Original Research Article

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20182410

The clinical spectrum of chronic diarrhoea in children in a tertiary care hospital in Bangalore, India

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Received: 11 May 2018 Accepted: 15 May 2018

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ABSTRACT

Background: In the developing world, chronic diarrhea is typically associated with serial enteric infections and malnutrition. There are many causes for chronic diarrhea and with better facilities these are being increasingly diagnosed in India. To study the clinical spectrum of chronic diarrhoea in children. in a tertiary care hospital in Bangalore

Methods: This was a prospective observational study conducted at the Dept of Pediatrics, Dr.B.R.Ambedkar Medical College, Bangalore from April 2015 to April 2017. All the patients who presented with symptoms suggestive of chronic diarrhoea were enrolled for the study. 50 children fulfilling inclusion criteria were selected for the study.

Results: Of 50 cases, 31(62%) showed cow milk protein intolerance (CMPI), 6 (12%) celiac disease, 5(10%) post infectious, 2(4%) glucose galactose intolerance, 1(2%) non-specific, 1(2%) cystic fibrosis, 1(2%) IBD, TB 1(2%) and 2(4%) lympangiectesia. In children below 2 years, cow milk protein intolerance was the most common cause of diarrhea whereas post infectious was the most common cause in 2-6 years age group and celiac disease in above 6 years of age group.

Conclusions: Cow milk protein intolerance is the most common etiological factor. The incidence of celiac disease was the second most common cause after CMPI in the present study. The incidence of CMPI as a cause of chronic diarrhoea reduces as the age increases as seen in present study. The high incidence of celiac diseases may be due to referral to our institution by various peripheral hospitals when they could not diagnose after routine investigations.

Keywords: Cow milk protein intolerance, Chronic diarrhoea, Celiac disease, Galactose intolerance

INTRODUCTION

Diarrhea is one of the most common causes of morbidity and mortality in children worldwide. In clinical terms, diarrhea refers to either an increased stool frequency or a decreased stool consistency, typically a watery quality. The World Health Organization (WHO) defines a case as the passage of three or more loose or watery stools per day. Nevertheless, absolute limits of normalcy are difficult to define; any deviation from the child's usual pattern should arouse some concern (particularly when the passage of blood or mucus, or dehydration occurs) regardless of the actual number of stools or their water content.

Diarrhea lasting more than two to four weeks occurs in up to 3 to 5 percent of the population worldwide. In developing countries, infants experience a median of six episodes annually; children experience a median of three episodes annually. Diarrheal illness may consist of acute

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watery diarrhea, invasive (bloody) diarrhea, or chronic diarrhea (persistent ≥14 days). The major causes and the prevalence of chronic diarrhea differ between developed and developing countries. In the developing world, chronic diarrhea is typically associated with serial enteric infections and malnutrition; it is manifested by a chronic enteropathy, with impaired mucosal healing and diminished digestive and absorptive capacity.1 In developed countries, chronic diarrhea is more likely to be induced by underlying disease-causing malabsorption or maldigestion. However, enteric infections (particularly in immunocompromised patients), malnutrition, and dietary factors (e.g. excessive consumption of juice), play a role in some cases. There are many causes for chronic diarrhea and with better facilities these are being increasingly diagnosed in India.²

No exact recent prevalence data on etiological spectrum of chronic diarrhea in children from India is available.³ In past studies done in last 2-3 decades have shown varied etiologies.^{4,5} Recent studies from developed countries show increased incidence of Inflammatory bowel diseases in children especially Crohn's disease,6 hence we tried to study any change in spectrum of chronic diarrhea over a period of 2 years with special emphasis to IBD, cow milk protein allergy, celiac disease and immunodeficiency.

METHODS

This was a prospective, observational study conducted at the Dept of Pediatrics, Dr. B. R. Ambedkar Medical College, Bangalore from April 2015 to April 2017. Our hospital is a tertiary care facility in a large urban centre and serves as the referral centre for the entire Karnataka and neighborhood states. Ethical approval was obtained from Institutional Ethical committee of the Institution prior to the start of the study.

All the patients who presented with symptoms suggestive of chronic diarrhea were enrolled for the study. 50 children visited hospital during study period and were included for the study. Clinical history (with specific emphasis on onset, frequency and duration of symptoms), relevant clinical examination, investigation findings, diagnosis and treatment were collected in pretested proforma specially designed for the study. All of them underwent stool routine, renal function tests, complete hemogram, albumin in all, followed by casebased IgA Tissue transglutaminase antibody testing by Elisa method, upper gastrointestinal endoscopy with proctosigmoidoscopy duodenal biopsy, or colonoscopy with colonic biopsy, Mantoux testing, ELISA for HIV, barium meal follow through, immunoglobulin levels, stool for fat and opportunistic pathogens. The etiological diagnosis was based on standard recommendations. Celiac disease was diagnosed on the basis of modified ESPGHAN criteria.7 CMPA was identified as per Iyngkaran criteria.8 Diagnosis of nonspecific diarrhea was ascribed in those who had

