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Original Article

Bone mineral density in pediatric celiac disease: Clinical, biochemical, and serologic profiles—a retrospective cohort study

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ABSTRACT

Objective: The aim of this study was delineate the burden of low lumbar bone mineral density (BMD) in children with CD (celiac disease) and evaluate differences in BMD according to assessment timing and gluten-free diet (GFD) adherence, using concurrent tissue transglutaminase IgA (c-tTG-IgA), and describe accompanying anthropometric and biochemical profiles.

Materials and Methods: This retrospective cohort included CD patients (n=123) aged 5–18 years who underwent dual-energy X-ray absorptiometry (DEXA) between January 1, 2022, and December 31, 2024. Age-adjusted and height-adjusted BMD z-scores (BMD-AAz and BMD-HAz) were calculated. Patients were grouped as diagnosis or follow-up (≥12 months), and follow-up was subdivided into GFD-non-adherent follow-up group (FU-NonAdh) and GFD-adherent follow-up group (FU-Adh).

Results: Low BMD based on BMD-HAz (≤−1) was present in 37.4% (osteopenia 24.4%; osteoporosis 13.0%). Compared with diagnosis group, follow-up group had higher BMD-AAz and BMD-HAz (p=0.022 and p=0.011). BMD-HAz was higher in FU-Adh group than in diagnosis and FU-NonAdh group (p<0.001 and p=0.005), whereas FU-NonAdh group did not differ from diagnosis group. The low BMD group had a lower body mass index (BMI) z-score and shorter GFD duration (p<0.001 and p=0.010). Serum calcium levels were lower in the osteoporosis group than in the normal BMD group (p=0.003).

Conclusion: Lumbar BMD impairment is frequent in pediatric CD, with the most evident improvement in the GFD-adherent follow-up group. In secondary analyses, lower BMI z-scores and shorter GFD duration were observed in children with low BMD, which may help inform risk stratification.

Keywords: Body mass index, calcium, dual-energy x-ray absorptiometry, gluten-free diet, tissue transglutaminase

Introduction

Celiac disease (CD) is a systemic autoimmune condition characterized by immune-mediated small intestinal damage induced by gluten intake. In childhood, it may present not only with gastrointestinal symptoms but also with extraintestinal manifestations such as growth failure, anemia, and reduced bone mineral density (BMD) (1–3). Osteopenia and osteoporosis are prevalent and clinically significant conditions in children with CD due to their association with long-term fracture risk (4,5).

Multiple mechanisms contribute to the emergence of low BMD in CD, including malabsorption, chronic inflammation, and hormonal alterations. Malabsorption of calcium (Ca) and 25-hydroxyvitamin D_3 ($25(OH)D_3$) due to villous atrophy can predispose patients to the onset of secondary hyperparathyroidism and enhanced bone resorption, while growth retardation and malnutrition may hinder the attainment of optimal bone mass (6,7). Despite this, it remains unclear which clinical and biochemical profiles are more strongly associated with BMD impairment and which children should be prioritized for screening with dual-energy X-ray absorptiometry (DEXA) (8,9).

A gluten-free diet (GFD) is the mainstay for achieving both mucosal recovery and enhancement of bone health. However, the relationship between serologic response and bone

mineralization has not been fully elucidated. Although tissue transglutaminase immunoglobulin A (tTG-IgA) levels are widely used indicators of dietary adherence, findings regarding their association with BMD remain inconsistent (4,10–12).

This study sought delineate the burden of low lumbar BMD in children with CD and to evaluate differences in BMD by assessment timing and GFD adherence, while describing accompanying anthropometric and biochemical profiles.

Materials and Methods

Study design and setting

This investigation was performed using the electronic medical records of CD patients followed in the Pediatric Gastroenterology Department of Gulhane Training and Research Hospital, University of Health Sciences. university hospital. All CD patients between 5 and 18 years of age who had BMD measurement with DEXA and had concurrent tissue transglutaminase immunoglobulin A (c-tTG-IgA) available at the time of BMD assessment between January 1, 2022, and December 31, 2024, were included.

