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# Evaluation of Demographic and Clinical Characteristics of Celiac Patients: A Single Center Experience

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## ABSTRACT

**Objective:** Celiac disease (CD) is an autoimmune disorder among genetically predisposed subjects exposed to gluten-containing foods. It is now appreciated that CD is now recognized as a common condition among persons of various ethnic groups and both adults and children, and that affects many organ systems. This study was conducted to evaluate the demographic and clinical characteristics of pediatric celiac patients.

**Patients and Methods:** A total of 122 individuals diagnosed with CD by serologic and histologic assessments between January 2010 and December 2016 were enrolled in the study.

**Results:** : Forty-three patients were boys (35.2%), and seventy-nine were girls (64.8%). The mean age was 12.6±5.7 years, and the mean age at diagnosis was 8.8±5.1 years. The most frequent presenting symptoms were abdominal pain (41%), failure to thrive (36.1%), and diarrhea (34.4%). Adherence to a gluten-free diet was 67.2%. Family history of CD was positive in 2.5% of patients. The most frequent comorbidities were iron deficiency anemia (36.1%), vitamin D deficiency (12.3%), and type-1 diabetes mellitus (7.4%). Endoscopic assessments revealed dentations in 61.5% of cases, and histologic evaluations told that Marsh 3b was the most frequent histologic grade (27.9%). IgA and IgG transglutaminase antibody levels were decreased significantly following the initiation of the gluten-free diet.

**Conclusion:** Celiac disease faces a very varied picture in terms of clinic and laboratory at the time of diagnosis and in the follow-up. Early diagnosis of CD is critical to prevent long-term complications; currently, the only effective treatment is a lifelong gluten-free diet.

**Keywords:** Celiac, gluten-sensitive enteropathy, tropical sprue, children, demographic characteristics, clinical characteristics

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## INTRODUCTION

Celiac disease (CD) is an autoimmune enteropathy triggered by gluten ingestion in genetically predisposed individuals. The diagnosis is based on serologic and histopathologic features, including anti-tissue transglutaminase antibodies and anti-endomysial antibodies, as well as histopathologic features of villous atrophy and crypt hyperplasia, respectively (1, 2).

CD is a severe autoimmune disorder that affects mainly the digestive system. As a concern, malabsorption develops, which results in malnutrition-related problems, including anemia,

vitamin deficiencies, and osteoporosis. The current treatment for CD patients is a strict lifelong Gluten-Free Diet. However, avoiding gluten intake is extremely difficult due to hidden gluten from food contamination. Besides, the CD individuals benefit from a supplementary diet with vita Hydrolysis of toxic gliadin peptides are being studied (5-7).

The prevalence of CD varies significantly across and within different countries (5-7). The prevalence rate in Turkey ranges between 0.5% and 1.3% (8)

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Although there has been a substantial increase in CD diagnoses over the last 30 years, many patients remain undiagnosed. Given the wide range of clinical spectrum of celiac disease, patients must be carefully evaluated and included in differential diagnosis since many extraintestinal findings were related. Furthermore, early diagnosis and prompt treatment prevent health problems such as growth retardation, osteoporosis, infertility, and autoimmune diseases (4).

This study evaluated pediatric celiac patients' demographic and clinical characteristics in a tertiary care hospital, a reference center for CD.

# MATERIALS AND METHODS

A retrospective analysis of 122 patients diagnosed with CD at the Pediatric Gastroenterology, Hepatology, and Nutrition department, Ondokuz Mayıs University Faculty of Medicine, was conducted between January 2011 and January 2016. Patients' electronic records were searched for the following search terms: celiac disease, gluten-sensitive enteropathy, chronic diarrhea, malabsorption, and small intestinal biopsies. The study included only children under the age of eighteen. Biochemical parameters were also recorded for analysis, including serological markers and small intestinal biopsy interpretation. Age, gender, nationality, clinical presentation, and biochemical parameters were all recorded. Pathological examinations were reported according to the Marsh-Oberhuber classification. Body weight, height, and body mass index were calculated using the patients' and size measurements. Standard deviation score (SDS): measured value - median value for age and sex / standard deviation for age and sex were noted. Body weights below -2 SDS were considered underweight, and those with a height below -2 SDS were considered stunted (9).

