ISSN No:-2456-2165

The Clinical Spectrum of Chronic Diarrhea in Children

Dr. Venugopal Reddy. I.
Medical Director and Consultant Pediatrician,
Ovum Hospital, Bangalore

Dr. Bhaskar Shenoy
HOD of Pediatrics, Manipal Hospital,
HAL Road, Bangalore

Dr. Obul Reddy
Pediatrician, Manipal Hospital, Bangalore
Kumudavalli.N, M.Tech, IT Consultant,
Bangalore

Abstract:- Diarrhea is a common manifestation of gastrointestinal disease, and its definition has traditionally been based on the frequency, volume, and consistency of stools. However, a consensus statement issued by the American Gastroenterological Association suggests that chronic diarrhea should be defined as a decrease in fecal consistency lasting for two or more weeks. Diarrhoea is one of the most common causes of morbidity and mortality in children worldwide, and the World Health Organization (WHO) defines a case as the passage of three or more loose or watery stools per day. A total of 50 children were included in the study, and the patient selection was based on age, presenting symptoms suggestive of chronic diarrhoea. This two-year study of chronic diarrhoea in children in Karnataka and neighboring states found that cow milk protein intolerance was the most common entity encountered, followed by celiac disease and post infectious diarrhoea.

The male preponderance encountered in this series is a reflection of the referral pattern in general, resulting from socio-cultural factors. The incidence of celiac disease is the 2nd most common cause of CD in this study (10%), likely due to referral to our institution by various peripheral hospitals when they could not diagnose after routine investigations. This study found that children of 1 year of age are the most at risk for chronic diarrhoea, with a male to female ratio of 3:2. Cow milk protein intolerance (CMPI) was the most common aetiological factor (62.0%), followed by celiac disease (CMI) and tuberculosis (TB). The referral pattern, prevalence of the disease, skills of the physician and availability of appropriate diagnostic facilities all influence the aetiological spectrum and outcome of chronic diarrhea.

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. Regional hospitals and laboratory diagnostics should be well equipped to diagnose these cases. Mortality of CD (2%) was a case of glucose galactose intolerance which has poor outcome.

I. INTRODUCTION

Diarrhea, derived from the Greek "to flow through," is a common manifestation of gastrointestinal disease. Its definition has traditionally been based upon the frequency, volume, and consistency of stools. However, the relationship between these features and patients' perception of diarrhea is variable. As a result, a consensus statement issued by the American Gastroenterological Association suggests that chronic diarrhea should be defined as a decrease in fecal consistency lasting for two or more weeks.

Diarrhoea is one of the most common causes of morbidity and mortality in children worldwide. In clinical terms, diarrhoea 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.

II. MATERIALS AND METHODOLOGY

A. MATERIALS

All the patients who presented with symptoms suggestive of chronic diarrhoea in Manipal hospital, Bangalore constituted the material for the study.

Total of 50 children were included in the study. This was a study conducted at The Department of Paediatrics, Manipal hospital, Bangalore. The patient Selection for the study was based on age, presenting symptoms suggestive of chronic diarrhoea.

B. METHODS

Our hospital is a tertiary care facility in a large urban centre and serves as the referral centre for the entire Karnataka and neighbourhood states. Cases admitted during April 2009 to April 2011 were analysed and follow up was done. The dates of the onset of illness, fulfilment of diagnostic criteria, diagnosis and treatment all were noted. All of them underwent stool routine,renal function tests and other routine laboratory investigations. Special tests including intestinal biopsy were done whenever clinically indicated.

ISSN No:-2456-2165

C. STUDY PERIOD

2 years

D. POPULATION

All children admitted to the paediatric ward, Manipal hospital, Bangalore from April 2009 to April 2011 was taken up for the study. A total of 50 children were included in the study.

E. DATA COLLECTION

Clinical history (with specific emphasis on onset, frequency and duration of symptoms), relevant clinical examination and investigation findings were noted as per the proforma.

F. CRITERIA FOR INCLUSION:

- Age : 6 months to 16 years
- loose stools.
- blood in stools
- chronicity or chronic and intermittent
- cow milk intake
- dehydration
- vomiting
- weight loss

G. CRITERIA FOR EXCLUSION:

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

H. METHODOLOGY

- PLACE OF STUDY: MANIPAL HOSPITAL, BANGALORE
- STUDY DESIGN: OBSERVATIONAL STUDY
- PERIOD OF STUDY: 24 MONTHS
- STUDY POPULATION: 50 CASES

I. OBSERVATION AND ANALYSIS

A total of 50 children with chronic diarrhoea were analysed and observed . During the time of admission/ visits patients are clinically assessed for dehydration and investigations(stool routine, biopsy findings etc) were noted .The results were tabulated and interpreted .

J. STUDY DESIGN

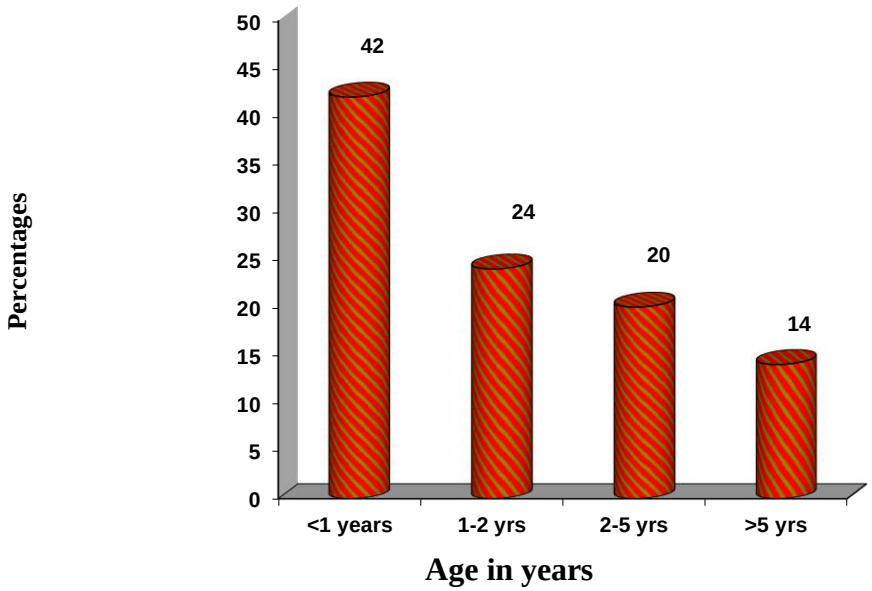
This is an observational descriptive clinical study consisting of 50 children with chronic diarrhoea. There were total of 50 patients of chronicdiarrhoea diagnosed from 2009 to 2011 at Manipal Hospital, Bangalore.