Diagnosis and eligibility criteria

The diagnosis of CD was confirmed by upper gastrointestinal endoscopy and small intestinal biopsy according to European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) 2020 criteria (13). Patients diagnosed without biopsy, those with IgA deficiency, those with endocrine or other chronic diseases, and those using medications that could affect bone metabolism were excluded. A cohort of 123 patients meeting the study-defined requirements was incorporated into the analysis.

Data collection

Demographic and clinical data, including age, gender, height, weight, and body mass index (BMI), as well as Ca, phosphorus (P), alkaline phosphatase (ALP), parathyroid hormone (PTH), and 25(OH)D_3 levels, were obtained from the medical records. Height z-score, weight z-score, and BMI z-score were calculated according to Neyzi growth references (14).

Dual-Energy X-ray absorptiometry and bone mineral density

BMD assessments were obtained at the lumbar vertebrae L2–L4 level using a Hologic QDR 4500 bone densitometer (Hologic Inc., Bedford, MA, USA). Age-adjusted BMD z-score (BMD-AAz) and height-adjusted BMD z-score (BMD-HAz) were calculated using reference curves derived from healthy Turkish children (15).

Grouping strategy

Participants were initially classified into two groups based on the timing of DEXA assessment: at diagnosis or at follow-up. The diagnosis group included patients assessed at diagnosis. The follow-up group included patients assessed ≥12 months after diagnosis. It was subdivided into two subgroups based on c-tTG-IgA status at the time of DEXA: the GFD-non-adherent follow-up group (FU-NonAdh), which was c-tTG-IgA positive, and the GFD-adherent follow-up group (FU-Adh), which was c-tTG-IgA negative (16).

For the secondary analysis, patients were categorized into three strata based on BMD-HAz: normal BMD group (BMD-HAz > –1), osteopenia group (–2 < BMD-HAz ≤ –1), and osteoporosis group (BMD-HAz ≤ –2) (17). Additionally, BMD-HAz ≤ –1 was defined as low BMD.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean andstandard deviation or median and interquartile range (IQR), and categorical variables as number and percentage. The distribution of continuous variables was assessed using the Shapiro–Wilk test and Q–Q plot. Between-group comparisons were performed using the independent samples t-test or Mann–Whitney U test, as appropriate. For comparisons across the three BMD categories, one-way ANOVA or the Kruskal-Wallis test was used, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. For subgroup analyses, pairwise comparisons were conducted as specified in the tables. A p-value < 0.050 was considered statistically significant in all analyses.

Results

BMD data from 123 children with CD were assessed. The mean age of the patients was 11.7±3.7 years, and 55.3% were female. The mean age at diagnosis was 8.7±3.8 years. Anthropometric assessment showed a mean height z-score of –0.40±1.08, a mean weight z-score of –0.62±1.22, and a mean BMI z-score of –0.54±1.19. Based on BMD-HAz values, 37.4% of the patients had low BMD (24.4% had osteopenia, and 13.0% had osteoporosis). Based on BMD-AAz values, 40.7% of the patients had low BMD (30.1% had osteopenia, and 10.6% had osteoporosis).

In total, 38 patients were assessed at diagnosis and 73 at follow-up; an additional 12 patients were evaluated after diagnosis but within <12 months and were not included in either group. Compared with the diagnosis group, the follow-up group had significantly higher densitometric indices, with higher BMD-AAz and BMD-HAz (p=0.022 and p=0.011, respectively) (Table I, Figure 1). In contrast, age, gender distribution, and biochemical parameters Ca, P, ALP, PTH, and 25(OH)D_3 levels were comparable across groups (Table I).

