

# Frequency Of Celiac Disease Among Patients With Chronic Gastrointestinal Symptoms

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## ABSTRACT

**Background:** Celiac disease is an immune-mediated enteropathy that may present with chronic gastrointestinal symptoms and remains underdiagnosed because of its diverse clinical manifestations. **Objective:** To determine the frequency of celiac disease among patients presenting with chronic gastrointestinal symptoms and identify associated clinical predictors. **Methods:** This cross-sectional analytical study was conducted at Nishtar hospital Multan from march 2025 to march 2026 including 168 patients presenting with chronic gastrointestinal symptoms for more than three months. **Results:** The mean age of participants was  $35.9 \pm 12.4$  years, with females comprising 56.0% of the study population. Anti-tTG serology was positive in 34 (20.2%) patients, while histologically confirmed celiac disease was identified in 22 (13.1%). Bloating (57.1%), abdominal pain (53.0%), and chronic diarrhea (42.9%) were the most common symptoms. Patients with confirmed celiac disease were younger ( $29.7 \pm 9.3$  vs.  $36.8 \pm 12.6$  years;  $p=0.01$ ) and had lower BMI ( $20.6 \pm 3.7$  vs.  $24.3 \pm 4.5$  kg/m<sup>2</sup>;  $p<0.001$ ). Positive anti-tTG serology was the strongest predictor of confirmed disease (aOR 6.84;  $p<0.001$ ), followed by iron deficiency anemia (aOR 4.18), chronic diarrhea (aOR 3.42), BMI  $<22$  kg/m<sup>2</sup> (aOR 3.06), and unexplained weight loss (aOR 2.89). **Conclusion:** Celiac disease is a significant underlying cause of chronic gastrointestinal symptoms and should be actively considered in patients with suggestive gastrointestinal and malabsorptive clinical features.

**Keywords:** Celiac disease; chronic gastrointestinal symptoms; anti-tTG; duodenal biopsy; chronic diarrhea; malabsorption.

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## INTRODUCTION

Celiac disease is an immune-mediated enteropathy that occurs in genetically susceptible persons as a consequence of gluten exposure which results in inflammation of the small intestinal mucosa, destruction of the villi and malabsorption of nutrients [1]. It is well established nowadays that it is a major gastrointestinal condition in children and adults that occurs worldwide, and it is now acknowledged that its clinical manifestations go beyond the classic symptoms of malabsorptive diarrhea [2]. While historically thought to be rare in developing areas, there is a significant disease burden in many populations that is now being diagnosed [3]. Patients with chronic gastrointestinal

symptoms often form a diagnostically difficult group, as these symptoms (chronic diarrhea, abdominal pain, bloating, constipation, dyspepsia, nausea, weight loss and altered bowel habits) are similar to several functional and organic gastrointestinal diseases [4]. Of these, celiac disease is an important but underdiagnosed cause because of its variable clinical manifestations and delayed diagnoses [5]. The classical symptoms of celiac disease include chronic diarrhea, steatorrhea, abdominal distention, weight loss, and malabsorption with subsequent nutritional deficiencies [6]. Non-classical presentations, such as isolated bloating, recurrent abdominal discomfort, constipation, dyspepsia, iron deficiency anemia, fatigue, osteoporosis, infertility, neurological symptoms and

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asymptomatic seropositivity are now well appreciated [7]. The wide variation in clinical presentation results in diagnostic delay and underestimation of disease prevalence. The mechanism of celiac disease is the abnormal reaction of the immune system to gluten peptides which leads to intestinal inflammation and increased immune activity, with the consequence of crypt hyperplasia, villous atrophy, and impaired absorption of nutrients [8]. Environmental and immunological factors also contribute to the disease but the genetic predisposition of the HLA-DQ2 and HLA-DQ8 haplotypes is a significant factor [9]. If it remains untreated, it can cause chronic malnutrition, failure to thrive, osteoporosis, reproductive disorders, autoimmune disorders and occasionally intestinal cancers [10].

