Volume 3, Issue 5, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

FACTORS AFFECTING BONE MINERAL DENSITY IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

Dr Sobia Ashfaq[*1], Prof Dr Naureen Akhter[2], Dr Ch Muhammad Umer Razaq[3], Dr Iqra Ashraf[4], Dr Adeela Chaudhry[5], Dr Saba Mukhtar[6]

*[*1,4,6]Fellow Pediatric nephrology, UCHS, CH Lahore*
[2]HOD Pediatric Nephrology, UCHS, CH Lahore
[3,5]Assistant Professor Department of Pediatric Nephrology, UCHS, CH Lahore

[*1]sobiahafeez4151@gmail.com

DOI: https://doi.org/10.5281/zenodo.17068138

Keywords:

Article History
Received: 15 May 2025
Accepted: 26 June 2025
Published: 3 July 2025

Corresponding Author: *
Dr Sobia Ashfaq

Abstract

Background: *Children with idiopathic nephrotic syndrome (INS) are at increased risk of developing bone mineral density (BMD) abnormalities due to the long-term use of corticosteroids, vitamin D deficiency, and physical inactivity.*
Objective: *This study aimed to investigate the factors affecting BMD in children with INS, with a focus on corticosteroid therapy, nutritional status (calcium and vitamin D levels), physical activity, and laboratory markers.*
Methods: *A cross-sectional observational study was conducted at the Department of Nephrology, The Children's Hospital Lahore from November 2024 to April 2025. A total of 70 children diagnosed with INS were included in the study. BMD was measured using dual-energy X-ray absorptiometry (DEXA) at the lumbar spine and femoral neck. The children's cumulative corticosteroid dose, calcium and vitamin D levels, physical activity levels, and serum albumin were recorded.*
Results: *The mean age of the participants was 8.6 ± 3.2 years, with a slight female predominance (51.4%). BMD classification revealed 40% of children had normal BMD, 45.7% had osteopenia, and 14.3% had osteoporosis. Corticosteroid use was negatively correlated with BMD ($r = -0.62$, $p < 0.01$). Serum calcium and vitamin D levels were significantly lower in children with osteopenia and osteoporosis ($p < 0.05$). Physical activity showed a positive correlation with BMD ($p < 0.05$), with children in the high activity group having higher BMD than those in the low activity group.*
Conclusion: *Corticosteroid therapy, vitamin D deficiency, and low physical activity are key factors influencing bone mineral density in children with INS. Optimizing corticosteroid use, ensuring adequate calcium and vitamin D intake, and promoting physical activity are essential strategies for preventing bone demineralization in this population. Early screening and intervention are recommended to reduce the risk of long-term skeletal complications in children with INS.*

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

INTRODUCTION

Bone mineral density (BMD) is a critical indicator of bone health, and its assessment is particularly important in pediatric populations with chronic diseases such as idiopathic nephrotic syndrome (INS) [1]. INS is a widespread renal condition in children, where nephrotic-range proteinuria, hypoalbuminemia, hyperlipidemia, and edema are present. Although the main issue in the INS is the management of renal functioning, recent research has noticed that bone health is a significant concern in such patients because of several factors that can lead to reduced BMD [2]. Children affected by INS are more susceptible to bone mineral disorders and these disorders may cause a fractured bone, stunted growth and permanent musculoskeletal problems. The pathophysiology in the cause of these bone-related problems is complex as it is a combination of disease-related factors and medications, which include corticosteroids, mostly used in the management of INS. Although effective in the management of the disease, corticosteroids have been found to interfere with calcium and vitamin D metabolism, which can cause secondary loss of bone minerals [3].

