



ASSOCIATION BETWEEN NEPHROTIC SYNDROME STATUS (ACTIVE DISEASE AND REMISSION) AND VITAMIN D AND CALCIUM LEVELS IN CHILDREN

Annike Indah Kencana¹, Oke Rina Ramayani¹, Johannes Harlan Saing¹, Rina Amelia², Rosmayanti Syafriani Siregar¹, Karina Sugih Arto¹

¹Department of Pediatrics, Faculty of Medicine, Universitas Sumatera Utara ¹

²Department of Community Medicine, Faculty of Medicine, Universitas Sumatera Utara ²

*annikeindah@students.usu.ac.id

ABSTRACT

Pediatric nephrotic syndrome causes massive proteinuria, resulting in urinary loss of albumin, vitamin D-binding protein, and calcium-binding proteins. These losses may lead to vitamin D deficiency and impaired calcium homeostasis. Evidence regarding the association of active disease and remission with vitamin D and calcium levels among Indonesian children remains limited. This study aimed to examine the association between nephrotic syndrome status (active disease and remission) and vitamin D and calcium levels in children at Adam Malik Hospital, Medan. This analytical observational study used a cross-sectional design and included children aged 1-18 years with active nephrotic syndrome or nephrotic syndrome in remission. Data were obtained from medical records and laboratory measurements of serum 25-hydroxyvitamin D [25(OH)D] and calcium. Univariate analysis was used to describe participant characteristics. Associations between variables were assessed using the chi-square test or Fisher's exact test, with statistical significance set at $p < 0.05$. A total of 66 patients were analyzed, including 33 with active nephrotic syndrome and 33 in remission. In the active-disease group, 90.9% had vitamin D deficiency and 78.8% had hypocalcemia. Fisher's exact test showed a significant association between nephrotic syndrome status and vitamin D status ($p = 0.033$). In contrast, nephrotic syndrome status was not significantly associated with calcium status ($p = 0.108$), although hypocalcemia was more frequent in the active-disease group than in the remission group. Active nephrotic syndrome was significantly associated with vitamin D deficiency but not with serum calcium status. Periodic monitoring of vitamin D levels should be considered as part of the evaluation of children with nephrotic syndrome, particularly during active disease, to prevent complications related to bone and mineral metabolism.

Keywords: nephrotic syndrome, vitamin D, calcium, children, remission, active disease

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INTRODUCTION

Disturbances in calcium homeostasis are common in nephrotic syndrome. Low serum total calcium and vitamin D levels are thought to result from urinary loss of their protein-bound fractions. However, whether free calcium and free vitamin D levels are also reduced remains uncertain. Several studies have reported low free calcium levels in nephrotic syndrome. Low vitamin D levels have been attributed to urinary losses of 25-hydroxyvitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)D], most of which circulate in protein-bound form (Yang et al., 2021a).

Nephrotic syndrome (NS) is a clinical syndrome characterized by massive proteinuria that causes hypoalbuminemia and is accompanied by hyperlipidemia, edema, and other complications. The condition results from increased permeability of the damaged glomerular basement membrane, with infection and thromboembolic events among its important complications. Abnormal glomerular permeability may result from intrinsic kidney disease (primary NS) or secondary causes, including congenital infections, diabetes, systemic lupus erythematosus, malignancy, and certain medications (Tapia, 2023).

Primary NS, an important cause of chronic kidney disease in childhood, has a reported annual incidence of 1.5-2 cases per 100,000 individuals and a prevalence of 16 per 100,000. NS is associated with substantial morbidity because of hypercoagulability, infection, recurrent hospitalization, adverse effects of immunosuppressive therapy, and the risk of progression to end-stage kidney disease (Taner et al., 2023). Globally, the annual incidence of NS among children younger than 18 years ranges from 2 to 7 cases per 100,000. Nephrotic syndrome occurs more frequently in boys during childhood, whereas its incidence in adulthood is similar in men and women. Minimal change disease is the most common cause in children, while diabetic nephropathy is the leading cause in adults (Piccini et al., 2023).

