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Original Article

Common Presentation and Clinical Correlates of Celiac Disease in Pediatric Population of Pakistan

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ABSTRACT

Objective: To explore the various clinical presentations in childhood celiac disease patients of Sindh, Pakistan.
Study Design: Cross-sectional study
Setting and Duration of Study: Pediatric Department, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, Khaipur Mirs Pakistan, from Sep 2018 to Mar 2020.
Methodology: A total of 140 children aged between 1-15 years, with diagnosed cases of celiac disease were enrolled in the study. Patients with inconclusive diagnosis, with multiple comorbidities, age >15 years, or children whose parents did not give consent to take part in the study were excluded from the current study. All children were further categorized according to the sociodemographic and clinical presentation.
Results: The mean age of patients at the onset of symptoms was 3.15±1.25 years. Out of 140 patients, 74(52.8%) were male and 66(47.1%) female. Out of 140 patients, 28(20%) patients had positive anti-endomysial antibody titers. About 8 patients had concomitant autoimmune diseases i.e. Type 1 diabetes mellitus, out of these 5 tested positive for anti-endomysial antibody titers. The most common presentation was chronic diarrhea, seen in 13(32%) of patients.
Conclusion: The current study revealed that the majority of the diagnosed pediatric patients presented with a typical clinical picture of celiac disease.

Keywords: Anti-endomysial antibody, Adult celiac disease, Clinical presentation, Hyderabad.

How to Cite This Article: *Bharo MA, Baloach KAS, Bhanbhro BA, Ishfaq H, Abbas K. Common Presentation and Clinical Correlates of Celiac Disease in Pediatric Population of Pakistan. Pak Armed Forces Med J 2024; 74(Suppl-2): S101-104. DOI: https://doi.org/10.51253/pafmj.v74iSUPPL-2.5082*

INTRODUCTION

Earlier, Celiac Disease (CD) was widely regarded as the gastrointestinal disease of youth affecting primarily white people, it is now acknowledged as a systemic disease that may target people of any age and many colors.[1,2] The data demonstrates that out of every 100 to 250 children, and adults there is a chance of presence of celiac disease (CD).[3] Sometimes, individuals have little, mild, or lack of symptoms at all and are distinguishable only by screening. The signs and symptoms of celiac disease include diarrhea, bloating, developmental delay, abdominal discomfort, and delayed puberty.[4,5] According to the international criteria,[6] the clinical diagnosis of celiac disease requires alterations in the intestinal mucosa moreover a reaction after a strict gluten-free diet in the form of settlement of histologic modifications or of clinical manifestations.[7] It is worth noting that celiac disease is an immune-mediated enteropathy which is caused by the consumption of gluten in people who are genetically vulnerable. In 90-95% of the individuals, the responsible genes are situated on chromosome six's HLA system.[8]

A considerable amount of literature has been published on celiac disease.[9] It is now well established from these studies that celiac disease has a wide variety of clinical manifestations which differ from one person to another making it difficult to diagnose.[2,10] The mechanisms that underpin signs and symptoms are not fully understood. Much uncertainty in several studies still exists about the typical and atypical manifestations of this disease in childhood. This paper attempts to examine the fore-mentioned problem. The objectives of this research were to explore the frequency and frequencies of signs and symptoms like bloating, diarrhea, failure to thrive etc. in this disease of gluten-sensitive individuals. The study aimed to contribute to the ongoing developments in research with respect to celiac disease in Pakistan.

METHODOLOGY

The cross sectional study was conducted from September 2018 to March 2020, for a duration of 18 months at the Pediatric Department of Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, Khaipur Mirs Pakistan. The sample size was

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Received: 19 Aug 2020; revision received: 04 Jan 2021; accepted: 04 Mar 2021

calculated using reference prevalence of celiac disease to be 1.4%, confidence interval of 95%, and a margin of error of 1.94%. Using select statistics sample size calculator, a sample size of 140 was obtained. Patients were recruited for the study using a non-probability consecutive sampling technique.

Inclusion Criteria: All children aged between one year to 15 years, with diagnosed cases of celiac disease were included.

Exclusion Criteria: Patients with inconclusive diagnosis, with multiple comorbidities, age of child over 15 years, or children whose parents did not give consent to take part in the study were excluded from the study.

After procuring ethical clearance from the ethical committee of the institutional review board, the data collection was initiated. Informed verbal as well as written consent was procured from the guardians of all patients. Detailed history and clinical examination were performed on all children and findings were recorded on a predefined pro forma. The diagnosis of celiac disease was based on consistent clinical history, anti-endomysial antibody titers, positive anti-tTG as detected by ELISA. The patients who had raised levels of Anti-tTGs were confirmed with endoscopic duodenal biopsy. All children were further categorized according to the sociodemographic and clinical presentation.

All data analysis was performed using Statistical Package for the Social Sciences (SPSS version 24). The continuous data like mean age and body mass index were calculated using mean & standard deviation whereas, the categorical data including the gender, the age groups, clinical presentations were presented as frequency and percentage. The descriptive results were illustrated with the aid of tables.

RESULTS

The mean age of patients was 3.15±1.25 years, with over one-fourth of the patients having symptoms since the age of 1 year. More than one-half of the children were male with a frequency of 74(52.8%) while there were 66(47.1%) female children. Consanguinity i.e. cousin marriages was commonly practiced in 59(42.1%) cases, whereas family history was positive in only 23(16.4%) patients.

