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Original Research Article

A Prospective Study to Evaluate the Clinical, Biochemical and Serological Profile in Children Diagnosed with Celiac Disease

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Abstract

Aim: The goal of this study was to look at the clinical symptoms and biochemical profile of celiac disease in children.

Methods: All children diagnosed with CD in the previous 5 years, as well as newly diagnosed celiac patients who meet the inclusion criteria for the next year. This is a prospective and retrospective observational descriptive study. CD was diagnosed in children with chronic diarrhoea and other suggestive signs based on a positive tTGA and duodenal biopsies. For complete follow-up data, hospital records were reviewed.

Results: In a study period of 12 months we diagnosed 42 children with Celiac Disease, who were studied prospectively, whereas 58 patients who were diagnosed within the last 3 years & were on regular follow up in OPD were studied retrospectively. In the total group of 100 patients in the age range of 1year to 15 years. The presenting clinical features of our group of patients were: chronic diarrhea (81 %), failure to thrive (78%), abdominal pain (41%), abdominal distention (37%), anorexia/vomiting (5%/ 2%), &weight loss (15%). Rare features were fever, fatigue, blood in stools & constipation.

Conclusion: Chronic diarrhea was the most common presenting complaint in all age groups (92%) followed by failure to thrive, not gaining weight and abdominal pain. Constipation was least common. Anemia was the most common laboratory-confirmed finding and the most common type of anemia was iron deficiency anemia. Prevalence Anemia was most common in below 5 yrs.

Keywords: chronic diarrhea, iron deficiency anemia, celiac disease

Introduction

Celiac disease is thought to be very rare in India, according to popular belief. There have been an increasing number of reports from North India recently (major wheat eating areas).[1, 2] The prevalence of the celiac disease is globally 1%, but large variations among countries have been shown. [3] Celiac disease (CD) is a chronic, immunologically determined form of enteropathy affecting the small intestine in genetically predisposed children and adults. It is precipitated by the ingestion of gluten containing foods.[4]

In children under two years of age gastrointestinal symptoms and failures to thrive are common. In older children and adults, symptoms are often nonspecific, such as abdominal pain, anemia, osteoporosis, fatigue, and even depression. Consequently, the diagnosis may easily be delayed or even missed. [5]

The clinical presentations are different in age groups such as shown by Santiago Vivas MD.They studied new cases of celiac disease diagnosed between 2000 and 2006 prospectively included (66 children and 54 adults). The clinical spectrum was categorized in two groups: (a) typical (malabsorption, chronic diarrhea, or failure to thrive) and (b) oligosymptomatic (abdominal pain, anemia, hyper transaminasemia). In the real sense worldwide, CD “out of the intestine” is 15 times more frequent than CD “in the intestine making the diagnosis extremely challenging.[6,7]

No foods or medications containing gluten from wheat, rye, and barley or their derivatives can be taken, as even small quantities of gluten may be harmful. Complete removal of gluten from the diet of celiac disease patients will result in symptomatic, serologic, and histological remission in most patients. [8]

This study was taken up to analyze clinical manifestations, biochemical profile and serology of children with celiac disease presenting at Darbhanga Medical College & Hospital, Darbhanga, Bihar, India for 12 months

Material and Methods:

Subjects: All children diagnosed as CD and satisfying inclusion criteria were enrolled in the study.

Study period: 12 months

Inclusion criteria

1. All children presenting to the hospital with clinical features suspected of celiac disease and confirmed by intestinal biopsy.
2. Age-1 to 15 years

Exclusion criteria

1. Age<1 or>15 years
2. Non-consent
3. Not confirmed as celiac

Methodology of study

Informed consent was taken from parents before the interview and inclusion of the study**.**

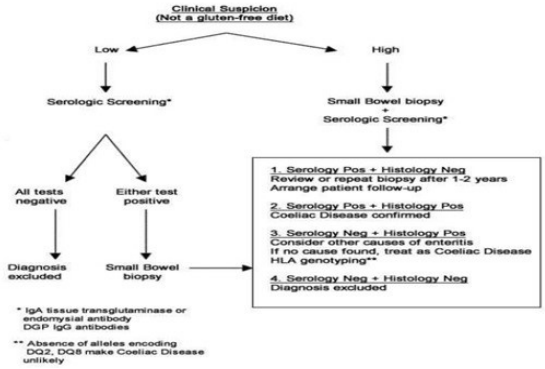
Clinical Examination: All patients were examined thoroughly for signs of anemia, lymphadenopathy, malnutrition, organomegaly, chest signs, murmur and CNS disease

Immunology: Tissue transglutaminase (tTGA) quantitative estimation was done in each suspected patient and the following values following enzyme immunoassay (ELISA) method of the lab was used:

- <20 IU-Negative
- 20-30 IU-Weak positive,
- 30IU-Positive

All suspected patients were subjected to intestinal biopsy following the flowchart proposed by WHO and the world gastroenterology association.