Observation and Analysis was made in children with CD which showed cow milk protein intolerance 31(62%), celiac disease 6 (12%), post infectious 5(10%) ,glucose galactose intolerance 2(4%), non specific 1(2%) ,cystic fibrosis 1(2%), IBD 1(2%) ,lympangiectesia 2(4%)

Table 1: Distribution of age in years

Age in years	Number of children	%
<1 years	21	42.0
1-2 years	12	24.0
2-5 years	10	20.0
>5 years	7	14.0
Total	50	100.0

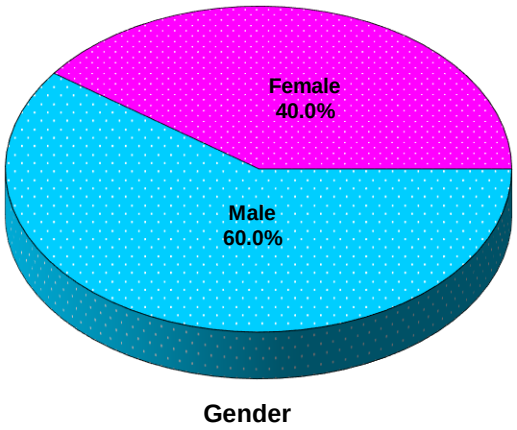
Mean ± SD: 2.95± 3.76



Most common age group with CD was < 1 year followed by 1-2 years, then 2-5 years and then 5-16 years.

Table 2: Gender distribution of patients studied

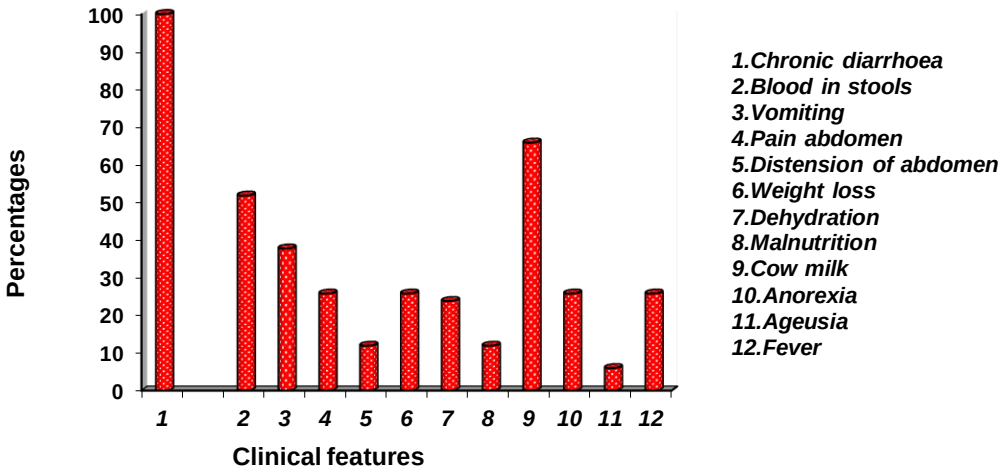
Gender	Number of children	%
Male	30	60.0
Female	20	40.0
Total	50	100.0



The male to female ratio was 3:2 with 30 boys and 20 girls.

Table 3: Clinical features of patients studied

Clinical features	Number of children (n=50)	%
1.Chronic diarrhoea	50	100.0
2.Blood in stools	26	52.0
3.Vomiting	19	38.0
4.Pain abdomen	13	26.0
5.Distension of abdomen	6	12.0
6.Weight loss	13	26.0
7.Dehydration	12	24.0
8.Malnutrition	6	12.0
9.Cow milk	33	66.0
10.Anorexia	13	26.0
11.Ageusia	3	6.0
12.Fever	13	26.0

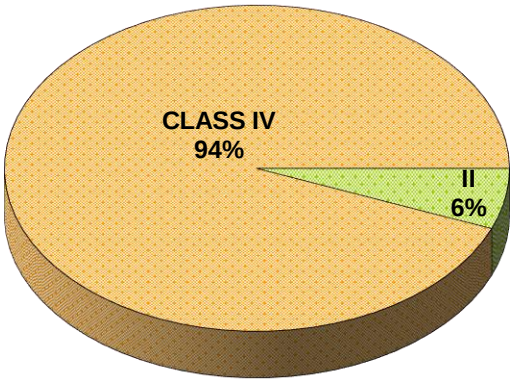


The most common presenting clinical features were diarrhea 50(100%) in which chronicity in 100% , blood in stools 26(52%) ,vomiting 19 (38%), , weight loss 13(26%) ,dehydration 12(24%) ,fever 12(26%) ,pain abdomen 13(26%) , distension of abdomen /odema 6(12%), and other features like failure to thrive, organomegaly, ageusia,anorexia and vitamin deficiency.

ISSN No:-2456-2165

Table 4: Socio-economic status

Socio-economic status	Number of children (n=50)	%
Class IV	3	6.0
Class II	47	94.0

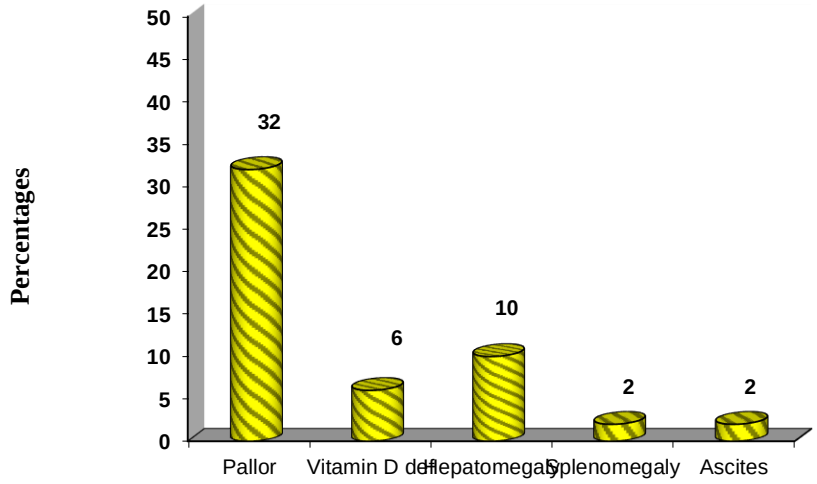


Socio-economic status

Socioeconomic class according to kuppuswamy classification:
Upper (I), Upper Middle (II),Middle Lower middle (III),Lower Upper lower (IV),Lower (V)

