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Original Research Article

Prevalence and clinical profile of celiac disease among malnourished children in South Rajasthan, India

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ABSTRACT

Background: Celiac disease (CD) is the most common genetically related food intolerance, worldwide. The objective of this study was to study the prevalence and clinical profile of malnourished children.
Methods: It was a prospective and observational study. The present study was conducted in the Department of Paediatrics, Geetanjali Medical College and Hospital, Udaipur, Rajasthan. Two hundred and one children were studied. All malnourished children were initially selected and those fulfilling inclusion criteria were included in the study. A detailed interview of all the children/parents was conducted regarding symptoms commonly associated with celiac disease. All cases found positive for t-TGA (>10au/ml) were subjected to upper GI Endoscopy. Subjects were labelled as celiac disease if tissue trans-glutaminase IgA antibodies were >10 au/ml and histopathology was suggestive. Statistical analysis was done by one way ANOVA test and Chi-square as per requirements also Fisher exact and Man Whitney were applied.
Results: Celiac disease was present in 23.9% of malnourished patients. Most common presenting symptoms were diarrhoea (40.2%), abdominal distension (39.9%) and abdominal pain (36.8%) and most common clinical sign was pallor, which was present in more than three-fourth of the patients (85.9%) followed by multivitamin deficiency (25.4%).
Conclusions: There is a high prevalence of Celiac disease in malnourished children. Screening for Celiac disease (especially in presence of diarrhoea and abdominal distension, pain abdomen) should be an essential part of work-up in all malnourished children.

Keywords: Celiac disease, IgA-anti tissue transglutaminase antibodies, Screening

INTRODUCTION

Celiac disease (CD) is the most common genetically related food intolerance, worldwide. It is an autoimmune disorder that occurs in genetically susceptible individuals.[1] It is triggered by a well-identified environmental factor (gluten and related prolamins present in wheat, rye, and barley), and the autoantigen is also well known (the ubiquitous enzyme tissue transglutaminase). The disease primarily affects the small intestine, where it progressively leads to flattening of the small intestinal mucosa. The genetic susceptibility to celiac disease is conferred by well-identified haplotypes in the human leukocyte antigen (HLA) class II region (DR3 or DR5/DR7 or HLA DR4). Celiac disease appears to start between the age 9 to 24 months after the introduction of foods that contain gluten. Infants and young children typically present with chronic diarrhoea, anorexia, abdominal distension, abdominal pain, poor weight gain or weight loss, vomiting and anemia.

Severe Malnutrition can occur if the diagnosis is delayed. Behavioural changes are common and include irritability, lethargy and delayed development. Older children presented with nausea, recurrent abdominal pain, bloating, constipation, intermittent diarrhoea and multivitamin deficiency.

The most common extra intestinal manifestations of celiac disease are iron-deficiency anemia (unresponsive to iron therapy) short stature, arthritis and arthralgia, epilepsy with bilateral occipital calcifications peripheral neuropathies, cardiomyopathy, isolated hypertransaminasemia, dental enamel, hypoplasia, aphthous stomatitis, and alopecia. The diagnosis of celiac disease is based on a combination of symptoms, antibodies, HLA, and duodenal histology.

METHODS

All malnourished children between 2 years to 18 years of age were included and children having any systemic disease affecting growth of child were excluded from the study.

After obtaining informed consent from parents, patients fulfilling the selection criteria were included in the study. Detailed clinical and dietary history was taken to determine the cause of malnutrition. A detailed interview of all the children/parents was conducted regarding following symptoms commonly associated with celiac disease.

Blood sample of 2 ml (plain and EDTA each) was collected and sent for t-TGA (tissue transglutaminase anti IgA antibodies) by Elisa technique (CHEMBELL) and complete blood count using automated machine (HORIBA).

All cases found positive for t-TGA (>10au/ml) were subjected to upper GI Endoscopy.[2] Endoscopic gross appearance of esophageal mucosa, stomach mucosa and intestinal mucosa were recorded and punch biopsies from duodenal blub and from distal duodenum were taken by Gastroenterologist.

