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Original Research Article

To Evaluate Incidence of Osteoporosis in Patients taking Corticosteroids for Biopsy Proven Primary Adult Nephrotic Syndrome

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Abstract

Background: Nephrotic syndrome (NS) in adults is commonly managed with corticosteroids, which, while effective in inducing remission, are strongly associated with steroid-induced osteoporosis. The combined effects of NS itself—through urinary loss of vitamin D–binding protein and altered calcium-phosphate metabolism—and glucocorticoid therapy may accelerate bone loss. Despite the high prevalence of vitamin D deficiency in India, data on osteoporosis incidence in Indian adults with biopsy-proven NS remain scarce.

Methods: This prospective cohort study enrolled 35 adults with biopsy-proven primary NS receiving corticosteroids and 70 age- and sex-matched non-NS controls between May 2022 and June 2024. Patients with pre-existing osteoporosis or secondary causes of NS were excluded. Bone mineral density (BMD) was assessed using dual-energy X-ray absorptiometry (DEXA) at baseline and after three months. Biochemical markers of bone metabolism were measured. Statistical analyses included chi-square, unpaired t-tests, and Fisher's Exact Test.

Results: At baseline, demographic and biochemical parameters were comparable between groups. After three months, NS patients showed a significant decline in mean T-score (–0.93 to –2.01; Δ –1.08), compared to minimal change in controls (–0.85 to –1.19; Δ –0.34; $p < 0.0001$). Osteopenia occurred in 57.14% of NS patients versus 24.29% of controls (RR 2.35; $p = 0.0012$). Osteoporosis was observed in 37.14% of NS patients compared to 8.57% of controls (RR 4.31; $p = 0.0008$).

Conclusion: Adults with NS treated with corticosteroids experience rapid and clinically significant bone loss within three months, with markedly higher incidence of osteopenia and osteoporosis. Early DEXA screening and prophylactic interventions, including calcium, vitamin D supplementation, and bisphosphonates in high-risk patients, are warranted.

Keywords: Nephrotic Syndrome; Corticosteroids; Osteoporosis; Bone Mineral Density; DEXA; T-Score.
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Introduction

Nephrotic syndrome (NS) in adults is a common glomerular disorder characterized by heavy proteinuria, hypoalbuminemia, edema, and dyslipidemia, and is associated with significant systemic morbidity. While renal outcomes remain the primary focus of management, the long-term complications arising from both the disease process and its treatment have important implications for overall patient health and quality of life [1].

Corticosteroids constitute the cornerstone of therapy for primary adult nephrotic syndrome and are strongly recommended by the kidney disease: Improving Global Outcomes (KDIGO) guidelines for inducing and maintaining remission [2,3]. Despite their proven efficacy, prolonged or high-dose glucocorticoid therapy is associated with a wide range of adverse effects, among which osteoporosis represents one of the most serious and potentially preventable complications. Glucocorticoid-induced osteoporosis is the most common form of secondary osteoporosis worldwide and is associated with an increased risk of fragility fractures, chronic pain, disability, and mortality [4–10].

The deleterious effects of corticosteroids on bone metabolism are well established. Glucocorticoids

suppress osteoblast differentiation and activity, enhance osteoclast-mediated bone resorption, reduce intestinal calcium absorption, and impair vitamin D metabolism, collectively leading to rapid bone loss and deterioration of bone microarchitecture [4–8]. Importantly, bone loss is most pronounced during the initial months of steroid therapy, emphasizing the need for early detection and preventive strategies [9,10].

In patients with nephrotic syndrome, the risk of osteoporosis is further amplified by disease-specific mechanisms. Heavy proteinuria results in urinary loss of vitamin D–binding protein, leading to reduced bioavailable vitamin D and subsequent disturbances in calcium-phosphate homeostasis [12]. Chronic inflammation, immobility during active disease, hypogonadism, and repeated disease relapses further contribute to skeletal fragility. Thus, adults with nephrotic syndrome receiving corticosteroids represent a uniquely vulnerable population exposed to a "double burden" of bone loss arising from both the underlying disease and its treatment.

Although the association between corticosteroid therapy and osteoporosis is well documented in Western populations, data from South Asia—and particularly India—remain limited. Ethnic differences in bone mineral density, dietary calcium intake, sun exposure, vitamin D status, and lifestyle factors may significantly influence fracture risk and skeletal outcomes [11,13]. Moreover, most existing studies have focused on paediatric nephrotic syndrome or secondary causes of NS, leaving a critical evidence gap regarding adult patients with biopsy-proven primary nephrotic syndrome.

