Bone mineral density in adolescents and young women with hypogonadism: a DXA-based comparative analysis

Nurşen Kurtoğlu, Neşe Hayırlıoğlu

Department of Obstetrics and Gynecology, University of Health Sciences Türkiye, Bağcılar Training and Research Hospital, İstanbul, Türkiye

Abstract

Objective: To evaluate bone mineral density (BMD) in adolescent girls and young women with hypogonadism from a gynecologic perspective, and to compare their results with those of patients referred for clinical indications associated with bone health, such as fracture history or chronic medication use.

Material and Methods: This retrospective study included females aged 12-21 years who underwent dual-energy X-ray absorptiometry (DXA) between January 2020 and April 2025 in a tertiary university hospital. Patients were categorized as hypogonadal or non-hypogonadal according to the indication for DXA. Lumbar spine (L1-L4) Z-scores were compared between these groups, with height adjustment applied for patients below the 3rd percentile. Demographic characteristics, vitamin D levels, and BMD Z-scores were analyzed across groups and among hypogonadism subtypes (hypergonadotropic, congenital hypogonadotropic, and functional hypothalamic amenorrhea).

Results: Of the 74 participants, 29 (39.1%) underwent DXA because of hypogonadism. Patients with primary amenorrhea had significantly lower lumbar spine Z-scores than those with secondary amenorrhea ($p<0.01$). The mean lumbar spine Z-score was numerically lower in the hypogonadism group (-1.95±1.04) compared with others (-1.38±1.31), however; this was not significant ($p=0.051$). No significant differences were observed among hypogonadism subtypes. Mean serum 25-hydroxyvitamin D levels were low across all groups (12.9±7.7 ng/mL), indicating widespread deficiency.

Conclusion: Adolescent girls and young women with hypoestrogenic conditions, particularly those with primary amenorrhea exhibited lower BMD, emphasizing the essential role of estrogen in bone mass accrual during adolescence. Early diagnosis, hormone replacement, and optimization of vitamin D and calcium intake will be important for preserving bone health in this high-risk population. [J Turk Ger Gynecol Assoc. 2026; 27(2): 114-9]

Keywords: Adolescent, hypogonadism, bone mineral density, vitamin D deficiency, estrogen deficiency, dual-energy X-ray absorptiometry

Received: December 17, 2025 **Accepted:** April 30, 2026 **Publication Date:** June 02, 2026

Introduction

Osteoporosis is the most common bone disease, affecting approximately one in four women over the age of 50 years, and prevalence increases with age (1). However, approximately 90% of peak bone mass, the key determinant of lifelong bone health, is acquired by the end of adolescence, particularly during puberty (2,3).

Dual-energy X-ray absorptiometry (DXA) is widely used to assess bone health (4) and, in adolescents, is recommended only for those with clinical conditions associated with impaired bone health rather than low-risk individuals (5). In this age

Address for Correspondence: *Nurşen Kurtoğlu*
e-mail: *kurtoglunursen@yahoo.com* ***ORCID:*** *orcid.org/0000-0002-8609-4487*

DOI: *10.4274/jtgga.galenos.2026.2025-12-7*

Cite this article as: *Kurtoğlu N, Hayırlıoğlu N. Bone mineral density in adolescents and young women with hypogonadism: a DXA-based comparative analysis. J Turk Ger Gynecol Assoc. 2026; 27(2): 114-9*

group, DXA results are interpreted using Z-scores and a Z-score below -2 is considered "low bone mineral density (BMD) for age" (4). The International Society for Clinical Densitometry (ISCD) recommends that a diagnosis of pediatric osteoporosis requires both low BMD and a clinically significant fracture history (5).

Peak bone mass is influenced by both genetic and modifiable factors including nutrition, vitamin D status, body mass index (BMI), chronic illnesses, and hormonal status (5,6). Hypogonadism represents a key risk factor because estrogen deficiency impairs bone formation and accelerates resorption (7,8). Therefore, BMD assessment is recommended in reproductive-age women with persistent hypogonadism (8).

