

# Celiac Disease and Celiac Crisis in Children

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## ABSTRACT

**Objective:** To determine the frequency of clinical features of Celiac disease (CD) and Celiac crisis in children.

**Study Design:** Case series.

**Place and Duration of Study:** Paediatrics Unit, Sheikh Zayed Medical College and Hospital, Rahim Yar Khan, from September 2009 to September 2010.

**Methodology:** Forty children aged between 4 to 13 years of either gender, presenting with complaints of recurrent diarrhea, abdominal distention, severe emaciation and dehydration were included. The information about breast feeding, weaning diets, age of introduction of wheat diets, onset of diarrhea, characteristics and frequency of stools, growth, vaccination status, symptoms in 1st degree relatives, restriction of Gluten diet in the past and anthropometric measures were recorded. Serological tests against anti-Tissue Transglutaminase (anti-tTG) antibodies were obtained in all cases. Upper gastrointestinal endoscopies were performed and multiple biopsies were taken from distal parts of duodenum.

**Results:** Among the forty children, twenty four (60%) were females and 16 were males (40%). The mean age was  $6.35 \pm 2.83$  years. Thirty five (87.5%) parents were cousins. Breast feeding was not exclusively given and the Gluten containing weaning diets were given as early as 3.5 months of age. Thirty (75%) children presented with typical sign and symptoms of CD. Celiac crisis presented with profuse diarrhea, severe dehydration; abdominal distention; pedal edema, carpopedal spasm due to tetany; wasted muscles; head drop and inability to stand. The serum tTG antibodies in thirty-eight cases (95%) were above the cut off level of 7u/ml ranging from 35-99 u/ml. The histopathology of specimens from distal duodenum revealed lesions of M3 type in thirteen (32.5%) and M2 type in eighteen cases (45%). All cases recovered and improved on follow-up after strict adherence to gluten-free diet (GFD).

**Conclusion:** Majority of children with Celiac disease presented with typical symptom, while Celiac crisis was characterized by severe dehydration, weakness and calcium deficiency signs. Most were the product of consanguineous marriages and were given Gluten - containing weaning foods as early as the 4th month of life.

**Key words:** Celiac Disease (CD). Children. Head drop. Celiac crisis. Biopsy. Gluten.

## INTRODUCTION

Celiac disease (Gluten sensitivity enteropathy) is an autoimmune chronic gastrointestinal disorder in which ingestion of Gliadin portion of Gluten present in wheat, rye and barley causes the damage to mucosa of the small intestine in genetically susceptible individuals.<sup>1,2</sup> The disease is associated with human leukocyte antigen (HLA)-DQ2/DQ8 in majority of cases,<sup>1,3</sup> but only about 4% of them develop the disease after introduction of Gluten diets. The prevalence of Celiac disease in world is about 1% of individuals being one of commonest genetically induced chronic disorder with female to male ratio of 2:1 to 3:1.<sup>4</sup>

Wheat is the staple food in Pakistan and is the first weaning diet (biscuits, porridge, bread) given to almost every child as early as third to fourth months of life. Therefore, the susceptible children have a potential risk

from infancy because the time of introduction and quantity of gluten are important factors. The occurrence of CD has been observed in areas of the world where wheat was consumed more than rice.

Celiac disease has a protean clinical manifestations ranging from silent, atypical, classical to life-threatening celiac crisis.<sup>7</sup> Celiac crisis is a constellation of profound diarrhea, weight loss, hypocalcaemia and hypoproteinemia.<sup>4-8</sup> This fatal condition warrants intensive care. Short stature may be the only stigmata of CD and needs screening for non-diarrhea CD. The awareness of the disease is needed in underdeveloped countries as it is treatable.<sup>9,10</sup>

Much data about occurrence of the disease is not known in Pakistan due to under diagnosis,<sup>10</sup> and treatment on empirical grounds as the facilities of serological screening, paediatrics gastric endoscope and histopathology of intestinal biopsy are still lacking even in tertiary care centres. The rationale of this study was to emphasize the importance of early recognition of CD and ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition) based diagnosis in all suspected children and lifelong adherence to gluten-free diet (GFD).<sup>3,7</sup> The aim of the study was to determine the frequency of clinical features of Celiac disease (CD) and Celiac crisis in children.