Vitamin D plays an essential role in normal physiological function and skeletal health. It is also crucial for maintaining calcium homeostasis. Serum 25(OH)D is considered the principal indicator of vitamin D stores, with levels above 30 ng/mL regarded as sufficient (Jesmin et al., 2025). Vitamin D-binding globulin, which has a lower molecular weight than albumin, binds up to 98% of circulating 25(OH)D. During active nephrotic syndrome, vitamin D-binding protein (VDBP) is lost in the urine together with albumin. Vitamin D deficiency in nephrotic syndrome may cause skeletal manifestations, including substantial trabecular bone loss in the axial skeleton, particularly the spine, pelvis, and ribs. This increases the risk of fractures, hypocalcemia, and long-term complications such as rickets and osteomalacia. Early vitamin D supplementation may therefore help prevent impaired bone mineralization caused by calcium-phosphorus imbalance (Maji et al., 2022).

A previous study by Yang et al. in adults with NS found low total and free serum calcium levels and low total 25(OH)D levels during active disease. Although 1,25(OH)D remained within the normal range, the level was considered inappropriately normal in the presence of hypocalcemia and hyperparathyroidism. Calcium and vitamin D metabolite levels improved during remission, although patients with incomplete remission continued to have low 25(OH)D levels (Yang et al., 2021a).

Thakor et al. reported lower serum calcium levels and several metabolic abnormalities in patients with NS than in controls. Their study examined the associations of serum calcium and vitamin D with other biochemical parameters in steroid-sensitive nephrotic syndrome (SSNS) and steroid-resistant nephrotic syndrome (SRNS) (Thakor et al., 2022). Liao et al. found that patients with NS had an approximately 3.3-fold higher risk of osteoporosis than individuals without NS. The principal risk factors were older age, low calcium intake, and high cumulative steroid exposure. Nephrotic syndrome may disrupt calcium and vitamin D homeostasis through hypocalcemia, reduced vitamin D metabolites, and hyperparathyroidism, which contribute to reduced bone mineral density (Liao et al., 2024). This study aimed to determine the association between nephrotic syndrome status (active disease and remission) and vitamin D and calcium levels in children.

METHOD

This analytical observational study used a cross-sectional design and included 66 children aged 1-18 years with active nephrotic syndrome or nephrotic syndrome in remission. Participants were recruited using consecutive sampling. Data were obtained from medical records and laboratory measurements of serum 25-hydroxyvitamin D [25(OH)D] and calcium. Univariate analysis was used to describe participant characteristics. Associations between variables were assessed using the chi-square test or Fisher's exact test, with statistical significance set at $p < 0.05$. The study received ethical approval from the Health Research Ethics Committee of Universitas Sumatera Utara (No. 18/KEPK/USU/2026).

RESULT

Participant Characteristics

The mean age of the participants was 11 ± 10.8 years, and the mean disease duration was 3 ± 2.06 years. The study included 66 children with nephrotic syndrome treated at Adam Malik Hospital. Most participants were male (45 patients, 68.2%), while 21 (31.8%) were female. Steroid-resistant nephrotic syndrome (SRNS) was the most common clinical type (29 patients, 43.9%), followed by steroid-dependent nephrotic syndrome (SDNS) in 22 patients (33.3%) and steroid-sensitive nephrotic syndrome (SSNS) in 15 patients (22.8%). Participant characteristics are presented in Tables 1 and 2.

Table 1.
Age and Disease Duration of Children with Nephrotic Syndrome

Variable	Mean $\pm$ SD
Age	11 ± 10.8
Disease duration	3 ± 2.06

Table 2.