The diagnosis of CD was confirmed in all patients by the presence of IgA-tTGA and/or IgG-tTGA serological markers and/or histopathological changes in small intestinal mucosal biopsies. It was further investigated why small intestinal biopsies were performed in cases with negative serology but positive histology. HLA-DQ2/DQ8 genetic testing had not been performed on patients in a private clinic setting due to cost concerns. Serum IgA measurements were performed to rule out a possible IgA deficiency in the measurement of patients' specific antibodies to celiac disease. In addition, tissue transglutaminases were performed with IgA and IgG-type antibody evaluations. Endomysial antibodies were also evaluated along with tissue transglutaminase antibodies to maximize diagnostic accuracy. Endomysial antibodies, dTG onset, dTG first month, dTG third month, and dTG sixth month levels of the patients were evaluated. The cut-off value for tissue transglutaminase enzyme was accepted as 15 U/mL. Patients with diarrhea, constipation, abdominal pain, and bloating symptoms were considered typical celiac patients. Those with extraintestinal symptoms such as growth retardation, inability to gain weight, short stature, vomiting, and anemia were considered atypical. As part of the evaluation of dietary compliance, antibody-negative results and family reports were considered, and patients were classified as following or not following the diet.

Institutional Ethics Review Board approved the study and conducted it following Helsinki Declaration principles with date and number: OMU KAEK 2017/163, 14.04.2017.

### Statistical Analyses

SPSS 21 ® (IBM Corp., Armonk, NY) software was used for statistical analysis. The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/ Shapiro-Wilk tests). Mann Whitney U test was used for non-normally distributed data. Nominal data were given using cross tables, and the difference between groups was compared using Chi-Square and Fisher tests, where appropriate. Mean and standard deviation values were used for numerical data, and frequency and percentage representations were used for categorical data. Whether the numerical data met the parametric distribution criteria was evaluated with the Kolmogorov-Smirnov test. Friedman's non-parametric analysis of variance was used for comparisons of more than two groups, and the Wilcoxon signed-rank test was used for pairwise group comparisons to compare the numerical data among the dependent groups in which the changes over time were evaluated. Wilcoxon signed ranks test with Bonferroni correction was used in post-hoc evaluations where statistical significance was found in multiple group comparisons. In independent group analysis, Kruskal-Wallis non-parametric analysis of variance was used in various groups, the Mann-Whitney U test was used in post-hoc and pairwise group comparisons, and Bonferroni correction was applied in post hoc analyses. A p-value below 0.05 was considered significant for all analyses.

# RESULTS

The study evaluated the data of 122 patients in total. A total of 43 patients (35.2%) were males, and 79 (64.8%) were females. The average age of the study participants was 12.6±5.7 years, ranging from 3 to 22 years of age. The mean age at diagnosis was 8.8 years±5.1 years; the youngest was 1, and the oldest was 18 (Table 1)

At a rate of 41%, abdominal pain was the most frequent complaint of patients, followed by growth retardation (36.1%), diarrhea (34.4%), anemia (32%), inability to gain weight (28.7%), and short stature, respectively. In addition, we observed an increase in abdominal distension (27%), constipation (6.6%), and vomiting (4.9%) symptoms in the patients. The CD was present in the families of three patients (2.5%). The most common comorbid conditions besides CD were iron deficiency anemias (76.1%), vitamin D deficiency (12.3%), and type-1 diabetes (7.4%). Pallor was the most common physical examination finding in 19 patients (15.6%), followed by abdominal distension in 10 patients (8.2%) and dental disorders in 10 patients (8.2%). Based on the dietary characteristics of the patients, it has been found that they were diagnosed and switched to gluten-free diets within an average of 2.6±2.1 months from the time of their admission to the hospital/clinic. The mean diet period of the patients was 48.1±22 months. Dietary compliance was found to be 67.2% among the patients.