Subjects were labelled as celiac disease if tissue trans-glutaminase IgA antibodies were >10 au/ml and histopathology was suggestive

RESULTS

It is a prospective and observational single centre study. Total 201 malnourished children were studied. Celiac disease was present in 23.9% of malnourished patients. Most of the patients i.e. 88, were observed to be of age group 5-10 years suffering from this disease. Comparative study of occurrence of celiac disease with gender showed that disease observed more in male (51.2%) patients than female (48.8%). The most common symptom seen among children in the present study was diarrhoea followed by abdominal distension, abdominal pain, anorexia and constipation i.e. 40.2%, 39.9%, 36.8%, 36.8% and 10% respectively. All of these symptoms were severe in celiac disease patient groups as compare to non-celiac patients.

Table 1: Prevalence of celiac disease in malnourished children and their comparison.

Age in years	Celiac disease				Total
	Yes	(%)	No	%	(n = 201)
<5 years	12	21.1	45	78.9	57
5-10 years	23	26.1	65	73.9	88
>10 years	13	23.2	43	76.8	56
Total	48	23.9	153	76.1	201

p = 0.77

Table 2: Distribution of patients according to presenting clinical symptoms and comparison of clinical symptoms in celiac and non-celiac group in different age group.

Symptoms	Age category						Total No. (%)	p Value
	<5 years		5-10 years		>10 years			
	Celiac disease group (%)	Non-Celiac disease group (%)	Celiac disease group (%)	Non-Celiac disease group (%)	Celiac disease group (%)	Non-Celiac disease group (%)		
Diarrhea	7 (58.3)	24 (53.3)	11 (47.8)	22 (33.8)	7 (76.9)	10 (23.2)	81 (40.2)	0.02
Abdominal distension	8 (75.0)	14 (31.1)	13 (56.5)	21 (32.3)	6 (46.1)	18 (41.8)	80 (39.9)	0.30
Abdominal pain	8 (75.0)	14 (31.1)	10 (43.4)	24 (36.9)	5 (38.4)	13 (30.2)	74 (36.8)	0.75
Anorexia	7 (58.3)	17 (37.7)	11 (47.8)	20 (30.7)	5 (38.4)	14 (32.5)	74 (36.8)	0.60
Constipation	0 (0.0)	4 (8.8)	3 (13.0)	4 (6.2)	2 (15.3)	7 (16.2)	20 (10.0)	0.19

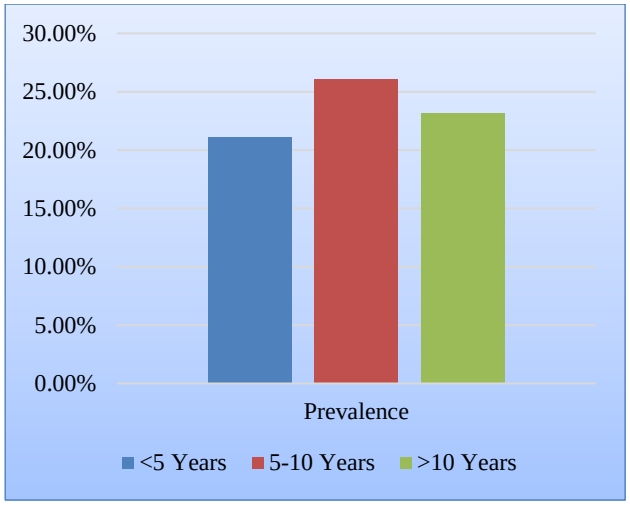

Figure 1: Prevalence of Celiac disease in different age group.