Given the high prevalence of vitamin D deficiency in India and the widespread use of corticosteroids in nephrology practice, there is a pressing need for region-specific data to quantify the burden of osteoporosis in this population. Such evidence is essential to guide screening strategies, preventive interventions, and long-term management protocols.

The present prospective cohort study was therefore designed to evaluate the incidence of osteoporosis in adults with biopsy-proven primary nephrotic syndrome receiving corticosteroid therapy, compared with age- and sex-matched non-nephrotic controls. Using dual-energy X-ray absorptiometry (DEXA) as the diagnostic standard, this study aims to generate clinically relevant data to inform routine practice and emphasize the importance of early bone health assessment and intervention in adult nephrotic syndrome.

Materials & Methods

This prospective cohort study was conducted to evaluate the incidence of osteoporosis in adults with biopsy-proven primary nephrotic syndrome (NS) receiving corticosteroid therapy. Patient recruitment was carried out between May 2022 and June 2024. All participants provided written informed consent, and the study protocol was approved by the institutional ethics committee. The nephrotic syndrome cohort was compared with a control group of non-NS patients not receiving corticosteroid, with propensity score matching performed to minimize confounding by age and sex.

Study Population: Patients were eligible if they were adults (≥18 years) with first-time diagnosed, biopsy-proven primary nephrotic syndrome. Additional requirements included an estimated glomerular filtration rate (eGFR) greater than 90 ml/min/1.73 m^2 and corticosteroid intake for a minimum duration of three months.

Patients were excluded if they had been diagnosed with nephrotic syndrome prior to May 2022, had osteoporosis before initiation of corticosteroid therapy, or were younger than 18 years. Individuals with incomplete data, secondary causes of nephrotic syndrome, or comorbidities strongly contributing to osteoporosis (except mild hypothyroidism and hypertension) were excluded. Patients with calcium or vitamin D deficiency, childhood nephrotic syndrome, or a history of corticosteroid intake for less than three months were also excluded.

Sample Size: A total of 35 adults with nephrotic syndrome receiving corticosteroids and 70 non-NS controls were enrolled. The ratio of 1:2 between NS and non-NS groups was maintained using propensity score matching to control for age and sex. Patients with a baseline T-score ≤ –1.0 on DEXA scan were excluded to ensure that only new cases of osteopenia or osteoporosis were captured during follow-up.

Outcome Parameters: The primary outcome parameter was the incidence of osteoporosis, defined by a T-score ≤ –2.5 on DEXA scan at the lumbar spine, femoral neck, or distal radius. Secondary outcomes included the incidence of osteopenia (T-score between –1.0 and –2.5), biochemical markers of bone metabolism (serum calcium, phosphorus, alkaline phosphatase, vitamin D3, and intact parathyroid hormone).

Data Collection: Detailed clinical histories were obtained, including dose and duration of corticosteroid intake, relapse episodes of nephrotic syndrome, and calcium intake from diet and supplementation. Clinical examination focused on vital signs, edema, and ascites. Laboratory investigations included serum creatinine, corrected

calcium, phosphorus, alkaline phosphatase, vitamin D3, and intact parathyroid hormone levels. Bone mineral density was measured using dual-energy X-ray absorptiometry (DEXA) at the lumbar spine, femoral neck, and left distal radius at baseline (index date) and after three months of corticosteroid therapy.

Methodology: All patients with nephrotic syndrome were treated with corticosteroids according to KDIGO guidelines. Primary membranous nephropathy patients additionally received cyclophosphamide for three months as part of a modified Ponticelli regimen; however, the effect of cyclophosphamide on bone density was not evaluated due to the low cumulative dose administered. Bone mineral density was assessed using the lowest T-score among the three skeletal sites. Patients were stratified into NS and non-NS cohorts, and propensity score matching was applied to control for selection bias.

Statistical Analysis: The distribution of demographic variables (age, sex), comorbidities, and corticosteroid use between NS and non-NS cohorts was compared using the chi-square (χ^2) test. Incidence rates of osteopenia and osteoporosis were calculated from the lowest BMD values. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Statistical significance was set at $p < 0.05$. All analyses were performed using standard statistical software.