Diagnosis is made by clinical suspicion, serological testing and histopathological confirmation. Anti-tissue transglutaminase IgA antibodies are still a highly effective screening tool, and in many clinical situations, confirmatory histological assessment is obtained from an endoscopic duodenal biopsy [11]. Early diagnosis is important because strict gluten free dietary treatment can have a major impact on symptoms as well as nutritional recovery and long term outcomes [12]. However, the prevalence of celiac disease has been reported to be different among patients with chronic gastrointestinal complaints, depending on the population, diagnostic criteria, and referral pattern [13]. The prevalence could be significantly higher in symptomatic gastrointestinal cohorts compared to the general population and is important to consider conducting targeted screening [14]. For many patients, however, the diagnosis is delayed for a considerable period, since the symptoms are not considered specific for inflammatory bowel disease, but rather for irritable bowel syndrome, dyspepsia, chronic infection or non-specific gastrointestinal disorders [15].

### Objective

To determine the frequency of celiac disease among patients presenting with chronic gastrointestinal symptoms and identify associated clinical predictors.

### METHODOLOGY

This was a cross-sectional analytical study conducted at Nishtar hospital Multan from march 2025 to march 2026, including 168 patients presenting with chronic gastrointestinal symptoms to determine the frequency of celiac disease and associated clinical characteristics.

### Inclusion Criteria

Patients aged 18 years and above presenting with chronic gastrointestinal symptoms lasting more than three months, including chronic diarrhea, abdominal pain, bloating,

constipation, dyspepsia, nausea, unexplained weight loss, or altered bowel habits, were included. Patients willing to undergo clinical evaluation, serological testing, and relevant diagnostic investigations with informed consent were included.

### Exclusion Criteria

Patients with previously diagnosed celiac disease, known inflammatory bowel disease, gastrointestinal malignancy, chronic pancreatitis, active gastrointestinal infection, prior major intestinal surgery, severe systemic illness affecting gastrointestinal function, immunodeficiency disorders, or incomplete diagnostic records were excluded from the study.

### Data Collection

After obtaining ethical approval, data were collected using a structured proforma. Baseline demographic and clinical variables included age, gender, duration and type of gastrointestinal symptoms, body mass index, family history of autoimmune disease, anemia status, nutritional deficiencies, and associated extraintestinal manifestations. All patients underwent clinical assessment and serological screening using anti-tissue transglutaminase IgA antibodies, with total serum IgA evaluation where indicated. Patients with positive serology or high clinical suspicion underwent upper gastrointestinal endoscopy with duodenal biopsy for histopathological confirmation according to standard diagnostic criteria. Clinical symptom patterns, laboratory findings, biopsy results, and confirmed celiac disease frequency were recorded.

### Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean  $\pm$  standard deviation, while categorical variables were presented as frequency and percentage. Chi-square tests and independent t-tests were used to compare characteristics between patients with and without confirmed celiac disease. Multivariable logistic regression analysis was performed to identify predictors associated with celiac disease diagnosis. A p-value  $\leq 0.05$  was considered statistically significant.

### RESULTS

The study included 168 patients with chronic gastrointestinal symptoms, with a mean age of  $35.9 \pm 12.4$  years. Females were slightly more common, comprising 94 (56.0%) patients. The mean BMI was  $23.8 \pm 4.6$  kg/m<sup>2</sup>, and mean symptom duration was  $11.4 \pm 5.9$  months. Iron deficiency anemia was present in 46 (27.4%) patients, while a history of vitamin deficiency was reported in 38 (22.6%).