When the diagnosis group and the follow-up subgroups were compared, the primary between-group differences were observed in BMD outcomes. BMD-HAz was higher in the GFD-adherent follow-up group than in the diagnosis group (p<0.001)

Table I: Comparison of clinical, biochemical, anthropometric, and densitometric parameters according to timing of assessment

Variable	Diagnosis Group	Follow-up Group	p
Total number of patients	38	73	-
BMD-AAz*	-0.98 ± 1.07	-0.45 ± 1.17	0.022§
BMD-HAz*	-1.05 ± 1.29	-0.41 ± 1.20	0.011§
Age (years)†	11.00 (9.00-14.75)	12.00 (9.00-15.00)	0.558¶
Gender (female)‡	22 (57.9%)	46 (63.0%)	0.749‖
Calcium (mg/dL)*	9.77 ± 0.40	9.84 ± 0.39	0.349§
Phosphorus (mg/dL)*	4.63 ± 0.65	4.52 ± 0.79	0.447§
Alkaline phosphatase (U/L)*	204.55 ± 74.53	203.80 ± 101.43	0.968§
Parathyroid hormone (pg/mL)†	35.50 (25.23-47.85)	34.30 (26.00-48.30)	0.936¶
25(OH)D_3 (ng/mL)†	20.61 (12.66-26.75)	22.00 (15.18-31.09)	0.291¶
Height z-score*	-0.35 ± 1.07	-0.38 ± 1.07	0.869§
Weight z-score*	-0.78 ± 1.13	-0.46 ± 1.28	0.194§
BMI z-score*	-0.82 ± 1.20	-0.35 ± 1.20	0.054§

:** *mean ± SD,* **†:** *median (IQR),* **‡:** *n(%),* **§:** *independent samples t-test,* **¶:** *Mann–Whitney U test,* **‖:** *chi-square test,* ***BMD-AAz: *Age-adjusted bone mineral density z-score,* ***BMD-HAz:*** *Height-adjusted bone mineral density z-score,* ***25(OH)D_3:*** *25-hydroxyvitamin D_3,* ***BMI:*** *Body mass index. The diagnosis group included patients assessed at diagnosis. The follow-up group included patients assessed ≥12 months after diagnosis.*

Table II: Comparison of clinical, biochemical, anthropometric, and densitometric parameters among the diagnosis group, the GFD-non-adherent follow-up group and the GFD-adherent follow-up group

Variable	Diagnosis Group	FU-NonAdh	FU-Adh Group	p^1	p^2	p^3
Total number of patients	38	24	49	-	-	-
BMD-AAz*	-0.98 ± 1.07	-0.78 ± 1.17	-0.29 ± 1.16	0.482§	0.005§	0.098§
BMD-HAz*	-1.05 ± 1.29	-0.96 ± 1.39	-0.14 ± 1.00	0.792§	<0.001§	0.005§
Age (years)†	11.00 (9.00-14.75)	12.50 (8.50–15.25)	12.00 (9.00–15.00)	0.896¶	0.468¶	0.621¶
Gender (female) ‡	22 (57.9)	11 (45.8)	35 (71.4)	0.506‖	0.276‖	0.061‖
Calcium (mg/dL)*	9.77 ± 0.40	9.77 ± 0.43	9.87 ± 0.37	0.963§	0.194§	0.294§
Phosphorus (mg/dL)†	4.70 (4.33–5.00)	4.75 (4.22–5.40)	4.50 (4.10–4.90)	0.669¶	0.288¶	0.223¶
Alkaline phosphatase (U/L)*	204.55 ± 74.53	188.88 ± 87.95	211.10 ± 107.51	0.455§	0.749ᵗ	0.383§
Parathyroid hormone (pg/mL)†	35.50 (25.23-47.85)	36.65 (25.93–51.20)	33.30 (26.60–45.00)	0.628¶	0.864¶	0.545¶
25(OH)D_3 (ng/mL)†	20.61 (12.66-26.75)	24.14 (16.65–30.92)	21.57 (14.70–31.09)	0.196¶	0.494¶	0.470¶
Height z-score†	-0.15 (-1.14–0.46)	-0.48 (-0.84–0.53)	-0.24 (-1.20–0.55)	0.691¶	0.952¶	0.738¶
Weight z-score*	-0.78 ± 1.13	-0.60 ± 1.12	-0.39 ± 1.36	0.546§	0.155§	0.507§
BMI z-score*	-0.82 ± 1.20	-0.58 ± 1.12	-0.24 ± 1.24	0.436§	0.030§	0.257§