Figure 1. Flowchart used for the diagnosis of celiac disease



Biopsy technique: Endoscopic biopsy was done for all subjects following the above flowchart. Endoscopy was done in a specialized endoscopy unit under propofol anesthesia. For duodenal biopsy a small-diameter, flexible and fiberoptic endoscopes, Olympus GIF 140, GIF 150, PQ 20 were used.

Each endoscope had its specifications and use. Endoscopic visualization of the intestinal mucosa along with 4 biopsy specimen taken—three from the second part of the duodenum distal to the papilla, and one from the duodenal bulb. All samples were preserved in formalin and sent to KEM lab for histopathologic examination. The patient was observed inward for any complications following the biopsy.

Results:

Table 1 shows 100 study cases among which the majority were below age 5.0 years that is 57 (57.0%), 33 (33.0%) had their age between 5.0 – 10.0 years and 10 cases (10.0%) had their age above 10.0 years. The mean ± standard deviation of the age of the entire group was 6.1 ± 4.8 years. Table 2 illustrates that 42.0% were males and 58% were females. The male: female sex ratio was 0.8: 1.0 in the entire study group. Table3 shows Among all the study participants 81.0% cases had chronic diarrhea, which thus is the most common clinical feature in our study, 78.0% cases had complained of not gaining weight, 41.0% cases had abdominal pain, 37.0% cases had abdominal distension, 30.0% had vomiting, 15.0% cases had weight loss, 5.0%cases had anorexia and 2.0% cases had other features (fever, blood in stools, fatigue and constipation).Table 4 shows that out Of 100 cases studied, 80.0%) were anemic with low hemoglobin, which was the most common lab abnormality.35 %) had elevated Liver Transaminase, of which 1% had Hepatomegaly on USG. 8.0% had positive Stool for Cryptosporidium. Table 5 depicts the prevalence of anemia differs significantly across three age groups of the cases with celiac disease studied (P-value<0.05). Anemia was most common in below 5 years (57 of 80 cases) and least common above 10 years of age in our study though in all age group anemia was a significant finding. Table 6 and 7 shows the mean value of tTGA was 165.89 and the

Median was 134.7 indicating the importance of high tTGA titres in CD.

Table 1. Age distribution of the cases studied with Celiac Disease (n= 100).

Age Group (years)	No. o f cases	% of cases
Below 5.0	57	57.0
5.0 – 10.0	33	33.0
Above 10.0	10	10.0
Total	100	100.0

Table 2: Gender Distribution of cases studied with Celiac Disease (n= 100)

Sex	No. of cases	% of cases
Male	42	42.0
Female	58	58.0
Total	100	100.0

Table 3. Clinical features of the cases studied with Celiac Disease (n=100

Clinical features	% of cases
Chronic diarrhea	81.0
Not gaining weight	78.0
Abdominal Pain	41.0
Abdominal distension	37.0
Vomiting	30.0
Weight loss	15.0
Anorexia	5.0
Other	2.0

Table 4. Distribution of abnormal findings - investigations at the time of diagnosis amongst the cases studied with Celiac Disease (n=100).

Investigations		% of cases
Hemoglobin	Normal	20%
	Anemia	80%
Liver Transaminase	Normal	65%
	Elevated	35%
Serum Electrolyte	Normal	93%
	Hypokalemia	7%
Prothrombin Time	Normal	97%
	Prolong	3%

Hypoalbuminemia	No	94%
	Yes	6%
Calcium	Normal	95%
	Low	5%
Phosphorous	Normal	95%
	Low	5%
Alk Phosphate	Normal	98%
	High	2%
Stool for Cryptosporidium	Negative	91%
	Positive	9%
USG	Non-specific	99%
	Hepatomegaly	1%
Renal Function test	Normal	98%
	Elevated	2%
Vitamin D	Normal	76%
	Deficient	24%

Table 5. Distribution of anemia according to various age groups of the cases studied with Celiac Disease (n= 100).