Several studies have investigated DXA indications in pediatric populations at risk (9,10). However, to the best of our knowledge, none have specifically evaluated hypogonadism-related bone outcomes in adolescents from a gynecologic perspective. Therefore, this study compared BMD and DXA indications in adolescents and young women with hypogonadism versus those referred for assessment because of other forms of clinical risk. Furthermore, within the hypogonadism cohort, we compared outcomes across etiologies (hypergonadotropic vs. hypogonadotropic hypogonadism) and between primary versus secondary amenorrhea to explore how variations in estrogen deficiency may influence bone mineralization.

Material and Methods

This retrospective study was conducted in the gynecology outpatient clinic of a tertiary university hospital in accordance with the Declaration of Helsinki (Clinical Trial ID: NCT07164248), after ethical approval was obtained from the University of Health Sciences Türkiye, Bağcılar Training and Research Hospital Ethics Committee (approval number: 2025/05/05/048, date: 22.05.2025). Female patients aged 12-21 years who underwent DXA between January 2020 and April 2025 were included. DXA data were retrieved from the hospital electronic medical record system.

DXA scans had been ordered by various specialties, including orthopedics, physical medicine and rehabilitation, neurology, pediatrics, endocrinology, and gynecology. Demographic information (date of birth, age, height, weight), clinical diagnosis, DXA indication, and 25-hydroxyvitamin D (25-OHD) levels (when available) were recorded. Patients were categorized according to DXA indication into hypogonadism and other clinical risk groups. The non-hypogonadal group comprised patients referred for a range of clinical conditions, including fracture history, scoliosis, chronic inflammatory or neurological disorders, and chronic medication use such as glucocorticoids, which may adversely affect bone health.

All scans were performed on the same densitometer (Stratos DR). BMD (g/cm^2) was measured at the lumbar spine (L1-L4) and total hip but only lumbar spine measurements were used in the analysis. As per the ISCD Pediatric Position Development Conference recommendations (11), DXA results were expressed as Z-scores based on chronological age. In patients whose height was <3rd percentile, lumbar spine Z-scores were adjusted using previously published regression equations (12,13).

Within the hypogonadism group, patients were further classified as hypergonadotropic or hypogonadotropic hypogonadism; the latter subgroup was categorized as congenital hypogonadotropic hypogonadism (CHH) or functional hypothalamic amenorrhea (FHA). Demographic parameters, vitamin D levels, and lumbar Z-scores were compared across groups.

Statistical analysis

Descriptive statistics for continuous variables included mean, standard deviation, median, minimum, and maximum; categorical variables were expressed as numbers and percentages. Normality was assessed using the Shapiro-Wilk test. The independent samples t-test was used for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. IBM SPSS, version 20 (SPSS, Chicago, IL, USA) was used for analysis. A $p<0.05$ was considered statistically significant.

Results

Data were obtained from 74 females aged 12-21 years. Of these, 29 (39.1%) were evaluated because of hypogonadism, and primary amenorrhea was the presenting complaint in approximately one-third of these patients. The remaining cases were referred for other risk factors associated with impaired bone health, occasionally with more than one indication. Overall, 17 patients (22.9% of all participants and 37.7% of those evaluated for non-hypogonadal reasons) had a history of fractures. Scoliosis was present in nine patients, and five were evaluated in the postpartum lactation period after adolescent pregnancy, most commonly due to back pain, with a mean lumbar spine Z-score of -2.44. Among non-hypogonadal referrals, multiple sclerosis and chronic steroid exposure each accounted for 13.3% of indications, and the most frequent clinical presentation was back pain and/or vertebral deformities.

As shown in Table 1, no significant differences were observed between the hypogonadism and non-hypogonadal groups in terms of age, height, weight, BMI, or serum 25-OHD levels (all $p>0.05$), indicating that the two cohorts were demographically and anthropometrically comparable.

