

Research Article

Chronic diarrhea in North Indian children: a widening etiological spectrum

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ABSTRACT

Background: Objectives of current study were to define the etiological spectrum and outcome of children with chronic diarrhea and to evaluate for any change in etiological spectrum of chronic diarrhea over five years.

Methods: In this retrospective study the hospital records of all patients with chronic diarrhea evaluated at the Department of Pediatric, Era's Lucknow medical college and hospital Lucknow & Vivekananda polyclinic & institute of medical sciences Lucknow, India over a period of five years i.e. from July 2006-July 2011, were reviewed.

Results: During the study period of 5 years, a total of 135 children [mean age 5.6 ± 4.2 year, 83 (61.48%) boys] of chronic diarrhea were seen (19 large bowel, 103 small bowel type, 13 mixed type). Of them 50 children with incomplete workup were excluded from data analysis, hence evaluation was done for a total 85 children, in which 6 cases (7.05%) had no definite etiology discerned and were labeled in indeterminate group. We had only 2 cases of abdominal tuberculosis presenting as chronic diarrhoea with other symptoms of fever, anorexia and lymphadenopathy. We had 1 case of inflammatory bowel disease (ulcerative colitis) & 1 cases of intestinal lymphangiectasia. Diagnosis was made on demonstration of AFB on ileal biopsy.

Conclusion: Chronic diarrhea accounted for 13-15% of total patients from two multispecialty hospitals of Lucknow which cater to a large population from U. P. Celiac disease remains the most important cause of chronic diarrhea in children from this region. Non-specific diarrhea and giardiasis still are important treatable etiologies. In case of chronic diarrhea with presence of blood in stool in young children, cow milk allergy was most common etiology. Immunodeficiency entity should be looked for in children, when routine work up for chronic diarrhea does not give any result. Intestinal TB is uncommon cause of chronic diarrhea as shown in our study; hence inadvertently ATT should not be prescribed for child presenting with diarrhea without any firm evidence.

Keywords: Chronic diarrhea, North India, Etiology

INTRODUCTION

Chronic diarrhea in children remains a common problem in community, leading to significant morbidity and at times mortality if left untreated. However, no exact recent prevalence data on etiological spectrum of chronic diarrhea in children from India is available.¹ In past studies²⁻⁵ done in last 2 - 3 decades have shown varied etiologies hence we tried to look into current scenario of

chronic diarrhea at 2 multispecialty teaching hospital which drain a large number of population from the state of U. P. 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 5 years with special emphasis to IBD, cow milk protein allergy, celiac disease and immunodeficiency.

The aims of this study were to 1) to define the etiological spectrum and outcome of children with chronic diarrhea and 2) to evaluate for any change in etiological spectrum of chronic diarrhea over five years.

METHODS

In this retrospective study the hospital records of all indoor patients with chronic diarrhea evaluated at the department of pediatric, Era's Lucknow medical college and hospital Lucknow & Vivekananda polyclinic & institute of medical sciences Lucknow, India over a period of five years i.e. from July 2006-July 2011, were reviewed.

Inclusion criteria: Children with diarrhea of more than 4 weeks duration, with insidious onset i.e. chronic diarrhea,⁷ up to 18 years of age were included in the study.

Case records of all patients were reviewed in detail for the presenting complaints, associated symptoms, age at presentation, duration of symptoms, examination and investigatory findings. Their final diagnosis and response to specific treatment was also seen. Workup of such cases was based on the type of diarrhea either small bowel (large volume diarrhea, watery diarrhea associated with vitamin or mineral deficiencies) or large bowel (small volume, associated with blood/mucus and often tenesmus/urgency) and likely differential diagnosis and investigation included complete hemogram, albumin in all, followed by case based IgA Tissue transglutaminase antibody testing by Elisa method (kit used: Dr Fening biomed), upper gastrointestinal endoscopy with duodenal biopsy, proctosigmoidoscopy or Full 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.⁸ CMPA was identified as per Iyngkaran criteria.⁹ Diagnosis of non-specific 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.¹⁰ Diagnosis of intestinal lymphangiectasia was confirmed on histological presence of dilated lacteals in small bowel biopsies.¹¹ 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.¹² 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.²⁷ 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. When no other cause was found, it was labeled as indeterminate group.

Statistics

Statistical analysis was done using SPSS 16.0 software. Continuous variables were expressed as mean \pm SD. Chi square and student t test was used for comparison of categorical and continuous variables. Significance was taken as $P < 0.05$.

RESULTS

During the study period of 5 years, a total of 135 children [mean age 5.6 ± 4.2 year, 83 (61.48%) boys] of chronic diarrhea were seen (19 large bowel, 103 small bowel type, 13 mixed type). Of them 50 children with incomplete workup were excluded from data analysis, hence evaluation was done for a total 85 children, in which 6 cases (7.05%) had no definite etiology discerned and were labeled in indeterminate group.

