiology of malabsorption among patients. Simadibrata, M. et al (2013)   studied small bowel diseases causing chronic diarrhea and reported that small intestine abnormalities detected endoscopically-histopathologically in 65 cases (82.6%), while the rest of the patients had normal small intestine. The abnormalities were found to be infective non-tuberculosis ileitis (26% of all cases), Infective non tuberculosis duodenitis (20, or 26%), non-infective jejunitis(18.2%), villous atrophy of the jejunum (3.9%), lymphoid nodular/follicle hyperplasia of the terminal ileum (15.6%) etc. Large intestinal abnormalities were found in 85.7 % of the chronic diarrhea cases. The frequent small intestinal abnormalities were infective ileitis, duodenitis and lymphoid nodular/follicle hyperplasia of the terminal ileum. The small intestinal abnormalities were found less than the large intestinal abnormalities. In this study, it was observed that liver biochemistry showed SGOT had statistically significant association in patients with and without malabsorption ($P < 0.05$) while serum bilirubin, SGPT, ALP, were did not show any statistically significant association. Similarly, serum ferritin levels were statistically significant in malabsorption.($p < 0.5$) and other biochemical parameters viz. blood urea, serum creatinine ,electrolytes , serum proteins , albumin showed no statistically significant association in patients with malabsorption.($p > 0.05$) Studies by Bertomeu A et al (1991) and Read NW et al (1990) observed low albumin in patients with chronic diarrhea along with a high specificity for the presence of organic disease, but no specific comment about association with malabsorption was commented.

CONCLUSION

We studied 30 patients of chronic diarrhea during 24 months. The commonest cause of chronic diarrhea is colonic in origin. The spectrum of etiology for chronic diarrhea revealed that irritable bowel syndrome tops the list followed by inflammatory colonic diseases. Only 26.7% patients of chronic diarrhea had malabsorption syndrome. In the clinical spectrum of chronic diarrhea with or without malabsorption; iron deficiency anaemia and carbohydrate malabsorption were noted as evidenced by low serum ferritin levels and positive D- Xylose test respectively.

ABBREVIATIONS

MCV: Mean corpuscular volume

ESR: Erythrocyte sedimentation rate

HbA1c: Glycosylated hemoglobin

LFT: Liver function test

RFT: renal function test

CRP: C reactive protein

SGPT: Serum glutamic pyruvic transaminase

SGOT: Serum glutamic oxaloacetic transaminase

ALP: Alkaline phosphatase

CE-CT: Contrast enhanced computed tomography

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