The mean lumbar spine BMD (L1-L4) Z-score was lower in patients with hypogonadism (-1.95±1.04) compared with

Table 1. Comparison of patients who underwent DXA due to hypogonadism with patients who underwent DXA due to other risk factors

	Total (n=74)	Hypogonadism (n=29)	Other risks (n=45)	p-value
	Mean ± SD Median (min-max)	Mean ± SD Median (min-max)	Mean ± SD Median (min-max)	
Height (cm)	159.11±6.25 160 (136-170)	159.00±6.66 160 (143-170)	159.18±6.05 160 (136-169)	0.906[a]
Weight (kg)	55.07±11.84 54 (33-85)	55.41±11.01 55 (39-78)	54.84±12.46 53 (33-85)	0.842[a]
BMI (kg/m^2)	21.75±4.59 20.9 (13.9-36.2)	22.08±5.17 20.9 (15.0-36.2)	21.54±4.22 21.0 (13.9-31.2)	0.624[a]
Age (years)	17.48±2.64 17 (12-21)	17.48±1.95 17 (14-21)	17.16±3.02 17 (12-21)	0.933[b]
L1-4 Z score	-1.54±1.28 -1.8 (-3.9-1.7)	-1.95±1.04 -1.9 [-3.9-(-1.0)]	-1.38±1.31 -1.6 (-3.9–1.7)	0.051[b]
25-OHD (ng/mL)	Total 47 patients 12.96±7.74 10 (3-31)	15 patients 14.00±8.70 10 (4-31)	32 patients 12.63±7.48 10 (3-31)	0.609[b]

[a]Independent groups t-test (independent samples t-test)
[b]Mann-Whitney U test
BMI: Body mass index, SD: Standard deviation, min: Minimum, max: Maximum, DXA: Dual-energy X-ray absorptiometry, L1-L4: Lumbar spine, 25-OHD: 25-hydroxyvitamin D

those evaluated for other risk factors (-1.38±1.31), however, this difference was not significant (p=0.051).

Serum 25-OHD values were available for 47 patients (59.5%), with an overall mean concentration of 12.96±7.74 ng/mL. Consistent with the group comparisons, no significant difference was observed between the hypogonadism and non-hypogonadal groups (p=0.609).

Of the 29 patients diagnosed with hypogonadism, 17 (58.6%) had hypergonadotropic hypogonadism, including 12 with secondary and five with primary amenorrhea. Notably, one patient with galactosemia presented with primary amenorrhea and had a markedly low lumbar spine (L1-L4) Z-score of -3.6. Among the chromosomal etiologies, one patient with Turner syndrome (16 years old, height 145 cm) had a raw Z-score of -3.9, which improved to -2.4 after height adjustment; another with Down syndrome (18 years old, height 143 cm) had a corrected Z-score of 1.0. Two patients with a history of chemotherapy (one for leukemia, one for osteosarcoma) were also present in this group.

Seven patients (24.1%) had FHA, all presenting with secondary amenorrhea, while four patients (13.8%) were diagnosed with CHH, all with primary amenorrhea. One patient (3.4%) had hyperprolactinemia related hypogonadism. Among patients with secondary amenorrhea, the mean age at menarche was 13.05±1.90 years and the mean duration of amenorrhea before DXA assessment was 16.1±9.9 months.

A significant difference was found between the lumbar spine (L1-L4) Z-scores of patients with primary amenorrhea and those with secondary amenorrhea (p<0.01). Patients with primary amenorrhea had lower L1-L4 Z-scores compared to those with secondary amenorrhea (Table 2).

Lumbar spine (L1-L4) Z-scores among hypogonadism subtypes are presented descriptively in Table 3. Mean Z-scores were lowest in patients with CHH, followed by those with hypergonadotropic hypogonadism, while patients with FHA exhibited relatively higher mean values. Given the small sample size, particularly in the CHH subgroup, no inferential statistical comparisons were performed, and these findings are presented for descriptive purposes only.

Discussion

In this study, adolescent girls with hypoestrogenic conditions exhibited lower BMD compared with patients evaluated for other clinical risk factors, although this difference did not quite reach statistical significance. Nevertheless, estrogen plays a well-established and critical role in skeletal development and the attainment of much of peak bone mass during adolescence, as consistently demonstrated in previous studies (14,15). In particular, patients with primary amenorrhea exhibited markedly reduced lumbar spine Z-scores compared with those with secondary amenorrhea, which may reflect earlier onset and longer duration of estrogen deficiency during the pubertal period. However, this difference should be interpreted with caution, as delayed skeletal maturation is common in adolescents with hypogonadism presenting with primary amenorrhea, and Z-scores calculated based on chronological

