Bone Mineral Density Screening and the Frequency of Osteopenia/Osteoporosis in Turkish Adult Patients With Celiac Disease

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ABSTRACT

Background: *The aim of this study was to evaluate the prevalence of osteopenia and osteoporosis in adult patients with celiac disease (CD) at diagnosis and/or in the follow-up after a gluten-free diet (GFD).*

Methods: *Adult patients diagnosed with CD were retrospectively screened through follow-up records and computer databases. Patients assessed by dual-energy X-ray absorptiometry (DEXA) at diagnosis and/or in the follow-up after a GFD were included in the study.*

Results: *One hundred patients who underwent a DEXA scan at least once after diagnosis or after being on a GFD were included in the study. The mean age of the patients at diagnosis was 34.61 ± 10.3 years, and 84% of the patients (n = 84) were female. At the time of diagnosis (n = 46), the prevalence of osteopenia and osteoporosis was 67.3% and 15.2%, respectively, at the lumbar spine, and 43.4% and 10.8%, respectively, at the femur. After a GFD (n = 78), the prevalence of osteopenia and osteoporosis was 61.5% and 8.9%, respectively, at the lumbar spine, and 37.1% and 2.5%, respectively, at the femur.*

Conclusion: *The prevalence of CD patients with low bone mineral density (BMD) is high after diagnosis and in the follow-up after a GFD. It is important for all patients with CD to undergo a DEXA scan to determine the follow-up and/or treatment characteristics.*

Keywords: *Celiac disease, bone mineral density, osteopenia, osteoporosis*

INTRODUCTION

Celiac disease (CD), triggered by gluten, occurs in genetically predisposed individuals. It is characterized by chronic intestinal mucosal inflammation and villous atrophy, and causes damage to the absorption function of the small intestine.[1] The typical and atypical form of the disease may be accompanied by many extraintestinal manifestations.[2] Osteomalacia, osteopenia, and osteoporosis can be the presenting features or the extraintestinal manifestations of CD.

Calcium and vitamin D deficiency can lead to secondary hyperparathyroidism, which is considered to be the main reason for osteopenia and osteoporosis in patients with CD.[3] The prevalence of osteoporosis in CD was reported at highly variable ranges (6-70%), and the presence of osteoporosis was found to be associated with an increase in the risk of bone fractures.[4]

Although it is recommended to evaluate the bone mineral density (BMD) at diagnosis or in the follow-up, there is no consensus on screening time with dual-energy X-ray absorptiometry (DEXA).[5] On the other hand, some real-life data found in the literature revealed that a substantial portion of patients with CD were not screened with DEXA.[6,7]

As far as we know, there are no data on the prevalence of osteopenia and osteoporosis in adult patients with CD in our country. The different genetic and environmental factors in each cohort, as well as the diagnostic features of CD, may affect bone health. Therefore, it is crucial to know the frequency of osteopenia/osteoporosis in our CD patients. Additionally, the evaluation of the frequency of osteopenia and osteoporosis in patients without well-known osteoporosis risk factors such as advanced age and menopause may be useful in determining screening strategies.

The aim of this study was to evaluate the prevalence of osteopenia and osteoporosis in patients with CD at diagnosis and in the follow-up after a gluten-free diet (GFD).

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MATERIALS AND METHODS

The follow-up files and the hospital's computer database records of the patients who were diagnosed with CD between January 2010 and December 2019 were evaluated retrospectively. Patients assessed by DEXA at diagnosis and/or in the follow-up after a GFD were included in the study.

A diagnosis of CD was made when an individual was positive for tissue transglutaminase immunoglobulin A (t-TGA) and/or endomysium immunoglobulin A (EMA), and demonstrated findings of at least Marsh grade II upon duodenal biopsy. Patients who were assessed by DEXA within 3 months before or after the diagnosis were considered "screened at the time of diagnosis," and those who underwent a DEXA scan at any time (at the 12th month at the earliest) after the GFD were considered "screened after a GFD." In patients screened after a GFD, the follow-up period was accepted as the time from the date of first diagnosis until the last DEXA scan date (month).

