e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(6); 104-109

Original Research Article

Clinicopathologic Features of Celiac Disease: A Retrospective Study from Tertiary Care Teaching Institute of Central India

Akanksha Jain[1], Kamal Malukani[2], Atishay Jain[3], Purti Agrawal Saini[4], Amit V Verma[5], Piyush Kumar Mishra[6]

[1]Demonstrator, Department of Pathology, N. S. C. B. Medical College, Jabalpur (M.P)
[2]Professor, Department of Pathology, SAMC & PGI, Indore (M.P)
[3]Assistant professor, N. S. C. B. Medical College, Jabalpur (M.P)
[4]Associate Professor, Department of Pathology, Nandkumar Singh Chauhan Govt Medical College, Khandwa (M.P)
[5]Professor, Department of Pathology, SAMC & PGI, Indore (M.P)
[6]Statistician, Department of Community Medicine, Nandkumar Singh Chauhan Govt Medical College, Khandwa (M.P)

Received: 20-03-2023 / Revised: 11-04-2023 / Accepted: 05-05-2023
Corresponding author: Dr Purti Agrawal Saini
Conflict of interest: Nil

Abstract

Background: Celiac disease (CD) is an immunologically mediated chronic inflammatory disorder of the small intestine presented with malabsorption symptoms after ingestion of gluten. The gold standard for the diagnosis of CD is duodenal biopsy with positive serologic tests either anti-tissue Transglutaminase (t-TG) or anti endomysial antibodies (EMA).

Material and Methods: This retrospective study was done in 36 duodenal biopsy confirmed cases of CD. The demographic characteristics such as age and gender, presenting features, ultrasonographic (USG) findings, upper gastrointestinal (UGI) endoscopic finding and serum t –TG levels were retrieved from previous records. The detailed microscopic examination of duodenal biopsy for villous architecture, crypt abnormality, villi to crypt ratio was done. The intraepithelial lymphocytes (IELs) were counted in 100 enterocytes. The staging was done according to Modified Marsh (Marsh–Oberhuber) criteria. The chi-square test was applied to know the association between modified marsh staging and t-TG levels, and endoscopic findings.

Results: The mean age was 33.6 years with range of 3 years to 65 years. Male to female ratio was 1.3:1. The commonest presentation was chronic diarrhoea in 80.5% cases. Serum t-TG level was raised in 92.6% cases and abnormal endoscopic features seen in 69.4% CD cases. The mild, moderate and severe villous atrophy was seen in 7 (19.4%), 13 (36.1%) and 16 (44.4%) patients.

Conclusion: The mainstay of the diagnosis of CD is duodenal biopsy. However, positive serologic tests like t-TG and mucosal abnormalities in UGI endoscopy help clinicians diagnose disease early and know the extent and severity of the disease.

Keywords: Celiac Disease, Villous Atrophy, Modified Marsh Staging, Intraepithelial Lymphocytes, Anti-Tissue Transglutaminase.

Introduction

Celiac disease (CD) is an immunologically mediated inflammatory disease of the gastrointestinal mucosa due to intolerance to a component of gliadin, a storage protein of the cereals wheat, barley and rye, in genetically susceptible individuals [1]. It is also known as gluten sensitive enteropathy or celiac sprue or nontropical sprue. Celiac disease usually seen in children, but adolescent, adult or elderly can be affected.

The pathogenesis involves inappropriate intestinal T-cell activation in HLA-DQ2- or HLA-DQ8-positive individuals triggered by antigenic peptides from wheat gluten or prolamins from barley and rye [2]. Circulating antibodies directed against gliadin, endomysium (EMA) or tissue transglutaminase (t-TG) are also present.

The clinical profile in CD varies with the age of the patient, extent of the involvement and presence of extraintestinal conditions. The typical presentation of CD in Indian children is chronic diarrhea, anemia and short stature [3,4].

For the diagnosis of CD, American College of Gastroenterology (ACG) in 2013 recommended the combination of small intestinal biopsy and serological tests such as anti-tissue transgluataminase (t TG) or anti-deamidated gliadin peptide (DGP) [5]. Villous atrophy is considered to be the most typical finding in CD. To grade mucosal abnormality in biopsy a modified Marsh – Oberhuber criteria is widely accepted by pathologist and clinicians [6].

Additional histological findings in CD, but with limited diagnostic values, are: (i) reduced height of enterocytes, (ii) pyknosis, (iii) loss of basal orientation and pseudostratification of the nuclei, (iv) reduced number of the goblet cells, and (v) reduction of the microvillous height. [1]

The present study was conducted to know the clinicomorphologic spectrum of CD in duodenal biopsies and its association with serologic tests and endoscopic findings.