Results

A total of 35 adults with nephrotic syndrome receiving corticosteroids and 70 non-NS controls not receiving steroid were enrolled.

The two groups were well-matched in terms of age, sex distribution, prevalence of hypertension and mild hypothyroidism, and body mass index (BMI), with no statistically significant differences (all p-values >0.05).

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variable	NS Group (n=35)	Control Group (n=70)	p value
Age (years, mean ± SD)	36.06 ± 14.00	35.83 ± 9.64	0.9216
Male sex (%)	19 (54.28)	39 (55.71)	>0.9999
Hypertension (%)	5 (14.29)	8 (11.43)	0.7561
Mild hypothyroidism (%)	3 (8.57)	4 (5.71)	0.6836
BMI (kg/m², mean ± SD)	22.43 ± 3.28	22.81 ± 3.59	0.6001

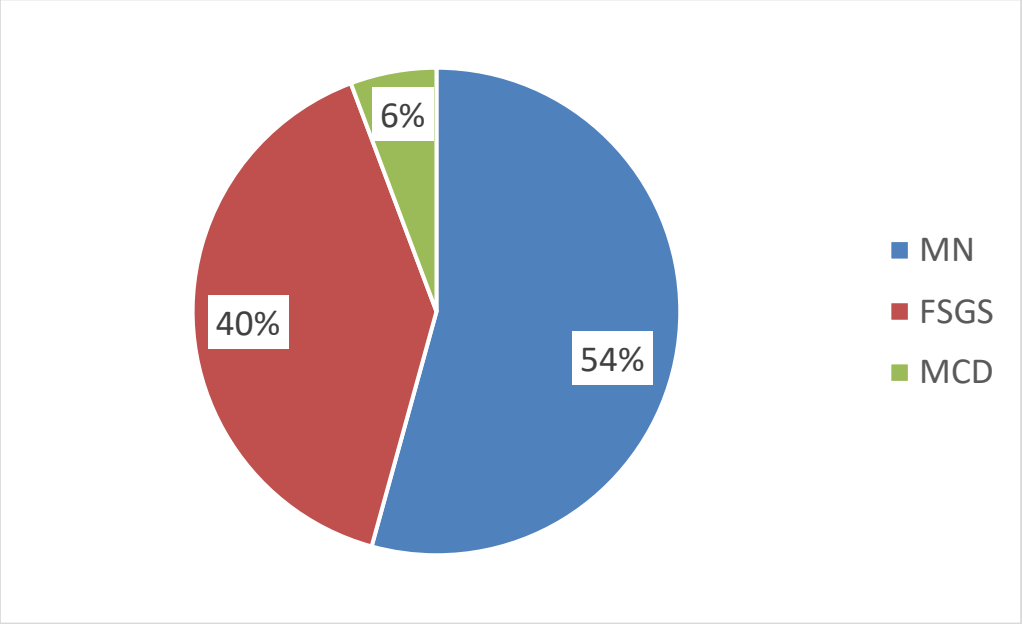

Figure 1: Distribution of Cases with respect to Basic Kidney Disease

Table 2 compares baseline biochemical parameters related to bone and mineral metabolism between the NS and control groups.

Key markers, including serum creatinine, corrected calcium, phosphorus, alkaline phosphatase, vitamin D3, and parathyroid hormone (PTH) levels, all showed no statistically significant differences (all p-values >0.05). This suggests that at the study's outset, both groups had similar renal function and mineral homeostasis, implying that any later observed differences in bone mineral density are unlikely to be attributed to pre-existing disparities in these standard biochemical parameters.

Table 2: Biochemical Parameters at Baseline

Parameter	Value in Mean ± SD		p value (Unpaired t test)
	NS Group (n=35)	Control Group (n=70)	
Serum creatinine (mg/dL)	0.94 ± 0.21	0.87 ± 0.29	0.2070
Corrected calcium (mg/dL)	8.22 ± 0.97	8.36 ± 0.59	0.3612
Phosphorus (mg/dL)	3.72 ± 0.69	3.61 ± 0.53	0.3680
Alkaline phosphatase (IU/L)	89.23 ± 30.73	85.05 ± 20.28	0.4067
Vitamin D3 (ng/mL)	22.43 ± 4.71	24.12 ± 5.87	0.1418
PTH (pg/mL)	53.83 ± 10.71	51.22 ± 11.56	0.2666

Table 3 displays the bone mineral density (BMD) results, measured by T-scores from DEXA scans, at baseline and after three months. While there was no significant difference in BMD at baseline (p=0.1435), a dramatic divergence occurred over three months.

