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Vitamin K2 deficiency associated with short stature in children: a cross-sectional study

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Abstract

Background Short stature in children is a common concern that can result from various underlying conditions. While factors such as growth hormone deficiency and nutritional deficiencies are well-known contributors, the role of vitamin K2 (VK2) in the development of short stature remains underexplored. This study aimed to investigate the association between VK2 status and short stature in children.

Methods A total of 730 children aged 3–16 years were enrolled and divided into three groups: short stature group ($n=191$), near-short stature group ($n=357$), and normal stature group ($n=182$). Clinical characteristics and growth-related indicators including serum VK2 levels, bone mineral density (BMD), insulin-like growth factor 1 (IGF-1), and 25-hydroxyvitamin D (25-(OH)D) were collected. VK2 was analyzed both as a categorical variable (VK2 deficiency vs. normal status) and as a continuous variable, logistic regression models were applied to assess the association between VK2 status and short stature using both approaches. Correlations between VK2 status and other growth-related indicators were also examined.

Results The prevalence of VK2 deficiency was higher in children with short stature (80.6%) and near-short stature (64.7%) compared to those with normal stature (32.4%) ($P<0.05$). Multiple logistic regression models showed that higher serum VK2 levels were significantly associated with a decreased risk of short stature (aOR = 0.005, 95% CI: 0.001–0.036) and near-short stature (aOR = 0.023, 95% CI: 0.006–0.085); and VK2 deficiency was significantly associated with increased risk of short stature (aOR = 5.934, 95% CI: 3.372–10.443) and near-short stature (aOR = 3.233, 95% CI: 2.095–4.989) after adjusting for covariates. Additionally, serum VK2 levels were positively correlated with IGF-1-SDS and 25(OH)D ($P<0.05$).

Conclusions VK2 deficiency was significantly associated with an increased risk of short stature in children. Further longitudinal studies are warranted to elucidate the causal relationship between VK2 deficiency and growth disorders in pediatric populations.

Keywords Vitamin K2, Short stature, Children

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Background

Short stature in children is a significant health concern with both physical and psychological consequences. It is clinically defined as a height that falls below the third percentile or more than two standard deviations below the mean for age, sex, and ethnicity under comparable environmental conditions [1]. Globally, it is estimated that 149 million children under 5 experience growth concerns [2], with approximately 3.2% of children in China diagnosed with short stature, equating to roughly 7 million affected children [3]. Alarmingly, less than 5% of these children receive standardized treatment [4]. The consequences of untreated short stature extend beyond physical growth deficits, affecting social interactions, self-esteem, and overall quality of life [5]. The underlying causes of short stature are multifactorial, including genetic factors, endocrine disorders, chronic diseases, and nutritional deficiencies [6]. While growth hormone deficiency and other hormonal imbalances have long been recognized as major contributors to short stature, emerging evidence have indicated that micronutrients—especially fat-soluble vitamins—may play an essential role in regulating growth and skeletal development [7–9].

Vitamin K2 (VK2) is a crucial fat-soluble vitamin with a wide range of roles in human health. Numerous studies have demonstrated a broadly positive correlation between VK2 supplementation and improved health outcomes [10–13]. VK2 plays a pivotal role in bone health, activating osteocalcin (OC) and matrix Gla protein, which is fundamental for proper skeletal development and growth in children [14, 15]. In addition, VK2 has been shown to influence other biological processes, including cellular growth, apoptosis, and angiogenesis, which may have indirect implications for overall development [16]. Therefore, VK2 deficiencies may hinder bone mineralization, impairing bone density and potentially leading to growth retardation [14, 17, 18]. VK2 is primarily found in fermented foods such as natto (fermented soybeans), cheese, and other dairy products, as well as animal-based foods like liver, egg yolks, and certain meats [19]. However, due to regional dietary patterns and shifts in eating habits, the intake of VK2 varies significantly among populations, which may influence its biological effects on growth and development. Additionally, children and adolescents have particularly high requirements for VK2, given that bone formation is most active during these stages [20]. Approximately 90% of peak bone mass is attained by the age of 18 or 19, with nearly 25% accruing during the two-year period surrounding the peak height velocity phase of bone growth [21, 22].