**Table 1: Baseline Demographic and Clinical Characteristics of Patients with Chronic Gastrointestinal Symptoms (n = 168)**

Variable	Total (n = 168)
Age (years), mean $\pm$ SD	35.9 $\pm$ 12.4
18–30 years, n (%)	58 (34.5%)
31–45 years, n (%)	67 (39.9%)
>45 years, n (%)	43 (25.6%)
Male, n (%)	74 (44.0%)
Female, n (%)	94 (56.0%)

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<b>BMI (kg/m<sup>2</sup>), mean ± SD</b>	23.8 ± 4.6
<b>Duration of Symptoms (months), mean ± SD</b>	11.4 ± 5.9
<b>Family History of Autoimmune Disease, n (%)</b>	19 (11.3%)
<b>Iron Deficiency Anemia, n (%)</b>	46 (27.4%)
<b>Vitamin Deficiency History, n (%)</b>	38 (22.6%)

Bloating was the most common symptom, reported in 96 (57.1%) patients, followed by abdominal pain in 89 (53.0%) and chronic diarrhea in 72 (42.9%). Altered bowel habits were present in 63 (37.5%), dyspepsia in 54 (32.1%), and fatigue in 52 (31.0%) patients. Weight loss was reported in 37 (22.0%), showing that both functional and malabsorptive symptoms were common.

**Table 2: Spectrum of Chronic Gastrointestinal Symptoms and Clinical Presentation (n = 168)**

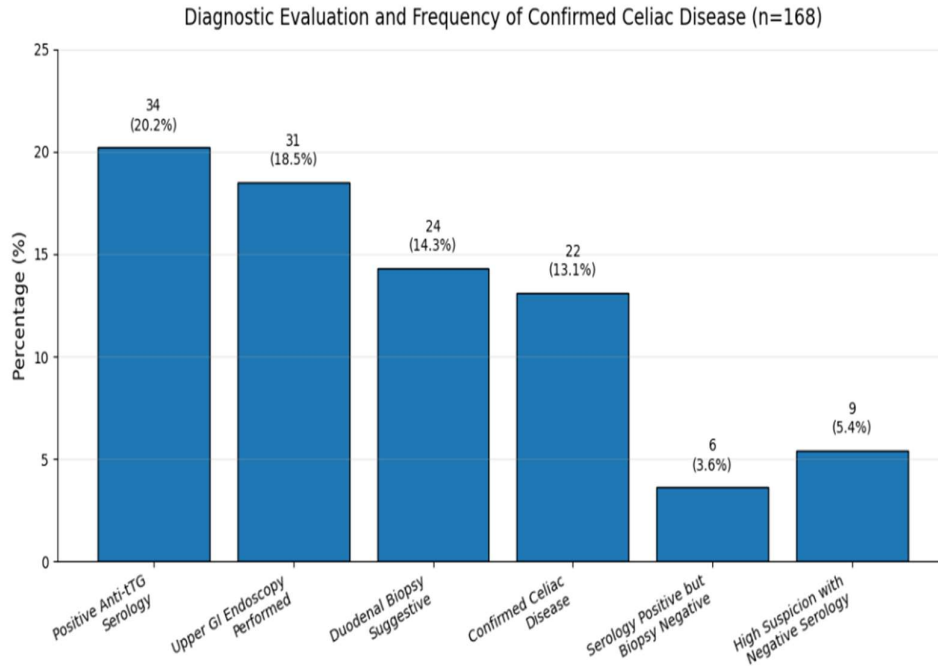
Variable	Frequency (n)	Percentage (%)
<b>Chronic Diarrhea</b>	72	42.9
<b>Abdominal Pain / Discomfort</b>	89	53.0
<b>Bloating / Abdominal Distension</b>	96	57.1
<b>Chronic Constipation</b>	41	24.4
<b>Dyspepsia</b>	54	32.1
<b>Nausea / Vomiting</b>	29	17.3
<b>Unexplained Weight Loss</b>	37	22.0
<b>Altered Bowel Habits</b>	63	37.5
<b>Fatigue</b>	52	31.0
<b>Recurrent Mouth Ulcers</b>	18	10.7

Anti-tTG serology was positive in 34 (20.2%) patients, while upper GI endoscopy was performed in 31 (18.5%). Duodenal biopsy was suggestive of celiac disease in 24 (14.3%) patients, and histologically confirmed celiac disease was found in 22 (13.1%). This indicates a notable frequency of celiac disease among patients with chronic gastrointestinal symptoms.

