ORIGINAL ARTICLE
CELIAC CRISIS: A RARE OR RARELY RECOGNIZED DISEASE
Nadia Waheed, Huma Arshad Cheema, Hassan Suleman, Zafar Fayyaz, Iqra Mushtaq, Muhammad, Almas Hashmi
Department of Hepatology & Nutrition, Children Hospital & Institute of Child Health, Lahore-Pakistan

Background: Celiac crisis is a serious life threatening complication of celiac disease characterized by profuse diarrhoea, severe dehydration and metabolic disturbances leading to neuromuscular weakness, cardiac arrhythmias and sudden death. It has been described as rare condition and not well documented in the literature. To improve awareness and facilitate diagnosis of this condition, we studied risk factors, pattern of presentation and management plans of celiac crisis. Methods: It was a descriptive cross sectional study. Patients presenting in emergency room (ER) with profuse diarrhoea leading to severe dehydration, neuromuscular weakness, and metabolic acidosis and electrolyte abnormalities enrolled in the studies after positive serology and small bowel biopsy suggestive of celiac disease. Results: Total 126 patients out of 350 fulfilled the criteria including 54 (42.8%) male and 71 (56.3%) female. The mean age at presentation was 5.25±1.18 years. Risk factors were poor social status (97.60%), consanguinity (96.77%), early weaning with gluten contained diet (93.54%), and Presenting complaints were loose motion (100%), loss of neck holding (96.77%), dehydration (96.77%), polyuria (95.96%), inability to walk (67.74%), abdominal distension (85.86%). Electrolytes imbalances were hypokalaemia (2.4±0.55), hypocalcaemia (7.29±0.66), hypomagnesaemia (1.89±0.50), hypophosphatemia (2.8±0.68), hypoaalbuminemia (3.05±0.48) and metabolic acidosis (96%). One hundred & twenty patients were stabilized with GFD and correction of dehydration, acidosis and electrolyte imbalance. Six patients needed parenteral steroids ant total parenteral nutrition (TPN). Recovery time from crisis was mean 5.4±2.73 days (range 3–20 days). Conclusion: Celiac crisis is a common but under recognized problem in developing countries. Commonest presenting feature is neuromuscular paralysis and biochemical abnormality is hypokalaemia.

Keywords: Celiac Disease; Celiac crisis; electrolyte abnormality; neuromuscular weakness

INTRODUCTION
Celiac disease is an immune mediated enteropathy caused by permanent sensitivity to gluten in genetically susceptible individuals. After dietary exposure to gluten, which is found in wheat, rye and barley, the bowel mucosal immunologic response results in villous atrophy, crypt hyperplasia and damage to surface epithelium in small intestine. This gluten sensitive enteropathy causes decrease in the absorptive surface area resulting in malabsorption syndrome. Epidemiologic studies in India, Middle East and North Africa suggests that it is common and may occur 0.14–1.17% in low risk group, and 2.4–4.4% in high risk group.

Celiac disease can occur at any age. Although classic gastrointestinal symptoms of celiac disease usually appear in children aged 9–18 months but long delays between onset of symptoms and diagnosis can occur. The mode of presentation can be quite variable too. The variation in symptoms, onset and mode of presentation depends on amount of gluten in the diet, time of introduction of gluten, duration of exposure to gluten and other environmental factors, such as duration of breast feeding. Evidence suggests that if gluten is introduced during breast feeding the symptoms tends to be less severe and appear later in life. Celiac crisis is a complication of celiac disease. It is a serious medical emergency resulting from acute onset or rapid progression of gastrointestinal symptoms and characterized by severe diarrhoea, dehydration and metabolic disturbances like hypokalaemia, hypomagnesaemia, hypocalcaemia, hypophosphatemia and metabolic acidosis. Celiac crisis is regarded as a rare complication of celiac disease and in recent published literature only few cases have been reported. In developing countries like Pakistan it is not uncommon and in one of the study from Pakistan it was first presenting feature in 25% of patient with celiac disease.