Furthermore, the nephrotic condition per se, which is a loss of albumin and other proteins, may lead to changes in the calcium homeostasis and the metabolism of vitamin D. Such disproportions may also increase the bone demineralization in predisposed people. Also, diet, physical exercise, and even genetic predisposition may have considerable influence on BMD in children with INS [4]. It is imperative to learn the mechanisms of these changes in bone density so that a comprehensive treatment strategy can be developed. Corticosteroids have a number of adverse effects on bone metabolism, such as reduced bone formation, elevated bone resorption, and hindered mineralization caused by prolonged use. The main mediating effects of these effects are the inhibition of the osteoblast's activity, heightened osteoclast activity and diminished gut absorption of calcium [5]. Long-term steroid treatment in children can cause bone mass to decrease and thereby make them prone to fractures due to the cumulative effects of such treatment [6]. Indeed, it has been established that vertebral and non-vertebral fractures are more common among INS children who are undergoing chronic steroid treatment than healthy children. Besides corticosteroid treatment, children with INS could also have a deficiency of vital nutrients in bone health, especially calcium and vitamin D [7]. Proteinuria may result in the depletion of calcium-binding proteins, which interfere with the absorption of calcium [8]. Moreover, hypoalbuminemia, which is a characteristic of INS, may influence the bioavailability of vitamin D, critical in the absorption of calcium and within bone [9]. Vitamin D deficiency is very common among children with INS and is regarded as a major factor that leads to low BMD. Consequently, children with INS tend to have to be supplemented both with calcium and vitamin D to avoid the occurrence of rickets and osteomalacia [10]. The dietary factors are also important in preserving bone in children with INS. The nephrotic syndrome may cause additional depletion of crucial nutrients that may adversely affect the nutritional status of the affected children [11]. Bone mineralization may further be compromised due to low-calcium, vitamin D intake, or other nutrients supporting bones. Besides, the high sodium and high protein diets that affect children with nephrotic syndrome because of the necessity to maintain the balance of nutritional elements can also result in higher levels of urinary calcium loss, which also promotes the process of bone demineralization [12].

Objective

This study aimed to investigate the factors affecting BMD in children with INS, with a focus on corticosteroid therapy, nutritional status (calcium and vitamin D levels), physical activity, and laboratory markers.

Methodology

This cross-sectional observational study was conducted at the Department of Nephrology, The Children's Hospital Lahore from November 2024 to April 2025. A total of 70 children diagnosed with INS were included in the study. A total of 70 children diagnosed with idiopathic nephrotic syndrome were included in the study. The sample size was determined using the standard sample size

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

calculation formula, considering an expected prevalence of bone mineral density reduction in this population, with a confidence level of 95% and a margin of error of 5%.

Inclusion Criteria:

1. Children aged 5–18 years.
2. Diagnosed with idiopathic nephrotic syndrome based on clinical and laboratory criteria, including nephrotic-range proteinuria and hypoalbuminemia.
3. Receiving corticosteroid therapy for at least 6 months, either as a part of induction or maintenance therapy.
4. No history of secondary causes of nephrotic syndrome (e.g., systemic lupus erythematosus, diabetes mellitus, infections).
5. Written informed consent obtained from the parent/guardian.

Exclusion Criteria:

1. Children with secondary nephrotic syndrome from systemic causes such as infections or autoimmune diseases.
2. History of congenital bone disorders (e.g., osteogenesis imperfecta, rickets).
3. Any bone fractures or surgeries within the last six months prior to the study.
4. Children with conditions or medications that could interfere with bone metabolism (e.g., bisphosphonates, steroids for conditions other than INS).

Data Collection:

Data collection involved both clinical assessments and laboratory investigations. Demographic details such as age, gender, and the duration of nephrotic syndrome were recorded.

Data related to the comorbidity, such as hypertension or diabetes, were also recorded, since they may impact the health of bone. The length and nature of corticosteroid therapy, dose and frequency was also recorded since corticosteroids are known to have effects on bone metabolism. BMD was evaluated on a basis of dual-energy X-ray absorptiometry (DEXA) scans to determine bone density and lumbar spine (L2-L4) and femoral neck. Analysis of the results was performed on the basis of age- and gender-specific reference values, and BMD was categorized as normal, osteopenia, or osteoporosis. Besides BMD determination, laboratory tests were conducted to determine levels of calcium, phosphate and vitamin D because they are essential in bone maintenance. The level of serum albumin and 24 hours urine protein excretion were also tested to ascertain the nephrotic stage and evaluate protein loss a major determinant of bone mineralization. They also measured bone turnover using bone turnover markers including osteocalcin and parathyroid hormone (PTH) to indicate bone metabolism. Nutritional status was assessed by the use of 24-hours dietary recall, with reference to the consumption of calcium and vitamin D. Food supplements (where applicable) taken by the kids were also recorded. The level of physical activity was measured by a validated questionnaire on pediatric physical activity that classified the level of physical activity as low, moderate, or high, according to the frequency and intensity of the weight-bearing activities.

