KASTAMONU MEDICAL JOURNAL

Original Article

DOI: 10.51271/KMJ-0171

Kastamonu Med J. 2024;4(4):196-199.

A comprehensive analysis of demographics, comorbidities, and laboratory findings in adult celiac disease patients: a single center experience

İbrahim Ethem Güven[1], Batuhan Başpınar[2]

[1]*Department of Gastroenterology, Yenimahalle Training and Research Hospital, Ankara, Turkiye*
[2]*Department of Gastroenterology, Prof. Dr. Alaeddin Yavaşça State Hospital, Kilis, Turkiye*

Received: 16/09/2024 ◆ **Accepted**: 01/10/2024 ◆ **Published**: 01/12/2024

ABSTRACT

Aims: This study aims to evaluate the demographics, comorbidities, and laboratory findings of patients with Celiac disease in our clinic.

Methods: A total of 91 celiac patients who were followed in our centre between January 2020 and September 2023 were included in the study. Demographic, laboratory and comorbidities data were analysed retrospectively.

Results: 72 (79.1%) patients were female, and the mean age of the participants was 42.3±15.1 years. Deficiency of iron was observed in 46 (50.6%) participants, vitamin B12 in 9 (9.9%) participants, folat in 11 (12.1%) participants, and vitamin D in 37 (40.7%) participants. Hypothyroidism and diabetes mellitus were found to be the two most common comorbidities of celiac disease. In addition, liver enzymes were demonstrated to be elevated in the 9 (9.9%) patients.

Conclusion: Celiac disease is associated with mineral and vitamine deficiency. In addition, mildly elevated liver enzymes may be observed in the clinical course. Notably, extraintestinal manifestations, especially hypothyroidism and diabetes, may accompany the disease.

Keywords: Celiac disease, iron deficiency, hypothyroidism, autoimmune disease

INTRODUCTION

Celiac disease (CD) is a chronic autoimmune condition triggered by the consumption of gluten, primarily affecting the small intestine.[1] In genetically predisposed individuals, gluten intake leads to inflammation, villous atrophy, and subsequent malabsorption of key nutrients.[2] The clinical presentation of CD can vary widely, from classic gastrointestinal symptoms like diarrhea and abdominal pain to more subtle signs due to malabsorption of nutrients such as anemia, osteoporosis etc.[3] Due to the lack of disease-specific signs and symptoms, along with the presence of asymptomatic patients, the diagnosis of CD is frequently delayed.[4]

The diagnosis of CD is typically established through a combination of serological tests and histopathological examination of duodenal biopsies. The presence of specific antibodies, such as anti-endomysium IgA, tissue transglutaminase IgA, and anti-gliadin IgA, is indicative of CD and is used as a preliminary screening tool.[4] Confirmatory diagnosis is made using the Marsh-Oberhuber classification, where patients with Marsh 3 pathology (showing villous atrophy) are diagnosed with CD.[5]

In addition to gastrointestinal involvement, CD is associated with a range of comorbid conditions, particularly other autoimmune diseases.[6] The relationship between CD and conditions like autoimmune thyroid disease, type 1 diabetes, and rheumatoid arthritis suggests a broader systemic immune dysregulation in these patients.[7] The aim of this study is to provide a detailed analysis of the demographic characteristics, comorbid conditions, serological markers, and laboratory findings in a cohort of adult patients diagnosed with CD at a tertiary medical center in Ankara, Turkiye.

METHODS

The presented study was a retrospective study conducted in Gastroenterology Unit of Yenimahalle Training and Research Hospital, a tertiary medical center in Ankara, Turkiye. All adult patients diagnosed with CD between January 2020-Semptember 2023 were included in the study. Patients with malignancy, severe chronic liver and kidney diseases, altered GI anatomy, and younger than 18 years old were excluded. In addition, patients with missing data were also

Corresponding Author: İbrahim Ethem Güven, drethemg@gmail.com

Cite this article as: Güven İE, Başpınar B. A comprehensive analysis of demographics, comorbidities, and laboratory findings in adult celiac disease patients: a single center experience. *Kastamonu Med J.* 2024; 4(4):196-199.

excluded. This study was conducted in accordance with the principles of the Declaration of Helsinki, reviewed ethically, and approved by the Medical and Health Researches Ethics Committee of Yenimahalle Training and Research Hospital (Date: 22.11.2023, Decision No: E-2023-60). Informed consent was not required due to the retrospective nature of the study.

Demographic data, comorbidity status, Celiac serology, laboratory results such as liver enzymes, lipid profiles, parameters for vitamin and iron deficiency, renal and thyroid function were collected from the electronic and printed files of the patients.