**Table 3: Diagnostic Evaluation and Frequency of Confirmed Celiac Disease (n = 168)**

Variable	Frequency (n)	Percentage (%)
<b>Positive Anti-tTG Serology</b>	34	20.2
<b>Upper GI Endoscopy Performed</b>	31	18.5
<b>Duodenal Biopsy Suggestive of Celiac Disease</b>	24	14.3
<b>Histologically Confirmed Celiac Disease</b>	22	13.1
<b>Serology Positive but Biopsy Negative</b>	6	3.6
<b>High Clinical Suspicion with Negative Serology</b>	9	5.4

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**Figure 1: Diagnostic Evaluation and Frequency of Confirmed Celiac Disease Among Patients With Chronic Gastrointestinal Symptoms**

Patients with confirmed celiac disease were younger than non-celiac patients ( $29.7 \pm 9.3$  vs.  $36.8 \pm 12.6$  years;  $p=0.01$ ) and had significantly lower BMI ( $20.6 \pm 3.7$  vs.  $24.3 \pm 4.5$  kg/m<sup>2</sup>;  $p<0.001$ ). Chronic diarrhea, bloating, weight loss, iron deficiency anemia, and fatigue were significantly more common in the celiac group, suggesting a stronger malabsorptive clinical pattern.

**Table 4: Comparative Clinical and Laboratory Characteristics Between Patients With and Without Confirmed Celiac Disease**

Variable	Celiac Disease Present (n=22)	Celiac Disease Absent (n=146)	p-value
Age (years), mean $\pm$ SD	$29.7 \pm 9.3$	$36.8 \pm 12.6$	0.01
Female Gender, n (%)	16 (72.7%)	78 (53.4%)	0.09
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	$20.6 \pm 3.7$	$24.3 \pm 4.5$	<0.001
Chronic Diarrhea, n (%)	16 (72.7%)	56 (38.4%)	0.003
Bloating, n (%)	18 (81.8%)	78 (53.4%)	0.01
Weight Loss, n (%)	11 (50.0%)	26 (17.8%)	0.001
Iron Deficiency Anemia, n (%)	14 (63.6%)	32 (21.9%)	<0.001
Fatigue, n (%)	13 (59.1%)	39 (26.7%)	0.003

Positive anti-tTG serology was the strongest predictor of confirmed celiac disease (aOR 6.84; 95% CI: 2.72–17.18;  $p<0.001$ ). Iron deficiency anemia (aOR 4.18), chronic diarrhea (aOR 3.42), BMI <22 kg/m<sup>2</sup> (aOR 3.06), and unexplained weight loss (aOR 2.89) were also significant predictors, highlighting key clinical clues for targeted screening.

**Table 5: Multivariable Logistic Regression Analysis for Predictors of Confirmed Celiac Disease**

Variable	Adjusted OR	95% CI	p-value
Chronic Diarrhea	3.42	1.41–8.28	0.006
Iron Deficiency Anemia	4.18	1.73–10.09	0.001
BMI <22 kg/m <sup>2</sup>	3.06	1.26–7.41	0.01
Unexplained Weight Loss	2.89	1.14–7.29	0.02
Positive Anti-tTG Serology	6.84	2.72–17.18	<0.001

