

Celiac Disease: Clinical, Endoscopic and Histological Profile

DILARAM KHAN, ADNAN U REHMAN, SHER REHMAN

ABSTRACT

Aim: To know the common clinical presentation, endoscopic and histological profile of celiac disease.

Methods: This cross sectional study was carried out in Gastroenterology unit HMC, Peshawar from July 2009 to July 2011. Fifty two patients of both gender and more than one year of age, having clinical suspicion of celiac disease and proven histologically were included in the study.

Results: Twenty five (48.1%) were male and 27 (51.9%) were female. The mean age was 20.19±10.68 years. Chronic diarrhea was present in 43(82.7%) cases, iron deficiency anemia in 39 (75%) cases, Weight loss in 34 (65.4%) cases, abdominal pain in 17 (32.7%) cases, failure to thrive in 15 (28.8%) cases and 15 (28.8%) cases were with short stature. Abdominal distension was present in 13 (25.0%) cases, vomiting in 8 (15.4%) cases, delayed puberty in 7 (13.5%) cases, infertility in 4 (7.7%) cases and dermatitis herpetiformis in 1 (1.9%) cases. Atrophic mucosa with mosaic pattern was present in 20 (38.5%) cases, nodular mucosa with scalloping in 15 (28.8%) cases, atrophic nodular mucosa without scalloping in 6 (11.5%) cases, normal mucosa in 6 (11.5%) cases and scalloping of duodenal folds in 5 (9.6 %) cases. **Conclusion:** Celiac disease is a gluten sensitive enteropathy which occurs in both gender of all age group with various intestinal and extra intestinal manifestations.

Keywords: Celiac disease, Intestinal, Extra-intestinal, Endoscopic, Histological profile

INTRODUCTION

Celiac disease is a systemic immune-mediated disorder triggered by dietary gluten in genetically susceptible persons. Celiac disease is characterized by a broad range of clinical presentations, a specific serum autoantibody response, and variable damage to the small intestinal mucosa.¹ This disorder has become more common than in the past, even if it frequently remains undetected for long periods of time. It affects 0.6 to 1.0% of the population worldwide^{2,3} occurs in all age group and females predominate over males, with a ratio of 2:1 or 3:1⁴, however, men may have a more severe form of the disease at presentation.⁵ Previously celiac disease used to be considered as the disease of European and Western population but now it has emerged as a global problem. It is recognized in every continent including Asia⁶, the Middle East⁷, North Africa⁸, South America⁹ and Cuba.¹⁰

The pathogenesis of celiac disease involves an external trigger (gluten), changes in intestinal permeability, enzymatically modified gluten, HLA recognition, and innate and adaptive immune responses to gluten peptides involving self-antigens, eventually leading to celiac enteropathy.^{11,12} Genetic background plays a key role in the predisposition to the disease. The *HLA-DQ2* haplotype is expressed in the majority of patients with celiac disease (90%),

whereas it is expressed in one third of the general population. In another 5% of patients with celiac disease, the *HLA-DQ8* haplotype is expressed, whereas almost all the remaining 5% of patients have at least one of the two genes encoding *DQ2*. *DQ2* and *DQ8* haplotypes expressed on the surface of antigen-presenting cells can bind activated gluten peptides, triggering an abnormal immune response.¹³

There had been a notion and wide belief that celiac disease is a disease of children. It is now recognized that children with celiac disease, in whom the diagnosis is delayed, present later in life either with typical manifestations such as chronic diarrhea and malabsorption, or with atypical manifestations like short stature, refractory anemia, metabolic bone disease or dental enamel defects.^{14,15} A significant number of adult patients with celiac disease remain either silent or asymptomatic.^{16,17} The aim of this study was to know the common clinical presentation, endoscopic, and histological profile of celiac disease in our local set up so that to create awareness about this disease.