The diagnosis of CD was made based on the GI endoscopy with duodenal biopsy due to suspicion of CD or other indications.

Cut-off values for vitamin and iron deficiency was determined as 200 pg/ml for vitamin B12, 4 ng/ml for folate, 20 ng/mL for vitamin D, 15% for transferrin saturation and 20 ml/ng for ferritin levels. The values below the cut-off level were considered as deficiency for the corresponding parameter. Both for alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, cut-off was considered as 35 U/L. Serologic parameters such as anti-endomysium IgA, tissue transglutaminase IgA, and anti-gliadin IgA was recorded as either positive or negative. Selective IgA deficiency was excluded by confirming that the patients' total IgA levels were within the normal range.

Statistical Analysis

Statistical analysis was performed using 24th version of Statistical Package for the Social Sciences (SPSS; IBM SPSS Statistics, United States). Categorical variables were described using as numbers and percentages. For continuous variables were tested with the Kolmogorov–Smirnov test for scattering pattern. Data were presented as median and standard deviation for continues variables with normal distribution, and median and minimum-maximum values (min-max) for non-parametric values. No comparative statistical analysis was performed in the study.

RESULTS

A total of 91 participants were included in the study, of whom 72 (79.1%) were female. The mean age of the participants was 42.3±15.1 years, and the median disease duration was 11.1 years, ranging from 1 to 42 years. The mean body-mass index (BMI) was 25.3±2.0 kg/m². Comorbid disease profiles were given in Table 1 with other demographic features. Of the study population, hypothyroidism was the most common comorbidity, observed in 18 (19.8%) participants. Other comorbidities included diabetes mellitus in 6 (6.6%) participants, Sjögren's disease in 3 (3.3%) participants, asthma and rheumatoid arthritis in 2 (2.2%) participants each, and inflammatory bowel disease, familial Mediterranean fever, and Graves' disease in 1 (1.1%) participant each.

The serological test results for celiac disease were given in Table 1. Anti-endomysium IgA antibody positivity was observed in 60 (65.9%) participants. Tissue transglutaminase IgA antibodies were positive in 71 (78.0%), and anti-gliadin IgA antibodies were detected in 49 (53.9%) participants.

Laboratory results other than serology for Celiac disease were given in Table 2. The median hemoglobin level was 13.1 g/dl (range: 8.6-16.5), and the median white blood cell count was 6.2×10³/µl (range: 3.3-13.5). Platelet counts had a median of

Table 1. Demographic characteristics, comorbid diseases and celiac test results of the participants

Parameter	n=91
Sex (female), n (%)	72 (79.1)
Age, mean (SD)	42.3 (15.1)
Disease duration, years, median (min-max)	11.1 (1.0-42.0)
BMI, kg/m², mean (SD)	25.3 (2.0)
Anti-endomysium IgA	
Negative, n (%)	31 (34.1%)
Positive, n (%)	60 (65.9%)
Tissue transglutaminase IgA	
Negative, n (%)	20 (22.0%)
Positive, n (%)	71 (78.0%)
Anti-gliadin IgA	
Negative, n (%)	42 (46.1%)
Positive, n (%)	49 (53.9%)
Comorbid disease	
Hypothyroidism, n (%)	18 (19.8%)
Diabetes mellitus, n (%)	6 (6.6%)
Sjögren disease, n (%)	3 (3.3%)
Asthma, n (%)	2 (2.2%)
Rheumatoid arthritis, n (%)	2 (2.2%)
Inflammatory bowel disease, n (%)	1 (1.1%)
Famillial mediterranean fewer, n (%)	1 (1.1%)
Graves disease, n (%)	1 (1.1%)