Table 2. Comparison of L1-4 Z score values between patients with primary amenorrhea and patients with secondary amenorrhea

	Primary amenorrhea (n=9)	Secondary amenorrhea (n=20)	p-value
	Mean ± SD Median (min-max)	Mean ± SD Median (min-max)	
L1-4 Z score	-2.94±0.93 -3.30 (-3.9-1.5)	-1.68±0.69 -1.8 (-2.9-0.1)	**0.002**[b]

[b]Mann-Whitney U test
SD: Standard deviation, min: Minimum, max: Maximum, L1-L4: Lumbar spine

Table 3. Comparisons of L1-4 Z score values between diagnoses in patients who requested DXA examination due to amenorrhea

	Hypergonadotropic hypogonadism (n=17)	FHA (n=7)	Congenital hypogonadotropic hypogonadism (n=4)
	Mean ± SD Median (min-max)	Mean ± SD Median (min-max)	Mean ± SD Median (min-max)
L1-4 Z score	-2.14±1.10 -1.9 (-3.9-0.1)	-1.77±0.60 -1.9 [-2.4-(-0.8)]	-2.52±0.75 -2.6 [-3.3-(-1.5)]

SD: Standard deviation, min: Minimum, max: Maximum, DXA: Dual-energy X-ray absorptiometry, L1-L4: Lumbar spine, FHA: Functional hypothalamic amenorrhea

age may overestimate the severity of low bone mass in this group. These findings support the importance of timely diagnosis and treatment in girls who fail to achieve menarche, while highlighting the need for bone age-adjusted assessments in future studies to more accurately characterize bone health.

Although the cohort size was relatively small, the inclusion of a well-defined adolescent population highlights the vulnerability of this age group, in whom estrogen deficiency may disrupt the acquisition of peak bone mass and increase lifetime fracture risk. Beyond hypoestrogenism, several other clinical conditions, such as chronic inflammatory disease, glucocorticoid exposure, neurological disorders, and adolescent pregnancy and lactation, also contributed to reduced BMD in our cohort. The comparison between hypogonadal and non-hypogonadal risk groups, as well as among distinct hypogonadal etiologies, suggests that various conditions leading to reduced estrogen exposure may influence lumbar spine bone density although not all differences reached statistical significance. The lack of a statistically significant difference in BMD between hypogonadal patients and the comparison group may be partly attributable to the non-healthy nature of the control population, which included individuals with clinical conditions known to adversely affect bone health. In this context, the absence of significance likely reflects underlying bone vulnerability in both groups rather than a true lack of effect of hypoestrogenism. Early recognition of high-risk profiles is therefore essential to guide individualized management strategies.

Among hypogonadal patients, the majority had hypergonadotropic hypogonadism, including individuals with primary ovarian insufficiency (POI). POI and related causes of ovarian failure are recognized contributors to hypoestrogenism and low BMD, with greater impact when diagnosis and hormonal treatment are delayed (14,16). Additional etiologies in our cohort, such as Turner syndrome, galactosemia, and treatment-related ovarian dysfunction, similarly impair bone accrual through a combination of estrogen deficiency and intrinsic skeletal vulnerability (17-19). Although the specific mechanisms differ, the common pathway involves disruption of pubertal estrogen exposure and consequent reduction in trabecular bone, particularly in the lumbar spine.

FHA and CHH represented additional hypoestrogenic states in our study. FHA is frequently associated with secondary amenorrhea in adolescents, while CHH typically presents as primary amenorrhea due to impaired GnRH secretion (7,20). In both conditions, delayed estrogen replacement may result in insufficient bone mineralization during adolescence, supporting recommendations for early evaluation and pubertal induction in individuals with persistent hypoestrogenism (21).

Of note, vitamin D deficiency was widespread in 60% of our cohort (mean serum 25-OHD: 12.96 ng/mL), consistent with previous reports linking low vitamin D status to impaired bone development during adolescence (22,23). Concentrations below 10-12 ng/mL are associated with impaired bone mineralization, whereas values <20 ng/mL indicate biochemical deficiency (22,23). Nevertheless, vitamin D levels did not differ significantly between hypogonadal and non-hypogonadal groups, suggesting

that low estrogen exposure rather than vitamin D deficiency may be the dominant determinant of BMD in this setting.