Although emerging evidence suggests a possible association between VK2 deficiency and short stature, current research remains limited and inconclusive [23, 24]. Most existing studies are conducted in populations with different dietary backgrounds, which complicates the generalization of findings across regions [25]. Moreover, variations in dietary intake and regional differences in VK2 levels may influence the outcomes [26], highlighting the need for region-specific studies to determine whether a significant association exists. Therefore, this cross-sectional study aims to investigate the association between VK2 deficiency and short stature in children in Guilin, China, and examining whether lower VK2 concentrations correlate with reduced growth outcomes in children diagnosed with short stature.

Methods

Study design and participants

This cross-sectional study was conducted at the Guilin Maternal and Child Health Hospital between September 2022 and September 2024. A total of 730 children aged 3 to 16 years were enrolled and categorized into three groups: short stature, the near-short stature, and the normal stature, based on standardized height percentiles. The short stature group comprised children who met the diagnostic criteria for short stature as outlined in the "Guidelines for the Diagnosis and Treatment of Children with Short Stature" [27], published by the Subspecialty Group of Endocrinologic, Hereditary, and Metabolic Diseases, The Society of Pediatrics, Chinese Medical Association. The near-short stature group included children whose height was between the 3rd and 25th percentiles, while the normal stature group consisted of children with height above the 25th percentile for their age and sex, and who did not have any known growth disorders or medical conditions that could affect growth.

The inclusion criteria were as follows: [1] children aged 3–16 years; [2] normal newborn size; [3] normal hearing and speech abilities; [4] no severe neurological or congenital organ/tissue abnormalities; and [5] no history of chronic illness or genetic conditions affecting growth, such as genetic bone metabolism disorders, myelodysplastic syndromes, or parathyroid dysfunction. Children with physical disabilities, recent use of medications (e.g., cyclophosphamide, vinorelbine) that inhibit bone marrow or erythropoiesis, recent illness or significant dietary changes within two weeks prior to the blood test, or participation in other clinical trials were excluded. This study was approved by the Ethics Committee of the Guilin Maternal and Child Health Hospital, and informed consent was obtained from both the children and their legal guardians.

Data collection

Data on clinical characteristics and growth-related indicators were collected for all participants. Clinical characteristics included age, sex, height, weight, body mass index (BMI), parents' height, family history, and results

from a general physical examination. Growth-related indicators included VK2, insulin-like growth factor 1 (IGF-I), 25-hydroxyvitamin D [25(OH)D], and bone mineral density (BMD) Z-score.

Measures

Physical measurements of all participants were recorded according to standard procedures. Height was measured using a standardized height-measuring instrument, according to the "Chinese Child Physical Growth Evaluation Recommendations" by the Chinese Pediatric Society. Measurements were taken three times, and the average value was recorded to a precision of 0.1 cm. Weight was recorded using a calibrated electronic scale, with an accuracy of 0.1 kg, while participants were in a fasting state and wearing light clothing without shoes. BMI was calculated using the formula: weight (kg) / height² (m^2).

Serum samples were meticulously collected from all participants and subsequently analyzed to evaluate the levels of VK2, IGF-I, and 25(OH)D. Serum VK2 levels were measured using high-performance liquid chromatography coupled with mass spectrometry (AB SCIEX Jasper HPLC MS TRIPLE QUAD 4500MD), a highly sensitive and specific analytical method that allows for precise measurement of low-concentration analytes in complex biological matrices [28]. The cutoff for VK2 deficiency (< 0.10 ng/mL) was derived from MDI Laboratory reference values and has been previously used in studies involving pediatric populations [17]. IGF-I concentrations were measured using microparticle chemiluminescence immunoassay (Autobio A6200), and the IGF-1 SDS was determined by comparing IGF-1 levels to those of Chinese children of the same age and sex [29]. 25(OH)D levels were determined by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS), 25(OH)D insufficiency was defined as serum levels between 12 and 20 ng/ml, and sufficiency as levels above 20 ng/ml [30]. BMD Z-score was assessed using dual-energy X-ray absorptiometry (DXA). To ensure the accuracy of the measurements, quality control specimens were randomly tested daily, maintaining an error rate within 5% and guaranteeing both the integrity of the measuring instruments and the reliability of the data.