The NS group showed a substantial decline in mean T-score (from -1.23 to -2.21), resulting in a mean change (Δ) of -0.98, whereas the control group had a minimal change of -0.24.

The differences in BMD at 3 months and in the degree of change were both highly statistically significant (p<0.0001). This indicates a rapid and significant loss of bone density specifically in the nephrotic syndrome patients on corticosteroids over a short period.

Table 3: Bone Mineral Density (BMD) by DEXA at Baseline and 3 Months

Time	Mean T-score ± SD		p value (Unpaired t test)
	NS Group (n=35)	Control Group (n=70)	
Baseline	–0.93 ± 0.68	-0.85 ± 0.54	0.5139
3 Months	–2.01 ± 0.95	–1.19 ± 0.61	<0.0001
Δ change	-1.08 ± 0.85	-0.34 ± 0.58	<0.0001

Table 4 summarizes the incidence of osteopenia and osteoporosis at the study's endpoint. The NS group had markedly higher rates of both conditions: 57.14% osteopenia and 37.14% osteoporosis, compared to 24.29% and 8.57% in the control group, respectively.

These correspond to significantly elevate relative risks of 2.35 for osteopenia and 4.31 for osteoporosis. The p-values from Fisher's Exact Test (0.0012 and 0.0008) confirm these differences are highly significant.

Consequently, only 5.72% of the NS group maintained normal BMD, versus 67.14% of controls, underscoring the profound negative impact of nephrotic syndrome combined with corticosteroid therapy on bone health.

Table 4: Incidence of Osteopenia and Osteoporosis

Outcome	NS Group (n=35)	Control Group (n=70)	Relative Risk (95% CI)	p value (Fisher's Exact Test)
Osteopenia (%)	20 (57.14)	17 (24.29)	2.35 (1.42 – 3.89)	0.0012
Osteoporosis (%)	13 (37.14)	6 (8.57)	4.31 (1.79 – 10.36)	0.0008
Normal BMD (%)	2 (5.72)	47 (67.14)	—	

Discussion

This prospective cohort study demonstrates a rapid and clinically significant decline in bone mineral density (BMD) among adults with nephrotic syndrome receiving corticosteroid therapy, with changes evident within just three months of treatment initiation. Patients with nephrotic syndrome exhibited markedly higher incidences of osteopenia (57.14%) and osteoporosis (37.14%) compared to non-nephrotic controls, highlighting the profound skeletal impact of corticosteroid therapy in this population.

The magnitude and rapidity of bone loss observed in this study underscore the concept of a "double insult" to skeletal health. Glucocorticoids exert direct catabolic effects on bone by suppressing osteoblastogenesis, enhancing osteoclast activity, and reducing calcium absorption from the gastrointestinal tract [4–8]. Simultaneously, nephrotic syndrome contributes independently to bone fragility through urinary loss of vitamin D–binding protein, impaired vitamin D bioavailability, altered mineral metabolism, and chronic inflammatory activity [12]. The combined effect of these mechanisms likely explains the pronounced reduction in BMD observed over a short duration.

Our findings are consistent with prior studies demonstrating early and substantial bone loss following initiation of high-dose corticosteroid therapy. Fujita et al. reported significant reductions in lumbar spine BMD within three months of steroid exposure in nephrotic patients, supporting

the observation that glucocorticoid-induced bone loss is an acute phenomenon rather than a slow, cumulative process [14]. Similarly, Hegarty et al. demonstrated reduced BMD in adults treated with high-dose corticosteroids for nephrotic syndrome, particularly at trabecular-rich skeletal sites [15]. While differences in study design and duration limit direct comparison, the overall evidence consistently points toward a high risk of early osteoporosis in this population.

Notably, baseline biochemical parameters related to mineral metabolism—including serum calcium, phosphorus, vitamin D3, and parathyroid hormone—did not differ significantly between nephrotic and control groups in our study. This finding parallels observations by Aggarwal et al., who emphasized that total vitamin D levels may not accurately reflect bioavailable vitamin D in nephrotic syndrome due to urinary protein losses [16]. Consequently, normal total vitamin D levels may mask underlying functional deficiency, contributing to ongoing bone loss despite apparently normal baseline biochemical values.