## DISCUSSION

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In this study, 13.1% (22) of 168 patients with any chronic gastrointestinal symptoms had a diagnosis of celiac disease, highlighting an important prevalence of the disease in this symptomatic group. Anti-tTG serology was positive in 34 (20.2%) patients and biopsy confirmed disease in 22 (13.1%) patients: a serological screen followed by histological confirmation is useful. A previous study also found that patients with chronic gastrointestinal complaints had a higher prevalence of celiac disease than the general population. The most common symptom overall was bloating (96, 57.1%), followed by abdominal pain (89, 53.0%), and chronic diarrhea (72, 42.9%). Chronic diarrhea was more common among celiac disease patients (16, 72.7%) than non-celiac patients (56, 38.4) ( $p=0.003$ ), and bloating was more common among celiac (18, 81.8%) than non-celiac (78, 53.4) patients ( $p=0.01$ ). Chronic diarrhea, abdominal bloating, and recurrent abdominal discomfort are also common presenting symptoms that have been observed in patients with CD in a previous study [16]. Patients with confirmed celiac disease were younger, with mean age of  $29.7 \pm 9.3$  years compared with  $36.8 \pm 12.6$  years in non-celiac patients ( $p=0.01$ ), and had significantly lower BMI ( $20.6 \pm 3.7$  vs.  $24.3 \pm 4.5$  kg/m<sup>2</sup>;  $p<0.001$ ). This indicates that there could be a component of malabsorption and chronic inflammation of the intestine that results in nutritional deficiency in celiac disease. Another study found that patients with newly diagnosed celiac disease who had GI symptoms had lower BMIs and were younger [17]. Malabsorptive features were highly correlated with confirmed diagnosis of celiac disease. Weight loss was present in 11 (50.0%) celiac patients compared with 26 (17.8%) non-celiac patients ( $p=0.001$ ), while iron deficiency anemia was reported in 14 (63.6%) versus 32 (21.9%) patients ( $p<0.001$ ). Fatigue also was significantly more prevalent in the celiac disease patients (13 [59.1%]) than in the non-celiac patients (39 [26.7%]). ( $p=0.003$ ) One earlier study also found that iron deficiency anemia, weight loss, and fatigue were other important extraintestinal and malabsorptive markers of celiac disease [18]. Positive anti-tTG was the strongest predictor of confirmed celiac disease (aOR 6.84;  $p<0.001$ ) in a regression analysis. Other factors such as Iron Deficiency Anemia (aOR 4.18), Chronic Diarrhea (aOR 3.42), BMI less than 22 kg/m<sup>2</sup> (aOR 3.06), and Unexplained Weight Loss (aOR 2.89) were also significant predictors. The present results indicate that screening should be encouraged in patients with chronic gastrointestinal symptoms who have anemia, low BMI, diarrhea and weight loss. A prior study also showed that serological and clinical risk factors are a better combination for the diagnosis of celiac disease [19][20]. The overall results indicate that celiac disease is not uncommon in patients with chronic gastrointestinal symptoms and can go undiagnosed if patients are not screened. Early diagnosis of celiac disease is facilitated by routine discussion of the condition in patients with persistent bloating, diarrhea, low BMI, iron deficiency anemia, fatigue and weight loss, potentially reducing long-term problems.

#### LIMITATIONS

This study has several limitations. Being a single-center cross-sectional study, causal relationships between clinical predictors and celiac disease diagnosis cannot be definitively established. The sample size was moderate, which may limit broader generalizability. Not all patients underwent endoscopic biopsy, particularly those with low clinical suspicion, which may have led to underestimation of true disease frequency. Serological testing may also be affected by IgA deficiency or false-positive results in selected cases. Dietary history, genetic predisposition, and long-term follow-up after diagnosis were not assessed.

#### CONCLUSION

It is concluded that celiac disease represents a notable cause of chronic gastrointestinal symptoms, with a confirmed frequency of 13.1% in this study population. Chronic diarrhea, bloating, low BMI, iron deficiency anemia, fatigue, and unexplained weight loss were significantly associated with confirmed celiac disease. Positive anti-tTG serology was the strongest diagnostic predictor. Early consideration of celiac disease in patients with persistent gastrointestinal symptoms and malabsorptive features may facilitate timely diagnosis, appropriate dietary intervention, and prevention of long-term complications.

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