Of 31 cases of celiac disease, 22 were boys, with mean age of presentation was 6.6 ± 3.2 (1-17) year with mean duration of symptoms 40.08 ± 35.6 month, range 1-190 mo. Anemia was seen in 26 (83.87%) with mean Hb value 8.0 ± 1.2 g/dl, both rickets and B complex vitamin deficiencies were seen in 7 (22.58%), hypoalbuminemia in 8 (25.80%). Thrombocytosis (platelet count more than four lakhs/mm³) was seen in 12 (38.70) and asymptomatic rise of transaminases (more than two times upper limit of normal) seen in 6 (19.35%) patients. Scalloping on upper gastrointestinal endoscopy was seen as prominent feature with duodenal biopsy showing subtotal villous atrophy in 20 (64.51%), total villous atrophy in 11 (35.48%). IgA tissue transglutaminase antibody was positive in all 31 cases. In follow up symptoms subsided and patients improved on gluten free diet in all cases.

Another major diagnosis was Cow Milk Protein Allergy (CMPA), Of total 10 cases, 6 were males, mean age of presentation was 1.65 ± 1.2 (0.3-6) year, with mean duration of symptoms being 8.8 ± 8.2 (1-42) months. Proctosigmoidoscopy showing aphthous ulcers in 7 (70%) and 6 (60%) had blood in stools as one of the presenting complaint. Anemia was seen in 6 (60%) with mean Hb value 8.5 ± 1.2 g/dl. All patients improved on milk and milk product free diet. Lactose free soy based formula alone was implemented in 3 (30%) patients who were either too young or not started on complementary diet, and milk and milk product free diet in the rest.

Non-specific diarrhoea/toddler diarrhoea was attributed as cause of diarrhoea in 17 children, 11 were boys, with mean age being 3.3 ± 1.5 year. Tissue transglutaminase

antibody was done in 15, which was negative and endoscopic evaluation with duodenal biopsy done in 13 cases was normal. Anemia was seen in 3 (17.64%) with mean Hb value 11 ± 1.2 g/dl. Follow up of 13 such cases showed subsidence of diarrhoea in which half of them were given added fat/butter (2 g/kg) as dietary intervention.

Of 15 children with giardiasis upper GI endoscopy was done in all, duodenal biopsy revealed giardia in 12 children (rest 3 diagnosed on basis of stool examination). Mean age of presentation being 5.5 ± 3.5 year and mean duration of diarrhoea being 19.8 ± 15.2 months, all cases improved with nitroimidazole group of drugs for recommended duration.

Table 1: Comparative table showing other studies on etiology of chronic diarrhea in children.

	Yachha et al. ²	Altuntas et al. ⁴	Lee et al. ³	Rastogi et al. ⁵	Present study
No of children	137	70	27	47	85
Country	India (Chandigarh)	Turkey	Malaysia	India (N. Delhi)	India (Lucknow)
Time period	1984-1989	1993-1996	1996-1997	1999	July 2006-July 2011
Age group	1-15 year	1 mo-15 year	New-born -9 mo	6 mo -12 year	1 mo-18 year
Etiology					
Celiac disease	26%	30%	-	6.8%	36.47%
Tropical enteropathy	-	10%	-	46.8%	-
CMA	6%	17%	29%	-	11.76%
Non-specific diarrhea	-	-	-	21.8%	20%
Parasitic infestation	9%	26%	26%	14.8%	17.64%
Intestinal TB	9%	-	-	-	2.35%
Int lymphangiectasia	-	-	7%	-	1.17%
IBS	-	10%	-	10.6%	-
Immunodeficiency	-	-	-	-	
A) HIV	-	-	-	-	1.17 %
B) CVID	-	-	-	-	1.17 %
Cystic fibrosis	-	10%	-	-	-
Sec Lac. intolerance	-	-	19%	-	-
IBD	--	-	-	-	1.17 %
Protracted diarrhea	33%	-	-	-	-
Unknown	13.1%	10%	11.1%	-	7.05%

Among uncommon cause of diarrhea, immunodeficiency as a cause was seen in 2 cases, of which Primary immunodeficiency was seen in 1 cases (Common variable immunodeficiency in 1), and 1 cases were of HIV related diarrhea. Age of primary immunodeficiency case was 7 (2.5-13) years with diarrhea alone as major presenting complaint. After initial workup was negative, their immune profile was sought for. Case of CVID who was on regular intravenous immunoglobulin infusions improved symptomatically, however patient with HIV on antiretroviral developed toxic megacolon and died.

We had only 2 cases of abdominal tuberculosis presenting as chronic diarrhoea with other symptoms of fever, anorexia and lymphadenopathy.