Celiac crisis can occur in already diagnosed celiac disease patients with poor dietary compliance and it can be the initial presentation. Pathophysiology of celiac crisis is not known exactly, poor compliance or under diagnosed celiac disease children are in catabolic starvation with depletion of total body stores of phosphorus, potassium, magnesium and calcium. An acute severe exacerbation of underlying mucosal inflammation leads to intractable diarrhoea resulting in loss of water and electrolytes in stool. This further worsens the metabolic disturbances and a vicious circle ensues leading to severe manifestation of
hypotension, neuromuscular weakness, respiratory muscle failure, tetany, cardiac arrhythmias and sudden death.\(^\text{10}\) If it is not diagnosed and managed timely it is associated with high morbidity and mortality. Therefore, we conducted this study to identify risk factors, to know pattern of presentation and to formulate treatment strategy of celiac crisis in children.

### MATERIAL AND METHODS

After taking approval from ethical review committee (ERC) this cross-sectional study was conducted at Gastroenterology & Hepatology Unit, Children Hospital and Institute of Child Health Lahore, from July 2014 to Dec 2015. There are no standardized diagnostic criteria for celiac crisis in the literature. We included all patient presented with acute onset of diarrhoea requiring hospitalization along with severe dehydration and/or neuromuscular weakness and/or metabolic disturbances like hypokalaemia, hypocalcaemia, hypomagnesaemia, hypophosphatemia, hypoalbuminemia and metabolic acidosis. Informed written consent was obtained. Already known cases of celiac disease were inquired for poor compliance, while in new cases serological test anti tissue transglutaminase antibodies (tTG) was sent on day of admission. Esophagastroduodenoscopy (OGD) with small bowel biopsy (SBB) was performed after stabilization of patients. All patients met the standard diagnostic criteria for celiac disease including: modified Marsh classification 3a or higher and positive anti tTG. Three patients could not be stabilized and SBB could not be carried out, they diagnosed only on positive anti tTG. Standard care treatment was provided to all patients with parental fluids, correction of dehydration, electrolyte imbalance, vital monitoring and input/output record. Details of biochemical parameters, i.e., serum K, Na, Ca, Mg, P, albumin, ABGs, urinary electrolytes and ECG were noted.

Hypokalaemia was defined as serum K concentration less than 3.5 mEq/L and further graded as mild if it was ranged between 3.0–3.4 mEq/L, moderate if between 2.5–2.9 mEq/L, and severe if less than 2.5 mEq/L. Hypocalcaemia was defined as serum Ca concentration less than 8.5 mg/dl, hypomagnesaemia as serum Mg concentration less than 1.5 mg/dl, hypophosphatemia as serum P concentration less than 2.4 mg/dl and hypoalbuminemia as serum albumin concentration less than 3.5 g/dl. Patients with severe hypokalaemia, hypocalcaemia with characteristic ECG changes or hypokalaemia with neuromuscular symptoms received rapid correction with concentrated potassium chloride solution (200 mEq/L) given at 0.3 mEq/kg/h with continuous ECG monitoring until normalization of ECG findings and neuromuscular symptoms. Hypocalcaemia was corrected with parenteral calcium gluconate solution and activated form of vitamin D. Hypomagnesaemia was corrected with 25 mg/kg/day slow parental infusion for three consecutive days. Hypophosphatemia corrected with oral phosphate solution keeping an eye on worsening of diarrhoea. All patients started on gluten free diet (GFD). Intravenous corticosteroids and total parenteral nutrition (TPN) also considered for patient with intractable diarrhoea. All data including demographic data, risk factors, clinical presentation, anthropometric parameters, clinical course, treatment given, time to recovery and outcome were documented on a Performa.

### RESULTS

Total 126 patients out of 350 fulfilled the criteria and included in the study. Male were 54 (42.8%), female were 71 (56.3%) with M: F ratio was 1:1.3. All patients had height and weight below 5\(^\text{th}\) percentile for age. The mean age at presentation was 5.25±1.18 with a range 1.8–8 years. Five patients were diagnosed celiac and 121 presented as celiac crisis for the first time. Risk factors were consanguinity (96.77%), more than 3 diarrheal episodes/year (89.52%), early weaning with gluten contained diet (93.54%), poor social status; no affected sibling was present in family.