Table 1 Baseline characteristics of study populations ($n = 730$)

Variable	*n* (%)/ M (SD)
Age (year)	7.29 (2.97)
Sex (n, %)	
Male	491 (67.3)
Female	239 (32.7)
BMI (kg/m^2)	15.13 (2.21)
BMI-SDS	-0.79 (1.09)
Height of father (cm)	167.30 (4.47)
Height of mother (cm)	155.15 (3.99)

BMI, body mass index; SD, standard deviation; SDS, standard deviation score

Statistical analysis

Missing data was handled using Multiple Imputation. Continuous variables were summarized as means with standard deviations (SD) for normally distributed data, or medians with interquartile ranges (IQR) for non-normally distributed data. Categorical variables were presented as frequencies (n) and proportions (%). For univariate analysis, one-way ANOVA was used for continuous variables, while chi-square tests or Fisher's exact tests were applied for categorical variables. The associations between serum VK2 levels and growth-related indicators were evaluated using Pearson correlation analysis.

Multiple logistic regression was employed to determine the independent contribution of VK2 to short stature since ordered logistic regression was unsuitable for multivariate analysis due to parallel lines test violations ($P < 0.05$). VK2 was evaluated both as a continuous variable as well as a categorical variable, it was then entered into distinct multiple logistic regression models in each form rather than simultaneously to avoid multicollinearity. Variables that were statistically significant in univariate analyses were included as covariates in multiple models. Results are presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). All statistical analyses were performed using SPSS 26.0 software and R software (version 4.4.2; https://www.r-project.org/). A two-tailed P value of < 0.05 was considered statistically significant.

Results

Characteristics of study populations

A total of 730 children participated in this study, comprising 191 (26.2%) with short stature, 357 (48.9%) with near short stature, and 182 (24.9%) with normal stature. The mean age of the participants was 7.30 (2.98) years, with a predominance of male subjects (67.3%). The BMI and SDS for BMI of study populations were 15.13 (2.21) kg/m^2 and −0.79 (1.09), and parents' heights of study populations were 167.30 (4.47) cm and 155.15 (3.98) cm for father and mother, respectively (shown in Table 1). The VK2 status and other growth-related indicators were summarized in Table 2.

Univariate association between study variables and short stature

The results of the univariate analyses are presented in Table 3. The mean age of the short stature group was significantly higher than that of the normal stature group ($P < 0.001$), while no significant difference was observed between the near-short stature and normal stature groups ($P > 0.05$). BMI and height of father were

Table 2 Distribution of growth-related indicators ($n=730$)

Variable	*n* (%)/ M (SD)
BMD Z-score	0.85 (0.85)
IGF-1 (ng/ml)	161.50 (89.46)
IGF-1-SDS	-0.57 (1.03)
25(OH)D (ng/ml)	31.10 (8.58)
25(OH)D group	
Sufficiency	679 (93.0)
Insufficiency	51 (7.0)
VK2 (ng/ml)	0.14 (0.16)
VK2 group	
Normal	286 (39.2)
Deficiency	444 (60.8)

BMD, bone mineral density; IGF-1, insulin-like growth factor 1; 25(OH)D, 25-hydroxyvitamin D; SD, standard deviation; SDS, standard deviation score; VK2, vitamin K2

Table 3 Univariate analyses between baseline characteristics and short stature ($n=730$)

Variable	Short stature (*n* = 191)	Near-short stature (*n* = 357)	Normal stature (*n* = 182)	*P* value
Age (year)	6.57 (3.09)	7.42 (2.78)	7.84 (3.10)	< 0.001
Sex (n, %)				0.273
Male	134 (70.2)	243 (68.1)	114 (62.6)	
Female	57 (29.8)	114 (31.9)	68 (37.4)	
BMI (kg/m^2)	14.73 (1.54)	14.99 (1.96)	15.86 (2.99)	< 0.001
BMI-SDS	-0.85 (1.01)	-0.76 (1.10)	-0.77 (1.16)	0.603
Height of father (cm)	166.61 (4.59)	167.24 (4.51)	168.13 (4.14)	0.004
Height of mother (cm)	154.18 (4.01)	155.28 (3.91)	155.89 (3.93)	< 0.001
BMD Z-score	0.61 (0.91)	0.95 (0.80)	0.89 (0.85)	< 0.001
IGF-1 (ng/ml)	110.65 (69.93)	161.70 (84.90)	213.32 (88.72)	< 0.001
IGF-1-SDS	-1.21 (0.91)	-0.55 (0.96)	0.06 (0.84)	< 0.001
25(OH)D (ng/ml)	28.79 (7.91)	29.42 (7.95)	36.80 (7.91)	< 0.001
25(OH)D group				0.822
Sufficiency	174 (91.1)	328 (91.9)	165 (90.7)	
Insufficiency	17 (8.9)	29 (8.1)	17 (9.3)	