Material and Methods

Study design and duration: The present retrospective observational study was conducted in the Department of Pathology, Sri Aurobindo Medical College and Post Graduate Institute, Indore, M.P. from January 2011 to June 2017.

Inclusion criteria: All duodenal biopsies received and diagnosed as celiac disease (CD) during study period were included in the study.

Exclusion criteria: Inadequate (less than 3 villi) and autolytic duodenal biopsies were excluded.

Data Collection: A detailed information including age, gender, clinical signs and symptoms, complete blood count, serum t-TG IgA antibodies and upper gastrointestinal (UGI) endoscopic findings were recorded from the case records. Histopathologic slides and paraffin blocks were retrieved from surgical pathology department and studied. Additional sections were cut to prepare fresh slides wherever required, stained and studied.

A detailed microscopic examination of properly oriented duodenal biopsies was done. The microscopic parameters such as villous architecture, villous to crypt ratio (V:C), intraepithelial lymphocytes (IELs) and crypt examination were done. The IELs were counted in 100 enterocytes and consider into normal (<30/100 enterocytes) and increased (≥30/100 enterocytes). The staging was also done according to Modified Marsh (Marsh–Oberhuber) criteria [7, 8]. We also tried to find out the association between modified marsh staging and t-TG levels, and endoscopic findings. Chi-square test was applied to know the statistical significance.

Results

A Total of 36 celiac disease cases were studied in properly orientated adequate biopsies. The age range was 3 years to 65 years with mean age of 33.6 years. Male to female ratio was 1.3:1 with male dominance. Maximum no of patients (33.3%) belonged to 15 to 30 years of age group (Table -1).

Table 1: Age and gender wise distribution

Age in years	No. of patients (N)		Total
	Male	Female	
<5	1	1	2
5-15	2	1	3
>15-30	6	6	12
>30-45	6	4	10
>45-60	5	3	8
>60	0	1	1
Total	**20**	**16**	**36**

The most common manifestation was chronic diarrhea with or without abdominal pain affected 80.5% (29/36) patients. The next common presentation was refractory anemia in 73% (19/26) individuals. A single case of atypical presentation in 23 year female patient found, who had short stature and failure to thrive along with diarrhea, weight loss and anemia.

Serum t-TG IgA level was available in 27 cases, of which 25 cases (92.6%) showed raised levels. 11 cases (40.7%) showed ≥100 IU/ml t-TG levels and 14 cases (51.8%) showed t-TG level between 15 to 99 IU/ml.

Ultrasonographic findings of whole abdomen were also available in 13 cases, of these 8 cases did not show any significant abnormality. Other remaining cases showed associated liver abnormality such as hepatomegaly (1 case), cirrhosis (2 cases), cirrhosis with portal hypertension (1 case) and parenchymal changes (1 case). UGI endoscopy revealed no abnormality in duodenal mucosa in 11 cases (30.5%), whereas remaining 25 cases showed different mucosal abnormalities such as granular mucosa (8 cases, 22.2%), attenuated folds (17 cases, 47.2%) and scalloped folds (12 cases, 33.3%).

In microscopic examination none of the biopsy revealed normal villous architecture. The mild, moderate [Figure 1] and severe [Figure 2] villous atrophy was seen in 7 (19.4%), 13 (36.1%) and 16 (44.4%) patients respectively along with crypt abnormality and raised IELs [Table 2].

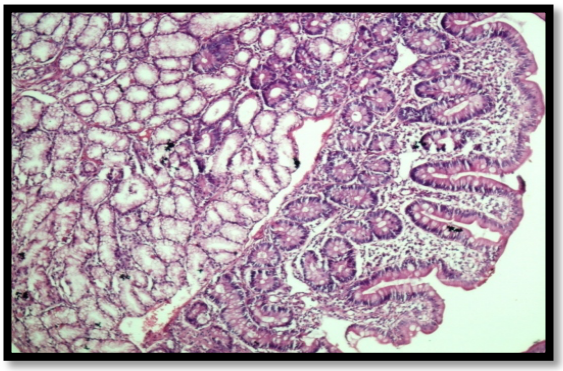

Figure 1 (Stage 3b): Duodenal mucosal biopsy showing moderate villous atrophy. (H&E, 40 X)