Osteoporosis was diagnosed when a patient had a T score ≤−2.5 at any localization, osteopenia was diagnosed when a patient was within the range of −1> T score >−2.5, and normal BMD was diagnosed when a patient had a T score ≥−1.[8] In addition, patients who did not have normal BMD according to the T score were defined as having low BMD. Furthermore, patients were analyzed according to the Z score (Z score <−2 or Z score ≥−2). A Z score <−2 was defined as low bone mass.[9]

Of the patients screened at the time of diagnosis, demographic characteristics (age/sex), body mass index (BMI), clinical presentation features, duodenal histopathology findings according to the Marsh classification, t-TGA and/or EMA status, menopausal status, habits of smoking or alcohol consumption, the total lumbar (L2-4) and femoral BMD values, and the T and Z scores identified by the DEXA scan were recorded.

Of the patients screened after a GFD, clinical presentation features (age/sex) and duodenal histopathology findings according to Marsh classification at the time of diagnosis were recorded. In addition, at the end of the follow-up period, the BMI, t-TGA, and/or EMA status, GFD compliance assessed by dietary history, menopausal status, smoking and drinking habits, treatments received for osteopenia or osteoporosis, the total lumbar (L2-4) and femoral BMD, and T and Z scores identified by the DEXA scan were recorded.

Patients diagnosed under the age of 17, patients with a negative t-TGA and/or EMA status at the time of diagnosis, those who had a history of steroid and levothyroxine use or endocrine disorders (hyperthyroidism, untreated hypothyroidism, hypogonadism, Cushing disease, primary hyperparathyroidism, diabetes mellitus), and patients with a malignant disease were excluded from the study.

Premenopausal women and male patients under the age of 50 years were defined as subgroups. The frequency of osteopenia and osteoporosis were analyzed.

The research was approved by the Local Ethics Committee dated April 14, 2020 and numbered B10.1.TKH.4.34.H.GP.0.01/90.

Statistical Analysis

The patients' data were analyzed with the SPSS 25.0 program. Descriptive information about the demographic features of the patients was presented as the mean (median for those without normal distribution), frequency, and percentage. The distribution of data according to the number of samples was evaluated by the Shapiro–Wilk and Kolmogorov–Smirnov tests. The mean of continuous variables found to be normally distributed was compared with the Student's *t*-test, and the mean of non-normally distributed variables was compared with the Mann–Whitney *U*-test. Paired *t*-tests for normally distributed data and the Wilcoxon signed-rank tests for non-normally distributed data were used for comparison of repeated measurement values. Chi-squared test and Fisher's exact test were used to compare categorical data. The statistical significance level (*P* value) was accepted as <.05, and the results are given within a 95% CI.

RESULTS

A total of 75.5% (n = 105) of adult CD patients (n = 139) were screened with DEXA at diagnosis and/or in the follow-up. After applying the exclusion criteria, 100 patients who underwent a DEXA scan at least once after diagnosis or a GFD were included in the study. The flowchart of the study is shown in Figure 1. At the time of diagnosis, the mean age of the patients was 34.61 ± 10.3 years, 84% of the patients were female, and the mean symptom duration before diagnosis was 14.2 ± 15.7 months. A total of 83% of the patients had received calcium and/or vitamin D supplements at any time after diagnosis.