:** *mean±SD,* **†:** *median (IQR),* **‡:** *n(%),* **§:** *independent samples t-test,* **¶:** *Mann–Whitney U test,* **‖:** *chi-square test,* ***GFD: *gluten-free diet,* ***BMD-AAz:*** *Age-adjusted bone mineral density z-score,* ***BMD-HAz:*** *Height-adjusted bone mineral density z-score,* ***25(OH)D_3:*** *25-hydroxyvitamin D_3,* ***BMI:*** *Body mass index,* ***p^1:*** *Diagnosis vs FU-NonAdh,* ***p^2:*** *Diagnosis vs FU-Adh;* ***p^3:*** *FU-NonAdh vs FU-Adh*

and the GFD-non-adherent follow-up group (p=0.005). BMD-AAz was also higher in the GFD-adherent follow-up group than in the diagnosis group (p=0.005), whereas the difference between the two follow-up subgroups did not reach statistical significance (p=0.098) (Table II, Figure 2). BMI z-score was higher in the GFD-adherent follow-up group than in the diagnosis group (p=0.030). In contrast, age, gender distribution, and biochemical parameters Ca, P, ALP, PTH, and 25(OH)D_3 levels were comparable across the diagnosis group and follow-up subgroups (Table II).

Compared with the normal BMD group, the low BMD group had a significantly lower BMI z-score (p<0.001) and shorter GFD duration (p=0.010). Age, gender distribution, and biochemical parameters were otherwise comparable between groups (Table III).

Table III: Comparison of clinical, biochemical, and anthropometric parameters between normal BMD and low BMD groups

Variable	Normal	Low	p
Total number of patients	77	46	-
Age (years)*	12.00 (9.00–16.00)	11.00 (8.25–13.00)	0.178§
Gender (Female)†	50 (64.9)	27 (58.7)	0.618¶
GFD duration (months)*	26.00 (4.00–58.00)	10.50 (2.25–30.75)	0.010§
Calcium (mg/dL)‡	9.87 ± 0.34	9.73 ± 0.47	0.055‖
Phosphorus (mg/dL)*	4.70 (4.20–5.00)	4.60 (4.20–5.00)	0.904§
Alkaline phosphatase (U/L)*	208.00 (133.0–259.0)	188.00 (142.5–227.7)	0.340§
Parathyroid hormone (pg/mL)*	35.00 (26.80–47.90)	31.75 (24.25–50.33)	0.724§
25(OH)D_3 (ng/mL)*	22.00 (15.18–29.80)	24.40 (14.04–31.24)	0.427§
Height z-score*	–0.45 (–1.20–0.39)	0.03 (–1.08–0.54)	0.304§
Weight z-score*	–0.50 (–1.36–0.21)	–1.06 (–1.50––0.29)	0.047§
BMI z-score ‡	–0.25 ± 1.12	–1.02 ± 1.17	<0.001‖

: median (IQR), †: n(%), ‡: mean±SD, §: Mann–Whitney U test, ¶: chi-square test, ‖: independent samples t-test, **BMD: bone mineral density, **GFD:** gluten-free diet, **25(OH)D_3:** 25-hydroxyvitamin D_3, **BMI:** body mass index. Normal BMD comprised patients with BMD-HAz>–1. Low BMD comprised patients with BMD-HAz ≤ –1 (osteopenia or osteoporosis).*

Table IV: Comparison of clinical, biochemical, and anthropometric parameters across BMD categories