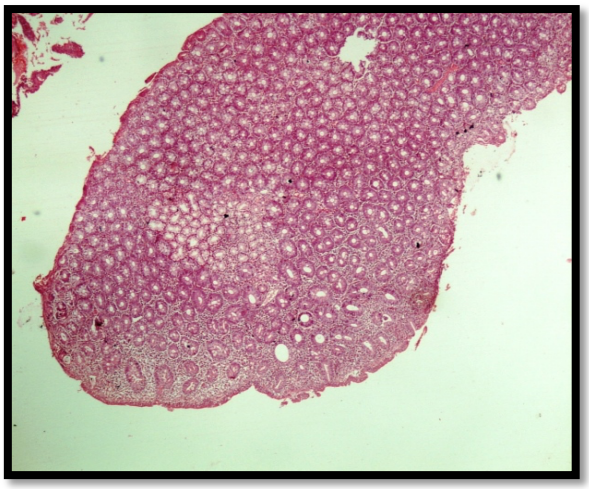

Figure 2: (Stage 3c): Duodenal mucosal biopsy showing total villous atrophy. (H&E, 40 X)

Table 2: Distribution of cases according to Modified Marsch-Oberhuber classification

Type	IELs	Crypts	Villous blunting	No of cases N (%)
3a	>30	hyperplastic	mild	7 (19.4%)
3b	>30	hyperplastic	modearte	13 (36.1%)
3c	>30	hyperplastic	Severe (flat)	16 (44.4%)

We tried to know the association of modified marsh grading with serum t-TG level and abnormal endoscopic findings and found it was not significant with t-TG level but it was statistically significant with endoscopic findings (table 3). In present study 85.7% (6/7 cases) patients with mild villous atrophy (Type 3a) had normal UGI endoscopy and 25% (1/4) of such patients had normal t-TG level. Whereas, 88.9% (8/9 cases) of moderate villous atrophy and 100% (14/14) of severe atrophic patients showed raised levels.

Table 3: Association of modified marsh grading with t-TG level and endoscopic findings

Type	t-TG level (IU/ml) N=27			X^2 (p-value)	Endoscopic finding N=36		X^2 (p-value)
	<15	>15-100	>100		Normal	Abnormal *	
3a	1	3	0	6.20 (0.815)	6	1	12.83 (0.016)**
3b	1	5	3		3	10	
3c	0	6	8		2	14	

* granular mucosa/attenuated/scalloped mucosal folds

** p value <0.05 statistically significant.

Discussion

In the present study, the mean age of CD patients was 33.6 years, with an age range of 3 years to 70 years. The findings were in accordance with Indian studies by Makharia et al [9], Karegar et al [10] and Balasubramanian et al [11], who reported mean age 28.7, 32.5 and 36 years respectively in their studies. A study conducted in Pakistan on 12 patients of seronegative CD also reported the similar finding [12]. The M:F ratio was1.3:1 with male dominance in the current study whereas, female predominance was noted in Indian as well as in western studies. [9-13]

The most common presentation was chronic diarrhea in 80.5% cases in the

present study. This finding was similar with Karegar et al [10] and Balasubramanian et al [11]who reported diarrhea as commonest presentation in 84% and 87.5% respectively in CD patients. Refractory anemia was observed in 73% cases in the present study and ranked second commonest manifestation. This finding was not in line with other studies, who reported anemia in lower frequency ranging from 16% to 32% in CD patients.[9-11,14] This discordant finding may be because of higher age and longer duration of symptoms in the present study population.

The current study also observed liver abnormality in 38.5% (5/13) cases in which sonographic evidence was available. The study by Makharia et al [9] also reported liver disease in 20% patients of CD. In UGI endoscopy, mucosal abnormalities in the index study were observed in 69.4% cases. Makharia et al [9] and Yadav P et al [15] reported mucosal abnormalities in 75.5% and 82% cases respectively in their studies. The specific abnormal findings like loss of folds, scalloping, mosaic pattern has a positive predictive value of 84% with 94% sensitivity and 92% specificity in diagnosis of CD in UGI endoscopy [16].

The present study reported increased levels of t-TG in 92.6% CD patients. Of these only 40.7% patients had ≥100 IU/ml t-TG levels and 51.8% patients had t-TG levels between 15 to 99 IU/ml. Mubarak et al [17] in his study reported t-TG positivity in 71% (130/183) CD patients. He also reported the 89% positive predictive value (PPV), 92% negative predictive value (NPV) with 97% sensitivity and 78% specificity for t-TG >10 IU/ml. Whereas, he reported 100% PPV, 66% NPV with 100% specificity, and 73% sensitivity for ≥ 100 IU/ml t-TG levels. Similar observation was reported by Hill et al [18] and he concluded that ≥ 100 IU/ml t-TG levels had 100% PPV and eliminates the necessity of biopsy for diagnosis of CD. The present study did not found any association between t-TG level and different stages of CD. We could not find any study in literature who studied this association.