PATIENTS AND METHODS

This cross sectional descriptive study including 52 patients was carried out in the Department of Gastroenterology & Hepatology Hayatabad Medical complex, Peshawar from July 2009 to July 2011. Patients of both gender and having clinical suspicion of celiac disease and proven histologically were included in the study. All those patients younger than

Department of Gastroenterology, Hayatabad Medical Complex, Peshawar

Correspondence to Dr. Dilaram Khan, e-mail: dilaramkhan03@yahoo.com

one year of age, patients already diagnosed as celiac disease and on gluten free diet and patients unfit for upper gastrointestinal endoscopy were excluded from the study to reduce bias in the study. Proper approval was taken from the Ethical Committee of the institution before starting the study. Informed consent was taken from all patients seen in OPD having suspicion of celiac disease, and either assessed in OPD or admitted to the ward and evaluated by detailed history, thorough clinical examination, and appropriate baseline investigations. All patients after necessary investigation were prepared for endoscopic examination, upper endoscopy was done, findings were recorded and at least 4 to 6 biopsies were taken from second or third part of the duodenum for histopathological confirmation. All those patients who fulfill the inclusion criteria and gave consent to be included, were included in the study. The information's thus collected through history, clinical examination, endoscopic assessment, histological and serological examinations were entered into a proforma and bias was controlled by following the exclusion criteria. Data was analyzed by using statistical software (SPSS version 17). Mean±SD was calculated for continuous variables like age. Frequencies were calculated for categorical variables like clinical presentation, endoscopic and histological profile.

RESULTS

A total of 52 patients were included in this study out of which 25 were male and 27 were female with a male to female ratio of 1:1.08. The mean age was 20.19±10.68 years with minimum age of 3 years and maximum age of 50 years. Majority of patients were in the age range of 11-20 years followed by age range of 21-30 years (Table 1). Chronic diarrhea was the most common clinical presentation present in 43 (82.7%) cases followed by iron deficiency anemia in 39 (75%) cases. Weight loss was present in 34 (65.4%) cases, abdominal pain in 17 (32.7%) cases, failure to thrive in 15 (28.8%) cases and 15 (28.8%) cases were with short stature. Abdominal distension was present in 13 (25.0%) cases, vomiting in 8 (15.4%) cases, delayed puberty in 7 (13.5%) cases, infertility in 4 (7.7%) cases and dermatitis herpetiformis in 1 (1.9%) case (Table 2). Atrophic mucosa with mosaic pattern in second part of the duodenum was the most common endoscopic finding present in 20(38.5%) cases followed by nodular mucosa with scalloping in 15(28.8%) cases. Nodular mucosa without scalloping was present in 6 (11.5%) cases, normal duodenal mucosa in 6 (11.5%) cases and scalloping of duodenal folds was present in 5 (9.6%) cases (Table 3). MARSH-III was the most

common histological finding in our study which was present in 47 (90.38%) cases followed by MARSH-II in 3 (5.76%) cases. MARSH-I was present in 1 (1.92%) case and MARSH-0 was also present in 1 (1.92%) case (Table 4).

Table 1: Frequency and percentage of ages

Age (years)	No.	%
1 – 10	12	23.0
11 – 20	21	40.6
21 – 30	14	26.9
31 – 40	4	7.6
41 – 50	1	1.9

Table 2: Frequency and percentage of clinical presentations

Clinical presentation	No.	%
Chronic diarrhea	43	82.7
Iron deficiency anemia	39	75.0
Weight loss	34	65.4
Abdominal pain	17	32.7
Failure to thrive	15	28.8
Short stature	15	28.8
Abdominal distension	13	25.0
Vomiting	8	15.4
Delayed puberty	7	13.5
Infertility	4	7.7
Dermatitis herpetiformis	1	1.9

Table 3: Frequency and percentage of endoscopic findings

Endoscopic finding	No.	%
Atrophic mucosa with mosaic pattern	20	38.5
Nodular mucosa with scalloping	15	28.8
Nodular mucosa without scalloping	6	11.5
Scalloping alone	5	9.6
Normal mucosa	6	11.5