Age Group (years)	Anemia (n=80)	Normal (n=20)	Total	p-value
	% of cases	% of cases	% of cases	
Below 5.0	57%	2%	100.0	0.001*
5.0 – 10.0	15%	8%	100.0	
Above 10.0	8%	10%	100.0	

Table 6. Distribution of the cases studied with Celiac Disease according to levels of TGA(n=100).

TGA Levels	% of cases
<20 (Negative)	15%
20 – 30 (Weak Positive)	7%
>30 (Positive)	78%
Total	100%

Table 7. Descriptive statistics of tTGA in Celiac Disease patients (n=50).

Parameter	No. of cases	Mean	Standard Deviation	Median	Min –Max
tTGA IgA (U/mL)	100	165.89	81.78	134.7	3.3-312

Discussion:

This study was conducted in Darbhanga Medical College & Hospital, Darbhanga, Bihar, India. Total 100 patients were enrolled with clinical presentation of adult celiac disease in relation of biochemical parameters.

The total number of children diagnosed with the Celiac disease was 100, who were followed after 1, 3, and 6months in a prospective study and single follow up in the retrospective study. All enrolled patients were assessed at admission and their clinical parameters were noted and patients were followed up as per proforma. Among all the biopsy-proven CD children and adolescents, various age-related characteristics were detected.

In this study majority of patients belonged to the age group <5yrs (50%), followed by the age group 5-10 years (32%). The mean ± standard deviation (SD) of the age of the entire group was 5.9 ± 3.7 years as in a study by Poddar et al. where the mean age at diagnosis 6.3 to 8.6. In the study by Stone et al. [9]infants less than 2 years of age represented only 12% of the study, 27% of patients were aged between 4 and 5 years, 36% were aged between 5 and 10 years and 26% were more than10 years of age. Lower age at diagnosis suggest improved awareness for celiac disease among pediatricians and improved availability of serological tests. [10]

Regarding the clinical manifestations, chronic diarrhea was the most common clinic manifestation (92%) overall in all age groups which was similar to the study done by Poddar et al. and by Mohindar et al [11]. Stone et al in his study showed the most common presenting symptom in younger children (those <5 years) was diarrhea (59%), followed by irritability (34%) and weight loss (38%). In older children (≥ 5 years), the most common presenting feature was abdominal pain (55%) followed by diarrhea (26%).[9] In our study abdominal pain was seen in 41% and 37% of the study population had abdominal distension which was mainly seen in school-aged and adolescence while abdominal pain and abdominal distension was reported to be 45% and 9% respectively by Tanpowpong et al.[10]

The significant age-related differences in the family history of CD were interesting but difficult to explain. School-aged children and adolescents, who were more likely to have no or less typical CD symptoms, might also be more likely to undergo CD screening solely because of positive family members with CD compared with the younger children. A similar reason might explain the borderline significant higher proportion of family history of irritable bowel syndrome among school-aged children as well. Another possible explanation might be because of differences in parental or patient reports across the age groups. These questions will need to be addressed with future research. Anemia was present in 76% of the study population (n=50) which was similar to the study of Poddar et al and Mohindar et al.[11] In the study by Stone et al [9]. Anemia was seen only in 21% of the study population. In our study percentage of iron deficiency anemia was 80% in confirmed iron deficiency.

10% of the study population had elevated transaminases,4% had abnormal renal function tests, 2% had hypokalemia, 14% had hypoalbuminemia, 2% had elevated prothrombin time, 10% had low ionic calcium, low phosphorous and high alkaline phopthatase.14% of our study children were

positive for stool cryptosporidium which was similar to study by Fassano et al. [12]

USG was non-specific in the present study and did not appear to have a role in celiac disease diagnosis which is against the study by Recabbona et al in which various sonographic anomalies in children with Celiac disease were observed: abdominal fluid in 76%, hyperperistalsis in 82%, pericardial effusion in 47% and unusual appearance of the small bowel wall in 94%.[13,14]

Conclusion

Females made up the bulk of the patients (58 percent. In all age categories, chronic diarrhea was the most prevalent presenting ailment (42 percent), followed by failure to thrive, inability to acquire weight, and stomach pain. The least common ailment was constipation.

Anemia was the most common laboratory-confirmed finding and the most common type of anemia was iron deficiency anemia. The majority of cases studied had Positive tTGA indicating its importance in the screening of CD.

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