Statistical Analysis

Data were analyzed using SPSS version 26. Descriptive statistics were used to summarize the baseline characteristics of the study participants. Continuous variables, such as age, duration of nephrotic syndrome, BMD, and calcium levels, were presented as means ± standard deviation (SD) or median and interquartile range (IQR), depending on the distribution of the data. Categorical variables, including gender and BMD classification, were expressed as frequencies and percentages. A p-value of less than 0.05 was considered statistically significant.

Results

In this study, a total of 70 children with idiopathic nephrotic syndrome (INS) were enrolled, with a mean age of 8.6 ± 3.2 years. The gender distribution was almost equal, with 34 males (48.6%) and 36 females (51.4%). The mean duration of nephrotic syndrome among participants was 3.2 ± 1.6 years. Comorbid conditions were present in a subset of

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

patients, including hypertension in 15 children (21.4%) and any kind of infection in 8 children (11.4%). Assessment of bone mineral density (BMD) revealed that only 28 children (40%) had normal BMD, while the majority demonstrated compromised bone health, with 32 children (45.7%) classified as having osteopenia and 10 children (14.3%) as having osteoporosis. Laboratory investigations demonstrated that the mean serum calcium level was 8.4 ± 1.2 mg/dL, phosphate 3.1 ± 0.9 mg/dL, and vitamin D 19.8 ± 6.5 ng/mL, indicating that a large proportion of children had suboptimal vitamin D and calcium levels. The mean serum albumin was 2.8 ± 0.5 g/dL, and the average 24-hour urine protein excretion was 4.2 ± 1.4 g, confirming ongoing protein loss consistent with nephrotic syndrome. Bone turnover markers also showed abnormalities, with mean osteocalcin at 18.4 ± 4.2 ng/mL and parathyroid hormone (PTH) at 52.3 ± 19.4 pg/mL, suggesting altered bone metabolism in these patients.

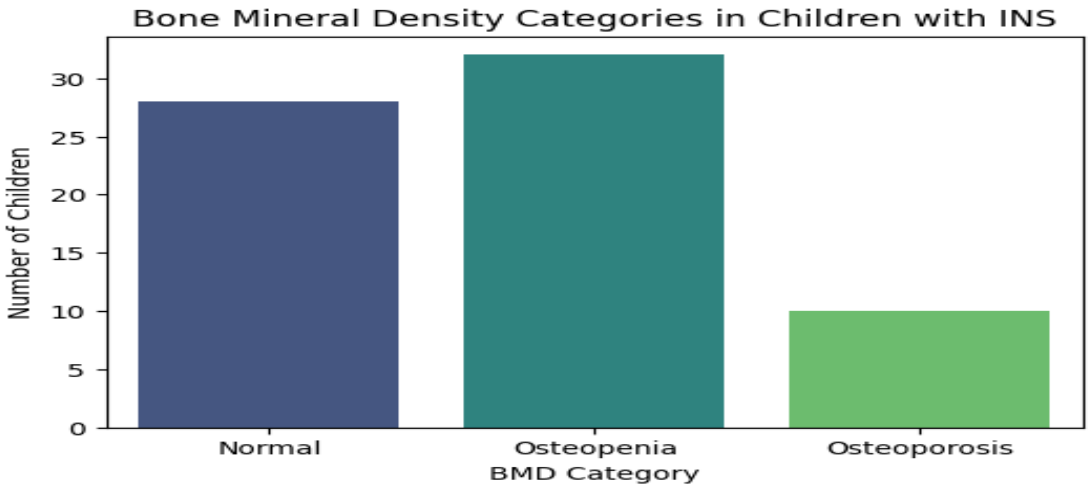
Table 1: Demographic Characteristics of Study Participants

