

Is Diarrhea the Commonest Clinical Presentation of Celiac Disease in Pakistan

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Abstract:-

➤ Objective:

To identify the common clinical presentation of coeliac disease in patients reporting to tertiary care hospital

➤ Type of Study:

Cross-sectional study

➤ Place and Duration:

Department of Gastroenterology, Pak Emirates Military Hospital Rawalpindi, from Feb - Aug 2023

➤ Methodology:

Patients with diagnosis of coeliac disease on the basis of serological, clinical and histopathological (biopsy) criteria were included. Patients with inflammatory bowel disease, chronic or acute diarrhea of any other origin, sepsis, and recent abdominal surgery were excluded. Laboratory investigations including full blood counts, liver function tests and serological tests for celiac disease were also performed. Patients with celiac serology positive underwent duodenal biopsies. Statistical analysis was conducted in Statistical Package for Social Sciences (SPSS) version 25.0.

➤ Results:

In this study, sixty-seven (n= 67) patients with median age of 37.00 (31.00-44.00) years were included. There were 30 (44.78%) males and 37 (55.22%) females with female predominance. In gastrointestinal system (GIT), the most common manifestation was diarrhea 35 (52.24%) sharing the place with abdominal pain 35 (52.24%). The least common manifestation was steatorrhea 5 (7.46%). In extra-intestinal manifestations, the anaemia 46 (68.66%) was the most common clinical abnormality followed by weight loss 24 (35.82%) and hypothyroidism 23 (34.23%). While idiopathic thrombocytopenic purpura (ITP) and limb ataxia was least common 2 (2.99%) extraintestinal feature.

➤ Conclusion:

The diarrhea and abdominal pain were most common gastrointestinal manifestation while anaemia, weight loss and hypothyroidism were the most common extraintestinal features.

Keywords:- Anaemia, Autoimmune Diseases, Celiac Disease, Diarrhea.

I. INTRODUCTION

Coeliac disease is a chronic condition with insidious onset and is genetically transferred.^{1,2} The individuals suffering from this condition have increased gluten sensitivity with HLA DQ-2 and HLA DQ-8 being the most important human leukocyte antigens (HLA) in its pathogenesis.^{3,4} It was found 1.4% prevalent in the basis of serological investigations and much lower (0.7%) on the basis of biopsy worldwide.⁵ In Pakistan, its incidence is much higher (29.3%) as reported by a study conducted by Jamila, et al.⁶ These figures given by Jamila, et al might not be the true incidence keeping in view the lesser number of medical facilities with the diagnostic modalities for coeliac disease, and not all people get tested, nor all can afford in private medical setups. So, the figures might be higher than the reported ones.

The clinical presentation varies greatly among different age groups but gastrointestinal (GIT) system the most commonly involved. People usually present with chronic diarrhea, weight loss, decreased haemoglobin (anaemia), abdominal pain, weight loss, loss of appetite and nausea.^{7,8,9} It has also wide range of extraintestinal features like ataxia, dermatitis herpetiform, migraine and seizures.^{7,8} These wide variety of non-specific symptoms and signs not only make the diagnosis difficult but also one of the causes of delayed diagnosis. Similarly, there is a history of failure to thrive, loss of muscle mass and fat.^{9,10} The coeliac disease not only brings the morbidity in affected individuals but also has a major impact on their quality life

There is very limited research in our country despite the such a high incidence of coeliac disease. This study was

planned to see most common presenting complaints of coeliac disease. This study will not only help in identifying the individuals with coeliac disease but it will also lower the threshold of the clinicians in suspecting the coeliac disease. Moreover, the resources can be directed towards targeted population in such resource limited community.

II. METHODOLOGY

This cross-sectional observational study was conducted at Department of Gastroenterology, Pak Emirates Military hospital (PEMH) Rawalpindi, Pakistan from 1st February 2023 to 31st August 2023. The institutional ethical approval was obtained from the institutes ethical committee vide A/28/ERC/46/24. The sample size was calculated using OpenEpi sample size calculator with confidence interval of 95%, margin of error 5% and population prevalence of coeliac disease as 1.4%, the sample size came out to be 22 individuals.⁵ The non-probability consecutive sampling technique was used. After the detailed explanation of purpose and method of study, verbal informed consent was acquired from all participants or their guardians (if below 18 years).

➤ Inclusion Criteria:

Patients with age greater than 18 years and less than 65 years, with diagnosis of coeliac disease on the basis of serological, clinical and histopathological (biopsy) criteria were included in the study.