Table 4: Frequency and percentage of histological findings

Histological findings	No.	%
Marsh - 0	1	1.9
Marsh - I	1	1.9
Marsh - II	3	5.8
Marsh - III	47	90.4

DISCUSSION

Celiac disease may present with classic clinical features including weight loss, diarrhea, and malabsorption of nutrients. However, there are reports of an increasing trend towards silent or subclinical presentations i.e. presentation with subtle symptoms not clearly related to gastrointestinal system. Nonspecific symptoms and nutritional deficiencies are especially common in older patients and as a result, the diagnosis of this treatable condition is often delayed or missed. Without active serologic screening, most cases of celiac disease probably remain undiagnosed. Though the celiac

disease can occur in all age groups, the mean age at diagnosis in this study was 20.19±10.68 years with minimum age of 3 years and maximum age of 50 years. Celiac disease is more common in women than men but this was not the case in our study and the occurrence of celiac disease was almost equal in male and female patients but since majority of female patients do not present to the hospitals or present very late in our set up which may be a reason that celiac disease prevalence was equal in male and females, however this needs further studies to know about the equal prevalence of celiac disease in our set up.

In recent years there has been increasing recognition that the mode of presentation of celiac disease may be changing.^{18,19} It often presents with symptoms not previously considered to be characteristic of the disease. While most gastroenterologists appreciate the broader spectrum of the disease, and its increasing prevalence, it is still perceived by most general practitioners as a rare condition of childhood or infancy, presenting mainly with gastrointestinal symptoms suggestive of malabsorption. Chronic diarrhea, and other malabsorptive features that are considered the typical presenting features of celiac disease, were the major complaint in our patients. This was same as in other studies done both nationally, Aziz et al²⁰ at Karachi and internationally Makharia et al²¹ in India however this was not in accordance with a study done by Ikram et al²² at Faisalabad. The presentation of celiac disease mainly as gastrointestinal disease in our study seem to be the general attitude of patients to seek medical care for gastrointestinal complaints from gastroenterology department, however certain no of patients in our study presented with some atypical gastrointestinal features like vomiting in 8 (15.4%) and extraintestinal features like failure to thrive in 15 (28.8%) cases, short stature in 15 (28.8%) cases, delayed puberty in 7 (13.5%) cases, infertility in 4 (7.7%) cases and dermatitis herpetiformis in 1 (1.9%) case, which show that patients presenting with these symptoms which are not explained by other causes should be evaluated for celiac disease.

The endoscopic and histological features of celiac disease in our study were almost similar to other studies done in Pakistan and internationally.²³ So an awareness is needed at primary, secondary and tertiary care level that celiac disease has various intestinal and extra intestinal presentations with a changing trend in presentation so that patients with celiac disease are diagnosed in time, and managed properly to prevent the occurrence of complication and the misery of patients and relatives.

CONCLUSION

Celiac disease is a gluten sensitive enteropathy which occurs in both gender of all age group with various intestinal and extra intestinal manifestations and a changing trend in presentations from typical to atypical gastrointestinal symptoms as well as extraintestinal features which need awareness in physicians to prevent delay in the diagnosis and treatment of celiac disease.