Sex and Clinical Type of Nephrotic Syndrome Among Children at Adam Malik Hospital, Medan

Variable	f	%
Sex		
Male	45	68.2
Female	21	31.8
Clinical type of nephrotic syndrome		
SSNS	15	22.8
SRNS	29	43.9
SDNS	22	33.3

Vitamin D Profile of Children with Nephrotic Syndrome

The mean vitamin D level was 13.7 ± 11.1 ng/mL. Values ranged from 2.3 to 56.8 ng/mL. Most patients had vitamin D deficiency (52 patients, 78.8%). Vitamin D insufficiency was identified in 10 patients (15.2%), and only 4 patients (6.1%) had normal vitamin D levels. These findings are presented in Tables 3 and 4.

Table 3.
Mean Vitamin D Level in Children with Nephrotic Syndrome

Vitamin D level	Mean $\pm$ SD	Range
Vitamin D level	13.7 ± 11.1	2.3-56.8

Table 4.

Vitamin D Status in Children with Nephrotic Syndrome at Adam Malik Hospital, Medan

Vitamin D status	f	%
Normal	4	6.1
Insufficiency	10	15.2
Deficiency	52	78.8

Calcium Profile of Children with Nephrotic Syndrome

The mean calcium level was 8.05 ± 0.80 mg/dL. Values ranged from 6.2 to 10.4 mg/dL. Most patients had hypocalcemia (46 patients, 69.7%), while 20 patients (30.3%) had calcium levels within the normal range. These findings are presented in Tables 5 and 6.

Table 5.
Mean Calcium Level in Children with Nephrotic Syndrome

Calcium level	Mean $\pm$ SD	Range
Calcium level	8.05 ± 0.80	6.2-10.4

Table 6.
Calcium Status in Children with Nephrotic Syndrome

Calcium status	f	%
Hypocalcemia	46	69.7
Normal	20	30.3

Association Between Vitamin D Status and Active Disease or Remission in Children With Nephrotic Syndrome

Vitamin D status differed between children with active nephrotic syndrome and those in remission. In the remission group, 22 patients (66.7%) had vitamin D deficiency, 7 (21.2%) had vitamin D insufficiency, and 4 (12.1%) had normal vitamin D levels. In the active-disease group, 30 patients (90.9%) had vitamin D deficiency, 3 (9.1%) had vitamin D insufficiency, and none had normal vitamin D levels. Fisher's exact test yielded $p = 0.033$ ($p < 0.05$), indicating a significant association between nephrotic syndrome status (active disease and remission) and vitamin D status in children at Adam Malik Hospital. These findings are presented in Table 7.

Table 7.
Association Between Vitamin D Status and Active Disease or Remission in Children with Nephrotic Syndrome

Vitamin D status	Nephrotic syndrome		Total f (%)	p-value
	Remission f (%)	Active disease f (%)		
Normal	4 (12.1)	0 (0)	4 (6.1)	
Insufficiency	7 (21.2)	3 (9.1)	10 (15.2)	
Deficiency	22 (66.7)	30 (90.9)	52 (78.8)	

Association Between Calcium Status and Active Disease or Remission in Children With Nephrotic Syndrome

Calcium status was compared between children with active nephrotic syndrome and those in remission. In the remission group, 20 patients (60.6%) had hypocalcemia and 13 (39.4%) had normal calcium levels. In the active-disease group, 26 patients (78.8%) had hypocalcemia and 7 (21.2%) had normal calcium levels. The chi-square test yielded $p = 0.108$ ($p > 0.05$), indicating no significant association between nephrotic syndrome status (active disease and remission) and calcium status in children at Adam Malik Hospital. These findings are presented in Table 8.

Table 8.
Association Between Calcium Status and Active Disease or Remission in Children with Nephrotic Syndrome

Calcium status	Nephrotic syndrome		Total f (%)	p-value
	Remission f (%)	Active disease f (%)		
Hypocalcemia	20 (60.6)	26 (78.8)	46 (69.7)	
Normal	13 (39.4)	7 (21.2)	20 (30.3)	

DISCUSSION

Male participants accounted for 68.2% of the study population, indicating that nephrotic syndrome was more common in boys than in girls. This finding is consistent with a 2023 study by Putra et al. at Prof. I.G.N.G. Ngoerah Hospital, which reported that 60% of children with nephrotic syndrome were male and 40% were female. Male predominance has also been reported in other clinical studies (Kresnandari, 2023). The Indonesian Ministry of Health reported that childhood nephrotic syndrome occurs more frequently in boys, with an approximate male-to-female ratio of 2:1 (Kemenkes, 2023). Ajarmeh et al. (2025) reported a similar finding, with boys accounting for 64% of pediatric nephrotic syndrome cases. The male predominance observed in this study is therefore consistent with previous reports and international guidelines (Kemenkes, 2023).