➤ Exclusion Criteria:

Patients with inflammatory bowel disease, chronic or acute diarrhea of any other origin, sepsis, recent abdominal surgery and nonsteroidal anti-inflammatory agents

(NSAIDS) abuse were excluded. Moreover, pregnant and nursing mothers and individuals on hematinic or blood transfusions for any other cause were also excluded. Patients with Marsh class 0, 1 or 2 or those with negative serology were excluded from the study.

Detailed history was taken, including history for risk factors for celiac disease and associated conditions like diabetes mellitus, thyroid disease etc. Physical examination including BMI calculation was done. Laboratory investigations including full blood counts, liver function tests and serological tests for celiac disease were also performed. Patients with celiac serology positive underwent duodenal biopsies. Patients were labelled to be having celiac disease if the histology showed Marsh class 3a, 3b, or 3c in addition to positive serology. Some asymptomatic patients who were in high-risk groups, also underwent serological tests and duodenal biopsies.

Statistical analysis was conducted in Statistical Package for Social Sciences (SPSS) version 25.0. The normality of data was checked using Shapiro-Wilk test. Mean and standard deviation (SD) were computed for normally distributed continuous variables while the median and interquartile range was checked for skewed variables. The frequencies along with percentages were used for qualitative variables.

In this study, there we included sixty-seven (n= 67) patients with median age of 37.00 (31.00-44.00) years. There were 30 (44.78%) males and 37 (55.22%) females with slight female predominance. In the total sample, 12 (17.91%) were diabetics and 6 (8.96%) were hypertensive. Table-I shows the basic demographic features of study population.

Table 1 Basic Demographic Features of Study Population (n=67)

Variable	Total Population (n=67)	Gender Distribution	
		Male (n=30)	Female (n=37)
Age (years)	37.00 (31.00-44.00)	36.50 (28.00-44.25)	38.00 (33.00-44.50)
Diabetes	12.00±1.10	3 (10.00%)	9 (24.32%)
Hypertension	6 (8.96%)	2 (6.67%)	4 (10.81%)
Hemoglobin	12 (17.91%)	12.73±0.86	11.42±0.91
BMI	19.91±1.81	19.20±1.63	20.48±1.76
Serology			
TTG IgA	53 (79.10%)	23 (76.67%)	30 (81.08%)
TTG IgG	1 (1.49%)	-	1 (2.70%)
Both	13 (19.40%)	7 (23.33%)	6 (16.22%)

In gastrointestinal system (GIT), the most common manifestation was diarrhea 35 (52.24%) sharing the place with abdominal pain 35 (52.24%). It was followed by loss of appetite 17 (25.37%) and constipation 15 (22.39%). In GIT,

the least common manifestation/ symptom was steatorrhea 5 (7.46%). Details of remaining manifestations are shown in Table-2.

Table 2 Gastrointestinal Manifestations of Coeliac Disease (n=67)

Clinical Manifestation	Values	
	Yes	No
Diarrhea	35 (52.24%)	32 (47.76%)
Abdominal Pain	35 (52.24%)	32 (47.76%)
Loss of Appetite	17 (25.37%)	50 (74.63%)
Constipation	15 (22.39%)	52 (77.61%)
Nausea	13 (19.40%)	54 (80.60%)
Bloating	9 (13.43%)	58 (86.57%)

Vomiting	8 (11.94%)	59 (88.06%)
Steatorrhea	5 (7.46%)	62 (92.54%)

In extra-intestinal manifestations of the coeliac disease, the anaemia 46 (68.66%) was the most common clinical abnormality followed by weight loss 24 (35.82%) and hypothyroidism 23 (34.23%). The dermatitis herpetiform was seen in 10 (14.93%) patients suffering from coeliac disease.

While idiopathic thrombocytopenic purpura (ITP) and limb ataxia was least common 2 (2.99%) extraintestinal manifestation. Details of various others extra-intestinal manifestations and associated diseases of coeliac disease are shown in Table 3.

Table 3 Extra-intestinal Manifestations of Coeliac Disease (n=67)

Clinical Manifestation	Values	
	Yes	No
Anaemia	46 (68.66%)	21 (31.34%)
Weight Loss	24 (35.82%)	43 (64.18%)
Hypothyroidism	23 (34.23%)	44 (65.67%)
Aphthous Ulcer	11 (16.42%)	56 (83.58%)
Atrophic Glossitis	11 (16.42%)	56 (83.58%)
Dermatitis Herpetiform	10 (14.93%)	57 (85.07%)
Psychiatric Symptoms	9 (13.39%)	58 (86.57%)
Menstrual Irregularities	9 (13.39%)	58 (86.57%)
Migraine	8 (11.98%)	59 (88.06%)
Fatigue	7 (10.45%)	60 (89.55%)
Hyperthyroidism	6 (8.96%)	61 (91.04%)
Psoriasis	6 (8.96%)	61 (91.04%)
SLE	6 (8.96%)	61 (91.04%)
Epilepsy	5 (7.46%)	62 (92.54%)
Autoimmune Hepatitis	5 (7.46%)	62 (92.54%)
ITP	2 (2.99%)	65 (97.01%)
Ataxia	2 (2.99%)	65 (97.01%)