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The Antibody Endomysial antibodies (EMA) levels, which reflect the mucosal inflammation severity in CD patients, were negative in 39 patients (32.0%), and +1 to +4 positive in 32 (26.2%), in 16 (13.1%), in 34 (27.9%), in 1 patient (0.8) respectively. A detailed description of the symptoms and clinical findings of the patients is in **Table 1**.

Endoscopic evaluations of the patients revealed the following findings: scalloped appearances in 75 patients (61.5%), edematous appearances in 39 patients (32%), atrophic appearances in 33 patients (27%), and both edematous and atrophic appearances in 17 patients (13.9%). Nodularity was detected in4 patients (3.3%). Twelve patients (9.8%) had no endoscopic findings. Based on the Mars-Oberhuber classification, 1 patient (0.8%) was in stage 1, and 1 patient (0.8%) was in stage 4. **Table 2** presents the endoscopic and clinical findings of pediatric celiac patients in detail.

A comparison between the tissue transglutaminase IgA and IgG values measured before the start of treatment and at the first, third, and sixth months following the diet indicated that both antibodies decreased over time as a consequence of the diet, and these decreases were statistically significant for both antibodies (**Fig. 1**).

Comparing the complaints of patients with and without diet adherence at the beginning of the treatment and the 6th-month controls, it was determined that complaints (except the shortness of the disease (p=0.072), not gaining weight (p=0.305), short stature (p=0.628) and anaemia (p=0.096)) in patients with diet adherence decreased significantly (**Table3**).

We determined that the 3rd month (p=0.014) and 6th month (dTG values in IgA structure were significantly lower in patients with diet compliance (p=0.002) (**Table 4**).

The distribution of symptoms according to the Marsh-Oberhuber classification showed no statistically significant differences (**Table 5**). There was no difference between the patients' ages at diagnosis according to the Marsh-Oberhuber classification (p=0.734). According to the pathological stages of the patients, the IgA-dTG values measured early in the treatment showed a statistically significant increase with the progression of the disease (p=0.011). The distribution of symptoms among the various age groups at diagnosis was examined. It was determined that diarrhea and abdominal distension were observed significantly at the highest rate in children between 0-60 months. In contrast, short stature was markedly observed at the lowest rate in this age group. Other symptoms were distributed similarly between age groups at diagnosis (**Table 6**).

**Table 1.** Evaluation of the patient's demographic, clinical and laboratory data

| **Demographic information** | **Number** |
|---|---|
| Number of patients male/female) number | 122 (43/79) |
| Age (years), mean +SD (min-max) | 12.6±5.7 (3-22) |
| Age of diagnosis (years), mean +SS (min-max) | 8.8±5.1 (1-18) |
| **Application complaints, n (%)** | |
| Stomach ache | 50 (41) |
| growth retardation | 44(36.1) |
| Diarrhea | 42(34.4) |
| Anemia | 39(32) |
| Not gaining weight | 35(28.7) |
| Short stature | 33(27) |
| Abdominal swelling | 21(17.2) |
| Constipation | 8(6.6) |
| Vomiting | 6(4.9) |
| Family history of Celiac disease, n (%) | 3 (2.5) |
| **Presence of additional diseases n (%)** | 90 (73.7) |
| **Diagnostic antibody analysis (EMA), n (%)** | |
| -Negative | 39 (32) |
| +Positive | 32(26.2) |
| ++ positive | 16 (13.1) |
| +++ positive | 34 (27.9) |
| ++++ positive | 1 (0.8) |

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**Table 2.** Endoscopy and histology results of the patients

| Demographic information | |
|---|---|
| **Endoscopic examination, , %** | |
| comb | 75, (61.5%) |
| edematous | 39, (32%) |
| atrophic | 33, (27%) |
| edematous+atrophic | 17, (13.9%) |
| Normal | 12, (9.8%) |
| nodularity | 4, (3.3%) |
| **Mars- Oberhuber classification n%** | |
| one | 1, (0.8%) |
| 2 | 28, (23%) |
| 3 a | 27, (22.1%) |
| 3b | 34, (27.9%) |
| 3c | 31, (25.4%) |
| 4 | 1, (0.8%) |