BMI, body mass index; BMD, bone mineral density; IGF-1, insulin-like growth factor 1; 25(OH)D, 25-hydroxyvitamin D; SDS, standard deviation score

significantly different between the short stature and normal stature groups, as well as between the near-short stature and normal stature groups ($P<0.05$); for height of mother, significant differences were observed between the short stature and normal stature groups, as well as between the short stature and near-short stature groups ($P<0.05$). For growth-related indicators, BMD Z-score were significantly different between the short stature and normal stature groups, as well as between the short stature and near-short stature groups ($P<0.05$); 25(OH)D levels were significantly different between the short stature and normal stature groups, near-short stature and normal stature groups ($P<0.05$). The IGF-1 levels and IGF-1-SDS differed significantly across the three groups ($P<0.05$).

Table 4 Differences in VK2 levels among study populations ($n=730$)

Variable	Short stature (*n* = 191)	Near-short stature (*n* = 357)	Normal stature (*n* = 182)	*P* value
VK2 (ng/ml)	0.09 (0.15)	0.11 (0.11)	0.23 (0.23)	< 0.001
VK2 group (n, %)				< 0.001
Normal	37 (19.4)	126 (35.3)	123 (67.6)	
Deficiency	154 (80.6)	231 (64.7)	59 (32.4)	

VK2, Vitamin K2

Table 5 Multiple logistic regression analyses in VK2 levels among study populations ($n=730$)

Variable	Short stature (*n* = 191)		Near-short stature (*n* = 357)	
	B	aOR(95%CI)	B	aOR(95%CI)
VK2 (ng/ml)	-5.39	0.005 (0.001–0.036)	-3.77	0.023 (0.006–0.085)
VK2 group	1.78	5.934 (3.372–10.443)	1.173	3.233 (2.095–4.989)

VK2, Vitamin k2; aOR, adjusted odds ratio; CI, confidence interval; Normal stature group was the reference group

Differences in VK2 status

Table 4 summarize the differences in VK2 status among three groups. There were significant differences in serum VK2 levels between the short stature and normal stature groups, as well as between the near-short stature and normal stature groups ($P<0.001$). In addition, the prevalence of VK2 deficiency was significantly higher in children with short stature (80.6%) and near-short stature (64.7%) compared to the normal stature group (32.4%) ($P<0.05$).

Multiple logistic regression analyses between VK2 and short stature

The results of the multiple logistic regression analyses examining the association between VK2 status and short stature are presented in Table 5. VK2 was evaluated both as a continuous variable as well as a categorical variable, with VK2 deficiency defined as < 0.10 ng/mL based on reference ranges. Variables that were statistically significant in univariate analyses—including age, parents' height, BMD Z-score, IGF-1-SDS, and 25(OH)D—were included as covariates in the multiple models. After adjusting for these covariates, higher VK2 levels were significantly associated with a decreased risk of short stature (aOR = 0.005, 95% CI: 0.001–0.036) and near-short stature (aOR = 0.023, 95% CI: 0.006–0.085); and VK2 deficiency was significantly associated with increased risk of short stature (aOR = 5.934, 95% CI: 3.372–10.443) and near-short stature (aOR = 3.233, 95% CI: 2.095–4.989).

Correlation between serum VK2 levels and growth-related indicators

The correlation between serum VK2 levels and growth-related indicators is shown in Table 6. BMI ($r = 0.10$, $P = 0.005$), IGF-1 ($r = 0.20$, $P < 0.001$), IGF-1-SDS ($r = 0.26$, $P < 0.001$) and 25(OH)D ($r = 0.15$, $P < 0.001$) were significantly correlated with serum VK2 levels. However, there was no significant correlation between serum VK2 levels and BMD Z-score ($P > 0.05$), indicating that VK2 levels may not show a direct association with BMD, despite its known biological role in bone metabolism.