III. DISCUSSION

The coeliac disease a wide variety of non-specific manifestations and gluten sensitivity being the most specific, which is later supported by certain serological tests like Anti-TTG A & B and duodenal biopsy during upper GI endoscopy. In our study, we found diarrhea 35 (52.24%) was the most common intestinal manifestation while anaemia 46 (68.66%) was the most common extra-intestinal manifestation. Anaemia is dependent on multiple factors like diet and nutrition, quality of food intake, iron deficiency and hemoglobinopathies, so it cannot be solely attributed to coeliac disease but Hussain, et al in their study concluded that the patients with anaemia should be evaluated for underlying malabsorption disorders as they found a statistically significant association between controls and cases of coeliac disease.¹¹ Spencer, et al also highlighted the under-testing of anaemia in coeliac disease.¹² In our study, among the other leading intestinal signs and symptoms, abdominal pain 35 (52.24%), loss/ decreased of appetite 17 (25.37%) and constipation 15 (22.39%) were present. In extra-intestinal features, weight loss 24 (35.82%), hypothyroidism 23 (34.23%), aphthous ulcer 11 (16.42%), atrophic glossitis 11 (16.42%) and dermatitis herpetiform 10 (14.93%) were the leading features. The limb ataxia 2 (2.99%) and ITP 2 (2.99%) were the least common extra-intestinal associated features while vomiting 8 (11.94%) and steatorrhea 5 (7.46%) were the least common GIT features.

In a study conducted by Butt et al in Karachi, Pakistan at a tertiary care centre found that females were found to affected more from coeliac disease.¹³ The gender and its association with coeliac disease has been reported to variable degrees as some have showed female predominance while others found no difference between the two.^{14,15} In our study, we found a slight female predominance of the disease. The difference in gender difference might be explained with ethnicity and genetic predisposition of certain ethnic groups in different parts of the world. Some researchers found the male predominance of coeliac disease contrary to findings of our study.¹⁶ The abdominal pain was found in 88.3% patients and diarrhea in 55.3% patients, and anaemia in 70.6% patients.¹³ The results of this study are comparable to their results except for very higher frequency of abdominal pain. The anaemia and diarrhea had comparable frequency with the present study. This increased frequency of abdominal pain might be due to its subjective perception or may be due to difference in study population and no validated scale was used in this study to measure the abdominal pain. But other researchers reported the diarrhea as the most common presenting complaint in coherence with the findings of our study, which also found the diarrhea as commonest finding in coeliac disease patients.^{17,18}

Arshad, et al in their study found diarrhea to be one of the most common intestinal feature of coeliac disease similar to the findings of our study.¹⁹ The extraintestinal manifestations of the coeliac disease are also common and usually found in asymptomatic patients later or earlier.

Among the extraintestinal features, the autoimmune diseases especially thyroid disease are most common.^{20,21} Among the thyroid diseases, the hypothyroidism like Hashimoto thyroiditis is most common. In a study conducted by Binicier, et al and Demirezer et al, they found Hashimoto thyroiditis as the most common autoimmune disease associated with coeliac disease.^{21,22} In this study too, the autoimmune diseases was found in higher frequency, the hypothyroidism (34.23%) followed by hyperthyroidism, psoriasis and systemic lupus erythematosus (SLE) as the most common findings. Most of the patients had more than one autoimmune disease. This poly-autoimmunity might due to distribution of common genetic pathology pathways. The autoimmune disease was also reported by Butt et al in our Pakistani population, thyroid illness being the most common similar to findings of our study.¹³

The coeliac disease presents with wide variety of signs and symptoms including, bloating, diarrhea, anaemia and other extraintestinal features including autoimmune diseases.^{7-10,23} The present study almost found all of these presenting features to a variable frequency in our population. This kind of presentation makes the coeliac disease as one of the difficult diseases to diagnose and might be the reasons for delay in its diagnosis.

IV. LIMITATIONS

There are certain limitations in our study. Firstly, the small sample size and cross-sectional type of the study limits the attributability of symptoms to coeliac disease. Secondly, due to cross-sectional study type, the duration of disease and time of diagnosis cannot be commented upon. Similarly, the cause and effect of certain findings like anaemia, hypothyroidism and other auto-immune disease cannot be seen. These limitations suggest a multi-centre, prospective, cohort-based research should be done to study the coeliac disease in more detailed pattern.

- **Conflict of Interest:** None
- **Funding Source:** None

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