Original Research Article

Clinical Spectrum in Celiac Patients Attending a Tertiary Care Centre in Northern India

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Abstract

Background: Celiac disease generally is characterized by gluten dependent clinical manifestations. Clinically there may be symptoms of frank mal-absorption or predominant extra intestinal manifestations.**Aim:** to study the clinical spectrum of children with celiac disease.**Methods:**360 children between the age group of 1-18 years diagnosed with celiac disease were enrolled into the studyand details about the symptoms were recorded.**Results:** 27.8% patients had purely gastrointestinal symptoms and 13.9% of the patients had non gastrointestinal presenting features alone. But the majority of the patients i.e. 58.3% of patients had both gastrointestinal and other clinical features.**Conclusion:** With such varied clinical spectrum, the diagnosis is often missed in search of a more defined and common diagnoses. Hence is the need to have a high index of suspicion for the diagnosis of celiac disease.

Keywords: clinical spectrum, atypical symptoms, celiac disease

Introduction

Celiac disease is a chronic small bowel enteropathy with an underlying autoimmune mechanism precipitated by exposure to dietary gluten in genetically predisposed people. It is characterized by gluten dependent clinical manifestations, specific auto antibodies, HLA DQ-2 and DQ-8 haplotypes and enteropathy.There is evidence that both humoral and cell mediated immune responses to gliadin and related prolamines are involved in the pathogenesis. Celiac specific antibodies comprise of auto antibodies against tissue Transglut-aminase (tTG) 2 including endomysial antibodies (EMA) and antibodies against deaminated forms of gliadin peptides.The prevalence of celiac disease varies in different parts of the world. In the western countries, it ranges from 0.7% to as high as 2%. In India most of the cases are reported from the Northern parts with an average prevalence of 1%[1].It is the most common cause of chronic diarrhea in children and accounts for 26% and 56% of chronic diarrhea among the adults in Western and Northern India respectively[2]. The silent celiac disease is approximately 7 times more common than symptomatic disease worldwide, and atypical presentation occurs in 30-40% of patients diagnosed with celiac disease in India[3].Thus the numbers represent only a tip of the ice berg and the actual burden of the disease is much more than what is apparent from them. The ratio of diagnosed to undiagnosed cases however varies widely from country to country[4-6].The diagnosis of celiac disease is made in a patient based on clinical, serological and histological findings. Clinically there may be typical or atypical symptoms with an unequivocal clinical response to gluten free diet. Clinical spectrum of celiac diseaseincludes symptomatic patients with symptoms of frank mal-absorption (chronic diarrhea, abdominal pain and distension, weight loss) or extra intestinal manifestations (anemia, fatigue, neurologic disorders, short stature, dental enamel defects, arthralgia, aphthous stomatitis etc.)[7].Symptoms usually appear early in life, around 6-24 months of age, after introduction of wheat products. Older children manifest commonly with extra intestinal symptoms like anemia, bone abnormalities, short stature, arthritis and arthralgia. Rare manifestations include epilepsy, occipital calcifications, peripheral neuropathies, cardiomyopathy, dental enamel hypoplasia, aphthous stomatitis and alopecia. Some diseases with autoimmune pathogenesis like type 1 diabetes, autoimmune thyroid disease, Addison disease, connective tissue disease, autoimmune atrophic gastritis, autoimmune hepatitis and psoriasis etc[7].are known to be associated with celiac disease.With such varied clinical spectrum, the diagnosis is often missed in search of a more defined and common diagnoses. Hence we decided to study the varied clinical spectrum we found in children with celiac disease attending our institution.

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Materials and Methods

The Cross Sectional Observational Study was conducted in the Department of Pediatrics, from 2015-2018. 360 children between the age group of 1-18 years diagnosed with celiac disease attending the Pediatric gastroenterology clinic, celiac camps, pediatric outpatient department and wards were enrolled into the study. Informed written consent was taken from all the participants before the enrollment. Demographic details and details about the symptoms were recorded for the children in pre-determined format.

For the purpose of study: Celiac disease was defined based on the guidelines by World Gastroenterology Organization -Guidelines for Celiac Disease2012 for Children[8].Children with clinical symptoms **OR** asymptomatic children with family history With positive serology* (IgA anti tTG antibodies)**And** biopsy findings (evidence of villous atrophy– Marsh staging 3b, c)Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. Data were checked for normality before statistical analysis.

Results

Among the 360 cases included, youngest was 3 years old while the oldest was 16years with a mean age of 7.72 ± 3.26 years. The control population was comparable in age distribution with a mean of 7.56 ± 3.18 years.Majority of the cases were <5years of age constituting 36.1%, followed by cases in the age group of 10-12 and 6-9 years who constituted 30.6% and 27.8% of the total number of cases respectively.Majority (86.1%) of the cases in our study presented with typical GI symptoms, including Diarrhea (66.7%), Vomiting (27.8%), and Constipation (8.3%), abdominaldistension (38.9%), Anorexia (30.6%) and pain abdomen (55.6%). Diarrhea and pain abdomen were the most frequent GI symptoms.Most of the cases also had associated non-GI symptoms including 3 (8.3%) patients who

had diabetes mellitus. 38.9% of the cases had anemia with progressive pallor as the presenting feature. A large number of cases (55.6%) presented with failure to thrive with complaints of not gaining weight and height. No neurological, dermatological or skeletal symptoms were noted.