The mean age of the participants was 11 ± 10.8 years. This differs from the 2023 study by Putra et al. at Prof. I.G.N.G. Ngoerah Hospital, Bali, which included patients aged 2-18 years and reported that most cases occurred in school-aged children (Kresnandari, 2023). Akter et al. (2024) found that children aged 4-7 years constituted the largest age group (50%), indicating that most cases first presented at a younger age than in the present study. Ajarmeh et al. (2025) also reported a median age at disease onset of 4 years among children with nephrotic syndrome. This difference may reflect the inclusion of patients who had reached remission after a relatively long disease course, resulting in an older age at enrollment than at initial diagnosis. Pediatric nephrology guidelines recognize that nephrotic syndrome may follow a prolonged course, particularly in children with frequent relapses or steroid dependence (KDIGO, 2013).

The vitamin D profile of patients with nephrotic syndrome in remission showed that most had vitamin D deficiency. Based on the vitamin D classification, the mean value was within the deficient range, indicating that low vitamin D levels persisted in many patients despite remission. This finding suggests that abnormalities in vitamin D metabolism may continue even after proteinuria improves (Jesmin et al., 2025). In nephrotic syndrome, vitamin D deficiency results from urinary loss of vitamin D-binding protein (VDBP) and 25(OH)D through the abnormally permeable glomerular filtration barrier. This protein loss reduces circulating vitamin D levels and increases the risk of deficiency. Long-term corticosteroid therapy may further impair vitamin D metabolism and compromise bone health. The 2024 KDIGO guideline identifies vitamin D and calcium supplementation as an important component of nephrotic syndrome management in children to reduce morbidity related to mineral and bone disorders (KDIGO, 2024).

The calcium profile of patients with nephrotic syndrome in remission showed that most had hypocalcemia. Calcium levels varied substantially within this group. Although the mean calcium level remained within the normal pediatric serum range, the high standard deviation indicated a wide distribution of values in the study sample. Calcium abnormalities in nephrotic syndrome are closely related to massive proteinuria, which causes urinary loss of important proteins, including albumin, vitamin D-binding protein (VDBP), and vitamin D metabolites. Loss of VDBP reduces circulating vitamin D levels and may impair intestinal calcium absorption. Long-term corticosteroid therapy may also reduce gastrointestinal calcium absorption and increase bone resorption. These effects place patients with nephrotic syndrome at risk of mineral and bone disorders. The 2025 KDIGO guideline recommends considering the monitoring and supplementation of vitamin D and calcium to reduce complications related to bone metabolism in children with nephrotic syndrome (KDIGO, 2025).

These findings are consistent with those of Yang et al. (2021), who investigated calcium and vitamin D homeostasis in patients with nephrotic syndrome. They found that total calcium and vitamin D levels decreased during active disease because of urinary protein loss. Calcium levels tended to improve after remission. However, patients who had not achieved complete remission continued to have lower vitamin D and calcium levels than healthy individuals (Yang et al., 2021b). Vitamin D status was significantly associated with nephrotic syndrome status. Lower vitamin D levels were more frequently observed during active disease, whereas higher levels tended to occur during remission. These findings indicate an association between vitamin D status and disease activity in childhood nephrotic syndrome.