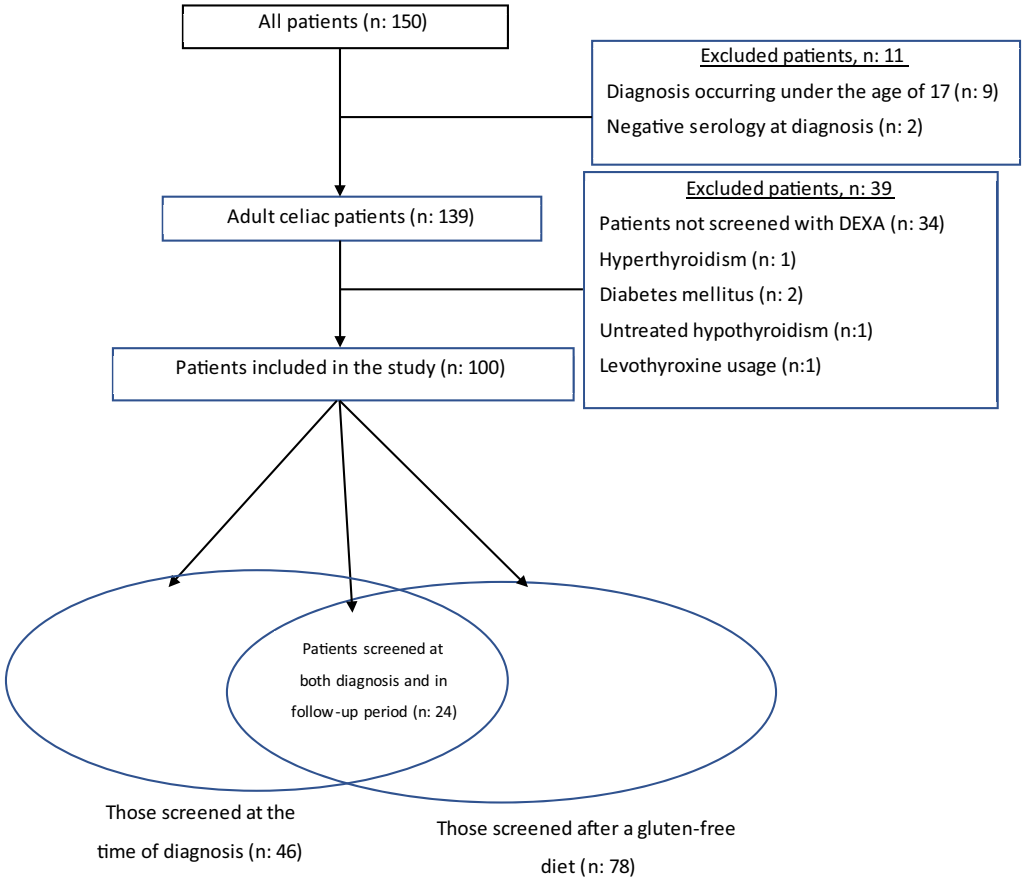

Figure 1. Flowchart of the study.

Patients Screened at the Time of Diagnosis

The general characteristics of the patients (*n* = 46) are shown in Table 1. At diagnosis, the prevalence of osteopenia and osteoporosis was 67.3% (*n* = 31) and 15.2% (*n* = 7) at the lumbar spine, and 43.4% (*n* = 20) and 10.8% (*n* = 5) at the femur. The lumbar and femoral DEXA results of the patients screened at the time of diagnosis are shown in Table 2.

Of the female patients, 15.2% (*n* = 7) were in menopause. In addition, 2.1% (*n* = 1) were male patients over 50 years old. In the total group, the frequency of osteoporosis was 37.5% (*n* = 3).

Patients Screened After a GFD

The general characteristics of the patients (*n* = 78) are shown in Table 3. The prevalence of osteopenia and osteoporosis after a GFD was 61.5% (*n* = 48) and 8.9% (*n* = 7) at the lumbar spine, and 37.1% (*n* = 29) and 2.5% (*n* = 2) at the femur. The femoral and lumbar DEXA results of these patients are shown in Table 4.

A total of 28.2% (*n* = 22) of the patients were in menopause. In these patients, the frequency of osteoporosis was 22.7% (*n* = 5).

Thirty seven percent of patients (*n* = 29) were taking supplements at the end of the follow-up period. At the end of the follow-up period, 1.2% (*n* = 1) of patients were found to have received bisphosphonate treatment.