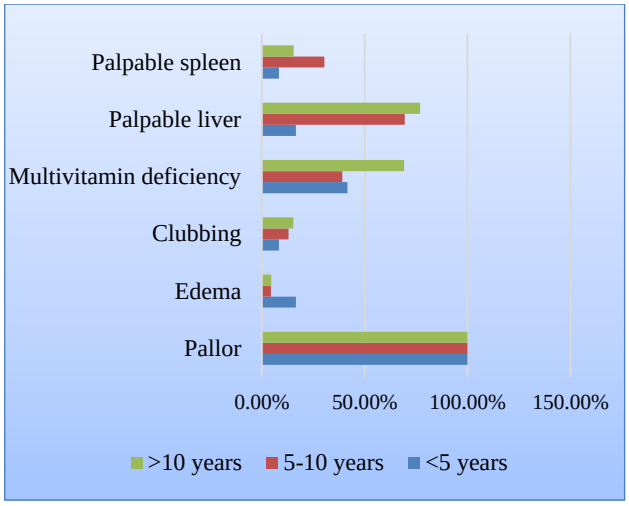

Figure 2: Distribution of presenting clinical signs in celiac disease patients

In present study, diarrhoea was the chief presenting symptom seen in 81% patients while in 29% cases frequent hospital admission was there for complain of diarrhoea in last 3 months. 7% of total patients noticed blood in stool.

Table 3: Distribution of patients according to presenting clinical signs and comparison of clinical signs among celiac and non-celiac group in different age group.

Clinical signs	Age category						Total No. (%)	p value
	<5 years		5-10 years		>10 years			
	Celiac disease group (%)	Non-celiac disease group (%)	Celiac disease group (%)	Non-celiac disease group (%)	Celiac disease group (%)	Non-Celiac disease group (%)		
Pallor	12 (100.0)	38 (84.4)	23 (100.0)	55 (84.6)	13 (100.0)	35 (83.7)	176 (85.9)	0.48
Multivitamin deficiency	5 (41.6)	9 (20.0)	9 (39.1)	12 (18.5)	9 (69.2)	7 (16.3)	51 (25.4)	0.80
Edema	2 (16.6)	0 (0.0)	1 (4.4)	0 (0.0)	0 (0.0)	2 (4.6)	5 (2.5)	0.27
Icterus	2 (16.6)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.3)	4 (2.0)	0.45
Palpable liver	2 (16.6)	18 (40.0)	16 (69.5)	46 (70.7)	10 (76.9)	34 (79.1)	126 (62.7)	0.11
Palpable spleen	1 (8.3)	24 (53.3)	7 (30.4)	5 (7.7)	2 (15.5)	5 (11.6)	44 (21.9)	0.08
Cyanosis	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0.28
Clubbing	1 (8.3)	0 (0.0)	3 (13.0)	1 (1.5)	2 (15.3)	0 (0.0)	7 (3.5)	0.37
Lymphadenopathy	0 (0.0)	0 (0.0)	1 (4.4)	4 (61.5)	0 (0.0)	0 (0.0)	5 (2.5)	0.03
Ascites	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)	1 (0.5)	0.27

Table 4: Distribution of patients according to severity of anemia, comparison of anemia in different age group and between celiac and non-celiac group.

Pallor grading	Age category						Total No. (%)
	<5 years		5-10 years		>10 years		
	Celiac disease Group (%)	Non-Celiac disease Group (%)	Celiac disease Group (%)	Non-Celiac disease Group (%)	Celiac disease Group (%)	Non-celiac disease Group (%)	
No pallor (>10 gm/dl)	0 (0.0)	7 (15.5)	0 (0.0)	10 (15.4)	0 (0.0)	8 (16.2)	25 (12.4%)
Mild (<10 gm/dl)	6 (50.0)	26 (57.7)	13 (56.5)	34 (52.3)	4 (23.1)	20 (46.5)	103 (51.3%)
Moderate (7-10 gm/dl)	5 (41.7)	12 (26.6)	9 (39.1)	21 (32.3)	9 (39.1)	15 (34.8)	71 (35.4%)
Severe (<7 gm/dl)	1 (8.3)	0 (0.0)	1 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0%)

Data collected on clinical signs suggested that most common clinical sign was pallor which was found in 85.9% of patients, maximum in age group of 5-10 years. On distribution of pallor according to grading, mild pallor was present in nearly half (46.5%) of the patients while one-third patients presented with moderate pallor (34.8%). Severe pallor was present in celiac group patients only. Multivitamin deficiency was another common sign noticed i.e.25.4%. Results of T-tIgA findings in the present study of different age-group suggested that 76.1% of children showed T-tIgA level up to 10 au/ml (negative) and maximum positive for T-tIgA (17.9%) were >200 au/ml on grading them according to biopsy marsh grading of celiac disease patients in different age category showed that stage 3a of celiac disease observed in maximum number of patients i.e. 62.5% followed by stage 3b i.e. 53.4%. Least occurrence of 2.1% observed for stage 3c in all the age groups of patients.