normal pattern of growth and development, and no evidence of malabsorption or enteric infections in the age group of 6 month to 5 year.9 Diagnosis of intestinal lymphangiectasia was confirmed on histological presence of dilated lacteals in small bowel biopsies.10 The diagnosis of inflammatory bowel disease (IBD) was based on Porto criteria and classified as Ulcerative colitis or Crohn's disease on the basis of characteristic clinical, endoscopic and histological changes.11 Common variable immunodeficiency was diagnosed by the standard criteria, including reductions of serum IgG, IgA, and/or IgM by two or more standard deviations from the normal mean. Presence of low serum immunoglobulins IgG, IgA, and IgM levels. Intestinal Tuberculosis was ascribed as a cause of chronic diarrhea only in those with histological evidence of tuberculosis with acid fast bacilli positivity and definite response to antitubercular treatment. Giardiasis was diagnosed in those with duodenal biopsies showing giardia or stool showing trophozoites of giardia. HIV related diarrhea patients had ELISA for HIV positive.

Inclusion criteria

- Age: 6 months to 16 years
- chronicity or chronic and intermittent loose stools for more than 2 weeks

Exclusion criteria

- Age: < 6 months and> 16 years
- loose stools <2 weeks

Statistical analysis was done using percentage and mean. Continuous variables were expressed as mean \pm SD.

RESULTS

During the study period, a total of 50 children with chronic diarrhea were observed and analyzed. Of 50 cases, 31(62%) showed cow milk protein intolerance (CMPI), 6 (12%) celiac disease, 5(10%) post infectious, 2(4%) glucose galactose intolerance, 1(2%) non-specific, 1(2%) cystic fibrosis, 1(2%) IBD, TB 1(2%) and 2(4%) lympangiectesia. In children below 2 years, cow milk protein intolerance was the most common cause of diarrhea whereas post infectious was the most common cause in 2-6 years age group and celiac disease in above 6 years of age group.

42% of children were < 1 year, 24% were in the age group between 1 and 2 years, 20% of children were between 2 and 5 years and 14% beyond 5 years of age. Mean age of presentation in present study was 1 year. The prevalence of the disease was more in males than females with 30 boys and 20 girls (3:2). The most common presenting clinical features associated with diarrhea were blood in stools 26(52%), vomiting 19 (38%), weight loss 13(26%), dehydration 12(24%), fever 12(26%), pain abdomen 13(26%), distension of

abdomen/edema 6(12%), and other features like failure to thrive, organomegaly, ageusia, anorexia and vitamin deficiency (Table 1) Out of 50 cases, 94% belonged to Kuppuswamy class II and 6% to Kuppuswamy class IV.

Table 1: Clinical features of patients.

Clinical features	No. of children (n=50)	%
Chronic diarrhea	50	100.0
Blood in stools	26	52.0
Vomiting	19	38.0
Pain abdomen	13	26.0
Distension of abdomen	6	12.0
Weight loss	13	26.0
Dehydration	12	24.0
Malnutrition	6	12.0
Cow milk	33	66.0
Anorexia	13	26.0
Ageusia	3	6.0
Fever	13	26.0

The most common presenting signs were anaemia 16(32%), vitamin deficiency in which all were vitamin D deficiencies 3(6%), hepatomegaly 5 (10%), splenomegaly 1(2%), and ascites with pedal edema 1(2%). [Chart 1] Out of 50 children, 12 children had dehydration at time of presentation- 8 (66% in 12) children had mild, 2 had moderate and 2 children had severe dehydration. Clinical symptoms as per different etiologies in chronic diarrhea patients is shown in chart 2. Microorganisms were isolated from 5 cases out of which cryptosporidium was seen in 2 cases, *E. coli* in 2 cases and Giardia in 1 case. Total Leukocyte count (TC /cu. mm) was elevated in 37

children with a range of 4500/cu.mm to 28040/cu.mm were predominantly polymorphs at initial presentation. Stool tests were abnormal in 39 patients (78%). In that 28 children (56%) had occult blood in stool which was more consistent with CMPI. In 8 children (16%) stool routine showed pus cells in HPF. Organisms that are associated with chronic diarrhea in this study are cryptosporidium, E. coli and Giardia. Abnormal urine examination in the form of traces of protein and numerous pus cells per high power field were present in 2 children (4%), renal parameters were normal in all children. Urine cultures grew E. Coli in 1 child. USG Abdomen evaluation has been performed in almost all children at the time of presentation. 92% of them were normal. Rest 4 patients showed features of hepatosplenomegaly. To confirm the diagnosis of cystic fibrosis in 1 case sweat chloride was done. In 9 cases (18%) intestinal biopsy was done to confirm the diagnosis. It revealed 6 cases of celiac disease, 2 cases of intestinal lymphangiectesia and 1 case of tuberculosis. Biopsy done in tuberculosis was normal. Intestinal biopsy in 5 case of celiac disease showed partial villous atrophy and 1 with total atrophy. All biopsies showed hyperplastic crypts, lymphotheliocytes, increased and mononuclear infiltration in lamina propria. 2 cases of intestinal lymphangiectesia showed epithelial lesions with intraepithelial lymphocytes and inflammation in the lamina propria. 1 child died and 1 did not improve, rest all 48 patients recovered from diarrhea.