Patients Screened Both at Diagnosis and After a GFD

While on a GFD, 23.5% (*n* = 24) of the patients were reassessed by DEXA, at an average of 34.25 ± 19.5 months after diagnosis. Women comprised 87.5% (*n* = 21) of the patients (19%, *n* = 4 in menopause) and all of the male patients were under the age of 50 years. The mean age of the patients was 36.2 ± 7.1 years, at the time of diagnosis. The prevalence of osteopenia and osteoporosis in these patients was 62.5% (*n* = 15) and 16.6% (*n* = 4), respectively, at diagnosis, and 66.6% (*n* = 16) and 4.1% (*n* = 1), respectively, after a GFD. the total

Table 1. General Characteristics of Patients Screened at the Time of Diagnosis (*n* = 46)

Age (mean ± SD)	35.3 ± 9.8
Sex, n (%)	
Male	9 (19.5%)
Female	37 (80.5%)
Male patients >50 years of age, n (%)	1 (2.1%)
Woman in menopause, n (%)	7 (15.2%)
BMI (kg/m^2) (mean ± SD)	23.3 ± 4.1
Clinical presentation, n (%)	
Anemia	17 (36.9%)
Chronic diarrhea	19 (41.3%)
Dyspepsia	4 (8.6%)
Abdominal pain	5 (10.8%)
Other	1 (2.1%)
Positive for EMA and/or t-TGA	46 (100%)
Duodenal histopathology, n (%)	
Marsh II	1 (2.17%)
Marsh IIIA	14 (30.43%)
Marsh IIIB	19 (41.3%)
Marsh IIIC	12 (26.1%)
Smoking, n (%)	8 (17.3%)
Alcohol, n (%)	0

BMI, body mass index; EMA, endomysium immunoglobulin A; SD, standard deviation; t-TGA, tissue transglutaminase immunoglobulin A.

femoral and lumbar mean BMD values and the T and Z scores were found to be significantly higher at the end of the follow-up period than at the time of diagnosis ($P < .05$) (Table 5). At the end of the follow-up period after a GFD, 50% (*n* = 12) of the patients were found to be positive for t-TGA and/or EMA, and 25% (*n* = 6) were not compliant with a GFD. All of the patients had received calcium and/or vitamin D supplements, and 4.1% (*n* = 1) of them had received bisphosphonate treatment at any time after diagnosis.

DISCUSSION

The worldwide frequency of CD varies between 0.6% and 1%, and in Turkey, seroprevalence has been reported in the range of 0.77-1.3%.[10,11,12] CD may show various clinical presentations. Patients may have classic malabsorption symptoms that include diarrhea, steatorrhea, and weight loss. Atypical CD, which has become a more commonly diagnosed CD disease type in recent years, may present with abnormal liver function tests, arthralgia/arthritis, dermatitis herpetiformis, alopecia, anemia, stomatitis, myalgia, psychiatric disorders, epileptic seizures, neuropathy, growth retardation, delayed puberty, and infertility.[2] Apart from gastrointestinal symptoms, bone mineralization disorders are the most common manifestations of CD.[13]

In CD, decreased digestive enzymes along with a loss of the absorptive surface of the small intestine may lead to insufficient absorption of calcium, micronutrients and vitamin D taken in with the diet (14).[14] Increasing levels of pro-inflammatory cytokines (TNF-alpha, IL-1β and IL-6), other endocrinological disorders, such as secondary hyperparathyroidism and hypogonadism, and, rarely, the presence of anti-osteoprotegerin antibodies can affect bone homeostasis in CD.[15,16,17]

The presence of osteoporosis is associated with increased risk of bone fracture. Some studies have shown

Table 2. Bone Mineral Density Results of Patients Screened at the Time of Diagnosis (*n* = 46)

	All Patients					
DEXA Localization	BMD*	T score*	Z score*	Osteopenia**	Osteoporosis**	−2 <Z score**
Femur	0.843	−1.02	−0.79	20 (43.4%)	5 (%10.8)	6 (13%)
Lumbar spine	0.883	−1.65	−1.27	31 (67.3%)	7 (%15.2)	11 (23.9%)
Premenopausal women (n = 30)						
Femur	0.825	−1.04	−0.88	14 (46.6%)	3 (10%)	4 (13.3%)
Lumbar spine	0.880	−1.35	−1.25	20 (66.6%)	3 (10%)	6 (20%)
Male patients >50 years of age (n = 8)						
Femur	0.920	−0.88	−0.58	2 (25%)	1 (12.5%)	1 (12.5%)
Lumbar spine	0.912	−1.73	−1.6	7 (87.5%)	1 (12.5%)	3 (37.5%)

*Values are medians; **Values are *n* (%).
BMD (g/cm^2), bone mineral density; DEXA, dual-energy X-ray absorptiometry.