Variable	Normal BMD	Osteopenia	Osteoporosis	p^1	p^2
Total number of patients	77	30	16		
Age (years)*	12.00 (9.00–16.00)	11.00 (8.00–12.75)	13.00 (9.75–15.50)	0.048§	0.783§
Gender (Female)†	50 (64.9)	20 (66.7)	7 (43.8)	1.000¶	0.159¶
GFD duration (months)*	26.00 (4.00-58.00)	10.50 (3.00-29.00)	10.00 (1.75-39.25)	0.012§	0.180§
Calcium (mg/dL)‡	9.87 ± 0.34	9.83 ± 0.39	9.54 ± 0.57	0.567‖	0.003‖
Phosphorus (mg/dL)*	4.70 (4.20–5.00)	4.65 (4.20–5.07)	4.60 (4.30–4.83)	0.848§	0.603§
Alkaline phosphatase (U/L)*	208.00 (133.0–259.0)	193.50 (155.2–226.2)	178.50 (127.2–235.7)	0.579§	0.299§
Parathyroid hormone (pg/mL)*	35.00 (26.80–47.90)	30.95 (24.40–44.42)	35.15 (24.27–57.92)	0.579§	0.903§
25(OH)D_3 (ng/mL)*	22.00 (15.18–29.80)	23.36 (13.28–30.76)	25.36 (14.67–33.15)	0.672§	0.357§
Height z-score*	–0.45 (–1.20–0.39)	–0.29 (–1.12–0.29)	0.54 (–0.84–1.02)	0.994§	0.047§
Weight z-score*	–0.50 (–1.36–0.21)	–1.04 (–1.56––0.29)	–1.23 (–1.50––0.43)	0.059§	0.276§
BMI z-score*	–0.36 (–1.00–0.40)	–0.73 (–1.77––0.14)	–1.25 (–2.03––0.83)	0.011§	0.003§

: median (IQR), †: n(%), ‡: mean±SD, §: Mann–Whitney U test, ¶: Fisher's exact test, ‖: independent samples t-test, **BMD: bone mineral density, **GFD:** gluten-free diet, **25(OH)D_3:** 25-hydroxyvitamin D_3, **BMI:** body mass index, **p^1:** Normal BMD group vs osteopenia group **p^2:** Normal BMD group vs osteoporosis group Normal BMD group comprised patients with BMD-HAz > –1; Osteopenia group comprised patients with –2 < BMD-HAz ≤ –1; and Osteoporosis group comprised patients with BMD-HAz ≤ –2.*

Across BMD categories, BMI z-score decreased stepwise from the normal BMD group to osteopenia and osteoporosis, with significant overall differences (p=0.002). BMI z-score was lower in both the osteopenia (p=0.011) and osteoporosis (p=0.003) groups compared with the normal BMD group. Serum Ca levels also differed across groups (p=0.010) and was lower in the osteoporosis group than in the normal BMD group (p=0.003) (Table IV).

Discussion

In this study, a notable frequency of lumbar BMD loss assessed by DEXA was demonstrated in children with CD; based on BMD-HAz, low BMD was identified in 37.4% of cases. Compared with patients assessed at diagnosis, the most prominent improvement was observed in the follow-up group that was serologically negative and considered