Table 6 Correlation between serum VK2 levels and growth-related indicators among study populations ($n = 730$)

Variables	*r* (VK2)	*P* value
BMI	0.10	0.005
BMI-SDS	-0.03	0.454
BMD Z-score	0.02	0.674
IGF-1	0.20	< 0.001
IGF-1-SDS (ng/ml)	0.26	< 0.001
25(OH)D (ng/ml)	0.15	< 0.001

BMD, bone mineral density; BMI, body mass index; IGF-1, insulin-like growth factor 1; 25(OH)D, 25-hydroxyvitamin D; SDS, standard deviation score

Discussion

This study identified a significant association between VK2 deficiency and short stature in children. The prevalence of VK2 deficiency was significantly higher among children with short stature (80.6%) and near-short stature (64.7%) compared to those with normal stature (32.4%). Children in the short stature and near-short stature groups also exhibited markedly lower serum VK2 levels than their normal-stature counterparts, suggesting that VK2 deficiency may contribute to impaired growth. Additionally, serum VK2 levels showed a positive correlation with key growth-related indicators, such as IGF-1 and 25(OH)D, supporting the potential role of VK2 in skeletal development. These findings suggest that VK2 deficiency may disrupt longitudinal bone growth. The novelty of this study lies in identifying VK2 as a potentially modifiable factor associated with childhood growth, offering new perspectives for nutritional or therapeutic interventions aimed at addressing growth disorders.

The results of this study were consistent with prior studies linking VK2 with bone health and growth [8, 15, 20]. Previous studies have highlighted the role of VK2 in bone metabolism, with several showing that VK2 plays a critical role in OC activation, which is essential for bone mineralization and overall bone health [14, 31]. For example, Kim et al. [32] reported that VK2 supplementation effectively counters vitamin C, enhances bone density, and offers neuroprotective, hepatoprotective, and anti-inflammatory benefits. A study conducted by Xie et al. [33] also reported that VK2 exhibited effects on maintaining or increasing lumbar spine BMD, and influencing the balance of carboxylated osteocalcin (cOC) and uncarboxylated osteocalcin (ucOC). However, studies specifically exploring the relationship between VK2 deficiency and short stature in children remain limited. Most of the current research focuses on the role of VK2 in preventing osteoporosis and increasing bone density in elderly and postmenopausal women [13, 25, 34], but similar studies in children are scarce [23]. Therefore, this study extends this body of evidence by suggesting that VK2 deficiency could impact growth and contribute to short stature in pediatric populations.

Additionally, the relationship between VK2 and short stature remained significant after adjusting for key covariates such as age, IGF-1, and 25(OH)D levels. These adjustments are critical because both 25(OH)D and other growth factors have been shown to influence bone health and linear growth in children [35–37]. By controlling for these factors, we were able to more clearly isolate the independent effect of VK2 on growth. The persistence of the observed associations after adjusting for potential confounders suggests that VK2 may have an independent, protective effect on height development. This strengthens the argument that VK2 is not merely a biomarker reflecting bone health, but an active participant in regulating growth.

Furthermore, this study explored the relationship between VK2 and other biomarkers associated with growth, particularly IGF-1, BMD, and 25(OH)D levels. VK2 plays a crucial role in bone health through its activation of OC, a protein that binds calcium to the bone matrix, promoting bone mineralization [38, 39]. Moreover, VK2 is also involved in regulating the growth hormone axis, particularly in its interaction with IGF-1 [40], a critical factor for longitudinal bone growth [37]. This study demonstrated a positive correlation between serum VK2 levels and IGF-1, suggesting that VK2 deficiency might impair IGF-1 signaling, thus inhibiting proper bone growth. In addition, VK2 is also thought to influence BMD and the mechanical properties of bones, making it an essential nutrient for skeletal development [32, 41]. However, in this study, no significant correlation was found between VK2 and BMD, which suggests that VK2 may not directly influence BMD in the study population. Although previous studies have suggested that VK2 contributes to bone health through its effects on BMD, this study did not find a significant correlation between serum VK2 levels and BMD. This discrepancy may be due to the cross-sectional nature of the study, age variability, or differences in BMD measurement sensitivity in children. It is also possible that VK2 influences bone health through other mechanisms not captured solely by BMD, such as improving bone quality or influencing bone metabolism markers. Future longitudinal studies incorporating a broader range of bone health indicators