Table 3. General Characteristics of Patients Screened After a Gluten-Free Diet (*n* = 78)

At diagnosis (n = 78)	
Age (mean ± SD)	34.1 ± 7.2
Sex, n (%)	
Male	10 (12.8%)
Female	68 (87.2%)
Clinical presentation at diagnosis, n (%)	
Anemia	32 (41%)
Chronic diarrhea	23 (29.5%)
Dyspepsia	11 (14.1%)
Abdominal pain	11 (14.1%)
Other	1 (1.3%)
Duodenal histopathology at diagnosis, n (%)	
Marsh II	1 (1.3%)
Marsh IIIA	26 (33.3%)
Marsh IIIB	37 (47.5%)
Marsh IIIC	14 (17.9%)
After a GFD (at the time of screening)	
Age (mean ± SD)	36.8 ± 7.7
BMI (kg/m^2) (mean ± SD)	23.79 ± 4.21
Overweight	21 (26.9%)
Obese	10 (12.8%)
Women in menopause, n (%)	22 (28.2%)
Male patients >50 years of age, n (%)	-
Smoking, n (%)	12 (15.3%)
Alcohol, n (%)	2 (2.5%)
GFD adherence, n (%)	
No	17 (21.8%)
On a GFD	61 (78.2%)
Seropositivity (positive EMA or t-TGA status) in GFD-compliant patients	15 (24.5%)
Seropositivity in GFD non-compliant patients	17 (%100)
Treatment, n (%)	
Calcium and/or vitamin D supplements	28 (35.8%)
Bisphosphonate	1 (1.2%)
Follow-up period (months)*	31 (IQR:25)

*Values are median.
BMI, body mass index; EMA, endomysium immunoglobulin A; GFD, gluten-free diet; SD, standard deviation; t-TGA, tissue transglutaminase immunoglobulin A.

that in CD, BMD increases with improvements in histopathological findings after a GFD. The British Society of Gastroenterology Guidelines for the diagnosis and management of CD recommend screening patients with osteoporosis risk factors at least 1 year after being on a GFD.[18] The European Society for the Study of Coeliac Disease (ESsCD) guidelines recommend that CD patients who have high risk factors for osteoporosis (men over 50 years of age, perimenopausal or postmenopausal women, and those with late-diagnosed, fragility fractures or diagnosed with malabsorption or bone disease) should be screened with DEXA at the time of diagnosis, and others should be screened before 30-35 years of age.[19]

We found that 24.4% of our adult CD patients had not been screened with DEXA. As in our study, some data in the literature revealed that patients with CD have been assessed by DEXA at varying rates. In one retrospective study, Fouda reported that only 36% of 128 adult patients had been assessed by DEXA, while in another study, 93% of 250 patients had been evaluated by DEXA at diagnosis and 60% in the follow-up period.[7,20] In our study, the fact that screening was not implemented for some patients may be associated with the lack of a standardized screening and/or follow-up process.

Literature data reported a low frequency of BMD, between 50% and 74%, at the time of diagnosis in untreated patients. In a study conducted by Pantaleoni et al. (*n* = 169), the prevalence of osteopenia at the lumbar vertebrae and femoral neck was 37% and 44%, respectively, and that of osteoporosis was 21% and 13%, respectively.[21,22,23] In this study, the prevalence of osteopenia at the lumbar vertebrae and femur at the time of diagnosis was 67% and 43%, respectively, and that of osteoporosis was 15% and 10%, respectively. In addition, we found that 23.9% and 13% of patients had low bone mass according to the total lumbar vertebra and femoral Z score, which indicates bone mass of patients with similar age and sex at diagnosis.

As far as we know, there are no data on the frequency of osteopenia or osteoporosis in adult CD patients in our country. We think that it is difficult to compare the literature data and the data of this study due to the differences in risk factors for osteoporosis (amount of calcium taken in compliance with diet, age, the presence of menopause, smoking, alcohol consumption, sex, exercise, and genetic factors) between the cohorts investigated and the factors associated with CD (the form of presentation, late diagnosis, the severity of villous atrophy, etc.).