We had 1 case of inflammatory bowel disease (ulcerative colitis) & 1 cases of intestinal lymphangiectasia. Diagnosis was made on demonstration of AFB on ileal biopsy.

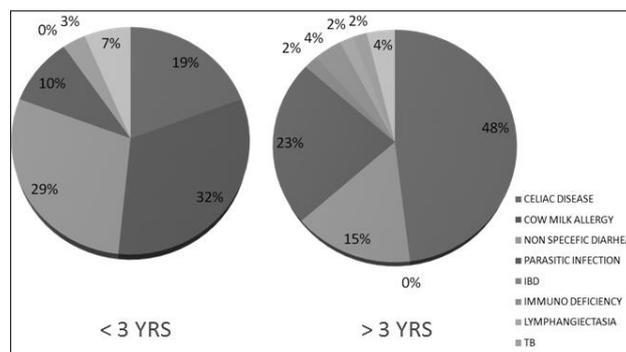


Figure 1: Comparative etiological profile of chronic diarrhea (<3 years vs. >3 years age).

DISCUSSION

The present study to our knowledge is the first from north India to elucidate various etiologies for chronic diarrhea in children where wheat is the staple diet.

Celiac disease in our study is the commonest cause of chronic diarrhea (36.47%); this is contrast to study by Rastogi et al.⁵ who showed tropical enteropathy as predominant cause (46.8%). The mean age at diagnosis of celiac cases in our study is much older 6.8 ± 3.2 year than studies from developed countries being under 2 year of age in 80%,¹⁴ but it is in accordance with other Indian studies.¹⁵

Cow Milk Allergy (CMA) was seen in 11.76% of our cases and it is also the leading cause of diarrhea in children less than 3 years of age. Thus reiterating the fact that this entity needs to be considered and investigated in young children accordingly before searching for inflammatory bowel diseases as generally done in adults. This is well reflected from our data that presentation of CMA is in much younger age group (1.65 ± 1.1 year) than IBD. In the West, symptoms suggestive of CMPA are seen in 5-15% of infants with prevalence of CMPA, confirmed by double blind placebo controlled challenge is 2-5%.¹⁶⁻¹⁸ Two studies from India^{2,19} have shown that CMPA is one of the common causes (6-30%) of chronic diarrhea in children even in a developing country like ours though we still don't have any information about its prevalence in general population.

Non-specific diarrhea was the second most common cause of chronic diarrhea in our study, constituting 20% of total cases similarly to that in study by Rastogi et al.⁵ who have reported 21% in children. In studies from developed countries²⁰ it is by far the most frequent cause of chronic diarrhea in children between 1 to 5 years of age. Absence of growth failure, no evidence of malabsorption with good prognosis is its hall mark. Their exact pathophysiology is still unclear, one of the postulates is of decreased intestinal transit time.²¹ It can be delayed by added fat in diet as tried in some of our children with beneficial results.

Giardiasis as a cause of chronic diarrhea was seen in 17.64% of study population which is similar to the study by Rastogi et al.⁵ In contrast to study by Yachha et al. and this difference may be attributed to the types of patient evaluated.

Primary intestinal lymphangiectasia was seen in 1 (1.17%) cases with diarrhea as major presentation, making it a rarer entity. From India only few data is available only too in the form of case reports.²²

Intestinal TB as a cause of chronic diarrhea has declined drastically as we had only 2 case of abdominal tuberculosis with diarrhea as presentation when compared to study by Yachha et al.² 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 & infant ATT has become a common tool for all prolonged ailments. This may alter the correct scenario in present situation.

Another striking point in our study was primary and acquired immunodeficiency related diarrhea that was seen in 2.34% cases whereas none of earlier series in past have not reported it to be the cause of diarrhea in children from India. However we anticipate the incidence of these two diseases much higher since we do not get direct referral of such patients to our hospital. Studies from west have shown that 7-23% of patients eventually diagnosed as having CVID had chronic diarrhea at the time of diagnosis.²³⁻²⁵ Surjit et al. have reported chronic diarrhea as presentation in 18.1% children amongst a total of 513 cases of HIV infection from a single centre in India.²⁶

CONCLUSIONS

Chronic diarrhea accounted for 13-15% of total patients from two multispecialty hospital of Lucknow which caters to a large population from U.P. Celiac disease remains the most important cause of chronic diarrhea in children from this region. Non-specific diarrhea and giardiasis still are important treatable etiologies. In case of chronic diarrhea with presence of blood in stool in young children, cow milk allergy was most common etiology. Immunodeficiency entity should be looked for in children when routine work up chronic diarrhea does not give any result. Intestinal TB is uncommon cause of chronic diarrhea as shown in our study; hence inadvertently ATT should not be prescribed for child presenting with diarrhea without any firm evidence.

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