SD: Standard deviation, BMI: Body-mass index, IgA: Selective immunoglobulin A

Table 2. Laboratory results of the participants

Hemoglobin (g/dl), median (min-max)	13.1 (8.6-16.5)
White blood cell count (×103/µl), median (min-max)	6.2 (3.3-13.5)
Platelet (×103/µl), median (min-max)	283.0 (145.0-550.0)
Ferritin (ml/ng), median (min-max) <20 ml/ng, n (%)	17.7 (2.0-158.0) 46 (50.6%)
Transferrin saturation (%), median <15%, n (%)	18.0 (1.0-120.0) 38 (41.8%)
Vitamin B12 (pg/ml), median (min-max) <200 pg/ml, n (%)	319.0 (130.0-924.0) 9 (9.9%)
Folate (ng/ml), median (min-max) <4 ng/ml, n (%)	8.0 (1.5-44.0) 11 (12.1%)
Vitamin D (ng/ml), median <20 ng/ml, n (%)	22.0 (4.0-49) 37 (40.7%)
ALT (U/L), median (min-max) >35 U/L, n (%)	17.1 (5.0-83.0) 9 (9.9%)
AST (U/L), median >35 U/L, n (%)	20.0 (12.0-80.0) 7 (7.7%)
Creatinine (mg/dl), mean (SD)	0.70 (0.19)
Albumin (g/dl), mean (SD)	4.13 (0.23)
Calcium (mg/dl), mean (SD)	9.58 (0.51)
TSH (mIU/L), median (min-max)	2.0 (0.01-65.0)
Total cholesterol (mg/dl), mean (SD)	181.3 (39.6)
Triglyceride (mg/dl), median (min-max)	124.0 (45.0-459.0)
HDL (mg/dl), mean (SD)	50.9 (12.7)
LDL (mg/dl), mean (SD)	104.4 (37.1)
Glucose (mg/dl), mean (SD)	86.4 (12.2)

Min: Minimum, Max: Maximum, SD: Standard deviation, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, TSH: Thyroid-stimulating hormone, HDL: High density lipoprotein, LDL: Low density lipoprotein

283.0×10³/µl (range: 145.0-550.0). The median ferritin value of the study population was 17.7 ng/ml (range: 2.0-158.0) for ferritin and 18.0% (range: 1.0-120.0) for transferrin saturation. While ferritin levels were below 20 ng/ml in 46 (50.6%) participants, transferrin saturation was below 15% in 38 (41.8%) participants. The median (min-max) levels of vitamin B12, folate and vitamin D were 319.0 pg/ml (130.0-924.0), 8.0 ng/ml (1.5-44.0), and 22.0 ng/ml (4.0-499.0), respectively. Among the study population, 9 (9.9%) participants had vitamin B12 levels below 200 pg/ml, 11 (12.1%) participants had folate levels below 4 ng/ml, and 37 (40.7%) participants had vitamin D levels below 20 ng/ml.

The median ALT level was 17.1 U/L (range: 5.0-83.0), and 9 participants (9.9%) had ALT levels above 35 U/L. The median aspartate aminotransferase (AST) level was 20.0 U/L (range: 12.0-80.0), with 7 participants (7.7%) having elevated AST levels. Creatinine levels had a mean of 0.70±0.19 mg/dl albumin levels had a mean of 4.13±0.23 g/dl, and calcium levels had a mean of 9.58±0.51 mg/dl. The median thyroid-stimulating hormone (TSH) level was 2.0 mIU/L, ranging in between 0.01 and 65. The mean total cholesterol level was 181.3±39.6 mg/dl, the median triglyceride level was 124.0 mg/dl (range: 45.0-49.0), and the mean HDL cholesterol level was 50.9±12.7 mg/dl. The mean LDL cholesterol level was 104.4±37.1 mg/dl. The mean glucose level was 86.4±12.2 mg/dl.

DISCUSSION

This study demonstrated that CD is associated with iron deficiency and vitamin deficiency including vitamin B12, folat, and vitamin D. Notably, it has also been demonstrated that many chronic inflammatory diseases may accompany CD.

In this study, the study population is predominantly female with a rate of 79.1%. According to the literature, it has been also observed that celiac disease is predominantly female in gender distribution, thus our findings is consistent with the literature.[8] The predominance of the female population in celiac disease suggests an autoimmune basis for the disease.[9] This autoimmune background also explains the occurrence of other autoimmune and inflammatory diseases in the clinical course of celiac disease.[10,11] In this study, hypothyroidism and diabetes mellitus were found to be the two most common comorbidities with a rate of 19.8% and 6.6%, respectively. This result is consistent with the findings of Freeman et al.,[12] which also demonstrated that the most common comorbid disease are hypothyroidism and diabetes mellitus in patients with CD. Although the rate was low in the study, it is noteworthy that autoimmune and inflammatory diseases such as Sjögren's disease, asthma, rheumatoid arthritis, IBD, inflammatory bowel disease, famillial mediterranean fewer and Graves' disease were also observed in some patients. However, the comorbidities associated with CD are not limited to our findings but can also be accompanied by many extraintestinal manifestations.

CD disease mainly involves small intestine. The chronic inflammatory condition caused by gluten sensitivity leads to damage to small intestinal cells. This damage causes disruption of the architecture of the villus structure and consequently malabsorption of key nutrients.[13] In this study, iron deficiency was observed in 46 (50.6%) participants according to ferritin results, and in 38 (41.8%) participants according to transferrin saturation results. The second most common deficiency was found in vitamin D with a rate of 40.7%. Folat and vitamin B12 deficiency was also absorved in participants with a rate of 12.1% and 9.9%, respectively. This study demonstrated that majority of the participants has vitamine and mineral deficiency. It should be emphasised that the literature shows that subclinical inflammation may persist even in diet-compliant patients.[14] Therefore, all patients should be screened for vitamin and mineral deficiencies in clinical controls, regardless of dietary compliance.