The fact that most of our patients were diagnosed when the clinical signs of CD were overt, may be related to

Table 4. Bone Mineral Density Results of Patients Screened After a Gluten-Free Diet (*n* = 78)

	All Patients					
DEXA Localization	BMD*	T score *	Z score*	Osteopenia**	Osteoporosis**	−2 < Z score**
Femur	0.879	−0.7	−0.4	29 (37.1%)	2 (2.5%)	4 (5.1%)
Lumbar spine	0.908	−1.3	−1.00	48 (61.5%)	7 (8.9%)	10 (12.8%)
Premenopausal women (n = 46)						
Femur	0.846	−0.7	−0.3	18 (39.1%)	1 (2.1%)	3 (6.5%)
Lumbar spine	0.908	−1.3	−0.90	30 (65.2%)	-	3 (6.5%)
Male patients <50 years of age (n = 10)						
Femur	0.930	−0.7	−0.5	2 (20%)	-	-
Lumbar spine	0.950	−1.3	−1.05	7 (70%)	1 (10%)	1 (10%)

*Values are medians; **Values are *n* (%).
BMD (g/cm^2), bone mineral density; DEXA, dual-energy X-ray absorptiometry.

Table 5. Comparison of DEXA Results of Patients Screened Both at the Time of Diagnosis and After a Gluten-Free Diet (*n* = 24)

Parameters	At Diagnosis (mean ± SD)	After a GFD (mean ± SD)	*P*
Femoral BMD	0.839 ± 0.098	0.905 ± 0.121	**.001***
T score	−0.89 ± 1.01	−0.47 ± 1.09	**.002***
Z score	−0.77 ± 1.04	−0.27 ± 1.11	**.004****
Lumbar spine BMD	0.853 ± 0.212	0.924 ± 0.093	**.026****
T score	−1.53 ± 1.03	−1.14 ± 0.88	**.013***
Z score	−1.31 ± 1.05	−0.92 ± 0.93	**.008****

*Paired *t*-test, **Wilcoxon signed-rank test.
BMD (g/cm^2), bone mineral density; GFD, gluten-free diet; SD, standard deviation.

the high rate of low bone density in this study. Recently, Tovolli et al. reported that CD patients diagnosed by screening had a significantly lower percentage of osteopenia/osteoporosis compared with those diagnosed with clinical suspicion. They concluded that early diagnosis protects from severe metabolic bone disease.[24] However, in our study, only 2 patients (screened for family history) were diagnosed without obvious clinical signs. On the other hand, moderate or severe villous atrophy was present in duodenal biopsies in two-thirds of our patients at the time of diagnosis, with findings of chronic diarrhea in more than one-third of our patients.[18,25]

Our study also revealed that 70.4% (osteopenia: 61.5% and osteoporosis: 8.9%) of the patients had low BMD after a GFD (*n* = 78). In adult CD, the main treatment for bone disease is a GFD; however, with GFD treatment, some patients achieve normal BMD levels.[26] In this study, only 21.2% of patients (*n* = 17) were not compliant with a GFD, but since 41.2% (*n* = 33) were positive for t-TGA or EMA, it can be assumed that some of the GFD-compliant patients unknowingly consumed some gluten.[19] In addition, Larussa et al.[27] found that normal BMD after a GFD in CD is associated with duodenal mucosal healing. Although we were not able to evaluate duodenal histopathology, post-GFD mucosal pathological findings are likely to persist in a significant number of our patients.

It has been reported that BMI increases in patients with GFD compliance.[28] Also, non-alcoholic fatty liver disease (NAFLD) develops in approximately one-third of the patients. It is known that chronic liver diseases increase the risk of osteoporosis. However, the relationship between osteoporosis and NAFLD is still not fully understood.[29] In this study, 26.9% (*n* = 21) of our patients were overweight and 12.8% (*n* = 10) were obese, after GFD. However, our patients were not evaluated for presence of NAFLD.