Study limitations

The main strength of this study is the evaluation of BMD in adolescents and young women with a spectrum of risk factors, allowing a gynecologic comparison of hypoestrogenic conditions within a broader at-risk population. The interdisciplinary referrals enabled examination of diverse etiologies that may affect peak bone mass during this critical developmental period.

Another strength is the demographic homogeneity between groups, which reduces confounding related to age, anthropometry, and vitamin D status and supports the validity of the observed differences in lumbar spine Z-scores.

However, the retrospective design limited the availability of potentially relevant variables such as nutritional status, physical activity, detailed medication history, and familial predisposition. Furthermore, menstrual history and age at menarche were often undocumented in patients referred from non-gynecologic specialties, limiting a more comprehensive endocrine assessment. The relatively small sample size also limits generalizability. It is important to note that the comparison group in this study comprised patients referred for DXA due to various clinical indications, including conditions known to be associated with reduced BMD, such as chronic steroid use. As a result, the true difference in BMD between hypogonadal patients and healthy adolescents may be greater than that observed in the present study but would require a healthy control group to confirm.

Although height-adjusted Z-scores were used in patients with short stature in accordance with pediatric DXA recommendations, the absence of bone age assessment remains a limitation of this study. In adolescents with hypogonadism and delayed puberty, bone age is frequently delayed. Consequently, Z-scores calculated based on chronological age may overestimate the severity of low bone mass (24). Future studies incorporating bone age adjusted assessments may help distinguish delayed skeletal maturation from true osteopenia.

Conclusion

This study highlights a significant difference in BMD between adolescents and young women with primary and secondary amenorrhea, with markedly lower lumbar spine Z-scores observed in those with primary amenorrhea. This finding suggests that earlier onset and longer duration of estrogen deficiency may adversely affect bone mineral accrual during adolescence, although this interpretation should be considered in light of delayed skeletal maturation in this group. The comparison between hypogonadal patients and those referred for other bone health-related indications did not demonstrate a significant difference in BMD. In addition, the uniformly low serum 25-OHD levels across the cohort indicate a widespread deficiency that may further compromise skeletal health.

Taken together, these results emphasize the importance of early identification of amenorrhea, particularly primary amenorrhea, and timely evaluation of bone health. Prompt hormonal management, along with optimization of vitamin D and calcium intake and lifestyle interventions, may be important for preserving bone mass during this vulnerable developmental period.

Ethics

Ethics Committee Approval: *Ethical approval for this study was obtained from the University of Health Sciences Türkiye, Bağcılar Training and Research Hospital Ethics Committee (approval number: 2025/05/05/048, date: 22.05.2025).*

Informed Consent: *Due to the retrospective design of the study, informed consent was waived by the Ethics Committee.*

Footnotes

Author Contributions: *Concept: N.K., Design: N.K., Data Collection or Processing: N.K., N.H., Analysis or Interpretation: N.K., N.H., Literature Search: N.K., N.H., Writing: N.K.*

Conflict of Interest: *No conflict of interest is declared by the authors.*

Financial Disclosure: *The authors declared that this study received no financial support.*

References

1. Yordanov A, Vasileva-Slaveva M, Tsoneva E, Kostov S, Yanachkova V. Bone health for gynaecologists. Medicina (Kaunas). 2025; 61: 530.
2. Gordon RJ, Gordon CM. Adolescents and bone health. Clin Obstet Gynecol. 2020; 63: 504-11.
3. Laine CM, Laine T. Diagnosis of osteoporosis in children and adolescents. Eur Endocrinol. 2013; 9: 141-4.
4. Adams JE. Bone densitometry in children. Semin Musculoskelet Radiol. 2016; 20: 254-68.
5. Guss CE, McAllister A, Gordon CM. DXA in children and adolescents. J Clin Densitom. 2021; 24: 28-35.
6. Zhu X, Zheng H. Factors influencing peak bone mass gain. Front Med. 2021; 15: 53-69.
7. Indirli R, Lanzi V, Mantovani G, Arosio M, Ferrante E. Bone health in functional hypothalamic amenorrhea: what the endocrinologist needs to know. Front Endocrinol (Lausanne). 2022; 13: 946695.
8. Jayasena CN, Devine K, Barber K, Comninos AN, Conway GS, Crown A, et al. Society for endocrinology guideline for understanding, diagnosing and treating female hypogonadism. Clin Endocrinol (Oxf). 2024; 101: 409-42.