Vitamin D deficiency in nephrotic syndrome is attributed to massive proteinuria and the resulting urinary loss of vitamin D-binding protein (VDBP) and vitamin D metabolites. This loss reduces circulating 25-hydroxyvitamin D [25(OH)D]. In addition to its role in calcium metabolism and skeletal health, vitamin D has immunomodulatory effects on T-cell activity, inflammatory cytokine production, and immune regulation. Low vitamin D levels may therefore be associated with greater

disease activity and a higher tendency toward relapse. Several studies also suggest that vitamin D contributes to maintaining podocyte integrity and the glomerular filtration barrier; deficiency may therefore aggravate kidney injury (Thakur et al., 2025).

These findings are consistent with those of Jesmin et al. (2025), who reported lower vitamin D levels in children with relapsing or active nephrotic syndrome than in those with stable remission. Although vitamin D levels increased after remission, most patients continued to have vitamin D insufficiency or deficiency. The authors concluded that vitamin D status was closely associated with disease activity and the clinical course of childhood nephrotic syndrome (Jesmin et al., 2025). Research on vitamin D receptor expression in children with primary nephrotic syndrome has also shown lower 25(OH)D levels during active disease than during remission, with an inverse association between 25(OH)D levels and the degree of proteinuria. Greater urinary protein loss was associated with lower serum vitamin D levels. Although vitamin D levels increased after remission, they often remained below the normal range reported for healthy children. These observations support the significant association between vitamin D status and active disease or remission found in the present study (Zhang et al., 2017).

Serum calcium status was not significantly associated with nephrotic syndrome status. This finding indicates that active disease and remission were not associated with a statistically significant difference in serum calcium status. The very weak correlation also suggests that changes in calcium levels had only a minimal relationship with disease activity. Serum calcium levels in patients with nephrotic syndrome may therefore be influenced by factors other than active disease or remission (Yang et al., 2021a). This finding is consistent with the study by Yang et al. (2021), which evaluated calcium and vitamin D homeostasis in patients with nephrotic syndrome. Calcium levels decreased during active disease because of proteinuria and hypoalbuminemia but tended to improve after remission. Nevertheless, changes in calcium levels did not consistently show a strong association with disease activity because of adaptive mechanisms in mineral metabolism. The authors concluded that calcium disturbances in nephrotic syndrome are complex and are not determined solely by active disease or remission.

Nephrotic syndrome increases glomerular permeability, resulting in urinary loss of proteins, including albumin, vitamin D-binding protein (VDBP), and calcium-binding proteins. This loss may reduce total serum calcium because most circulating calcium is bound to albumin. However, ionized calcium, the biologically active fraction, often remains within the normal range through hormonal compensatory mechanisms involving parathyroid hormone (PTH), active vitamin D, and the kidneys. Total serum calcium may therefore not accurately reflect calcium homeostasis in patients with nephrotic syndrome (Yang et al., 2021a). Another study of children with relapsing nephrotic syndrome and those in remission reported that total and ionized calcium levels tended to be lower during active disease than during remission, although the differences were not consistently statistically significant. More pronounced differences were observed in vitamin D and parathyroid hormone levels than in serum calcium levels. These findings suggest that compensatory mechanisms may maintain calcium homeostasis despite urinary protein loss and altered vitamin D metabolism during the course of nephrotic syndrome (Jesmin et al., 2025).

CONCLUSION

Children with active nephrotic syndrome had high proportions of vitamin D deficiency and hypocalcemia. Vitamin D status was significantly associated with active nephrotic syndrome. In contrast, calcium status was not significantly associated with active nephrotic syndrome.