Variable	**Value (n = 70)**
Age (Mean ± SD)	8.6 ± 3.2 years
Gender (n, %)	
- Male	34 (48.6%)
- Female	36 (51.4%)
Duration of Nephrotic Syndrome (Mean ± SD)	3.2 ± 1.6 years
Comorbid Conditions (n, %)	
- Hypertension	15 (21.4%)
- any Infections	8 (11.4%)
BMD Classification	
Normal	28 (40%)
Osteopenia	32 (45.7%)
Osteoporosis	10 (14.3%)
Laboratory Parameter	
Calcium	8.4 ± 1.2 mg/dL
Phosphate	3.1 ± 0.9 mg/dL
Vitamin D	19.8 ± 6.5 ng/mL
Serum Albumin	2.8 ± 0.5 g/dL
24-hour Urine Protein Excretion	4.2 ± 1.4 g
Osteocalcin	18.4 ± 4.2 ng/mL
Parathyroid Hormone (PTH)	52.3 ± 19.4 pg/mL

Volume 3, Issue 5, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

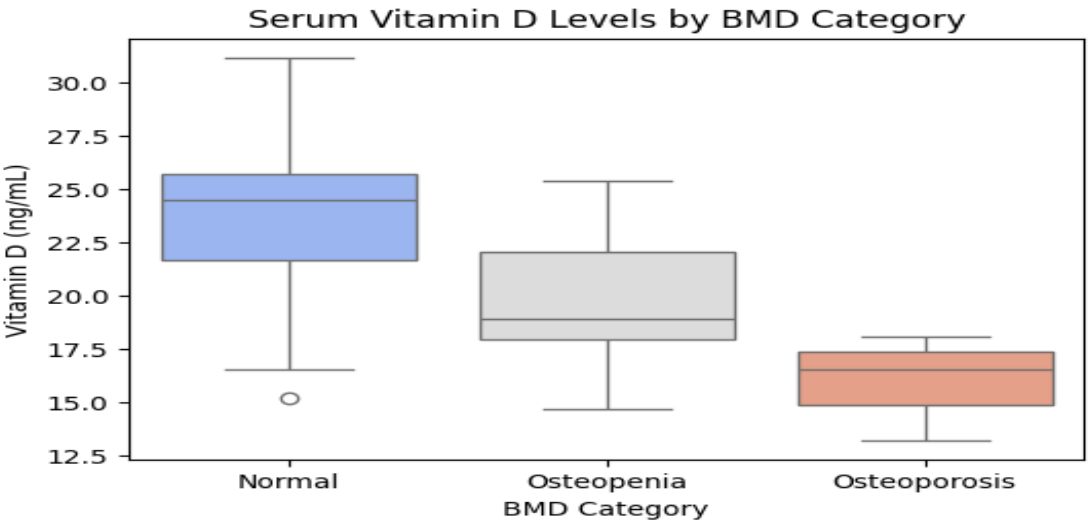


Nutritional assessment revealed a mean daily calcium intake of 480 ± 110 mg/day and vitamin D intake of 200 ± 95 IU/day, reflecting suboptimal intake relative to recommended pediatric levels.

Physical activity assessment showed that 18 children (25.7%) had low activity, 38 (54.3%) had moderate activity, and only 14 (20%) were highly active.

Table 2: Nutritional Status and Physical Activity

Parameter	**Value (n = 70)**
Calcium Intake (Mean ± SD)	480 ± 110 mg/day
Vitamin D Intake (Mean ± SD)	200 ± 95 IU/day
Physical Activity Level (n, %)	
- Low	18 (25.7%)
- Moderate	38 (54.3%)
- High	14 (20%)