Table 5: Clinical signs

Clinical signs	Number of children (n=50)	%
Pallor	16	32.0
Vitamin D deficiency	3	6.0
Hepatomegaly	5	10.0
Splenomegaly	1	2.0
Ascites +pedal oedema	1	2.0



Clinical signs

The most common presenting signs were anaemia16(32%) ,vitamin deficiency in which all were vitamin D deficiencies 3(6%), hepatomegaly 5 (10%), splenomegaly 1(2%) ,and ascites with pedal oedema 1(2%),

Table 6: Degree of Dehydration in CD

DEGREE OF DEHYDRATION	NO. OF CASES(N=12)	PERCENT 24%
Mild dehydration	8	66%
Moderate dehydration	2	16.6%
Severe dehydration	2	16.6%

ISSN No:-2456-2165

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 16% had severe dehydration.

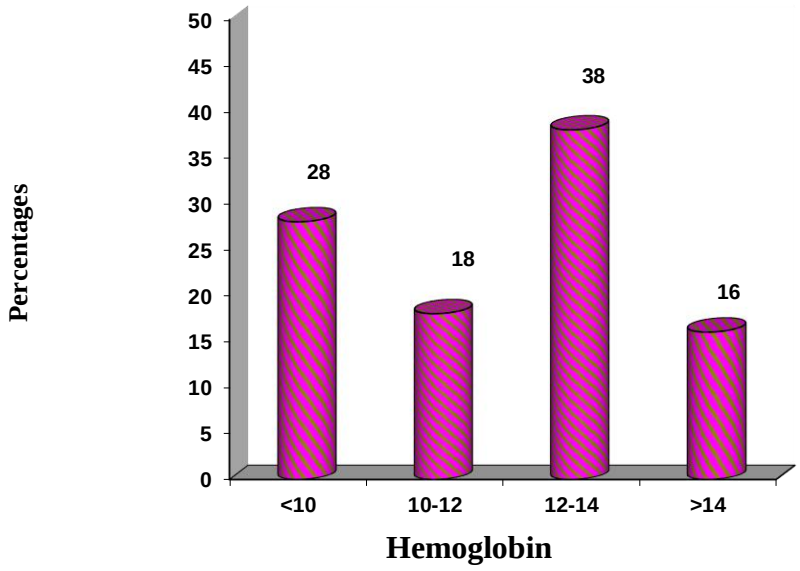
Table 7: Organism isolated

Organism	Number of children (n=50)	%
Nil	45	90.0
Yes	5	10.0
• Cryptosporidium	2	4.0
• E. Coli	2	4.0
• Giardia	1	2.0

Table 8: Levels of hemoglobin

Hemoglobin	Number of children (n=50)	%
<10	14	28.0
10-12	9	18.0
12-14	19	38.0
>14	8	16.0

Mean ± SD: 12.50±2.39



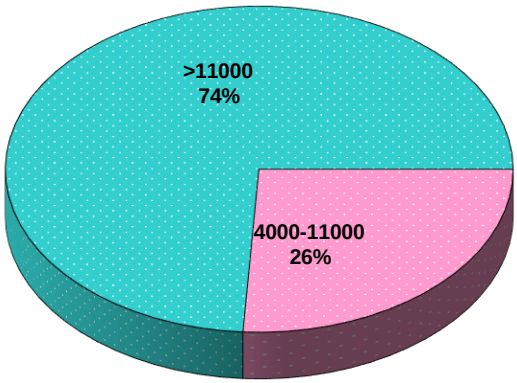
Haemoglobin (Hb gm/dl) from 6 to 16.8 in all children at the time of presentation. 14 children anemia at the time of presentation. Mean haemoglobin is 12.50.

Table 9: Total count

Total count	Number of children (n=50)	%
4000-11000	13	26.0
>11000	37	74.0

Mean ± SD: 14487.00±5486.52

ISSN No:-2456-2165

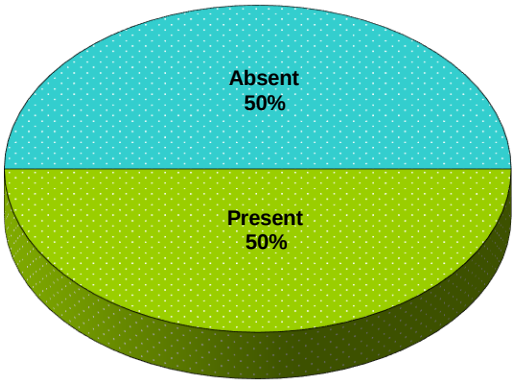


Total count

Total Leukocyte count (TC /cu. mm) was elevated in 37 children with a range of 4500/cu.mm to 28040/cu.mm and was predominantly polymorphs at initial presentation.

Table 10: Stool analysis

Stool analysis	Number of children (n=50)	%
Normal	11	22.0
Abnormal	39	78.0



DM

Table 11: Stool analysis

Stool analysis	Number of children (n=50)	%
Normal	11	22.0
Occult blood	28	56.0
WBC	8	16.0
Mucus	3	6.0
Blood+WBC	3	6.0
Cryptosporidium	2	4.0
E.Coli	1	2.0
Giardia	1	2.0
Abnormal	39	78.0

Stool tests were abnormal in 39 patients(78%). In that 28 children (56%) had occult blood in stool which was more consistant with CMPI. 8 children(16%) stool routine showed pus cells in HPF. Organisms that are associated with CD in this study are cryptosporidium, E.Coli and Giardia.