**Table 3.** Comparison of complaints at the start of treatment and 6th month follow-up in patients with and without diet compliance

| | Dietary compliance (-) (n=40) | | | Dietary compliance (+) (n=82) | | |
|---|---|---|---|---|---|---|
| | Beginning n (%) | 6 months n (%) | p | Beginning n (%) | 6 months n (%) | *p |
| **Diarrhea** | **13 (32.5)** | **4 (10)** | **0.015** | **29 (35.4)** | **7 (8.5)** | **<0.001** |
| **Constipation** | 2 (5) | - | - | 6 (7.3) | - | - |
| **Stomach ache** | **17 (42.5)** | **6 (15)** | **0.007** | **33 (40.2)** | **10 (12.2)** | **<0.001** |
| **Abdominal swelling** | **6 (15)** | **3 (7.5)** | **0.292** | **15 (18.3)** | **6 (7.3)** | **0.036** |
| **growth retardation** | **16 (40)** | **4 (10)** | **0.002** | **28 (34.1)** | **8 (9.8)** | **<0.001** |
| **not gaining weight** | 12 (30) | 8 (20) | 0.305 | **23 (28)** | **12 (14.6)** | **0.037** |
| **short stature** | 13 (32.5) | 11 (27.5) | 0.628 | 20 (24.4) | 11 (13.4) | 0.072 |
| **Vomiting** | 1 (2.5) | - | - | 5 (6.1) | - | - |
| **Anemia** | 11 (27.5) | 5 (12.5) | 0.096 | **28 (34.1)** | **10 (12.2)** | **<0.001** |

**Table 4.** Comparison of dTG values according to dietary compliance of the cases

| | Dietary compliance (-) (n=40) | | | | Dietary compliance (+) (n=82) | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | Cover | SS | min | Max | Cover | SS | min | Max | |
| **dTG - IgA** | | | | | | | | | |
| *Treatment start* | 128.8 | 92.5 | 0.4 | 276 | 120.2 | 88.2 | 1.7 | 278 | 0.63 |
| 1 month | 71.3 | 79.1 | 0.1 | 200 | 60.7 | 77.9 | 0.2 | 207 | 0.3 |
| **3 months** | 48.1 | 70.3 | 0.1 | 200 | **24.6** | **44.5** | **0.2** | **200** | **0.014** |
| **6 months** | 29 | 60.1 | 0.1 | 249 | **9.8** | **27.1** | **0.1** | **200** | **0.002** |
| **dTG - IgG** | | | | | | | | | |
| *Treatment start* | 92.8 | 73.3 | 3 | 200 | 75.9 | 68.8 | 0.6 | 202 | 0.177 |
| 1 month | 59.5 | 72.2 | 1.1 | 200 | 44.2 | 60.7 | 0.4 | 200 | 0.377 |
| 3 months | 26.3 | 47.9 | 0.8 | 200 | 25.8 | 49.6 | 0.6 | 200 | 0.839 |
| 6 months | 15.7 | 42.5 | 0.1 | 200 | 6.8 | 19.4 | 0.1 | 135 | 0.118 |

**Table 5.** Cases Symptom distribution according to the Marsh-Oberhuber classification

| | Stage 1 (n=1) | | Stage 2 (n=28) | | Stage 3a (n=27) | | Stage 3b (n=34) | | Stage 3c (n=31) | | Stage 4 (n=1) | | *p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % | n | % | |
| Diarrhea | - | - | 8 | 28.6 | 9 | 33.3 | 10 | 29.4 | 14 | 45.2 | 1 | 100 | 0.454 |
| Constipation | - | - | 1 | 3.6 | 3 | 11.1 | 1 | 2.9 | 3 | 9.7 | - | - | 0.553 |
| Stomach ache | 1 | 100 | 12 | 42.9 | 14 | 51.9 | 9 | 26.5 | 13 | 41.9 | 1 | 100 | 0.151 |
| Abdominal swelling | - | - | 6 | 21.4 | 3 | 11.1 | 6 | 17.6 | 6 | 19.4 | - | - | 0.848 |
| growth retardation | 1 | 100 | 13 | 46.4 | 6 | 22.2 | 15 | 44.1 | 8 | 25.8 | 1 | 100 | 0.062 |
| not gaining weight | 1 | 100 | 5 | 17.9 | 9 | 33.3 | 12 | 35.3 | 8 | 25.8 | - | - | 0.343 |
| short stature | 1 | 100 | 8 | 28.6 | 5 | 18.5 | 10 | 29.4 | 9 | 29 | - | - | 0.565 |
| Vomiting | - | - | 2 | 7.1 | 1 | 3.7 | 2 | 5.9 | 1 | 3.2 | - | - | 0.949 |
| Anemia | - | - | 6 | 21.4 | 10 | 37 | 14 | 41.2 | 9 | 29 | - | - | 0.560 |