Table 5: TGIgA Finding in different age group.

	Age category						Total No. (%)
	<5 years		5-10 years		>10 years		
	Celiac disease Group (%)	Non-celiac disease Group (%)	Celiac disease Group (%)	Non-celiac disease Group (%)	Celiac disease Group (%)	Non-celiac disease Group (%)	
Up to 10	0 (0.0)	45 (22.3.0)	0 (0.0)	65 (32.4)	0 (0.0)	43 (21.4)	153 (76.1)
10-20	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
20-200	7 (3.5)	0 (0.0)	2 (1)	0 (0.0)	3 (1.5)	0 (0.0)	12 (6.0)
>200	5 (2.5)	0 (0.0)	21 (10.5)	0 (0.0)	10 (4.9)	0 (0.0)	36 (17.9)

Table 6. Marsh Grading of celiac disease patients in different age category.

Marsh grading	Age category			Total No. (%)
	<5 years	5-10 years	>10 years	
	No. (%)	No. (%)	No. (%)	
Stage 3a	7 (58.3%)	13 (56.5%)	10 (76.9%)	30 (62.5%)
Stage 3b	5 41.7%)	10 (43.5%)	2 (15.4%)	17 (35.4%)
Stage 3c	0 (0.0%)	0 (0.0%)	1 (7.7%)	1 (2.1%)

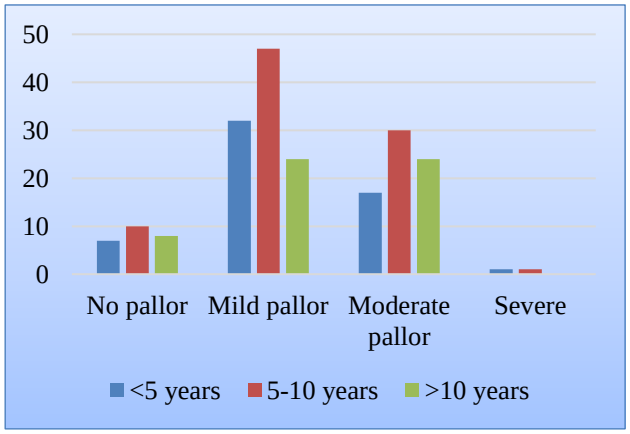

Figure 3: Distribution of patients according to severity of anemia.

Results of the study shows that all signs and symptoms of malnutrition discussed above also presents with celiac disease but in more severe form and could be missed by healthcare workers. Hence all malnourished patients should be screened for celiac disease also.

Celiac disease was present in 23.9% of patients and was more prevalent in 5-10 years age group i.e. 26.1%. According to Figure 1 celiac disease was almost equally present in all age groups slightly more in 5-10 years age group.

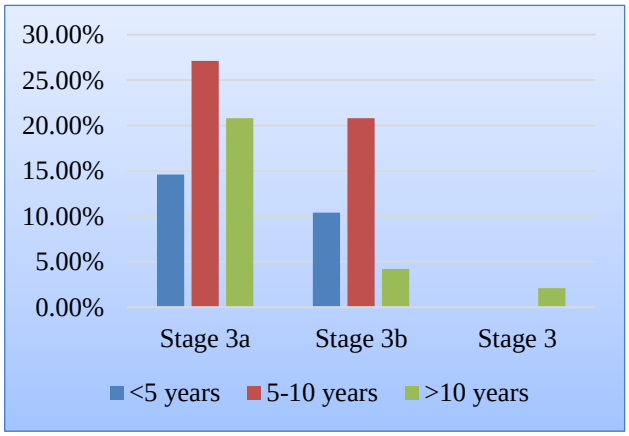

Figure 4. Marsh grading of celiac disease patients in different age category.