ISSN No:-2456-2165

Table 12: Urine Examination

Urine Examination	Number of children (n=50)	%
Normal	47	94.0
Abnormal	3	6.0

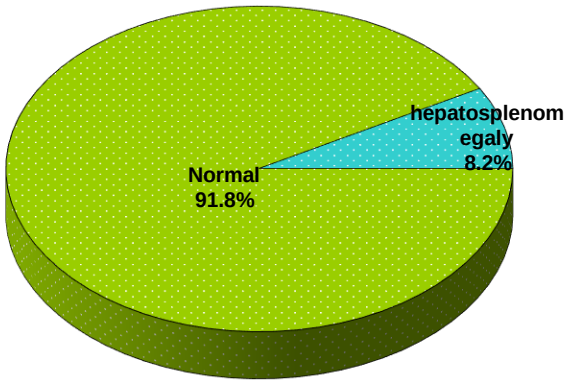
Urine Examination	Number of children (n=50)	%
Normal	47	94.0
WBC	2	4.0
E.Coli	1	2.0
Abnormal	3	6.0

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 2%

Table 13: USG abdomen

USG abdomen	Number of children (n=49)	%
Normal	45	91.8
hepatosplenomegaly	4	8.2

1: Not done



USG abdomen

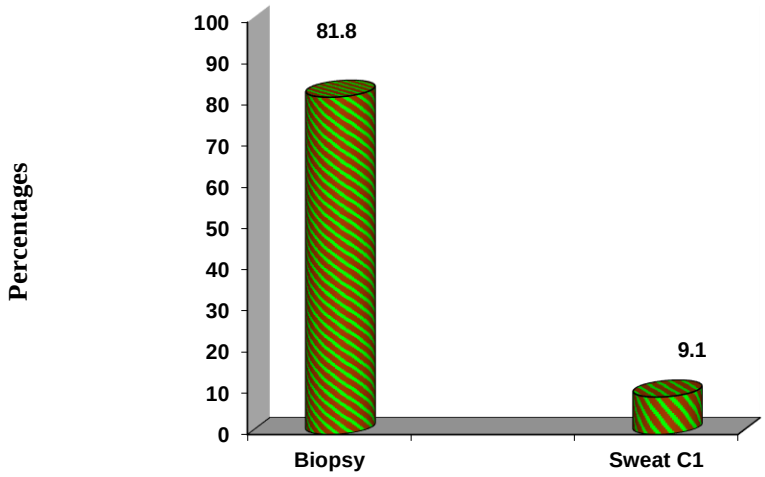
USG Abdomen evaluation has been performed in almost all children atthe time of presentation. 92% of them were normal. Rest 4 patients showed features of hepato-splenomegaly .

Table 14: Special tests

Special tests	Number of children (n=11)	%
Biopsy	9	81.8
Sweat Cl	1	9.1

Not done: 40

ISSN No:-2456-2165



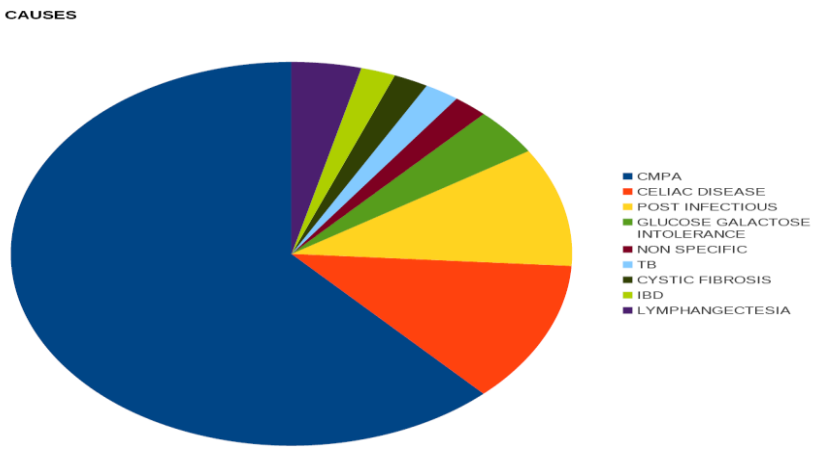
Special tests

- 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 case of celiac disease 5 showed partial villous atrophy and 1 with total atrophy.

All biopsies showed hyperplastic crypts, increased lymphotheliocytes, and mononuclear infiltration in lamina propria. 2 cases of intestinal lymphangiectesia showed epithelial lesions with intraepithelial lymphocytes and inflammation in the lamina propria.

Table 15: Aetiology

CAUSES	**N=50**
CMPI	31 (62%)
CELIAC DISEASE	6 (12%)
POST INFECTIOUS	5 (10%)
GLUCOSE GALACTOSE INTOLERANCE	2 (4 %)
NON SPECIFIC	1 (2 %)
TB	1 (2 %)
CYSTIC FIBROSIS	1 (2%)
IBD	1 (2 %)
LYMPHANGIECTESIA	2 (4 %)



aetiology according to age groups is an important out come of my study which correlates with other studies done in india

Table 16: CAUSES AND AGE RELATION

AGE GROUP 6 MONTH TO 1 YEAR(N=23)	
COW MILK INTOLERANCE	21 (91.3%)
GLU-GALAC INTOLERANCE	2 (8.69%)

ISSN No:-2456-2165

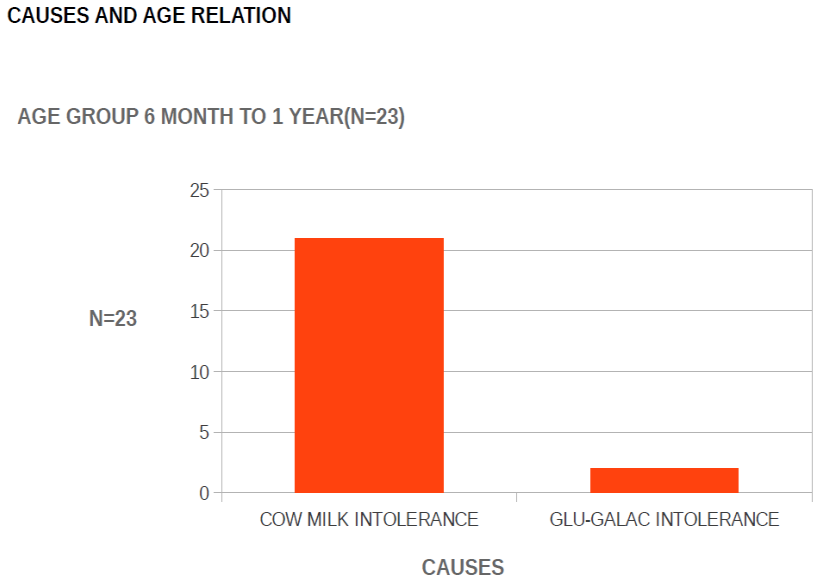


Table 17:

AGE GROUP 1 YEAR TO 2 YEARS(N=12)	
COW MILK INTOLERANCE	10 (83.3%)
POST INFECTIOUS	2 (16.6 %)