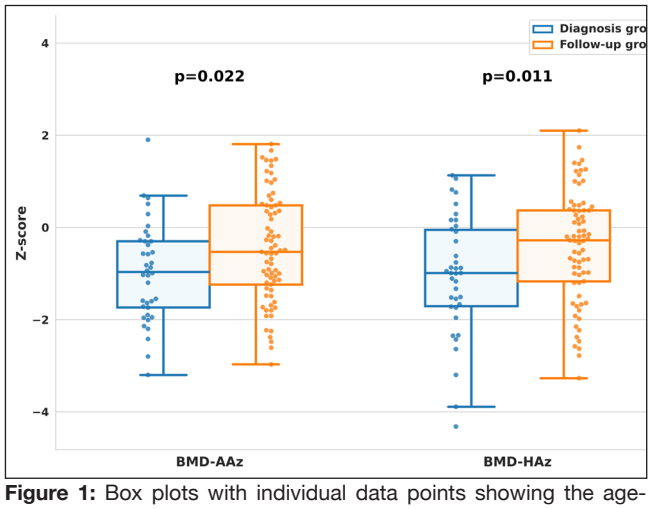

Figure 1: Box plots with individual data points showing the age-adjusted bone mineral density z-score (BMD-AAz) and height-adjusted bone mineral density z-score (BMD-HAz) in the Diagnosis and Follow-up groups. Boxes show the median (center line) and interquartile range (IQR), and points represent individual patient z-score values.

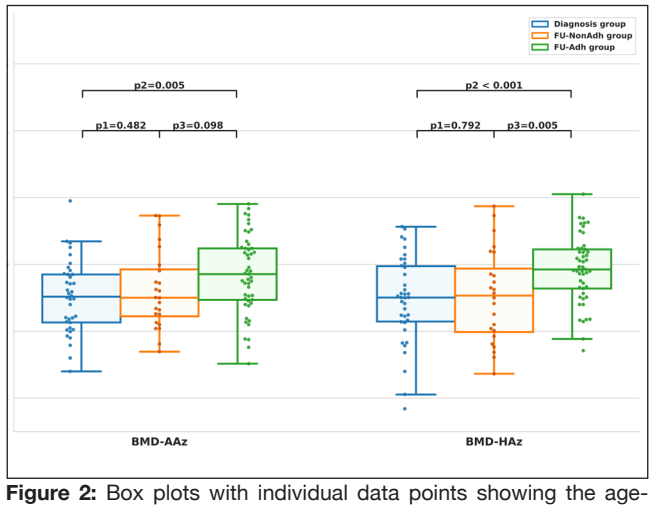

Figure 2: Box plots with individual data points showing the age-adjusted bone mineral density z-score (BMD-AAz) and height-adjusted bone mineral density z-score (BMD-HAz) in the diagnosis group, GFD-non-adherent follow-up group (FU-NonAdh group), and GFD-adherent follow-up group (FU-Adh group). Boxes show the median (center line) and interquartile range (IQR), and points represent individual patient z-score values. p1: Diagnosis group vs. FU-NonAdh group, p2: Diagnosis group vs. FU-Adh group, p3: FU-NonAdh group vs. FU-Adh group.

adherent to the GFD, in whom both BMD-AAz and BMD-HAz were significantly higher. In contrast, BMD measurements in patients who remained seropositive during follow-up and were considered non-adherent to the GFD did not differ from those in the diagnosis group. In secondary analyses, the low BMD group had a lower BMI z-score and a shorter GFD duration. These findings suggest that improvement in bone mineralization may be more closely related to seronegativity achieved through GFD adherence and a higher BMI during follow-up rather than to characteristics at diagnosis.

In our cohort, osteopenia was identified in 24.4% of patients and osteoporosis in 13.0%. Reported rates of osteopenia and osteoporosis in the literature vary widely, largely due to methodological heterogeneity, including differences in study populations, timing of assessment, reference curves, and the use of alternative adjustment approaches based on age and/or height (10,12,18). At diagnosis, Kırsaçlıoğlu reported low BMD rates of 56.7% based on BMD-AAz and 21.6% based on BMD-HAz, while Çamtosun reported osteoporosis rates of 12.8% using BMD-HAz and 26.7% using BMD-AAz (12,19). Across studies from different regions, osteoporosis has been reported in 13–32% and low BMD in 22–78% of children with CD (4,11,20). Collectively, these findings indicate that osteopenia and osteoporosis can occur at clinically meaningful frequencies in pediatric CD, and that between-study variability is likely driven largely by methodological differences.