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## METHODOLOGY

Forty (n = 40) children between age 4 to 13 years of either gender, presented with complaints of recurrent diarrhea, abdominal distention, severe emaciation and dehydration were included. Children with acute diarrhea, atypical CD such as dermatitis, herpetiformis (DH) or short stature as the sole presentation; negative serology for tTG antibodies, whose gastrointestinal endoscopy were not possible and other systemic chronic illnesses like tuberculosis were excluded. Information about breast feeding, weaning diets, age of introduction of wheat diets, onset of diarrhea, frequency of stools, growth, vaccinations, symptoms in 1st degree relatives, restriction of Gluten diet and anthropometric measures were recorded on a proforma. Majority of the investigations including complete blood count, ESR, X-rays of chest and skeleton, urine and stool examination, blood gas analysis, blood sugar, serum electrolytes (Na and K), calcium, creatinine, albumin, iron and transaminase estimations were done in the Pathology Laboratory of Sheikh Zayed Hospital, Rahim Yar Khan. The serological test anti-Tissue Transglutaminase (anti-tTG) antibodies analysis was obtained from the Aga Khan University Pathology Laboratory, Karachi. HLA typing was not done due to cost limitation. Upper gastrointestinal endoscopies (EGD) were performed by Gastroenterologist and multiple biopsies were taken from distal parts of duodenum. The histopathological reports were evaluated on Modified Marsh Classification for Celiac disease.<sup>10</sup> M2 (increased intraepithelial lymphocytes plus hyperplastic crypts) and M3 (M2 plus villous atrophy of variable degree) were considered as confirmed cases of celiac disease. The data was entered and analyzed in SPSS 16. Quantitative variables like age, weight, height and serum tTG were presented as mean and standard deviation and qualitative variables like gender and biopsy reports were presented in frequency and percentages.

## RESULTS

Among forty children, there were 24 (60%) females and 16 males (40%). Female to male ratio was 1.5:1 ranging from 4 to 13 years. The mean age was  $6.35 \pm 2.83$  years. The anthropometric measures included height and standard deviations of weight, height and serum tTG level are given in Table I. None of the cases had co-existing diseases like type 1 Diabetes mellitus, Down syndrome, Turner's syndrome, William's syndrome or clinical evidence of thyroiditis. Thirty-five n=35 (87.5%) parents were cousins. Two n=2 (5%) cases had one younger sister in each family with clinical diagnosis of CD. All cases had exclusive breast feeding till 3.5 months of age and later added buffalo milk as supplement. They started weaning diet like biscuit and piece of bread mixed in milk as early as 3.5 months of age. They were given wheat porridge, minced pieces of

**Table I:** General statistics of variable; found in children of celiac disease.

Statistics	Age (years)	Height (cm)	Weight (kg)	Serum tTG level (u/ml)
Mean	6.35	109.45	16.39	65.69
Standard deviation	2.83	13.35	6.15	32.45

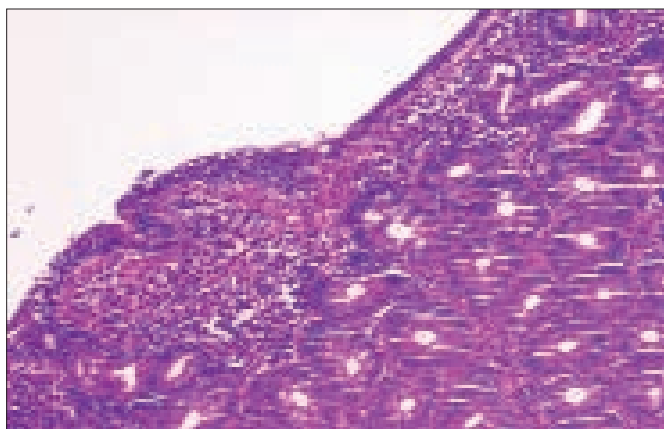
**Table II:** Clinicopathological features of celiac disease .

Feature	Frequency (n=40)	Percentage
Short stature	40	100%
Diarrhea and abdominal distension	30	75%
Celiac crisis	10	25%
Cheilosis	10	25%
Tetany	10	25%
Clubbing	06	15%
Delayed puberty	03	7.5%
Head drop	10	25%
Serum TtG	38	95%
Histopathology (M2)	18	45%
Histopathology (M3)	13	32.5%

flat bread mixed in butter and shortening (*choori*) at 6 months; cake-rusk with tea was the preferred breakfast from 9 months of age to adolescences. All cases suffered acute episodes of diarrhea since late infancy; got treatment but they used to pass one or two semisolid, frothy foul smelling stools followed by constipation. The parents were conscious of the ill health of their children and concerned about emaciation and short stature. Twenty-five (62.5%) were empirically diagnosed and advised to avoid gluten diet, but they could not strictly follow it.

Twenty-eight (70%) were admitted in the months of May to September. Twenty-six (65%) were from rural areas of Rahim Yar Khan. Thirty n=30 (75%) children presented with typical symptoms of CD. The clinical signs were anaemia, short stature, emaciation in all cases, cheilosis pedal edema, carpopedal spasm and clubbing (Table II).

Puberty was delayed in three n=3 (7.5%) patients. Anemia was moderate to severe according to WHO classification based on Hb%. Serum iron was consistently less than 50 microgram/ml and peripheral blood picture revealed hypochromic microcytic anaemia. The 10 cases of Celiac crisis presented with profuse diarrhea, severe dehydration; abdominal distention; pedal edema, carpopedal spasm due to tetany; wasted muscles; head drop and inability to stand. These cases required intensive care. Serum albumin ranged 1.7 to 2.1 g/dl in those 10 cases. Serum potassium was in the lower range of 2.5 to 3.3 meq/L. Renal profile and liver function tests were normal. Blood gases analysis revealed metabolic acidosis in 6 (15%) cases. Serological results of 38 (95%) cases were above the cut off level of 7 ml ranging from 35-99 ml. The histopathology of specimens from distal duodenum revealed lesions of M3 type in 13 cases (32.5%, Figure 1) and M2 type in 18 cases (45%).