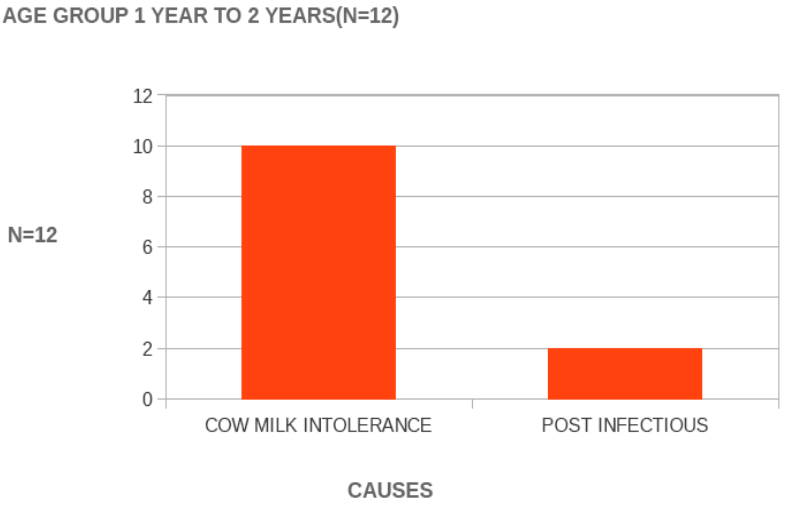


Table 18:

AGE GROUP 2 YEARS TO 6 YEARS(N=9)	
POST INFECTIOUS	3 (33.3%)
LYMPHANGIECTESIA	2 (22.2%)
CELIAC DISEASE	2 (22.2%)
NON SPECIFIC	1 (11.1%)
CMPA	1 (11.1%)

ISSN No:-2456-2165

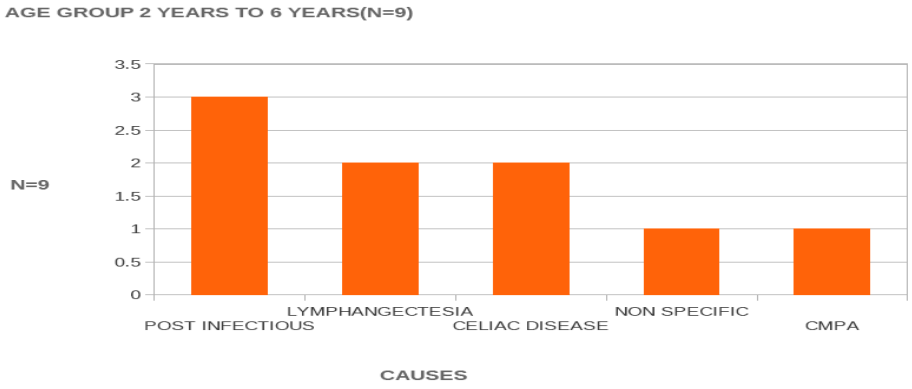


Table 19:

AGE GROUP 6 YEARS TO 16 YEARS(N=6)	
CELIAC DISEASE	4 (66.6%)
TUBERCULOSIS	1 (16.6%)
IBD	1 (16.6%)

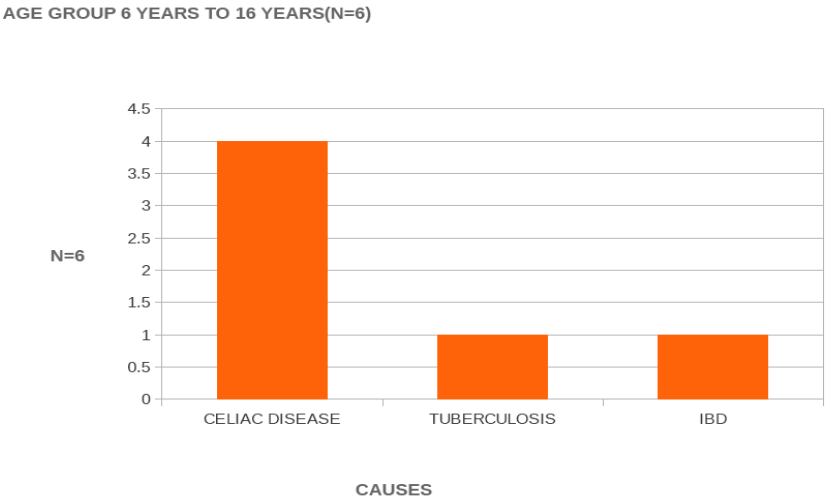


Table 20: Aetiological Diagnosis

Diagnosis	**Number of children (n=50)**	**%**
CMPA	31	62.0
CELIAC	6	12.0
POST	5	10.0
GL_GAL + I L	4	8.0
CYSTIC FIB + OTHERS	4	8.0