9. Topor LS, Melvin P, Giancaterino C, Gordon CM. Factors associated with low bone density in patients referred for assessment of bone health. Int J Pediatr Endocrinol. 2013; 2013: 4.
10. Bianchi ML, Leonard MB, Bechtold S, Högler W, Mughal MZ, Schönau E, et al. Bone health in children and adolescents with chronic diseases that may affect the skeleton: the 2013 ISCD Pediatric Official Positions. J Clin Densitom. 2014; 17: 281-94.
11. Gordon CM, Leonard MB, Zemel BS; International Society for Clinical Densitometry. 2013 Pediatric Position Development Conference: executive summary and reflections. J Clin Densitom. 2014; 17: 219-24.
12. Zemel BS, Leonard MB, Kelly A, Lappe JM, Gilsanz V, Oberfield S, et al. Height adjustment in assessing dual energy x-ray absorptiometry measurements of bone mass and density in children. J Clin Endocrinol Metab. 2010; 95: 1265-73.
13. Zemel BS, Kalkwarf HJ, Gilsanz V, Lappe JM, Oberfield S, Shepherd JA, et al. Revised reference curves for bone mineral content and areal bone mineral density according to age and sex for black and non-black children: results of the bone mineral density in childhood study. J Clin Endocrinol Metab. 2011; 96: 3160-9. Erratum in: J Clin Endocrinol Metab. 2013; 98: 420.
14. Popat VB, Calis KA, Vanderhoof VH, Cizza G, Reynolds JC, Sebring N, Bone mineral density in estrogen-deficient young women. J Clin Endocrinol Metab. 2009; 94: 2277-83.
15. Lu Y, Lu P, Lin L, Chen H, Zhang F, Li X. Characteristics of bone mineral density in patients with functional hypothalamic amenorrhoea and its association with reproductive hormones and body composition. Clin Endocrinol (Oxf). 2024; 100: 358-65.
16. Federici S, Rossetti R, Moleri S, Munari EV, Frixou M, Bonomi M, et al. Primary ovarian insufficiency: update on clinical and genetic findings. Front Endocrinol (Lausanne). 2024; 15: 1464803.
17. Chiarito M, Brunetti G, D'Amato G, Faienza MF. Monitoring and maintaining bone health in patients with Turner syndrome. Expert Rev Endocrinol Metab. 2020; 15: 431-8.
18. Wasserman H, O'Donnell JM, Gordon CM. Use of dual energy X-ray absorptiometry in pediatric patients. Bone. 2017; 104: 84-90.
19. Thakur M, Feldman G, Puscheck EE. Primary ovarian insufficiency in classic galactosemia: current understanding and future research opportunities. J Assist Reprod Genet. 2018; 35: 3-16.
20. Young J, Xu C, Papadakis GE, Acierno JS, Maione L, Hietamäki J, et al. Clinical management of congenital hypogonadotropic hypogonadism. Endocr Rev. 2019; 40: 669-710.
21. Voutsadaki K, Matalliotakis M, Ladomenou F. Hypogonadism in adolescent girls: treatment and long-term effects. Acta Biomed. 2022; 93: e2022317.
22. Smith TJ, Tripkovic L, Lanham-New SA, Hart KH. Vitamin D in adolescence: evidence-based dietary requirements and implications for public health policy. Proc Nutr Soc. 2018; 77: 292-301.
23. Płudowski P, Kos-Kudła B, Walczak M, Fal A, Zozulińska-Ziółkiewicz D, Sieroszewski P, et al. Guidelines for preventing and treating vitamin d deficiency: a 2023 update in Poland. Nutrients 2023; 15: 695.
24. Gordon CM, Bachrach LK, Carpenter TO, Crabtree N, El-Hajj Fuleihan G, Kutilek S, et al. Dual energy X-ray absorptiometry interpretation and reporting in children and adolescents: the 2007 ISCD Pediatric Official Positions. J Clin Densitom. 2008; 11: 43-58.