**Figure 1:** M3 type histopathological changes in the specimen of distal duodenal biopsy.

The cases presenting with Celiac crisis were admitted in intensive care unit. Acidosis corrected by rehydration. The cases recovered after this initial treatment and the oral foods like bananas and yogurt were well tolerated and gluten diet like custard allowed till the EGD for collection of distal duodenum biopsy specimens. Thirty-one (77.5%) cases with positive serology and histopathological biopsy reports of M2 and M3 lesions were declared the confirmed cases of CD. The parents were counselled in the presence of the child and understandable pathogenesis of the disease was explained. The importance of lifelong GFD was emphasized and parents were fully convinced to keep away the gluten diets. The cases were called regularly for follow-up at OPD to monitor the improvement by keeping record of height and weight, and adherence to GFD. Serum tTG antibody was advised to be evaluated at 6 months intervals. All cases developed a sense of well-being, improved appetite and decrease in frequency and bulk of stool and the weight was increased.

## DISCUSSION

Celiac disease is the commonest cause of malabsorption in children.<sup>10</sup> There is a dearth of data about prevalence of CD in Pakistan.<sup>10</sup> The disease remains undiagnosed in most of the patients due to the lack of laboratory facilities. However, the magnitude of clinically diagnosed patients is much more than expected. The current study has emphasized the diagnosis of CD by following the ESPGHAN criteria. The biopsy samples were taken according to recent recommendations.<sup>11</sup>

The age of presentation due to delayed diagnosis, use of wheat as staple diet, malnutrition as recurrent gastro-intestinal infections as in these cases is consistent with other studies.<sup>12</sup> The majority of admissions in peak summer season indicate environmental triggers like infections and episodes of acute diarrhea, leading to decompensated dehydration and metabolic disturbances. The prevalence of disease in first degree

relatives, either silent or classical, is found to be as high as 5% to 20% in many studies.<sup>13</sup> Two siblings had typical CD in this study; the relatives of all cases could not be detected due to lack of screening facilities in our setup. Optimum breast feeding (BF) provides protection against CD. ESPGHAN recommends not introducing gluten containing diet below 4 months of age, but contrary to that there was partial BF and early start of gluten diets at < 4 months of age in these cases.

Clinical features in this study were typical of CD. Severe wastage of muscles was due to maldigestion and malabsorption of macro and micronutrients, chronicity, recurrent infections, off and on diarrhea and hypokalemia. The neck muscles were wasted to the extent of inducing head drop was a specific presentation in this study. The examination of the motor system in those cases was otherwise normal. Stunted growth is a universal presentation of CD and idiopathic short stature (ISS) may be the sole presentation as studied in Iranian children.<sup>14</sup> Cheilosis indicated vitamin B Complex deficiency and clubbing was the sign of a chronic disorder.<sup>15</sup> Iron deficiency anaemia (IDA) found in all cases was consistent with other studies on CD.<sup>16</sup> Response to oral iron therapy ruled out refractory iron deficiency anaemia.

Celiac crisis in 25% of cases is a distinguishing feature. It has been considered rare in many studies.<sup>17-19</sup> This study addressed an early recognition of this fatal complication of CD. The condition could be missed as an acute gastroenteritis and misguided management would raise the mortality in already undiagnosed Celiac child. The use of steroids in this critical condition has been justified.<sup>13,20</sup> Such cases in this study were provided with intensive life saving treatment and later the diagnosis of CD was confirmed by ESPGHAN criteria.

tTG-A is a universally accepted test for screening CD. But negative serology does not rule out CD. It is believed that typical clinical features and positive serology is enough to advise GFD for life. Cases with positive serology in this study were confirmed as Celiac disease after histopathology of the distal duodenal biopsies. The current recommendation to take both distal duodenal and duodenal bulb biopsies is based on the patchy distribution of lesions in CD. Some portion of duodenum sample may be normal but the bulb portion is usually involved. Subtotal villous atrophy is also seen in giardiasis, protein-milk enteropathy, transient gluten enteropathy, bacterial overgrowth, and *E. coli* and *Salmonellae* infections.<sup>20</sup>

GFD for life is the mainstay of treatment. Adherence to this nutritional therapy, GFD will not only improve the quality of life, but also prevent malignancies like intestinal lymphoma in adulthood and reduce the high fatality and morbidity of celiac crisis. Counselling, moral

support and follow-up of these cases yielded encouraging results i.e. relief from symptoms and improvement in anthropometrics measures.

## CONCLUSION

A majority of children with Celiac disease presented with typical symptom while Celiac crisis was characterized by severe dehydration, weakness and calcium deficiency signs. Most were the product of consanguineous marriages and were given Gluten - containing weaning foods as early as the 4th month of life.

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