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**Table 6.** Comparison of dTG values of cases according to Marsh-Oberhuber classification

| | Stage 1 (n=1) | Stage 2 (n=28) | | Stage 3a (n=27) | | Stage 3b (n=34) | | Stage 3c (n=31) | | Stage 4 (n=1) | *p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cover | SS | Cover | SS | Cover | SS | Cover | SS | | |
| **dTG - IgA** | | | | | | | | | | | |
| ***Treatment start*** | **23** | 108.7 | 87.1 | **82.7** | 85.3 | **138.3** | 91.2 | **155.1** | 80 | 200 | **0.011** |
| One month | 11th | 56.1 | 77.6 | 61.3 | 79.3 | 72.8 | 82.5 | 66.1 | 77.7 | 68 | 0.748 |
| Three months | 2.3 | 38.9 | 61.2 | 25.2 | 49.9 | 24.1 | 40.1 | 44.5 | 68.9 | 4.2 | 0.424 |
| Six months | 1,2 | 12.6 | 37.9 | 22.5 | 53.3 | 15 | 43.3 | 16.2 | 34.3 | 2 | 0.825 |
| **dTG - IgG** | | | | | | | | | | | |
| *Treatment start* | 9 | 72 | 69.5 | 61.8 | 59.7 | 108.5 | 80.1 | 79.8 | 64.2 | 76 | 0.204 |
| One month | 7.7 | 40.9 | 63.8 | 42.1 | 55.2 | 53.4 | 69.6 | 60.3 | 71.2 | 45 | 0.498 |
| Three months | 6.4 | 25.6 | 47.8 | 19.4 | 40.1 | 28 | 56.1 | 30.6 | 51.4 | 21 | 0.783 |
| Six months | 1 | 11th | 29.9 | 9.8 | 23.7 | 13.5 | 43.3 | 5 | 5.5 | 3.7 | 0.396 |

# DISCUSSION

We evaluated the features of 122 children with CD. The disease is known to be more frequent among females as shown in our study. Clinical features at presentation are very variable. The first onset of the disease coincides with the weaning periods of 6 to 12 months. Atypical CD with a more asymptomatic course can also be seen in older children or adolescents. Although the mean age of diagnosis in our patient group was high, it was observed that approximately one-third of the patients were 3 years or less at diagnosis. The fact that the diagnosis age of our remaining patients was later than the rates reported in the literature may be due to the asymptomatic course in childhood. In one of the studies conducted in our country to evaluate celiac patients by Soylu et al. retrospectively analyzed 37 celiac patients and stated that the mean age at diagnosis was 7.5±4.7 years. The age range at diagnosis was between 1 and 16.3 years (10). Another study on this subject by Dinler et al. on celiac patients who were followed up in the Pediatric Gastroenterology department of Ondokuz Mayıs University between 2000 and 2007 (11). According to the results of the study, it was reported that the mean age at diagnosis was 8.2 years and ranged from 1 to 18 years (8). Many studies show that CD is more common in girls than in boys (11, 12). Our findings show similar characteristics in terms of gender distribution with studies conducted in the Turkish population may be due to a common genetic background (10, 11). It is known that the clinical presentation of CD can spread to a wide range. In the literature, it has been reported that diarrhoea, growth retardation, and short stature are the predominant symptoms at presentation in childhood patients. Other frequently observed symptoms include anorexia, muscle wasting, apathy, abdominal distension, irritability, and vomiting (13). In children with celiac disease, non-gastrointestinal symptoms such as short stature, refractory iron deficiency anaemia, hair loss, and headache without any gastrointestinal complaints are defined as atypical presentation. These symptoms mostly appear after 5-6 years of age. A study by Telega et al. reported that more than half of the patients diagnosed after age seven presented with an atypical presentation (14).