may provide more clarity. Additionally, this study found that higher serum VK2 levels were associated with higher 25(OH)D levels, reinforcing the idea of a synergistic relationship between VK2 and Vitamin D in bone health [42]. As Vitamin D is crucial for calcium absorption, and VK2 enhances calcium binding in the bone matrix, the combination of these two vitamins appears to play a critical role in skeletal development [43]. This potential disruption in bone metabolism and growth processes could explain the association between VK2 deficiency and short stature.

However, this study has some limitations to consider. Firstly, this was a cross-sectional study, which cannot establish a causal relationship between VK2 deficiency and growth, longitudinal studies are needed to clarify causality. Secondly, we only measured serum VK2 levels at a single time point, and potential fluctuations over time may influence its relationship with growth. Thirdly, this study did not collect data on pubertal stage (e.g., Tanner staging), age at menarche in girls, all of which are important factors influencing growth potential, future studies could address these limitations to validate and refine our results. Moreover, the generalizability of our findings may be limited by the specific population, further studies in diverse populations, including children from different ethnic backgrounds and regions, would be valuable to confirm the broader applicability.

Conclusions

This study demonstrates a significant association between VK2 deficiency and short stature, suggesting its potential role in height growth. The persistent association after covariates adjustment warrants further investigation into its therapeutic potential. Longitudinal and interventional studies are needed to confirm causality and explore therapeutic applications of VK2 for growth disorders.

Abbreviations

aOR	Adjusted odds ratio
BMI	Body mass index
BMD	Bone mineral density
cOC	Carboxylated osteocalcin
CI	Confidence Interval
IGF-1	Insulin-like growth factor 1
IQR	Interquartile range
25-(OH)D	25-hydroxyvitamin D
OC	Osteocalcin
SD	Standard deviation
SDS	Standard deviation score
ucOC	Uncarboxylated osteocalcin
VK2	Vitamin K2

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Author contributions

Y.S. contributed to the concept and design of this study, project administration, resources, conceptualization, funding acquisition, methodology, software, formal analysis, visualization and validation. G.S., S.W., W.L., K.W. contributed to the methodology, investigation, data curation, supervision and validation. Y.S. drafted the main manuscript text. All authors critically revised the manuscript for important intellectual content and approved the final version of manuscript.

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Data availability

The datasets used and/or analyzed during the current study are deposited in the related files.

Declarations

Ethics approval and consent to participate

This study was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki. The research protocol received formal approval from the Institutional Review Board of Guilin Maternal and Child Health Hospital (No. 2023-006KY). Written informed consent was obtained from all participating children's legal guardians, with additional assent acquired from the children themselves when appropriate.

Competing interests

The authors declare no competing interests.