ISSN No:-2456-2165

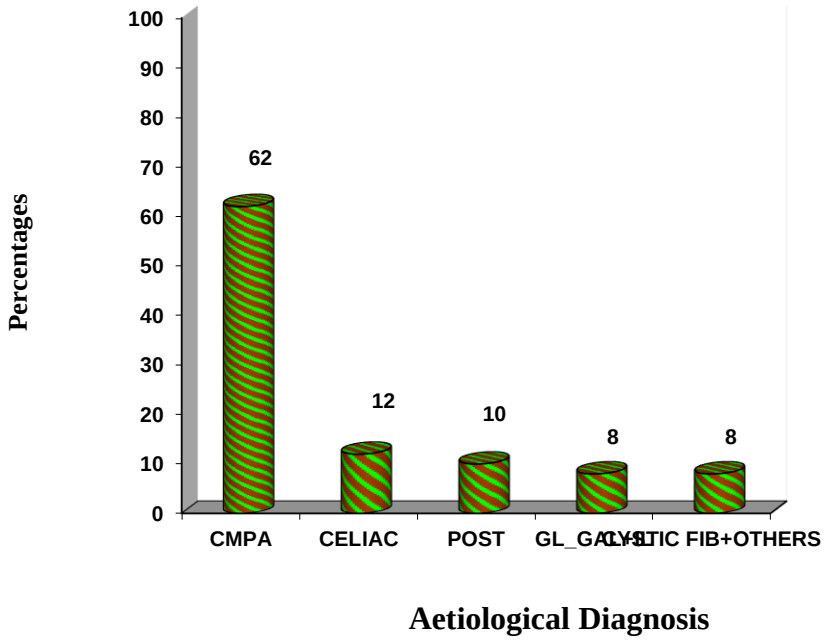
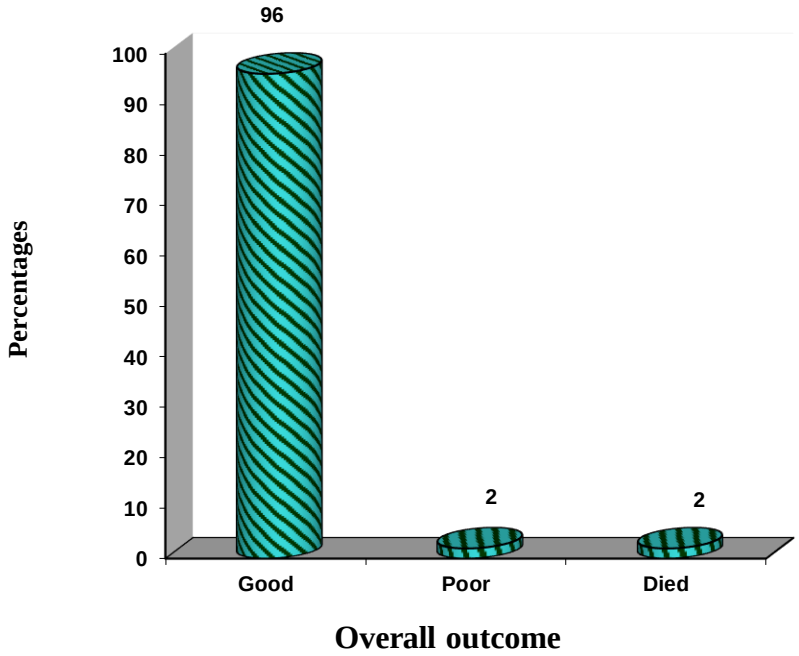


Table 21: Overall outcome

Overall outcome	Number of children (n=50)	%
Improved	48	96.0
Unimproved	1	2.0
Died	1	2.0