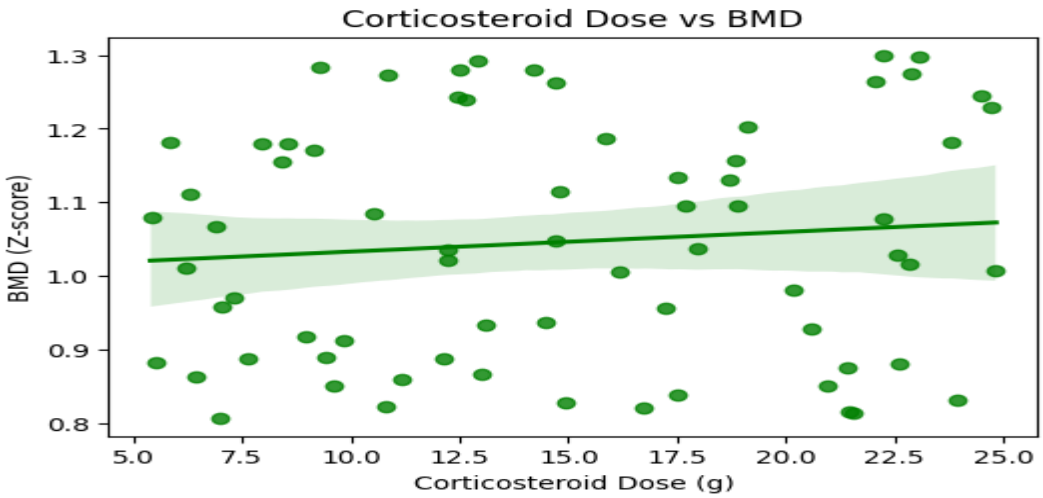
Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Multivariate linear regression analysis was performed to identify independent predictors of bone mineral density in children with idiopathic nephrotic syndrome. The analysis revealed that corticosteroid dose was a significant negative predictor of BMD (β = -0.46, p < 0.01), indicating that higher cumulative corticosteroid exposure was associated with lower bone density. Serum vitamin D emerged as a significant positive predictor (β = 0.33, p = 0.02), suggesting that higher vitamin D levels were associated with improved BMD. Physical activity showed a positive but non-significant association with BMD (β = 0.15, p = 0.08), whereas serum albumin had a negative but non-significant relationship (β = -0.20, p = 0.12).

Table 3: Regression Analysis for Predictors of BMD

Variable	β Coefficient	p-value
Corticosteroid Dose	-0.46	< 0.01
Serum Vitamin D	0.33	0.02
Physical Activity	0.15	0.08
Serum Albumin	-0.20	0.12
R^2 for model	0.42	



Discussion

This study aimed to evaluate the factors affecting bone mineral density (BMD) in children with idiopathic nephrotic syndrome (INS), focusing on the role of corticosteroid therapy, nutritional status, physical activity, and bone metabolism. Based on our results, we propose that the length of corticosteroid therapy, lack of calcium, vitamin D, and reduced physical exercise significantly contribute to a high incidence of osteopenia and osteoporosis in children with INS. Negative relationship between corticosteroid therapy and BMD was the most outstanding observation in this research. Long-term corticosteroid administration has been known to affect bone metabolism and it tends to raise bone resorption and reduce bone formation. The children with longer-lasting corticosteroid usage in our study showed worse BMD, which agrees with prior literature that emphasizes corticosteroid-mediated osteopenia and osteoporosis [13] [14]. This process is mediated by inhibition of osteoblast and bone turnover-imbalance due to increased osteoclast differentiation. The findings of our study support the necessity of close attention to bone health development in children receiving a long-term course of corticosteroid treatment, as well as to bone protective measures (calcium and vitamin D supplementation, the inclusion of physical activities