REFERENCES

- Ajarmeh, S. (2025). Steroid response and outcomes in childhood nephrotic syndrome: A multicenter, cross-sectional study from Jordan. *WJCP*, 14(4), 1–10. <https://doi.org/10.5409/wjcp.v14.i4.109671>
- Akter, S. et al. (2024). Socio-Demographic Factors of Children with Nephrotic Syndrome and Their Clinical Correlation. *Scholars Journal of Applied Medical Sciences*, 6691(10), 1410–1416.
- Jesmin, T. et al. (2025). Vitamin D status on remission of relapsing nephrotic syndrome among children at a South Asian tertiary hospital. *Egyptian Pediatric Association Gazette*, 73(1). <https://doi.org/10.1186/s43054-025-00374-7>
- KDIGO. (2013). *Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl.* ; 3(1): 1–150.
- KDIGO. (2024). *KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.*
- KDIGO. (2025). KDIGO 2025 Clinical Practice Guideline for the Management of Nephrotic Syndrome in Children. *Kidney Disease Improving Global Outcomes*. <https://kdigo.org/wp-content/uploads/2025/04/KDIGO-2025-Guideline-for-Nephrotic-Syndrome-in-Children>
- Kemenkes. (2023). *Mengenal Sindrom Nefrotik Pada Anak*. https://keslan.kemkes.go.id/view_artikel/2858/mengenal-sindrom-nefrotik-pada-anak
- Kresnandari, L. (2023). The quality of life in children with nephrotic syndrome at Prof I.G.N.G Ngoerah Hospital, Denpasar, Bali. *Isains Medis*, 14(1), 401–406. <https://doi.org/10.15562/ism.v14i1.1658>
- Liao, C. Y. et al. (2024). Do patients with nephrotic syndrome have an increased risk of osteoporosis? A nationwide population-based retrospective cohort study in Taiwan. *BMJ Open*, 14(5). <https://doi.org/10.1136/bmjopen-2023-080858>
- Mainnah, N. M. et al. (2019). GAMBARAN KADAR KALSIUM TOTAL DAN VITAMIN D PADA ANAK SINDROM NEFROTİK DI RSUD ULIN BANJARMASIN. *Homeostasis*, 451–460.
- Maji, M. et al. (2022). Severity of Vitamin D Deficiency in Children with Nephrotic Syndrome: A Study from Tertiary Care Center in Northern India. *Saudi Journal of Kidney Diseases and Transplantation*, 33(5), 608–616. <https://doi.org/10.4103/1319-2442.389421>
- Piccini, C. D. et al. (2023). *Increased cerebrospinal fluid pressure and nephrotic syndrome: A case report and literature review. Clinical Neurology and Neurosurgery*, 225, 107567.
- Siregar, R. S. et al. (2021). *Relationship between Serum 25 (OH) D Levels and Blood Pressure in Children with Nephrotic Syndrome*. 9, 260–264.
- Sultana et al. (2024). *Comparison of Calcium , Vitamin D and PTH in Different Subgroups of Steroid Sensitive Nephrotic Syndrome*. 9–16. <https://doi.org/10.4103/pnjb.pnjb>
- Taner, S. et al. (2023). Evaluation of Children with Nephrotic Syndrome: A Single Center Experience. *Journal of Pediatric Research*, 10(2), 118–124. <https://doi.org/10.4274/jpr.galenos.2023.37928>
- Tapia, C. (2023). Nephrotic Syndrome. *National Library of Medicine*. <https://www.ncbi.nlm.nih.gov/books/NBK470444/>
- Thakor, J. M. et al. (2022). Association between serum calcium and biochemical parameters among nephrotic syndrome patients: a case-control study. *Egyptian Pediatric Association Gazette*, 70(1), 4–9. <https://doi.org/10.1186/s43054-022-00110-5>
- Thakur, S. et al. (2025). *Vitamin D Levels in Children of Nephrotic Syndrome During Active Nephrosis and it ' s Correlation to Serum Albumin Levels*. 11(1). <https://doi.org/10.46347/jmsh.v11.i1.24.231>
- Yang, S. P. et al. (2021a). Calcium, vitamin d, and bone derangement in nephrotic syndrome. *Journal of the ASEAN Federation of Endocrine Societies*, 36(1), 50–55. <https://doi.org/10.15605/JAFES.036.01.12>
- Yang, S. P. et al. (2021b). *Calcium , Vitamin D , and Bone Derangement in Nephrotic Syndrome*.

36(1), 50–55.

Zhang, X. et al. (2017). *Vitamin D levels and vitamin D receptor expression in children with primary nephrotic syndrome* . 28(February 2013), 9658–9662.