DISCUSSION

During the 2-year period of study in about 5400 pediatric admissions, 0.9% were admitted with history of diarrhea of >2 weeks.

Table 2: Aetiological comparisons of different studies

Rastogi et al n=47	Yachha et al n=137	Lee et al n=27	Altunas et al n=70	Present study n=50
Tropical enteropathy 47%	Protracted diarrhea 33%		Post infectious 10% Other infections 4.2%	Post infectious-10%
Parasitic-15%	Parasitic-9%	Parasitic-26%	Parasitic 19%	Parasitic-0
Celiac-7%	Celiac -26% CMPI- 6%	CMPI-29%	Celiac 30% CMPI 17%	Celiac-12% CMPI -62%
IBS-11%	TB-5%	Sec. lactose intolerance 19%		TB-2% IBD-2%
NON-SP- 22%	OTHERS: 8% Cystic fibrosis Acrodermatitis enteropathica	Lymphangiectesia 7% Glucose galactose malabsorption 7.5%	Cystic fibrosis 10%	Nonspecific2% Lymphangiectesia-4% Cystic fibrosis-2% Glucose galactose malabsorption-4%
Unknown-nil	Unknown 13%	Unknown 11%	Unknown10%	Unknown-nil

The referral pattern, prevalence of the disease, skills of the physician and the availability of appropriate diagnostic facilities, influence the etiological spectrum and outcome of chronic diarrhea. Aetiological comparisons of different studies is shown in table 2. This two-year study comprising 50 children has shown that cow milk protein intolerance is the most common entity encountered. The next most common cause was celiac disease, followed by post infectious diarrhea. The male preponderance encountered in this study is similar to study conducted by Yaccha et al It is also a reflection of the referral pattern in general, resulting from sociocultural factors. 12

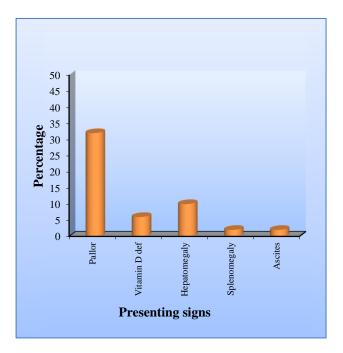


Figure 1: Presenting signs in patients with chronic diarrhoea.

Yaccha et al have published the profile of chronic diarrhea in children and the data from these studies showed that cow milk allergy and celiac disease were the most common entity encountered. The incidence of celiac disease is the 2nd most common cause of chronic diarrhoea in this study (10%). The high incidence of celiac diseases may be due to referral to our institution by various peripheral hospitals when they could not diagnose after routine investigations.

Intestinal TB as a cause of chronic diarrhea has declined drastically as we had only 1 case of abdominal tuberculosis with diarrhea as presentation when compared to study by Yachha et al. who reported it to be in 9% of total cases. The confounding factor in this observation may be the fact that presently at community level Tuberculosis is over diagnosed on weak grounds & infact ATT has become a common tool for all prolonged ailments. Mortality in present study is a case of glucose galactose intolerance which has poor outcome. Primary intestinal lymphangiectasia was seen in 2 (4%) cases with

diarrhea as major presentation, making it a rarer entity. From India only, few data are available only too in the form of case reports.

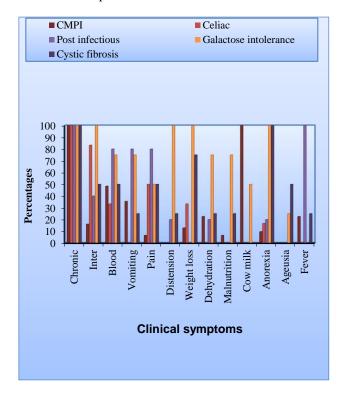


Figure 2: Clinical symptoms as per different etiologies in chronic diarrhoea patients

CONCLUSION

The high-risk groups as per present study for chronic diarrhea are children of <1 year of age (42.0%). Cow milk protein intolerance is one of the major subgroups in present study and it is the most common etiological factor (62.0%). The percentage of CMPI in children < 1 year in present study was 91.3% and 1-2 years is 83.3%. In view of high incidence, CMPI should be thought of in case of cow milk intake history and undiagnosed cases. The incidence of celiac disease was the second most common cause after CMPI in the present study. The incidence of CMPI as a cause of chronic diarrhea reduces as the age increases as seen in present study. The high incidence of celiac diseases may be due to referral to our institution by various peripheral hospitals when they could not diagnose after routine investigations.

ACKNOWLEDGEMENTS

Authors would like to Acknowledge Principal of Dr. B. R. Ambedkar Medical College for the guidance and support of the study.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

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Cite this article as: Shenoy B, Dodderi SK. The clinical spectrum of chronic diarrhoea in children in a tertiary care hospital in Bangalore, India. Int J Contemp Pediatr 2018;5:1267-71.