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

that involve weight-bearing) [15]. In this study, there was a considerable number of children with low levels of serum calcium and vitamin D, and this level was much lower among children with osteopenia and osteoporosis. Bone mineralization requires calcium and vitamin D and shortages of these nutrients may increase the risk of bone loss. We have discovered that there is a positive correlation between physical activity and BMD with children in high physical activity group showing better BMD than that of children in the low activity group [16]. Exercise especially weight-bearing exercises is an important activity in the prevention of bone by means of osteoblastic action and improvement of bone mineralization. This observation is in line with other researches that indicate children with chronic illnesses such as INS gain advantages of physical activity in preserving bone health. With the correlation between lack of exercise and low bone density, there is a strong need to ensure that children with INS are encouraged to exercise frequently so as to reduce the chances of osteoporosis [17]. Similar to earlier researchers, our bone turnover measures showed an increase in the levels of parathyroid hormone (PTH) and osteocalcin, which show a disturbed bone metabolism in children with INS. Certainly, greater levels of PTH are frequently a compensatory reaction to hypocalcemia, and higher levels of osteocalcin are indicative of high bone turnover [18-20]. This indicates that bone formation can be lagging behind bone resorption, which continues to contribute to the lower BMD, which is seen in our cohort. These results indicate that close monitoring of bone turnover markers in children with INS is necessary to learn more about their bone state and make changes in treatment regimens. We also measured dietary intake, calcium, and vitamin D in particular, and the mean values of these nutrients did not match the recommended values. Poor calcium and vitamin D may increase the bone loss in children with nephrotic syndrome who are already at risk secondary to corticosteroid therapy and protein loss [21].

Limitations:

This study has some limitations. The cross-sectional design does not allow us to establish causal relationships between the factors and BMD. A longitudinal study would provide more insight into how these factors interact over time to affect bone health. Additionally, while we assessed dietary intake and physical activity, these were based on self-reported data, which may introduce recall bias. Finally, the sample size, though sufficient for descriptive analysis, may limit the generalizability of our findings to broader populations.

Conclusion

It is concluded that children with idiopathic nephrotic syndrome (INS) are at significant risk of bone mineral density (BMD) reduction, primarily due to prolonged corticosteroid therapy, vitamin D deficiency, and insufficient physical activity. Higher cumulative corticosteroid doses were strongly associated with lower BMD, highlighting the need for careful steroid management. Additionally, inadequate calcium and vitamin D intake, along with a lack of physical activity, further contribute to bone demineralization.

References

Sharawat IK, Dawman L, Kumkhaniya MV, Devpura K, Mehta A. Bone mineral density and its influencing factors in children with idiopathic nephrotic syndrome: a prospective observational study. Trop Doct. 2019 Oct;49(4):292-298. doi: 10.1177/0049475519868055. Epub 2019 Aug 13. PMID: 31408410.

El-Mashad GM, El-Hawy MA, El-Hefnawy SM, Mohamed SM. Bone mineral density in children with idiopathic nephrotic syndrome. J Pediatr (Rio J). 2017 Mar-Apr;93(2):142-147. doi: 10.1016/j.jped.2016.05.010. Epub 2016 Nov 5. PMID: 27821253.

Kaczmarek U, Wrzyszcz-Kowalczyk A, Jankowska K, Prościak K, Mysiak-Dębska M, Przywitowska I, Makulska I. Oral health conditions in children with idiopathic nephrotic syndrome: a cross-sectional study. BMC Oral Health. 2020 Jul 29;20(1):213. doi: 10.1186/s12903-020-01197-1. PMID: 32727436; PMCID: PMC7391815.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Kamel AS, AlGhawass MME, Sayed MA, Roby SA. Evaluation of carotid intima media thickness in children with idiopathic nephrotic syndrome. Ital J Pediatr. 2022 Dec 9;48(1):195. doi: 10.1186/s13052-022-01383-7. PMID: 36494853; PMCID: PMC9733087.

Banerjee S, Basu S, Sen A, Sengupta J. The effect of vitamin D and calcium supplementation in pediatric steroid-sensitive nephrotic syndrome. Pediatr Nephrol. 2017 Nov;32(11):2063-2070. doi: 10.1007/s00467-017-3716-2. Epub 2017 Jul 19. PMID: 28725977.

Liu C, Yang D, Chen X, Liao Y, Ning G, Qu H. Opportunistic screening for bone mineral density deficits in pediatric patients from abdominal computed tomography scans obtained for other indications: a cross-sectional study. Pediatr Radiol. 2025 May;55(5):1006-1013. doi: 10.1007/s00247-025-06195-5. Epub 2025 Feb 18. PMID: 39964436.

Ahmed HM, Ameen EE, Awad MS, Botrous OE. Assessment of Carotid Intima Media Thickness and Left Ventricular Mass Index in Children with Idiopathic Nephrotic Syndrome. Vasc Health Risk Manag. 2021 Jun 10;17:349-356. doi: 10.2147/VHRM.S295868. PMID: 34140775; PMCID: PMC8203195.