REFERENCES

1. Green PHR, Cellier C. Celiac disease. *N Engl J Med* 2007;357:1731-43.
2. Fasano A, Berti I, Gerarduzzi T, Not T, Colletti RB, Drago S, et al. Prevalence of celiac disease in at-risk and not-at risk groups in the United States: a large multicenter study. *Arch Intern Med* 2003;163:286-92.
3. Biagi F, Klersy C, Balducci D, Corazza GR. Are we not over-estimating the prevalence of celiac disease in the general population? *Ann Med* 2010;42:557-61.
4. Green PHR, Stavropoulos SN, Panagi SG, Goldstein SL, McMahon DJ, Absan H, et al. Characteristics of adult celiac disease in the USA: results of a national survey. *Am J Gastroenterol* 2001;96:126.
5. Bai D, Brar P, Holleran S, Amakrishnan R, Green PH. Effect of gender on the manifestations of celiac disease: evidence for greater malabsorption in men. *Scand J Gastroenterol* 2005;40:183.
6. Puri AS, Garg S, Monga R, Tyagi P, Saraswat MK. Spectrum of atypical celiac disease in North Indian children. *Indian Pediatr* 2004;41:822.
7. al-Hassany M. Coeliac disease in Iraqi children. *J Trop Pediatr Environ Child Health* 1975;21:178.
8. Catassi C, Ratsch IM, Gandolfi L, Pratesi R, Fabiani E, El Asmar R, et al. Why is coeliac disease endemic in the people of the Sahara? *Lancet* 1999;354:647.
9. Gomez JC, Selvaggio GS, Viola M, Pizarro B, la Motta G, de Barrio S, et al. Prevalence of celiac disease in Argentina: screening of an adult population in the La Plata area. *Am J Gastroenterol* 2001;96:2700.
10. Sagaro E, Jimenez N. Family studies of coeliac disease in Cuba. *Arch Dis Child* 1981;56:132.
11. Jabri B, Sollid LM. Tissue-mediated control of immunopathology in celiac disease. *Nat Rev Immunol* 2009;9:858-70.
12. Schuppan D, Yunker Y, Barisani D. Celiac disease: from pathogenesis to novel therapies. *Gastroenterology* 2009;137:1912-33.
13. Karel K, Louka AS, Moodie SJ, Ascher H, Clot F, Greco L, Ciclitira PJ, et al. HLA types in celiac disease patients not carrying the DQA1*05-DQB1*02 (DQ2) heterodimer: results from the European Genetics Cluster on Celiac Disease. *Hum Immunol* 2003;64(4):469-77.
14. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology* 2001; 120: 636-51.
15. Dube C, Rostom A, Sy R, Cranney A, Saloojee N, Garrity C, et al. The prevalence of celiac disease in

- average-risk and at-risk Western European populations: a systematic review. *Gastroenterology* 2005;128 (4 Suppl 1):S57-S67.
16. Makharia GK. Where are adult Indian celiacs? *Trop Gastroenterol* 2006;27:1-3.
 17. Murray JA. Celiac disease in patients with an affected member, type 1 diabetes, iron-deficiency, or osteoporosis? *Gastroenterology* 2005;128 (Suppl 1):S52-S56.
 18. Bottaro G, Cataldo F, Rotolo N, Spina M, Corazza GR. The clinical pattern of subclinical/silent celiac disease: an analysis on 1026 consecutive cases. *Am J Gastroenterol* 1999, 94:691-696.
 19. Green PHR, Stavropoulos SN, Panagi SG, Goldstein SL, McMahon DJ, Absan H, et al. Characteristics of adult celiac disease in the USA: results of a national survey. *Am J Gastroenterol* 2001, 96:126-131.
 20. Aziz S, Muzaffar R, Zafar MN, Mehnaz A, Mubarak M, Abbas Z, et al. Celiac disease in children with persistent diarrhoea and failure to thrive. *J Coll Physicians Surg Pak* 2007;17:554-7.
 21. Makharia GK, Baba CS, Khadgawat R, Lal S, Tevatia MS, Madan K, Dattagupta S. Celiac disease: variations of presentations in adults. *Indian J Gastroenterol* 2007; 26:162-6.
 22. Ikram MA, Sajid A, Hameed S, Arshad K, Irshad-ul-Haq. Coeliac disease in children presenting with failure to thrive. *J Ayub Med Coll Abbottabad* 2011,23:6-9.
 23. Ravelli AM, Tobanelli P, Minelli LM, Villanacci V, Cestari R. Endoscopic features of celiac disease in children. *Gastrointestinal Endoscopy* 2001;54:736-42.