Discussion

Celiac disease is a systemic autoimmune disease characterized by a chronic inflammatory response to a complex of water insoluble protein present in wheat called gluten. The disease is characterized by antibodies against host tissue antigens like tissue Transglut-aminase (TTG), Endomysial Antigen (EMA) and Deaminated Gliad in Peptides (DGP) which have become the mainstay of diagnosis of the disease.Though Celiac disease is typically defined as a chronic gastrointestinal disease it also affects various organ systems directly or indirectly. Celiac disease is a systemic disorder affecting almost all organs. Usual age of onset coincides with weaning with wheat products and i.e. around 6-24 months of age. In children diagnosed within the first two years of life, intestinal symptoms are more common where as those diagnosed later in childhood or the asymptomatic patients diagnosed through a screening process, are most likely have extra intestinal manifestations. Celiac disease being an autoimmune disease, it is associated with many other diseases with autoimmune basis and vice versa.The wide clinical spectrum of celiac disease can be grouped into three categories[9]:

- Silent celiac disease- it is approximately seven times more common than symptomatic disease worldwide. These are the asymptomatic patients, who on screening, test positive for celiac serology as well show histological findings on biopsy.
- Potential celiac disease- these patients are either symptomatic or asymptomatic with positive serology but have not developed histological changes.
- Latent celiac disease- patients with normal biopsy findings with present or past history of gluten dependent enteropathy

The intestinal symptoms in Celiac disease are mainly due to mucosal damage and consequent mal-absorption, like diarrhea, vomiting, abdominal distension, bloating, constipation, anorexia, weight loss, failure to thrive, rectal prolapse, aphthous stomatitis, intussusception etc. In our study, majority (86.1%) of the cases had typical GI symptoms. 66.7% of the patients had Diarrhea, 27.8% had Vomiting, 8.3% had Constipation, Abdominal distension, 38.9% had Anorexia(30.6%) and 55.6% had pain abdomen at presentation. Diarrhea and pain abdomen were the most common GI symptoms. Mean age at diagnosis among the patients with GI symptoms at presentation was 3.42 ± 1.16 years.In India, approximately 30-40% of all the adults and children have atypical presentation as found in previous studies[3,10] Non-gastrointestinal complaints are more common than classic presentation with diarrhea in most of the western countries. Extra intestinal manifestations are mainly due to nutrient deficiencies and include chronic fatigue, arthritis/arthralgia, anemia, rickets, enamel hypoplasia, pubertastarda, secondary hyper-parathyroidism, short stature, peripheral neuropathy, epilepsy, irritability, cerebral calcification, cerebellar ataxia, chronic migraine and others. The most common symptoms seen in Indian children are stunting, seen in almost 100% of the patients, anemia (90-100%) and chronic diarrhea (88-94%) in that order[11,12]Similarly most of the cases in our study also had associated non-GI symptoms including 30 (8.3%) patients who had diabetes mellitus (type 1). 38.9% of the cases had anemia with progressive pallor as the presenting feature. A large number of cases (55.6%) presented with failure to thrive with complaints of not gaining weight and height. No neurological, dermatological or skeletal symptoms were noted. Mean age among the patients with non-GI symptoms at presentation was 9.73 ± 2.68 years. Thus younger children tend to present with gastrointestinal symptoms or those with gastrointestinal symptoms at presentation are usually diagnosed at an early age because of better awareness for the evaluation of such symptoms. Similarly non gastrointestinal symptoms are more common as the age advances or those children go undiagnosed at an early age due to non-specific nature of their symptoms.

Table 1:Clinical spectrum in patients with celiac disease

SYMPTOMS	Frequency	%
GI SYMPTOMS	**310**	**86.1**
Diarrhea	240	66.7
Vomiting	100	27.8
Constipation	30	8.3
Abdominal distension	140	38.9
Anorexia	110	30.6
Pain abdomen	200	55.6
NON-GI SYMPTOMS	**260**	**72.2**
Failure to thrive	200	55.6
Hematological	140	38.9
Endocrinal	30	8.3
Skeletal	00	0
Neurological	00	0
Dermatological	00	0
Others	00	0

Conclusion

27.8% of the cases predominantly consisting of younger children had purely gastrointestinal symptoms and 13.9% of the patients mainly those aged more than 5 years old had non gastrointestinal features alone at presentation. But the majority of the patients i.e. 58.3% of patients had both gastrointestinal and other clinical features. There is a need to have a high index of suspicion for the diagnosis of celiac disease especially to diagnosis patients with mild and atypical clinical spectrum.

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