Cetin, Nuran[1]; Gencler, Aylin[1]; Sivrikoz, Ilknur Ak[2]. Bone Mineral Density and Vitamin D Status in Children with Remission Phase of Steroid-Sensitive Nephrotic Syndrome. Saudi Journal of Kidney Diseases and Transplantation 30(4):p 853-862, Jul–Aug 2019. | DOI: 10.4103/1319-2442.265461

Ahangar Davoodi M, Nokhbe Zaeim H, Yousefichaijan P. Bone Mineral Density in Children with Nephrotic Syndrome Treated under GC for More than 2 Years. Int J Pediatr 2023; 11 (11):18391 18397. DOI: 10.22038/ijp.2023.74679.5361

Jesmin, Tahmina[1]; Al Mamun, Abdullah[1]; Rahman, Md Azizur[2]; Santa, Samina Masud[1]; Huque, Syed Saimul[1]; Begum, Afroza[1]; Roy, Ranjit Ranjan[1]; Rahman, Md Habibur[1]; Uddin, Golam Muin[1]. Bone Mineral Density in Children with Relapsing Nephrotic Syndrome: A Hospital-Based Study. Saudi Journal of Kidney Diseases and Transplantation 30(6):p 1415-1422, Nov–Dec 2019. | DOI: 10.4103/1319-2442.275486

Pavlou M, Serbis A, Kostara M, et al. (April 24, 2025) Bone Metabolism Defects in Children With Idiopathic Hypercalciuria: An Update. Cureus 17(4): e82931. DOI 10.7759/cureus.82931

Yang, Y., Chen, Z., Huang, Z. *et al.* Risk factors associated with low bone mineral density in children with idiopathic scoliosis: a scoping review. *BMC Musculoskelet Disord* **24**, 48 (2023). https://doi.org/10.1186/s12891-023-06157-8

Yuan Y, Chen X, Zhang L, Wu J, Guo J, Zou D, et al. The roles of exercise in bone remodeling and in prevention and treatment of osteoporosis. Prog Biophys Mol Biol. 2016;122(2):122–30.

Gómez-Bruton A, Matute-Llorente Á, González-Agüero A, Casajús JA, Vicente-Rodríguez G. Plyometric exercise and bone health in children and adolescents: a systematic review. World J Pediatr. 2017;13(2):112–21.

Miyagi M, Saito W, Imura T, Nakazawa T, Shirasawa E, Kawakubo A, et al. Body composition in Japanese girls with adolescent idiopathic scoliosis. Spine Surg Relat Res. 2021;5(2):68–74.

Bahrami A, Sadeghnia HR, Tabatabaeizadeh SA, Bahrami-Taghanaki H, Behboodi N, Esmaeili H, et al. Genetic and epigenetic factors influencing vitamin D status. J Cell Physiol. 2018;233(5):4033–43.

Alessa HB, Chomistek AK, Hankinson SE, Barnett JB, Rood J, Matthews CE, et al. Objective measures of physical activity and cardiometabolic and endocrine biomarkers. Med Sci Sports Exerc. 2017;49(9):1817–25.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Blüher S, Panagiotou G, Petroff D, Markert J, Wagner A, Klemm T, et al. Effects of a 1-year exercise and lifestyle intervention on irisin, adipokines, and inflammatory markers in obese children. Obesity. 2014;22(7):1701–8.

Fang Y, Zhu J, Fan J, Sun L, Cai S, Fan C, et al. Dietary Inflammatory Index in relation to bone mineral density, osteoporosis risk and fracture risk: a systematic review and meta-analysis. Osteoporos Int. 2021;32(4):633–43.

Bianchi ML. Osteoporosis in children and adolescents. Bone. 2007;41(4):486–95.

Bishop N, Arundel P, Clark E, Dimitri P, Farr J, Jones G, et al. Fracture prediction and the definition of osteoporosis in children and adolescents: the ISCD 2013 Pediatric Official Positions. J Clin Densitom. 2014;17(2):275–80.