The mild, moderate and severe villous atrophy was seen in 7 (19.4%), 13 (36.1%) and 16 (44.4%) patients in the current study. The observation was similar with Makharia et al [9] who reported mild, moderate and severe villous atrophy in 22.2%, 33.3% and 42.2% cases respectively. The present study highlighted the fact that as the villous atrophy becomes severe, duodenal mucosal abnormalities in the form of attenuated fold, scalloping and fissuring becomes more evident. This finding was in relation with Karegar et al [10].

Conclusion

CD not only limited to the children but also affects adult and adolescents. The commonest presentation was chronic diarrhea. UGI endoscopic abnormalities increased with stages of villous atrophy. The serum t-TG level was also raised in 92.6% of CD patients. Thus in patients with chronic diarrhea and refractory anemia serum t –TG and endoscopy should be advised along with duodenal biopsy to rule out or confirm the possibility of CD and to know the extent and severity of disease.

Reference

1. Dickson BC, Streutker CJ, Chetty R. C oeliac disease: an update for pathologists. J Clin Pathol. 2006; 59: 1008-16.
2. McManus R, Kelleher D. Celiac disease – the villain unmasked? N Engl J Med. 2003; 348:2573-4.
3. Poddar U, Thapa BR, Singh K. Clinical features of celiac disease in Indian children: are they different from the West? J Pediatr Gastroenterol Nutr. 2006;43(3):313-7.
4. Bharadia L, Kanojiya L, Choudhary S, Shivpuri D. Celiac Disease – A Case

Series from North India. Indian J Pediatr. 2016; 83(1):89.
5. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA. ACG clinical guidelines: Diagnosis and management of celiac disease. Am J Gastroenterol. 2013; 108:656–76.
6. Svajdler M, Daum O, Rychly B. Diagnosing celiac disease: role of the pathologists. Intl J Celiac Dis. 2014; 2:70-5.
7. Oberhuber G, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol. 1999; 1:1185–94.
8. Oberhuber G. Histopathology of celiac disease. Biomed Pharmacother. 2000; 54(7):368-72.
9. Makharia G, Baba CS, Khadgawat R, Lal S, Tevatia MS, Madan K et al. Celiac disease: Variations of presentation in adults. Indian J Gastroenterol. 2007; 26:162-6.
10. Karegar MM, Kothari K, Mirjolkar AS. Duodenal biopsy in malabsorption- A clinicopathological study. Indian J Pathol Oncol. 2016; 3(2); 197-201.
11. Balasubramanian P, Badhe BA, Ganesh RN, Panicker LC, Mohan P. Morphologic Spectrum of Duodenal Biopsies in Malabsorption: A Study from Southern India. Journal of clinical and diagnostic research. 2017;11(7): EC17–EC21.
12. Farina MH, Kumar Mandhwani R, Hassan Luck N, Abbas Z, Mubarak M, Laeeq SM et al. Clinicopathological Study of Seronegative Celiac Disease in Adults in Pakistan: A Pilot Study. Middle East journal of digestive diseases. 2017; 9(2): 94–99.
13. Stone ML, Bohane TD, Whitten KE, Tobias VH, Day AS. Age related clinical features of childhood coeliac disease in Australia. BMC Pediatr. 2005; 5(1):11.
14. Abu Daya H, Lebwohl B, Lewis SK, Green PH. Celiac disease patients presenting with anemia have more severe disease than those presenting with diarrhea. Clin Gastroenterol Hepatol. 2013; 11(11):1472-7.
15. Yadav P, Das P, Mirdha BR, Gupta SD, Bhatnagar S, Pandey RM, et al. Current spectrum of malabsorption syndrome in adults in India. Indian J Gastroenterol. 2011; 30:22–28.
16. Oxentenko AS, Grisolano SW, Murray JA. The insensitivity of endoscopic markers in coeliac disease. Am J Gastroenterol. 2002; 97:933-38.
17. Mubarak A, Wolters VM, Gmelig-Meyling FH, Ten Kate FJ, Houwen RH. Tissue transglutaminase levels above 100 U/mL and celiac disease: a prospective study. World J Gastroenterol. 2012 Aug 28; 18(32): 4399-403.
18. Hill PG, Holmes GK. Coeliac disease: a biopsy is not always necessary for diagnosis. Aliment Pharmacol Ther. 2008; 27(7):572-7.