Most common presenting symptoms were diarrhoea (40.2%), abdominal distension (39.9%) and abdominal pain (36.8%) in all patients but symptoms in celiac group patients were severe.

Most common clinical sign was pallor, which was present in more than three-fourth of the patients (85.9%) followed by multivitamin deficiency (25.4%).

Mild pallor was present in nearly half (46.5%) of the patients while one-third patients presented with moderate pallor (34.8%). Severe pallor was present in celiac group patients only.

17.9% patients had T-tIgA >200 au/ml and 6% had between 20- 200. All of these were positive for celiac disease (P = 0.25). Maximum number of patients in celiac disease group were of stage 3a (62.5%) followed by of stage 3b (17%) and of stage 3c (1%).

DISCUSSION

Celiac disease (CD) is a permanent intolerance to dietary gluten that is characterized by immune-mediated inflammatory lesions of the intestinal mucosa. Owing to its variable manifestations and age at onset, CD has emerged as a worldwide public health problem (Green and Cellier).[3] Although the "classical" malabsorption syndrome that is characterized by diarrhoea, steatorrhea, weight loss, and fatigue may occur in severe cases, most patients present with a milder constellation of symptoms, such as abdominal discomfort and bloating that mimic irritable bowel syndrome or non-gastrointestinal symptoms that include anemia and osteoporosis, or no symptoms at all. In most patients with CD, a gluten-free diet assures full recovery.

Many patients with milder presentation of CD are diagnosed at a relatively advanced stage of the disease. The prompt diagnosis and treatment of CD are associated with symptomatic improvement, reduction of potential complications (including malignancies), and decreased mortality (Baker, Farell et al).[4,5] Therefore, it is necessary to increase the awareness of physicians about the variable manifestations of CD and to emphasize the importance of screening.

Total 201 patients both, male and female of age ranges from 2 years to 18 years included in this study, among which maximum number ie.103 were male and 98 were female. Maximum patients included in the study group were of age group 5-10 years of both male and female followed by <5 years patients (57) and then >10 years of patients (56) of both sex. Hatlani A, performed epidemiological studies on celiac disease (CD) in among the Saudi children of age group ranges from 6-18 years, who are at a high risk of developing CD.[6] This study is also in line with previous study stated that celiac disease was more prevalent among males than females (Altwaty and Elbaratty).[7] The most common symptoms seen among the children suffering from CD were diarrhoea, abdominal distension, abdominal pain, anorexia and constipation were seen. As maximum of patients were observed to be of 5-10 years age group, hence related clinical symptoms were maximally observed in the same age group of celiac as well as non-celiac group. Whereas children of <5 years age and > 10 years age group, both celiac as well as non-celiac group, showed almost similar distribution of related clinical symptoms. After distribution of patients according to pallor grading, maximum of 51.3% cases belongs to mild anaemia group which was followed by moderate anaemia i.e. 35.4% of patients. Sherwani RK et al observed the pallor in all the 45 cases studied, authors also observed that mean haemoglobin was 8.1±1.6 gm%.[8] MCV, MCH and MCHC were 79.1±8.6 fl, 26.9±3 pg and 29.6±2.3 g/dl respectively. Mean serum iron was 32.1±1.2 g/ dl and TIBC was 432±3.2 g/ dl. On peripheral smear, 28 cases (82.4%) showed microcytichypochromic anaemia. Overall result suggested that most common presenting symptom was diarrhoea (40.2%), abdominal distension (39.9%) and abdominal pain (36.8%). According to Ludvigsson et al that main clinical presentations of celiac disease in the paediatric population include persistent diarrhoea followed by high mortality.[9] Thapa also clinically manifest the celiac disease on the basis following clinical manifests like diarrhoea, abdominal distension, abdominal pain, anorexia and constipation.[10] Immunoglobulin A (IgA) deficiency occurs more frequently in patients with celiac disease (CD) than in the general population and can lead to false-negative results in the best serologic test for CD. Results of T-tIgA findings in the present study of different age-group suggested that 76.1% of children showed T-tIgA level up to 10 au/ml(negative) and maximum positive for T-tIgA (17.9%) were >200 au/ml. One another study conducted in PBM Children Hospital, Bikaner from July 2012 through December 2013 by Beniwal N et al.[11] All consecutively admitted children with SAM were recruited. All subjects were screened for Celiac disease by serological test for IgA-anti tissue Transglutaminase (IgA tTG) antibodies. The sero-prevalence (IgA tTg positivity) of celiac disease was found to be 15.38%