The incidence rates of osteopenia and osteoporosis observed in our study are clinically alarming. More than one-third of nephrotic patients progressed to osteoporosis within three months, compared with fewer than 10% of controls. These findings reinforce the need for routine baseline and early follow-up DEXA screening in adults with nephrotic syndrome, particularly those initiated on corticosteroid therapy. Current international recommendations emphasize fracture risk assessment in patients receiving long-term glucocorticoids, yet implementation remains inconsistent in routine nephrology practice [8–10].

Although this study did not evaluate preventive or therapeutic interventions, existing literature strongly supports the role of early prophylaxis. Calcium and vitamin D supplementation have been shown to attenuate steroid-induced bone loss, particularly when initiated concurrently with corticosteroid therapy [17,18]. In patients at high risk or those demonstrating significant early bone loss, bisphosphonates such as risedronate have proven effective in preventing further decline in BMD [19,20]. These strategies are particularly relevant in nephrotic syndrome, where repeated disease relapses and cumulative steroid exposure further amplify skeletal risk [15,19].

The study has certain limitations. The relatively small sample size and short follow-up period limit the ability to assess long-term outcomes such as fracture incidence and sustained bone loss. Additionally, bioavailable vitamin D levels were not measured, which may have provided further insight into mineral metabolism abnormalities specific to nephrotic syndrome. Nonetheless, the prospective design, exclusion of patients with pre-existing osteoporosis, and use of matched controls strengthen the validity of the findings.

Overall, this study adds important region-specific evidence demonstrating that adults with primary nephrotic syndrome are at exceptionally high risk of rapid bone loss following corticosteroid therapy, underscoring the urgency of preventive bone health strategies in this population.

Conclusion

In conclusion, this prospective study demonstrates that adults with biopsy-proven primary nephrotic syndrome undergoing corticosteroid therapy experience rapid and clinically significant bone mineral density loss within a short period of three months. The incidence of osteopenia and osteoporosis was markedly higher in nephrotic patients compared with non-nephrotic controls, emphasizing the severe skeletal consequences of combined disease-related and treatment-related factors.

These findings highlight that bone loss in nephrotic syndrome is an early and aggressive complication rather than a late sequela of prolonged therapy. Routine baseline and early follow-up DEXA screening should therefore be integrated into standard care for adults with nephrotic syndrome initiating corticosteroids. Prophylactic measures—including calcium and vitamin D supplementation—and timely consideration of anti-resorptive therapy in high-risk patients are essential to reduce long-term fracture risk and morbidity.

By generating data from an Indian adult cohort, this study fills an important gap in existing literature and reinforces the need for heightened awareness of bone health in nephrology practice. Early recognition and intervention can help balance the benefits of corticosteroid therapy with the prevention of irreversible skeletal complications, ultimately improving long-term outcomes in patients with nephrotic syndrome.

References

1. Kodner C. Diagnosis and Management of Nephrotic Syndrome in Adults. Am Fam Physician. 2016 Mar 15;93(6):479-85. PMID: 26977832.
2. Canetta PA, Radhakrishnan J. The Evidence-Based Approach to Adult-Onset Idiopathic Nephrotic Syndrome. Front Pediatr. 2015 Sep 25;3:78. doi: 10.3389/fped.2015.00078.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021.