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References

1. Rani D, Shrestha R, Kanchan T, Krishan K. Short stature. StatPearls. Treasure Island (FL): StatPearls publishing copyright © 2025. StatPearls Publishing LLC.; 2025.
2. Malnutrition. Available at: https://www.who.int/news-room/fact-sheets/detail/malnutrition/. Accessed 1 Januarary 2025.
3. Li F, Liu K, Zhao Q, Chen J, Liu L, Xie Q, et al. Prevalence of short stature among children in China: A systematic review. Pediatr Investig. 2021;5(2):140–7.
4. Xiaoping L, Wei w. Paying attention to the standardized diagnosis and treatment for children with short stature in Chinese. Chin Pediatr Integr Traditional Western Med. 2024;16(05):369–71.
5. Backeljauw P, Cappa M, Kiess W, Law L, Cookson C, Sert C, et al. Impact of short stature on quality of life: A systematic literature review. Growth Horm IGF Res. 2021;57–58:101392.
6. Rajput R, Rani M, Rajput M, Garg R. Etiological profile of short stature in children and adolescents. Indian J Endocrinol Metab. 2021;25(3):247–51.
7. Aaseth JO, Finnes TE, Askim M, Alexander J. The importance of vitamin K and the combination of vitamins K and D for calcium metabolism and bone health: A review. Nutrients. 2024;16(15).
8. Capozzi A, Scambia G, Lello S. Calcium, vitamin D, vitamin K2, and magnesium supplementation and skeletal health. Maturitas. 2020;140:55–63.
9. Tsugawa N, Shiraki M, Vitamin K. Nutr Bone Health Nutrients. 2020;12(7).
10. Zhang T, O'Connor C, Sheridan H, Barlow JW. Vitamin K2 in health and disease: A clinical perspective. Foods. 2024;13(11).
11. Barna M, Dunovska K, Cepova J, Werle J, Prusa R, Bjørklud G et al. Short-term impact of vitamin K2 supplementation on biochemical parameters and lipoprotein fractions. Electrophoresis. 2024.
12. Su X, Wang W, Fang C, Ni C, Zhou J, Wang X, et al. Vitamin K2 alleviates insulin resistance in skeletal muscle by improving mitochondrial function via SIRT1 signaling. Antioxid Redox Signal. 2021;34(2):99–117.
13. Zhang Y, Liu Z, Duan L, Ji Y, Yang S, Zhang Y, et al. Effect of Low-Dose vitamin K2 supplementation on bone mineral density in Middle-Aged and elderly Chinese: A randomized controlled study. Calcif Tissue Int. 2020;106(5):476–85.
14. Capozzi A, Scambia G, Migliaccio S, Lello S. Role of vitamin K(2) in bone metabolism: a point of view and a short reappraisal of the literature. Gynecol Endocrinol. 2020;36(4):285–8.
15. Rodríguez-Olleros Rodríguez C, Díaz Curiel M. Vitamin K and bone health: A review on the effects of vitamin K deficiency and supplementation and the effect of Non-Vitamin K antagonist oral anticoagulants on different bone parameters. J Osteoporos. 2019;2019:2069176.