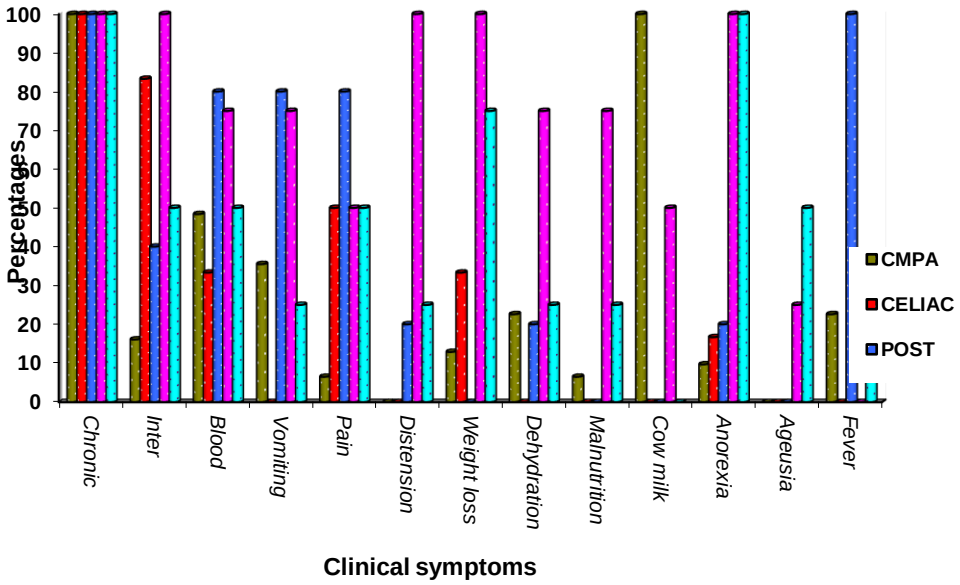


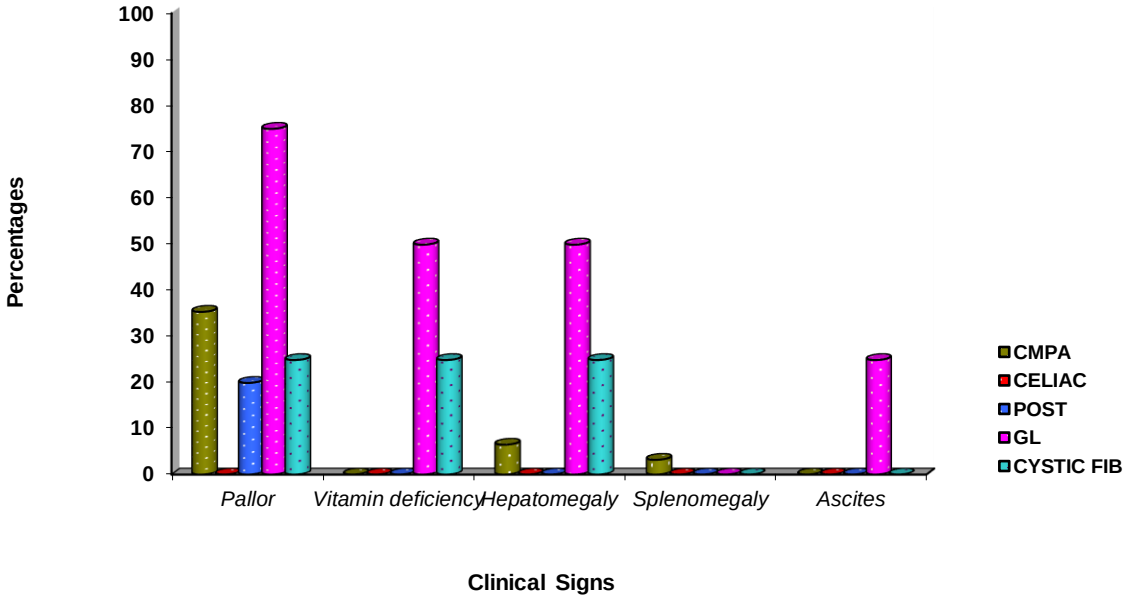
ISSN No:-2456-2165

Table 22: Correlation of clinical variables with final diagnosis

Variables	Diagnosis					P value
	CMPA (n=31)	CELIAC (n=6)	POST (n=5)	GL_GAL + I L (n=4)	CYSTIC FIB + OTHERS (n=4)	
Age in years						
• <1 years	19(61.3%)	0(0%)	0(0%)	2(50%)	0(0%)	<0.001**
• 1-2 years	10(32.3%)	0(0%)	2(40%)	0(0%)	0(0%)	
• 2-5 years	1(3.2%)	2(33.3%)	3(60%)	2(50%)	2(50%)	
• >5 years	1(3.2%)	4(66.7%)	0(0%)	0(0%)	2(50%)	
Gender						
• Male	17(54.8%)	4(66.7%)	2(40%)	3(75%)	4(100%)	0.416
• Female	14(45.2%)	2(33.3%)	3(60%)	1(25%)	0(0%)	
SES						
• Low SES	0(0%)	0(0%)	0(0%)	2(50%)	1(25%)	0.004**
• Middle SES	31(100%)	6(100%)	5(100%)	2(50%)	3(75%)	
Clinical symptoms						
• Chronic diarrhoea	31(100%)	6(100%)	5(100%)	4(100%)	4(100%)	1.000
• Intermittent	5(16.1%)	5(83.3%)	2(40%)	4(100%)	2(50%)	<0.001**
• Blood in stools	15(48.4%)	2(33.3%)	4(80%)	3(75%)	2(50%)	0.538
• Vomiting	11(35.5%)	0(0%)	4(80%)	3(75%)	1(25%)	0.030*
• Pain abdomen	2(6.5%)	3(50%)	4(80%)	2(50%)	2(50%)	<0.001**
• Distension of abdomen	0(0%)	0(0%)	1(20%)	4(100%)	1(25%)	<0.001**
• Weight loss	4(12.9%)	2(33.3%)	0(0%)	4(100%)	3(75%)	<0.001**
• Dehydration	7(22.6%)	0(0%)	1(20%)	3(75%)	1(25%)	0.114
• Malnutrition	2(6.5%)	0(0%)	0(0%)	3(75%)	1(25%)	0.010*
• Cow milk	31(100%)	0(0%)	0(0%)	2(50%)	0(0%)	<0.001**
• Anorexia	3(9.7%)	1(16.7%)	1(20%)	4(100%)	4(100%)	<0.001**
• Ageusia	0(0%)	0(0%)	0(0%)	1(25%)	2(50%)	0.004**
• Fever	7(22.6%)	0(0%)	5(100%)	0(0%)	1(25%)	0.002**
Clinical Signs						
• Pallor	11(35.5%)	0(0%)	1(20%)	3(75%)	1(25%)	0.143
• Vitamin deficiency	0(0%)	0(0%)	0(0%)	2(50%)	1(25%)	0.004**
• Hepatomegaly	2(6.5%)	0(0%)	0(0%)	2(50%)	1(25%)	0.074+
• Splenomegaly	1(3.2%)	0(0%)	0(0%)	0(0%)	0(0%)	1.000
• Ascites	0(0%)	0(0%)	0(0%)	1(25%)	0(0%)	0.160

ISSN No:-2456-2165





Statistical analysis shows strong correlation between

- Intermittent diarrhoea is more associated with glucose-galactose malabsorption, celiac disease then with CMPI in order .
- Cow milk ingestion less than 1 year of age has strong association with CMPI

III. OBSERVATIONS

Epidemiology out of 50 children with chronic diarrhoea, youngest was 6 month old male baby and oldest was 15-years.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. The higher incidence in our study is similar to the Arab studies done by Felix et al, other Indian studies including Yachha S.K3 et al, Sharma B.C et al studies.

- The prevalence of the disease was more in males than females (3:2) in present study and is similar to Yachha S.K et al, and Felix et al studies.
- Mean age of presentation in our study 1 year which is higher compared to Felix et al which was about 3.5 months
- Aetiological comparisions of different studies all over the world is as follows.

Table 23:

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 diarrhea33%		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

IV. DISCUSSION

During the 2 year period of study in about 5400 paediatric admissions 0.9% were admitted with history of diarrhea of > 2 weeks. The referral pattern, prevalence of the disease, skills of the physician and the availability of appropriate diagnostic facilities, influence the aetiological spectrum and outcome of chronic diarrhoea. 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 diarrhoea. The male preponderance encountered in this series is a reflection of the referral pattern in general, resulting from socio-cultural factors.

Some Indian authors have published the profile of chronic diarrhoea in children and the data from these studies show that cow milk allergy and celiac disease were the most common entity encountered in the earlier reports (Yaccha and et al).

The incidence of celiac disease is the 2 nd most common cause of CD 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.

V. CONCLUSIONS

- The high risk groups as per present study for chronic diarrhoea are children of < 1 year of age (42.0%) .
- Present study has shown male preponderance for chronic diarrhoea. The male to female ratio is 3:2.
- Cow milk protein intolerance is one of the major subgroups in our study and it is the most common aetiological 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 CD reduces as the age increases as seen in present study.
- Interestingly, the incidence of tuberculosis has been very less 1 case out of 50. Not encountered any case of acrodermatitis enteropathica.
- The referral pattern, prevalence of the disease, skills of the physician and the availability of appropriate diagnostic facilities, influence the aetiological spectrum and outcome of chronic diarrhoea.
- 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
- The regional hospitals and laboratory diagnostics should be well equipped to diagnose these cases.
- Mortality of CD (2%) in our study is a case of glucose galactose intolerance which has poor out come.

REFERENCES

[1.] Darrow DC, Yannet H. The changes in the distribution of body water accompanying increase and decrease in extracellular electrolyte. J Clin Invest 1935;14:266-75.
[2.] Hirschhorn N, McCarthy BJ, Ranney B, et al. Ad libitum oral glucose-electrolyte therapy for acute diarrhea in Apache children. J Pediatr 1973;83:562-71.
[3.] Hirschhorn N. The treatment of acute diarrhea in children: an historical and physiological perspective. Am J Clin Nutr 1980;33:637-63.
[4.] Gavin N, Merrick N, Davidson B. Efficacy of glucose-based oral rehydration therapy. Pediatrics 1996;98:45-51.
[5.] Santosham M, Burns B, Nadkarni V, et al. Oral rehydration therapy for acute diarrhea in ambulatory children in the United States: a double-blind comparison of four different solutions. Pediatrics 1985;76:159-66.
[6.] Holliday M. The evolution of therapy for dehydration: should deficit therapy still be taught? Pediatrics 1996;98(2 Pt 1):171-7.
[7.] Ulshen MH. Refeeding during recovery from acute diarrhea. J Pediatr 1988;112:239-40.
[8.] Sandhu BK, Isolauri E, Walker-Smith JA, et al. A multicentre study on behalf of the European Society