Several findings from our cohort underscore the importance of dietary adherence for bone recovery in pediatric CD. The GFD-adherent group had higher BMD-AAz and BMD-HAz than the diagnosis group, and BMD-HAz was also higher in the GFD-adherent group than in the GFD-non-adherent group, suggesting that sustained adherence to a GFD may be a key determinant of improvement in bone mineralization.

Data from different populations likewise show that BMD tends to be lower in patients who have not yet initiated a GFD or who remain non-adherent, and that bone outcomes improve following dietary treatment (4,6,9,11,20). Moreover, pediatric series have reported BMD improvement as early as 6 months after diagnosis when vitamin D and Ca supplementation is appropriately provided, and have highlighted the first year as a particularly critical period for recovery (19,21). Along the same lines, the longer GFD duration observed in the normal BMD group compared with the osteopenia group in our study supports a time-dependent benefit of remaining on a GFD. Overall, these results suggest that gains in bone health in pediatric CD may be more closely related to sustained GFD adherence during follow-up, together with intestinal healing and improved absorption, than to baseline characteristics at diagnosis.

In our cohort, the low BMD group had a lower BMI z-score than the normal BMD group, and BMI z-scores decreased stepwise from the normal BMD group to the osteopenia and osteoporosis groups, suggesting that impaired bone mineralization may accompany a less favorable anthropometric profile. This pattern is biologically plausible, as malabsorption and inadequate weight gain in CD may limit bone mass accrual, and lower body mass may reduce mechanical loading on the skeleton. Prior pediatric data have similarly suggested that a lower BMI may increase the likelihood of low BMD and that BMI could serve as a practical marker for clinical screening of reduced bone density (4,18). However, some pediatric series have reported BMD improvement shortly after diagnosis despite no clear differences in BMI SDS across BMD categories, implying that BMI-independent factors, such as mucosal healing

and improved nutrient absorption, may also contribute to bone recovery (11,21). In this context, and as shown in our study, children with lower BMI z-scores during follow-up may warrant closer evaluation for low BMD, and BMI may be considered a pragmatic clinical indicator within risk-based monitoring strategies.

In our study, Ca, P, ALP, PTH, and 25(OH)D_3 levels were comparable across the diagnosis and follow-up groups and between follow-up subgroups; however, when analyses were stratified by BMD categories, serum Ca levels, while remaining within the normal reference range, were lower in the osteoporosis group than in the normal BMD group. In CD, impaired intestinal absorption of Ca and 25(OH)D_3 due to villous injury and secondary hyperparathyroidism are among the key mechanisms underlying bone loss, and several series have reported lower serum Ca levels in patients who have not yet initiated treatment (4,6,9,11). The absence of between-group differences in 25(OH)D_3 in our cohort may be related to the increasingly widespread use of vitamin D supplementation in the community and routine clinical practice.

Limitations

Limitations should be acknowledged. Due to the retrospective nature of the study, data on the use of supplements such as Ca and/or vitamin D, pubertal characteristics, and fracture history were not available. In addition, the limited sample size in the osteoporosis group may have reduced statistical power for certain comparisons, including those related to GFD duration.

Conclusion

Low BMD is common in children with CD, and the most prominent improvement is observed during follow-up in patients considered adherent to a GFD. Patients in the diagnostic period, those who remain non-adherent during follow-up, and children with a low BMI may be prioritized for closer monitoring. Although routine biochemical parameters are often comparable, lower Ca levels may serve as a warning sign for osteoporosis. Overall, our findings suggest that improvements in bone health during follow-up tend to accompany intestinal healing achieved through GFD adherence, better nutrition, and a higher BMI.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by University of Health Sciences Gülhane Scientific Research Ethics Committee (03.06.2025, reference number: 2025-339).

Contribution of the authors

Study conception and design: ST; data collection: ST, EGB; analysis and interpretation of results: ST, EGB; draft manuscript preparation: ST. All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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