In our patient group, consistent with the literature, it was determined that the symptoms related to the gastrointestinal tract were prominent. Still, extraintestinal symptoms such as growth retardation and short stature were also observed in some patients. When the typical/atypical symptoms of our patient group were evaluated, typical symptoms were observed in 65.1% of boys and 64.6% of girls, 34.9% of boys and 35.4% of girls had atypical symptoms, and typical symptoms in both genders /atypical symptom rates were found to be similar. Similarly, in the guideline published by the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition for the diagnosis and treatment of CD in children, it was stated that the most common findings of CD are related to the gastrointestinal system (15, 16). When the studies conducted in our country were examined, Soylu et al. reported that the most common symptoms in children with CD were abdominal pain, abdominal swelling, and diarrhea, which were seen in approximately 60% of the patients (10).

In our study, the evaluations we made regarding the gluten-free diet regimens that the patients started after the diagnosis determined that the diet was applied for an average of 48 months, and 67% of the patients had diet compliance. In this regard, there are different studies in the literature on the dietary compliance of patients. Ramirez-Cervantes et al. evaluated adherence to a gluten-free diet in a study conducted by Mexican celiac patients. It was reported that the rate of those who strictly followed the gluten-free diet in the patient group was 57.5%. Still, although they adhered to the diet, approximately 40% of the patients were inevitably exposed to gluten-containing foods (17). Taghdir et al evaluated the compliance of Iranian pediatric and adolescent celiac patients with a gluten-free diet. It has been reported that they take the food (18).

When the factors affecting diet compliance were examined in the study, it was determined that the dietary compliance of men, patients with a family history of CD and those living in large families was lower. Dietary compliance was evaluated in the celiac patient group comprising 17 children and 13 adolescents, and it was found that 76.5% of the patients in the pediatric age group and 69.2% of the patients in the adolescent age group adhered to a gluten-free diet (19). Our study observed that the diet compliance rates in the patient

group whose data were analyzed were generally similar to those in the literature. Comparing the demographic characteristics of our patients with and without diet compliance, it was determined that there was no significant difference. When we compared the Marsh stage, which indicates the severity of the disease, between patients with and without diet compliance, it was found that there was no statistically significant relationship. However, although a statistical relationship was not detected, it was seen in the analyses that there was a decrease in dietary adherence rates as the Marsh stage increased. In the literature review, no study evaluated the relationship between diet compliance and disease stage in patients with celiac disease. Our current findings determined that the complaints other than short stature at the 6th-month follow-up of our patients with diet compliance showed a statistically significant regression compared to the evaluations made at the beginning of the treatment. In patients who did not comply with the diet, complaints other than not gaining weight, short stature, and anemia were similarly significantly regressed. At the beginning of the treatment, patients who were non-compliant with the diet had a lower incidence of diarrhea, constipation, abdominal pain, abdominal distention, growth retardation, short stature, inability to gain weight, vomiting, and anemia compared to those who were compliant. However, in the follow-up controls, there was no significant difference in the incidence of these complaints between the two groups. As a result of longer follow-ups of our patients, more comprehensive results can be obtained about the factors that may affect their dietary compliance.

In our study, we investigated the relationship between disease severity and serological markers. We observed that both endomysial and tissue transglutaminase antibodies in IgA and IgG structures tended to increase in parallel with histological deterioration. Still, only tissue transglutaminase in IgA structure showed a statistically significant increase. Dalgic et al. In the study performed by IgA, it was reported that tissue transglutaminase levels in the IgA structure increase as the Marsh-Oberhuber stage progresses (20). This increase is also more pronounced in patients with positive endomysial antibodies in the IgA structure (20).