4. Compston J. Glucocorticoid-induced osteoporosis: an update. Endocrine. 2018 Jul;61(1):7-16. doi: 10.1007/s12020-018-1588-2. Epub 2018 Apr 24. PMID: 29691807; PMCID: PMC5997116.
5. van Staa TP, Leufkens HG, Abenhaim L, Begaud S, Zhang B, Cooper C. Use of oral corticosteroids in the United Kingdom. Q Med J. 2000; 93:105–111. doi: 10.1093/qjmed/93.2.105.
6. Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years. Rheumatology. 2011;50(11):1982–1990. doi: 10.1093/rheumatology/ker017.
7. Overman RA, Yeh JY, Deal CL. Prevalence of oral glucocorticoid usage in the United States: a general population perspective. Arthritis Care Res. 2013;65(2):294–298. doi: 10.1002/acr.21796.
8. Silverman S, Curtis J, Saag K, Flahive J, Adachi J, Anderson F, Chapurlat R, Cooper C, Diez-Perez A, Greenspan S, Hooven F, Le Croix A, March L, Netelenbos JC, Nieves J, Pfeilschifter J, Rossini M, Roux C, Siris E, Watts N, Compston J. International management of bone health in glucocorticoid-exposed individuals in the observational GLOW study. Osteoporos. Int. 2015;26(1):419–420. doi: 10.1007/s00198-014-2883-2.
9. Van Staa TP, Leufkens HGM, Cooper C. A meta-analysis of the epidemiology of corticosteroid-induced osteoporosis. Osteoporos. Int. 2002;13:777–787. doi: 10.1007/s001980200108.
10. Amiche MA, Albaum JM, Tadrous M, Pechlivanoglou P, Lévesque LE, Adachi JD, Cadarette SM. Fracture risk in oral glucocorticoid users: a Bayesian meta-regression leveraging control arms of osteoporosis clinical trials. Osteoporos. Int. 2016;27(5):1709–1718. doi: 10.1007/s00198-015-3455-9.
11. Redmond J, Jarjou LM, Zhou B, Prentice A, Schoenmakers I. Ethnic differences in calcium, phosphate and bone metabolism. Proc Nutr Soc. 2014 May;73(2):340-51. doi: 10.1017/S0029665114000068.
12. Yang SP, Ong L, Loh TP, Chua HR, Tham C, Meng KC, Pin L. Calcium, Vitamin D, and Bone Derangement in Nephrotic Syndrome. J ASEAN Fed Endocr Soc. 2021;36(1):50-55. doi: 10.15605/jafes.036.01.12.
13. Aparna P, Muthathal S, Nongkynrih B, Gupta SK. Vitamin D deficiency in India. J Family Med Prim Care. 2018 Mar-Apr;7(2):324-330. doi: 10.4103/jfmpc.jfmpc_78_18.
14. Fujita T, Satomura A, Hidaka M, Ohsawa I, Endo M, Ohi H. Acute alteration in bone mineral density and biochemical markers for bone metabolism in nephrotic patients receiving high-dose glucocorticoid and one-cycle etidronate therapy. Calcified tissue international. 2000 Mar;66(3):195-9.
15. Hegarty J, Mughal MZ, Adams J, Webb NJ. Reduced bone mineral density in adults treated with high-dose corticosteroids for childhood nephrotic syndrome. Kidney international. 2005 Nov 1;68(5):2304-9.
16. Aggarwal A, Yadav AK, Ramachandran R, Kumar V, Kumar V, Sachdeva N, Khandelwal N, Jha V. Bioavailable vitamin D levels are reduced and correlate with bone mineral density and markers of mineral metabolism in adults with nephrotic syndrome. Nephrology. 2016 Jun;21(6):483-9.
17. Choudhary S, Agarwal I, Seshadri MS. Calcium and vitamin D for osteoprotection in children with new-onset nephrotic syndrome treated with steroids: a prospective, randomized, controlled, interventional study. Pediatric Nephrology. 2014 Jun;29(6):1025-32.
18. Gruppen MP, Davin JC, Oosterveld MJ, Schreuder MF, Dorresteijn EM, Kramer SP, Bouts AH. Prevention of steroid-induced low bone mineral density in children with renal diseases: a systematic review. Nephrology Dialysis Transplantation. 2013 Aug 1;28(8):2099-106.
19. Takei T, Itabashi M, Tsukada M, Sugiura H, Moriyama T, Kojima C, Shiohira S, Shimizu A, Karasawa K, Amemiya N, Kawanishi K. Risedronate therapy for the prevention of steroid-induced osteoporosis in patients with minimal-change nephrotic syndrome. Internal Medicine. 2010;49(19):2065-70.
20. Kikuchi Y, Imakiire T, Yamada M, Saigusa T, Hyodo T, Kushiyama T, Higashi K, Hyodo N, Yamamoto K, Suzuki S, Miura S. Effect of risedronate on high-dose corticosteroid-induced bone loss in patients with glomerular disease. Nephrology Dialysis Transplantation. 2007 Jun 1;22(6):1593-600.
21. Krishna SH, Saini DK. Study on Bone Mineral Density in Adults with Nephrotic Syndrome. European Journal of Cardiovascular Medicine. 2023 Jul 1;13(3):598.