of Paediatric Gastroenterology and Nutrition Working Group on Acute Diarrhoea. Early feeding in childhood gastroenteritis. J Pediatr Gastroenterol Nutr 1997;24:522-7.
[9.] Brown KH, Gastanaduy AS, Saavedra JM, et al. Effect of continued oral feeding on clinical and nutritional outcomes of acute diarrhea in children. J Pediatr 1988;112:191-200.
[10.] Beattie RM, Vieira MC, Phillips AD, Meadows N, Walker-Smith JA. Carbohydrate intolerance after rotavirus gastroenteritis: a rare problem in the 1990s. Arch Dis Child 1995;72:466 (letter).
[11.] Brown KH, Peerson JM, Fontaine O. Use of nonhuman milks in the dietary management of young children with acute diarrhea: a meta-analysis of clinical trials. Pediatrics 1994;93:17-27.
[12.] Brown KH. Dietary management of acute childhood diarrhea: optimal timing of feeding and appropriate use of milks and mixed diets. J Pediatr 1991;118(4 Pt 2):S92-8.
[13.] Lifschitz CH, Torun B, Chew F, Boutton TW, Garza C, Klein PD. Absorption of carbon 13 C-rice in milk by infants during acute gastroenteritis. J Pediatr 1991;118:526-30.
[14.] Melton L. Lifesaving vaccine caught in an ethical minefield. Lancet 2000;356:318.
[15.] Weijer C. The future of research into rotavirus vaccine. Br Med J 2000;321:525-6.
[16.] Diarrhoeal Diseases Study Group (UK). Loperamide in acute diarrhoea in childhood: results of a double-blind, placebo controlled multicentre clinical trial. Br Med J (Clin Res Ed) 1984;289:1263-7.
[17.] Bowie MD, Hill ID, Mann MD. Loperamide for treatment of acute diarrhoea in infants and young children. A double-blind placebo-controlled trial. S Afr Med J 1995;85:885-7.
[18.] Soriano-Brucher H, Avendano P, O'Ryan M, et al. Bismuth subsalicylate in the treatment of acute diarrhea in children: a clinical study. Pediatrics 1991;87:18-27.
[19.] Isolauri E, Juntunen M, Rautanen T, Sillanaukee P, Koivula T. A human Lactobacillus strain (Lactobacillus casei sp strain GG) promotes recovery from acute diarrhea in children. Pediatrics 1991;88:90-7.
[20.] Pant AR, Graham SM, Allen SJ, et al. Lactobacillus GG and acute diarrhoea in young children in the tropics. J Trop Pediatr 1996;42:162-5.
[21.] Hyams JS, Krause PJ, Gleason PA. Lactose malabsorption following rotavirus infection in young children. J Pediatr 1981;99:916-8.
[22.] Penny ME, Paredes P, Brown KH. Clinical and nutritional consequences of lactose feeding during persistent post-enteritis diarrhea. Pediatrics 1989;84:835-44.
[23.] Walker-Smith JA. Cow's milk intolerance as a cause of post-enteritis diarrhoea. J Pediatr Gastroenterol Nutr 1982;1:163-73.
[24.] Penny ME, Brown KH. Lactose feeding during persistent diarrhoea. Acta Paediatr Suppl 1992;381:133-8.
[25.] Lebenthal E, Lee PC. Glucoamylase and disaccharidase activities in normal subjects and in patients with mucosal injury of the small intestine. J Pediatr 1980;97:389-93.
[26.] Solomons NW, Garcia R, Schneider R, Viteri F, Argueta von Kaenel V. H2 breath test during diarrhea. Acta Paediatr Scand 1979;68:171-2.
[27.] Davidson GP, Goodwin D, Robb TA. Incidence and duration of lactose malabsorption in children hospitalized with acute enteritis: study in a well-nourished urban population. J Pediatr 1984;105:587-90.
[28.] Lifschitz CH, Bautista A, Gopalakrishna GS, Stuff J, Garza C. Absorption and tolerance of lactose in infants recovering from severe diarrhea. J Pediatr Gastroenterol Nutr 1985;4:942-8.
[29.] Naim HY, Roth J, Sterchi EE, et al. Sucrase-isomaltase deficiency in humans. Different mutations disrupt intracellular transport, processing, and function of an intestinal brush border enzyme. J Clin Invest 1988;82:667-79.
[30.] Treem WR, McAdams L, Stanford L, Kastoff G, Justinich C, Hyams J. Sacrosidase therapy for congenital sucrase-isomaltase deficiency. J Pediatr Gastroenterol Nutr 1999;28:137-42.
[31.] Turk E, Klisak I, Bacallao R, Sparkes RS, Wright EM. Assignment of the human Na+/glucose cotransporter gene SGLT1 to chromosome 22q13.1. Genomics 1993;17:752-4.
[32.] Abad-Sinden A, Borowitz S, Meyers R, Sutphen J. Nutrition management of congenital glucose-galactose malabsorption: a case study. J Am Diet Assoc 1997;97:1417-21.
[33.] Greene HL, Ghishan FK. Excessive fluid intake as a cause for chronic diarrhea in young children. J Pediatr 1983;102:836-40.
[34.] Kneepkens CM, Hoekstra JH. Fruit juice and chronic nonspecific diarrhea. J Pediatr 1993;122:499.
[35.] Lifschitz CH. Carbohydrate absorption from fruit juices in infants. Pediatrics 2000;105:e4.
[36.] Sullivan PB, Marsh MN, Mirakian R, Hill SM, Milla PJ, Neale G. Chronic diarrhea and malnutrition - histology of the small intestinal lesion. J Pediatr Gastroenterol Nutr 1991;12:195-203.
[37.] Gryboski JD. The role of allergy in diarrhea: cow's milk protein allergy. Pediatr Ann 1985;14:31-2, 33-4, 36.
[38.] Nichols VN, Fraley JK, Evans KD, Nichols BL. Acquired monosaccharide intolerance in infants. J Pediatr Gastroenterol Nutr 1989;8:51-7.
[39.] Murch SH. The molecular basis of intractable diarrhoea of infancy. Baillieres Clin Gastroenterol 1997;11:413-40.
[40.] Greenberg HB, Clark HF, Offit PA. Rotavirus pathology and pathophysiology. Curr Top Microbiol Immunol 1994;185:255-83.