In our study, when the dTG values of the patients were compared according to the Marsh stages, it was determined that only the dTG values in the IgA structure in the initial measurements showed a statistically significant difference. Accordingly, it was determined that dTG values increased significantly in parallel with the increase in the disease stage. The difference between dTG values according to the disease stage disappeared with the transition to a gluten-free diet. Different studies in the literature evaluate the relationship between dTG values and disease stage. A study reported that dTG values that were increased 11.4 times the normal value had a positive predictive value of 98.6% for villous atrophy in the gastrointestinal mucosa (21). In another study conducted by Marsh, it was determined that 93% of patients with marsh stage 3 disease had anti-dTG levels above 76 U/ml, and all patients with anti-dTG values above 200 were found to be marsh 3 (22). Another study by Emami et al. on dTG reported that the sensitivity of dTG values predicting marsh stage 3 CD was 80% (23). Accordingly, anti-dTG antibodies with a titer of 62.5 U/mL have a sensitivity of 95.4% and a specificity of 98%. In our study, a decrease to normal was found in dTG values in accordance with the information in the literature. Although biopsy is not routinely used for histological confirmation of mucosal healing, patients still require close monitoring and periodic serology evaluations. When dTG values of patients with and without diet adherence were measured during our follow-ups, it was determined that the dTG values at the 3rd and 6th months were statistically significantly lower in the patient group with diet adherence. This agrees with the results obtained in previous studies in the literature. Accordingly, we think that dTG measurements in the IgA structure will be helpful in the follow-up of the disease.

Our study found no significant difference in dTG levels or Marsh disease stages between patients who used and did not use flour when transitioning to solid food. However, endoscopic evaluations revealed a higher incidence of atrophic + edematous appearance in patients who used flour during the transition.The literature has reported that the duration of exposure to gluten is associated with the development process of autoimmune diseases (24). Studies have reported that continuing breast milk for a long time and switching to complementary foods are beneficial (15). It is recommended to switch to supplementary foods with cereals between the fourth and seventh months while breastfeeding (25, 26). Preferring foods with rice during this transition may be beneficial in delaying the encounter with gluten. According to the findings of our study, considering that the patients who use flour during the transition to solid food are exposed to gluten for a longer time, the fact that the edematous + atrophic appearance was detected in the endoscopy can be interpreted as an indicator of more advanced histopathological damage in these children. The main limitation of our study is that although all patients with CD were reached, it was carried out retrospectively.

# CONCLUSION

In conclusion, our study found and verified that gastrointestinal symptoms and growth retardation were the most common presenting symptoms of celiac disease in childhood. Early diagnosis of CD is critical to prevent long-term complications; currently, the only effective treatment is a lifelong gluten-free diet.