Results of marsh grading of celiac disease patients in different age category showed that stage 3a of celiac disease observed in maximum number of patients i.e. 62.5% followed by stage 3b i.e. 53.4%. Least occurrence of 2.1% observed for stage 3c in all the age groups of patients. Jora et al also performed similar type of study on marsh grading of duodenal histopathology in Celiac disease (CD) Waheed N et al from Lahore, Pakistan concluded in his study that celiac disease is not a rare disease in Asia, but an under diagnosed entity.[12,13] He conducted a descriptive cross-sectional study among 126 patients presenting in emergency room (ER) with profuse diarrhoea leading to severe dehydration, neuromuscular weakness, metabolic acidosis and electrolyte abnormalities. All patients met the standard diagnostic criteria for celiac disease including: modified Marsh

classification 3a or higher and positive t-TG-IgA. Total 126 patients out of 350 fulfilled the criteria and included in the study. Male were 54 (42.8%), females were 71 (56.3%) with M: F ratio of 1:1.3. All patients had height and weight below 5th percentile for age. The mean age at presentation was 5.25±1.18 with a range 1.8-8 year.

CONCLUSION

There is a high prevalence of Celiac disease in malnourished children. Screening for Celiac disease (especially in presence of diarrhoea and abdominal distension, pain abdomen) should be an essential part of work-up in all malnourished children.

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REFERENCES

1. Gautam A, Jain BK, Midha V, Sood A, Sood N. Prevalence of celiac disease among siblings of celiac disease patients. Indian J Gastroenterol. 2006;25(5):233-5.
2. Gluten Sensitive Enteropathy. In: Nelson W, Behrman RE, Kliegman RM, Arvin AM, eds. Nelson Textbook of Pediatrics. 15th edition. WB Saunders, Philadelphia; 1996;1095-6.
3. Green PH, Cellier C. Celiac disease. N Engl J Med. 2007;357:1731-43.
4. Baker SS. Rethinking strategies to screen for celiac disease. Pediatr. 2014;133:331-2.
5. Farrell RJ, Kelly CP. Celiac sprue. N Engl J Med. 2002;346:180-8.
6. Al Hatlani MM. Prevalence of celiac disease among symptom-free children from the eastern province of Saudi Arabia. Saudi J Gastroenterol. 2015;21(6):367-71.
7. Al-Tawaty AI, Elbargathy SM. Celiac disease in north-eastern Libya. Ann Trop Pediatric. 1998;18:27-30.
8. Sherwani RK, Alam S, Akhtar K, Abid B, Rahman K, Mehdi R. Prevalence of iron deficiency anemia in chronic diarrhoea and celiac disease: a western UP experience. Indian J Hematol Blood Transfusion. 2008;24(1):12-5.
9. Ludvigsson JF, Bai JC, Biagi F, Card TR, Ciacci C, Ciclitira PJ, et al. Diagnosis and management of adult coeliac disease: guidelines from the British Society of Gastroenterology. Gut. 2014;63:1210-28.
10. Thapa. Celiac disease in chidren: Recent Concepts. JK Sci. 2010;3:3-12.
11. Beniwal N, Ameta G, Chahar CK. Celiac disease in children with severe acute malnutrition (SAM) a hospital-based study. Indian J Pediatr. 2017;84(5):339-43.
12. Jora R, Raghuvanshi V, Payal V, Sharma P, Vishnoi SK. Correlation of tissue transglutaminase with modified marsh grading in celiac disease: a prospective cohort study. Indian J Pediatr. 2017;84(7):515-20.
13. Waheed N, Cheema AH, Suleman H, Fayyaz Z, Mushtaq I, Muhammad, et al. Celiac crisis; electrolyte abnormality; neuromuscular weakness. J Ayub Med Coll Abbottabad. 2016;28(4):672-5.

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