Out of 140 patients, 28(20%) children had positive anti-endomysial antibody titers. All children with positive biopsy underwent distal duodenal biopsy with histo-pathological examination of the biopsy specimens. The findings were consistent with diagnosis of celiac disease. Majority 77(55%) showed atrophy of duodenal folds, while 63(45%) patients showed cobblestone appearance on endoscopy. Histopathological examination revealed total villous atrophy in 74(53%) specimens and near normal villous architecture with a prominent intraepithelial lymphocytosis in 66(47%) of biopsy specimens.

Younger children (1 year to 5 years) more frequently presented with chronic diarrhea while older children (6 years to 15 years) presented with iron deficiency anemia.

About 8 patients were suffering from other associated autoimmune diseases i.e. Type 1 DM, out of these 5 tested positive for anti-endomysial antibody titers.

Table-I. Patient Demographic and Clinical Characteristics in our Study (n=140)

Patient Characteristics	Frequency n(%)
Gender	
Male	74(52.8%)
Female	66(47.1%)
Age group	
< 5 years	42(30%)
5 years to 10 years	70(50%)
>10 years	28(20%)
Consanguinity	
Yes	59(42.1%)
No	81(57.8%)
Family History	
Yes	23(16.4%)
No	117(83.5%)
History of Autoimmune disorders	
Yes	8(5.7%)
No	132(94.2%)

In the study, 13(32%) of patients presented with chronic diarrhea followed by short stature in 9(22.5%) patients as the second most common feature of celiac disease in our patients. was the most common presentation and was seen in 32%(n=13) of patients. Iron deficiency anemia was found in 8(20%) patients. See Table-II.

Table-II. Clinical Presentation among Patients with Diagnosed Celiac Disease (n=140)

Clinical manifestation	Frequency n(%)
Chronic Diarrhea	9(32.14%)
Iron deficiency anemia	6(21.43%)
Abdominal pain	5(17.86%)
Short stature	7(25.00%)
Failure to thrive	1(3.57%)

DISCUSSION

Celiac disease is an immune-mediated systemic disease manifested as the inability of the patient to digest gluten-containing grains such as wheat, rye, or barley.[11] The present study aimed to explore the demographic and clinical correlates of celiac disease in our population. We observed that about two-fifth of parents of children with celiac disease were cousins by relation with about one-fourth children having a positive family history. In a study by Mouzan *et al*., the relationship between consanguinity and inflammatory bowel disease was investigated. However, they did not find any significant difference in frequency of consanguinity among the cases and the controls (p=0.95, p=0.78, p=0.33, respectively).[12] They concluded that family history along with consanguinity might increase susceptibility of these diseases further reinforcing the current findings. Genetic predilection is a major contributor of these autoimmune-mediated diseases and the role of genetic mutations in the development and progression of the disease is well-established.[13-15] Neuhausen *et al*., revealed a significantly increased number of patients with insulin dependent diabetes mellitus and hypothyroidism among subjects with celiac disease. Moreover, they reported that the incidence of juvenile rheumatoid arthritis was increased among patients who had a family history of celiac disease highlighting the significance of shared genetics increasing an individual's susceptibility to multiple auto-immune mediated disease.[14] Another study highlighting the importance of family history was conducted by Cosnes *et al*., reporting that patients with celiac disease had the progressive risk of developing an autoimmune disease of about 8.1%±1% at age fifteen which increased to 15.7%±1.5% by the age thirty.[15] Family history of autoimmunity was an important risk factor along with the diagnosis of celiac disease prior to age 36 years with hazard ratios of 2.36(95% confidence interval, 1.71–3.31) and 2.65(95% confidence interval, 1.79–3.85), respectively.[15]

The current study reported that the most common manifestation with which the patient presented was chronic diarrhoea, followed by short stature and iron deficiency anemia. According to the literature, the presentation of celiac disease may vary according to the age of the patients and the duration of illness.[16-18] In a 30 yearlong study, significant changes observed in the pattern of the celiac disease in the pediatric population. The authors observed female dominance throughout the study unlike in the present study. Moreover, the study highlighted that there was a significant change of trends towards older age at the time of diagnosis (p<0.001) and lesser number of patients presented with the classical i.e. gastrointestinal symptoms at presentation (p<0.001). In fact, between the year 1978–1987 54/72(75%) presented with diarrhea compared to 54/141(38%) between the period of 1998-2007, the difference was statistically significant (p<0.0001). Between the years 1998-2007, about one-fourth population were asymptomatic (p<0.001). About 36 percent of patients had non-classical symptoms at presentation (p<0.001) in the last decade compared to earlier times.[15] In a local study, 96 patients with celiac disease were evaluated.[18] The authors observed in the majority of the patients however, some of the atypical presentations included constipation 21(21.9%), hypertransaminasemia 38(39.6 %) and neurological signs in 41(42.7%) patients.[18]

Despite the classical symptoms prevalent in the current study, it is advised that the clinician must also look for atypical symptoms in the pediatric population to avoid misdiagnosis and delay in the treatment. In patients with atypical presentation, diagnosis is often delayed, as clinicians do not look for atypical features of the disease. Celiac disease may also present as asymptomatic silent disease, with positive serology and villous atrophy or as latent disease where the patient has no clinical symptoms or atrophy accompanied by positive serology.[19-20] Therefore, it is highly recommended that the clinicians should not rule out celiac disease based solely on the non-classical presentations seen in clinical practice.

CONCLUSION

The current study indicated that the majority of the diagnosed pediatric patients presented with a typical clinical picture of celiac disease. It is however, noted that many children with celiac disease also present with atypical symptoms which must be comprehensively evaluated.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MAB & KASB: Study design, data interpretation, critical review, approval of the final version to be published.

BAB & HI: Data acquisition, data analysis, approval of the final version to be published.

KA: Concept, data analysis, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of

any part of the work are appropriately investigated and resolved.

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