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# REFERENCES


1. Decker E, Hornef M, Stockinger S. Cesarean delivery is associated with celiac disease but not inflammatory bowel disease in children. Gut microbes. 2011;2(2):91-8.
2. Onur T, Karaca Ü, Çelik MG. Use of Cerebral Oximetry in Elective Cesarean Section Procedures Performed Under Spinal Anesthesia: A Randomized Prospective Study. Medical Bulletin of Haseki/Haseki Tip Bulteni. 2021;59(1).
3. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. Gastroenterology. 2001;120(3):636-51.
4. Caio G, Volta U, Sapone A, Leffler DA, De Giorgio R, Catassi C, et al. Celiac disease: a comprehensive current review. BMC medicine. 2019;17(1):1-20.
5. Cichewicz AB, Mearns ES, Taylor A, Boulanger T, Gerber M, Leffler DA, et al. Diagnosis and treatment patterns in celiac disease. Digestive diseases and sciences. 2019;64(8):2095-106.
6. Oxentenko AS, Rubio-Tapia A, editors. Celiac disease. Mayo Clinic Proceedings; 2019: Elsevier.
7. Karasu D, Karaca U, Ozgunay SE, Yilmaz C, Yetik F, Ozkaya G. The frequency of emergence delirium in children undergoing outpatient anaesthesia for magnetic resonance imaging. International Journal of Clinical Practice. 2021;75(11):e14763.
8. Kuloğlu Z. Çölyak hastalığı. Türkiye Çocuk Hastalıkları Dergisi. 2014;8(2):105-11.
9. Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Archives of disease in childhood. 1976;51(3):170-9.
10. Soylu Ö, Ecevit ÖÇ. Clinical evaluation of cases followed-up for celiac disease. Journal of Dr Behcet Uz Children's Hospital. 2013;3(1):38-43.
11. Dinler G, Atalay E, Kalaycı AG. Celiac disease in 87 children with typical and atypical symptoms in Black Sea region of Turkey. World Journal of Pediatrics. 2009;5(4):282-6.
12. Megiorni F, Mora B, Bonamico M, Barbato M, Montuori M, Viola F, et al. HLA-DQ and susceptibility to celiac disease: evidence for gender differences and parent-of-origin effects. Official journal of the American College of Gastroenterology| ACG. 2008;103(4):997-1003.
13. Tokgöz Y, Terlemez S, Karul A. Fat soluble vitamin levels in children with newly diagnosed celiac disease, a case control study. BMC pediatrics. 2018;18(1):1-5.
14. Telega G, Bennet TR, Werlin S. Emerging new clinical patterns in the presentation of celiac disease. Archives of pediatrics & adolescent medicine. 2008;162(2):164-8.
15. Hill ID, Dirks MH, Liptak GS, Colletti RB, Fasano A, Guandalini S, et al. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Journal of pediatric gastroenterology and nutrition. 2005;40(1):1-19.
16. Karaca Ü, Karasu D, Eminoğlu Ş, Özgünay ŞE, Onur T, Kılıçarslan N. Evaluation of state and trait anxiety levels in adolescents undergoing endoscopy under anesthesia: A prospective study. 2022.
17. Ramírez-Cervantes KL, Romero-López AV, Núñez-Álvarez CA, Uscanga-Domínguez LF. Adherence to a gluten-free diet in Mexican subjects with gluten-related disorders: a high prevalence of inadvertent gluten intake. Revista de Investigación Clínica. 2017;68(5):229-34.
18. Taghdir M, Honar N, Mazloomi SM, Sepandi M, Ashourpour M, Salehi M. Dietary compliance in Iranian children and adolescents with celiac disease. Journal of Multidisciplinary Healthcare. 2016;9:365.
19. Esenyel S, Ünal F. Depression and anxiety in child and adolescents with follow-up celiac disease and in their families. 2014.
20. Dalgic B, Sari S, Basturk B, Ensari A, Egritas O, Bukulmez A, et al. Prevalence of celiac disease in healthy Turkish school children. Official journal of the American College of Gastroenterology| ACG. 2011;106(8):1512-7.
21. Rahmati A, Shakeri R, Sohrabi M, Alipour A, Boghratian A, Setareh M, et al. Correlation of tissue transglutaminase antibody with duodenal histologic marsh grading. Middle East journal of digestive diseases. 2014;6(3):131.
22. Ganji A, Esmaeilzadeh A, Bahari A, Ghafarzadegan K, Aghayee MA, Mozafari HM, et al. Correlation between cut-off level of tissue transglutaminase antibody and marsh classification. Middle East Journal of Digestive Diseases. 2016;8(4):318.
23. Emami MH, Karimi S, Kouhestani S, Hashemi M, Taheri H. Diagnostic accuracy of IgA anti-tissue transglutaminase in patients suspected of having coeliac disease in Iran. J Gastrointestin Liver Dis. 2008;17(2):141-6.
24. Bibbò S, Pes GM, Usai-Satta P, Salis R, Soro S, Colosso BMQ, et al. Chronic autoimmune disorders are increased in coeliac disease: a case–control study. Medicine. 2017;96(47).
25. Cosnes J, Cellier C, Viola S, Colombel JF, Michaud L, Sarles J, et al. Incidence of autoimmune diseases in celiac disease: protective effect of the gluten-free diet. Clinical Gastroenterology and Hepatology. 2008;6(7):753-8.
26. Viljamaa M, Kaukinen K, Huhtala H, Kyrönpalo S, Rasmussen M, Collin P. Coeliac disease, autoimmune diseases and gluten exposure. Scandinavian journal of gastroenterology. 2005;40(4):437-43.