Presenting complaints were (Figure-1) loose motion (100%) & vomiting (24%), loss of neck holding (96.77%), inability to walk (67.74%), abdominal distension (85.86%), tetany (4.03%), polyuria (95.96%), clubbing (65.56%), rickets (72.55%), body swelling (57.27%), dehydration (96.77%), hypotension (49.2%). Electrolytes imbalances were (Table-1) hypokalaemia (2.4±0.55), hypocalcaemia (7.29±0.66), hypomagnesaemia (1.89±0.50), hypophosphatemia (2.8±0.68), hypoalbuminemia (3.05±0.48) and metabolic acidosis (96%). Frequency of patients presented with different electrolytes abnormalities are shown in Figure-2. One hundred and twenty (120) 95% patients were stabilized with GFD and correction of dehydration, acidosis and electrolyte imbalance. Six (6) 4.76% patient needed parenteral steroids and total parenteral nutrition (TPN). Out of them 3 were expired unfortunately. Recovery time from crisis was mean 5.4 ±2.73 days (range 3–20 days).

![Figure-1: Clinical presentation of patients with celiac crisis.](http://www.jamc.ayubmed.edu.pk)
DISCUSSION

The term celiac crisis has been used since 1952, when Anderson and diSant-Agnese described 58 case of celiac disease, out of these 35 presented with acute fulminant form of celiac disease with 3(9%) fatalities. Since this initial report no individual publication has described more than three cases, as celiac crisis has nearly disappeared in developed countries. The reasons for this change are most likely related to improved vaccination, control of infection, early diagnosis and management of celiac disease and availability of gluten free diet. Our study identified that; the risk factors are same that were controlled in developed countries. Most of our cases belonged to poor social economic status, large family size, and early discontinuation of mother feed and start of unpasteurized doorstep milk along with early introduction of wheat contained weaning diet. All these factors lead to intestinal mucosal exposure to microorganism and antigens causing severe mucosal inflammation, immune activation and disruption of normal pattern of motility. In malnourished children who are already depleted in micro and macronutrients any trigger leads to exacerbation of the celiac disease ending in celiac crisis. Most of our patient diagnosed for the first time with celiac crisis supporting that they were under diagnosed, if diagnosed and started on gluten free diet at appropriate time this presentation could have been prevented. Common presenting feature in these patients besides dehydration is neuromuscular paralysis due to electrolytes disturbances especially hypokalaemia and hypophosphatemia this comply with all case reports published in literature. A possible explanation of this finding could be an acute exacerbation of underlying mucosal inflammation causes severe diarrhea leading to massive loss of water and electrolytes in stool. This leads to dehydration, shock, electrolytes disturbances and metabolic acidosis. Compensatory rise in renin and aldosterone in response to a volume contracted state results in kaliuresis and further worsens hypokalaemia. Chronic hypokalaemia itself causes nephrogenic diabetes insipidus leading to polyuria, thus worsening dehydration. Polyuria was one of the major clinical features in our study. In celiac crisis urinary potassium and trans-tubular gradient of potassium are high at the same time urinary chloride are also high, leading to negative urinary anion gap. This indicates primary extra-renal source of potassium loss.

This hypokalaemia is responsible for hyper polarization of resting membrane potential leading to decrease nerve cell excitability and ultimately resulting in neuromuscular weakness. Our study also confirms other biochemical parameters characteristic of celiac crisis found in case reports, such as hypomagnesaemia, hypocalcaemia, hypoalbuminemia and metabolic acidosis. Lloyd-Still JD et al reported role of steroids in celiac crisis, but in our study only 6 patients required steroids. Steroids can help in case of protracted diarrhoea as it will act as an immunosuppressive and anti-inflammatory and will heal the intestinal mucosa. At the same time it will promote hyperglycaemia leading to release of anabolic hormone insulin that will trap all electrolytes in anabolic process and will further worsens the metabolic abnormalities.

CONCLUSION

Celiac crisis is not an uncommon but underdiagnosed entity in developing countries mostly effecting population of low socioeconomic status. Most common presentation is profuse diarrhoea, dehydration and neuromuscular weakness. Hypokalaemia is a consistent biochemical abnormality in celiac crisis. Treatment strategy in these patients should be correction of metabolic and electrolytes abnormalities with gluten free diet.

AUTHORS’ CONTRIBUTION

NW: Conceived & designed research, collected data, analysed and drew results, organized manuscript.

HAC: Critical revision for important intellectual
REFERENCES


Address for Correspondence:
Dr. Nadia Waheed, Department of Hepatology & Nutrition, Children Hospital & Institute of Child Health, Lahore-Pakistan.
Cell: +92 333 446 1116
Email: drnadiasalman@gmail.com