16. Villa JKD, Diaz MAN, Pizziolo VR, Martino HSD. Effect of vitamin K in bone metabolism and vascular calcification: A review of mechanisms of action and evidences. Crit Rev Food Sci Nutr. 2017;57(18):3959–70.
17. Du CX, Li N. [Serum vitamin K(2) level and its association with bone metabolism markers in 1 732 children]. Zhongguo Dang Dai Er Ke Za Zhi. 2022;24(10):1130–5.
18. Skalny AV, Aschner M, Tsatsakis A, Rocha JBT, Santamaria A, Spandidos DA et al. Role of vitamins beyond vitamin D(3) in bone health and osteoporosis (Review). Int J Mol Med. 2024;53(1).
19. Simes DC, Viegas CSB, Araújo N, Marreiros C. Vitamin K as a diet supplement with impact in human health: current evidence in Age-Related diseases. Nutrients. 2020;12(1).
20. Kozioł-Kozakowska A, Maresz K. The Impact of Vitamin K2 (Menaquionones) in Children's Health and Diseases: A Review of the Literature. Child (Basel). 2022;9(1).
21. Bailey DA. The Saskatchewan pediatric bone mineral accrual study: bone mineral acquisition during the growing years. Int J Sports Med. 1997;18(Suppl 3):S191–4.
22. Cashman KD. Diet, nutrition, and bone health. J Nutr. 2007;137(11 Suppl):s2507–12.
23. Chen LL, Xu KW, Cao RX, Shen GH, Liu JR, Zhou F, et al. Vitamin K2 deficiency and its association with short stature in children: A cross-sectional study. Nutrition. 2024;131:112660.
24. Al-Agha AE, Kabli YO, AlBeiruty MG, Daftardar HE, Alkhattabi SZ, Badauod WM, et al. Quantitative ultrasound screening of bone mineral density on children with short stature. Saudi Med J. 2020;41(6):597–601.
25. Ma ML, Ma ZJ, He YL, Sun H, Yang B, Ruan BJ, et al. Efficacy of vitamin K2 in the prevention and treatment of postmenopausal osteoporosis: A systematic review and meta-analysis of randomized controlled trials. Front Public Health. 2022;10:979649.
26. Kojima T, Asoh M, Yamawaki N, Kanno T, Hasegawa H, Yonekubo A. Vitamin K concentrations in the maternal milk of Japanese women. Acta Paediatr. 2004;93(4):457–63.
27. The Subspecialty Group of Endocrinologic HaMD, The Society of Pediatrics, Chinese Medical Association. Guidelines for diagnosis and treatment of children with short stature in Chinese. Chin J Pediatr. 2008;46(6):428–30.
28. Fusaro M, Gallieni M, Rizzo MA, Stucchi A, Delanaye P, Cavalier E, et al. Vitamin K plasma levels determination in human health. Clin Chem Lab Med. 2017;55(6):789–99.
29. Cao B, Peng Y, Song W, Peng X, Hu L, Liu Z, et al. Pediatric continuous reference intervals of serum Insulin-like growth factor 1 levels in a healthy Chinese children Population - Based on PRINCE study. Endocr Pract. 2022;28(7):696–702.
30. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Tmava Berisha A, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. Eur J Clin Nutr. 2020;74(11):1498–513.
31. Myneni VD, Mezey E. Regulation of bone remodeling by vitamin K2. Oral Dis. 2017;23(8):1021–8.
32. Kim TH, Kim H, Lee HH, Sang JH, Vitamin K. Calcium metabolism modulator for menopausal women. J Menopausal Med. 2024;30(3):152–63.
33. Xie C, Gong J, Zheng C, Zhang J, Gao J, Tian C, et al. Effects of vitamin K supplementation on bone mineral density at different sites and bone metabolism in the middle-aged and elderly population. Bone Joint Res. 2024;13(12):750–63.
34. Zhou M, Han S, Zhang W, Wu D. Efficacy and safety of vitamin K2 for postmenopausal women with osteoporosis at a long-term follow-up: meta-analysis and systematic review. J Bone Min Metab. 2022;40(5):763–72.
35. Ganmaa D, Bromage S, Khudyakov P, Erdenenbaatar S, Delgererekh B, Martineau AR. Influence of vitamin D supplementation on growth, body composition, and pubertal development among School-aged children in an area with a high prevalence of vitamin D deficiency: A randomized clinical trial. JAMA Pediatr. 2023;177(1):32–41.
36. Huey SL, Acharya N, Silver A, Sheni R, Yu EA, Peña-Rosas JP, et al. Effects of oral vitamin D supplementation on linear growth and other health outcomes among children under five years of age. Cochrane Database Syst Rev. 2020;12(12):Cd012875.
37. Racine HL, Serrat MA. The actions of IGF-1 in the growth plate and its role in postnatal bone elongation. Curr Osteoporos Rep. 2020;18(3):210–27.
38. Jadhav N, Ajgaonkar S, Saha P, Gurav P, Pandey A, Basudkar V, et al. Molecular pathways and roles for vitamin K2-7 as a Health-Beneficial nutraceutical: challenges and opportunities. Front Pharmacol. 2022;13:896920.
39. Sato T, Inaba N, Yamashita T. MK-7 and its effects on bone quality and strength. Nutrients. 2020;12(4).
40. Iwamoto J, Sato Y, Takeda T, Matsumoto H. Bone quality and vitamin K2 in type 2 diabetes: review of preclinical and clinical studies. Nutr Rev. 2011;69(3):162–7.
41. Amizuka N, Li M, Kobayashi M, Hara K, Akahane S, Takeuchi K, et al. Vitamin K2, a gamma-carboxylating factor of gla-proteins, normalizes the bone crystal nucleation impaired by Mg-insufficiency. Histol Histopathol. 2008;23(11):1353–66.
42. Gasmi A, Bjørklund G, Peana M, Mujawdiya PK, Pivina L, Ongenae A, et al. Phosphocalcic metabolism and the role of vitamin D, vitamin K2, and nattokinase supplementation. Crit Rev Food Sci Nutr. 2022;62(25):7062–71.
43. Kuang X, Liu C, Guo X, Li K, Deng Q, Li D. The combination effect of vitamin K and vitamin D on human bone quality: a meta-analysis of randomized controlled trials. Food Funct. 2020;11(4):3280–97.

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