Another important finding of the current study was high ALT and AST levels with a rate of 9.9% and 7.7%, respectively. Previous studies have also shown that mild elevation of liver enzymes can be observed in celiac patients.[15,16] These findings emphasise the importance of the possibility of celiac disease in the etiology of patients investigated with elevated liver enzymes. In addition, it has been shown that in some patients a gluten-free diet induces normalisation of liver enzymes, so patients should be monitored in this respect.[17]

Limitations

The major limitation of the present study is its retrospective design. In addition, the study has a relatively small sample size since it is a single center study. Lastly, the effects of dynamic dietary adaptation changes on these data could not be analyzed.

CONCLUSION

In conclusion, this study demonstrated that vitamin and mineral deficiencies are present in the majority of patients with celiac disease. In addition, inflammation in celiac disease is not limited to the small intestine and may be accompanied by various inflammatory and autoimmune diseases in the clinical course of the disease.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Medical and Health Researches Ethics Committee of Yenimahalle Training and Research Hospital (Date: 22.11.2023, Decision No: E-2023-60).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Caio G, Volta U, Sapone A, et al. Celiac disease: a comprehensive current review. *BMC Med.* 2019;17(1):142.
2. Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology guidelines update: diagnosis and management of celiac disease. *Am J Gastroenterol.* 2023;118(1):59-76.
3. Guandalini S, Assiri A. Celiac disease: a review. *JAMA Pediatr.* 2014;168(3): 272-278.
4. Lebwohl B, Rubio-Tapia A. Epidemiology, presentation, and diagnosis of Celiac disease. *Gastroenterology.* 2021;160(1):63-75.
5. Husby S, Murray JA, Katzka DA. AGA clinical practice update on diagnosis and monitoring of celiac disease-changing utility of serology and histologic measures: expert review. *Gastroenterology.* 2019;156(4):885-889.
6. Therrien A, Kelly CP, Silvester JA. Celiac disease: extraintestinal manifestations and associated conditions. *J Clin Gastroenterol.* 2020;54(1): 8-21.
7. Durazzo M, Ferro A, Brascugli I, Mattivi S, Fagoonee S, Pellicano R. Extra-intestinal manifestations of celiac disease: what should we know in 2022? *J Clin Med.* 2022;11(1):258.
8. Jansson-Knodell CL, King KS, Larson JJ, Van Dyke CT, Murray JA, Rubio-Tapia A. Gender-based differences in a population-based cohort with celiac disease: more alike than unalike. *Dig Dis Sci.* 2018;63(1):184-192.
9. Parzanese I, Qehajaj D, Patrinicola F, et al. Celiac disease: from pathophysiology to treatment. *World J Gastrointest Pathophysiol.* 2017; 8(2):27-38.
10. Aboulaghras S, Piancatelli D, Oumhani K, Balahbib A, Bouyahya A, Taghzouti K. Pathophysiology and immunogenetics of celiac disease. *Clin Chim Acta.* 2022;528:74-83.
11. Laurikka P, Nurminen S, Kivelä L, Kurppa K. Extraintestinal manifestations of Celiac disease: early detection for better long-term outcomes. *Nutrients.* 2018;10(8):1015.
12. Freeman HJ. Endocrine manifestations in celiac disease. *World J Gastroenterol.* 2016;22(38):8472-8479.
13. Wierdsma NJ, van Bokhorst-de van der Schueren MA, Berkenpas M, Mulder CJ, van Bodegraven AA. Vitamin and mineral deficiencies are highly prevalent in newly diagnosed celiac disease patients. *Nutrients.* 2013;5(10):3975-3992.
14. Cardo A, Churruca I, Lasa A, et al. Nutritional imbalances in adult celiac patients following a gluten-free diet. *Nutrients.* 2021;13(8):2877.
15. Villavicencio Kim J, Wu GY. Celiac disease and elevated liver enzymes: a review. *J Clin Transl Hepatol.* 2021;9(1):116-124.
16. Beenet L, Tonesi D. Celiac disease and elevated liver enzymes: a still not fully defined pathogenesis. *J Clin Transl Hepatol.* 2021;9(2):274-275.
17. Casella G, Antonelli E, Di Bella C, et al. Prevalence and causes of abnormal liver function in patients with coeliac disease. *Liver Int.* 2013;33(7):1128-1131.