Age and menopause are common risk factors for osteoporosis. In a systematic review, Ganji et al.[30] reported the prevalence of osteopenia and osteoporosis at the time of diagnosis as 39.6% and 14.4%, in men and premenopausal women, respectively. In this study, the prevalence of osteoporosis was 10.5% at the time of diagnosis and 3.5% (*n* = 2) after a GFD in premenopausal women and men under the age of 50. In contrast, the prevalence of osteoporosis in menopausal women and in men over the age of 50 was higher (37.5% at diagnosis and 22.7% after a GFD).

The important limitations of this study are that it was a single-center and retrospective study involving a small

number of patients. The other limitations are the inability to evaluate mucosal healing and other risk factors for osteoporosis. However, we think that it is important to report the first literature data from our country that show the frequency of evaluation for bone disease in adult CD patients and the results of BMD as real-life data.

As a result, we found that the rate of patients with low BMD at diagnosis and at follow-up after a GFD was high in adult CD patients, and that BMD increased significantly after a GFD. It is important for all of these patients to undergo a DEXA scan to determine the follow-up characteristics and to receive treatment to increase the bone mass and reduce the risk of fractures. However, we think that the prevalence of osteopenia, osteoporosis, and risk factors at the time of diagnosis and in the follow-up period should be evaluated with prospective studies.

Ethics Committee Approval: This study was approved by the Umranıye Training and Research Hospital Ethics Committee (April 14, 2020/B10.1.TKH.4.34.H.GP.0.01/90).

Informed Consent: N/A.

Peer review: Externally peer-reviewed.

Author contributions: Concept – S.S.; Design – S.S., G.A.; Supervision – S.S., H.L.D.; Resources – R.K.; Materials – K.K., Ö.K., H.A., Ç.A.; Data Collection and/or Processing – K.K., Ö.K., H.A., Ç.A., R.K.; Analysis and/or Interpretation – S.S., P.G., G.A.; Literature Search – S.S., G.A.; Writing Manuscript – S.S.; Critical Review – G.A., K.Ö., N.M.B.

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REFERENCES

1. Di Sabatino A, Corazza GR. Coeliac disease. Lancet. 2009;373:1480-1493. [CrossRef]
2. Jericho H, Sansotta N, Guandalini S. Extraintestinal manifestations of celiac disease: effectiveness of the gluten-free diet. J Pediatr Gastroenterol Nutr. 2017;65:75-79. [CrossRef]
3. Oh HJ, Ryu KH, Park BJ, Yoon BH. Osteoporosis and osteoporotic fractures in gastrointestinal disease. J Bone Metab. 2018;25:213-217. [CrossRef]
4. Walker MD, Williams J, Lewis SK et al. Measurement of forearm bone density by dual energy X-ray absorptiometry increases the prevalence of osteoporosis in men with celiac disease. Clin Gastroenterol Hepatol. 2020;18:99-106. [CrossRef]
5. Larussa T, Suraci E, Nazionale I et al. Bone mineralization in celiac disease. Gastroenterol Res Pract. 2012;2012:198025. [CrossRef]
6. Singh P, Garber JJ. Implementation and adherence to osteoporosis screening guidelines among coeliac disease patients. Dig Liver Dis. 2016;48:1451-1456. [CrossRef]
7. Fouda MA. Celiac disease-related osteopathy among Saudi celiac patients: are we adherent to recommendations? Saudi J Gastroenterol. 2017;23:291-295. [CrossRef]
8. Camacho PM, Petak SM, Binkley N et al. American association of clinical endocrinologists and american college of endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis - 2016--executive summary. Endocr Pract. 2016;22:1111-1118. [CrossRef]
9. Abdallah Ismail N. Avoiding the under-diagnosis of low bone mineral density in egyptian children with chronic medical conditions affecting bone health. Arch Med Sci. 2011;7:700-705. [CrossRef]
10. Singh P, Arora A, Strand TA et al. Global Prevalence of celiac disease: systematic Reviewa nd Meta-analysis. Clin Gastroenterol Hepatol. 2018;16:823-836.e2. [CrossRef]
11. Tatar G, Elsurer R, Simsek H et al. Screening of tissue transglutaminase antibody in healthy blood donors for celiac disease screening in the Turkish population. Dig Dis Sci. 2004;49:1479-1484. [CrossRef]
12. Sezgin O, Sarıtaş B, Aydın İ, Şaşmaz T, Lınke ES. Celiac disease prevalence in Turkey: a population based cross-sectional study. Acta Med Mediterr. 2016;32:719.
14. Reilly NR, Fasano A, Green PH. Presentation of celiac disease. Gastrointest Endosc Clin N Am. 2012;22:613-621. [CrossRef]
13. Rubio-Tapia A, Hill ID, Kelly CP et al. ACG clinical guidelines: diagnosis and management of celiac disease. Am J Gastroenterol. 2013;108:656-76; quiz 677. [CrossRef]
15. Selby PL, Davies M, Adams JE, Mawer EB. Bone loss in celiac disease is related to secondary hyperparathyroidism. J Bone Miner Res. 1999;14:652-657. [CrossRef]
16. Fornari MC, Pedreira S, Niveloni S et al. Pre- and post-treatment serum levels of cytokines IL-1beta, IL-6, and IL-1 receptor antagonist in celiac disease. Are they related to the associated osteopenia? Am J Gastroenterol. 1998;93:413-418. [CrossRef]
17. Riches PL, McRorie E, Fraser WD et al. Osteoporosis associated with neutralizing autoantibodies against osteoprotegerin. N Engl J Med. 2009;361:1459-1465. [CrossRef]
18. Ludvigsson JF, Bai JC, Biagi F et al. Diagnosis and management of adult coeliac disease: guidelines from the british society of gastroenterology. Gut. 2014;63:1210-1228. [CrossRef]
19. Al-Toma A, Volta U, Auricchio R et al. European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. United European gastroenterology journal. 2019;7(5):583-613. [CrossRef]
20. Burger JPW, van der Laan JJH, Jansen TA et al. Low yield for routine laboratory checks in follow-up of coeliac disease. J Gastrointestin Liver Dis. 2018;27:233-239. [CrossRef]
21. Duerksen D, Pinto-Sanchez MI, Anca A et al. Management of bone health in patients with celiac disease: practical guide for clinicians. Can Fam Physician. 2018;64:433-438.
22. Zanchetta MB, Longobardi V, Bai JC. Bone and celiac disease. Curr Osteoporos Rep. 2016;14:43-48. [CrossRef]
23. Pantaleoni S, Luchino M, Adriani A et al. Bone mineral density at diagnosis of celiac disease and after 1 year of gluten-free diet. ScientificWorldJournal. 2014;2014:173082. [CrossRef]

24. Tovoli F, Negrini G, Sansone V et al. Celiac disease diagnosed through screening programs in at-risk adults is not associated with worse adherence to the gluten-free diet and might protect from osteopenia/osteoporosis. Nutrients. 2018;10:1940. [CrossRef]
25. Stazi AV, Trecca A, Trinti B. Osteoporosis in celiac disease and in endocrine and reproductive disorders. World J Gastroenterol. 2008;14:498-505. [CrossRef]
26. Krupa-Kozak U. Pathologic bone alterations in celiac disease: etiology, epidemiology, and treatment. Nutrition. 2014;30:16-24. [CrossRef]
27. Larussa T, Suraci E, Imeneo M, Marasco R, Luzza F. Normal bone mineral density associates with duodenal mucosa healing in adult patients with celiac disease on a gluten-free diet. Nutrients. 2017;9. [CrossRef]
28. Kabbani TA, Goldberg A, Kelly CP et al. Body mass index and the risk of obesity in coeliac disease treated with the gluten-free diet. Aliment Pharmacol Ther. 2012;35:723-729. [CrossRef]
29. Tovoli F, Negrini G, Farì R et al. Increased risk of nonalcoholic fatty liver disease in patients with coeliac disease on a gluten-free diet: beyond traditional metabolic factors. Aliment Pharmacol Ther. 2018;48:538-546. [CrossRef]
30. Ganji R, Moghbeli M, Sadeghi R, Bayat G, Ganji A. Prevalence of osteoporosis and osteopenia in men and premenopausal women with celiac disease: a systematic review. Nutr J. 2019;18:9. [CrossRef]