Readers Insight
Publisher of open access books and journals
PJMLS
Print ISSN: 2707-4471. Online ISSN: 2707-448X

| Research Article | Pak-Euro Journal of Medical and Life Sciences |
|---|---|
| DOI: 10.31580/pjmls.v6i3.2866 | Copyright © All rights are reserved by Corresponding Author |
| Vol. 6 No.3, 2023: pp. 253-260 | |
| www.readersinsight.net/pjmls | **Revised:** August 31, 2023 **Accepted:** September 12, 2023 |
| **Submission:** June 20, 2023 | **Published Online:** September 31, 2023 |


# PREVALENCE OF VITAMIN D DEFICIENCY IN CHILDREN WITH NEPHROTIC SYNDROME IN OUTPATIENT NEPHROLOGY DEPARTMENT, CHILDREN HOSPITAL, PIMS – A SINGLE-CENTER STUDY

Saima Sikandar[1]*, Nadia Waheed[1], Khizer Ilyas[1]

[1]**Department of Pediatric Medicine,** Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan

*** Corresponding author:** Dr. Saima Sikandar. Email. saimasikandar347@gmail.com

**Abstract**

**Background:** *Nephrotic syndrome is a common pediatric disease characterized by proteinuria, low serum albumin, and edema. Vitamin D deficiency has been implicated in various conditions, including nephrotic syndrome. This study aimed to determine the frequency of vitamin D deficiency in children with nephrotic syndrome and its potential impact on the disease.* **Methods:** *A cross-sectional study was conducted involving 180 pediatric patients with nephrotic syndrome. Vitamin D levels were categorized as deficient (<12 ng/ml), insufficient (12-20 ng/ml), or sufficient (20-100 ng/ml). The study also examined demographic and clinical variables and their correlation with vitamin D levels.* **Results:** *The study revealed that 36.1% of participants had vitamin D deficiency, and 26.7% had severe deficiency. No significant gender-based differences in vitamin D levels were observed. The duration of nephrotic syndrome did not significantly impact vitamin D levels. Hypocalcemia was present in 53.3% of participants. The 6-month post-follow-up status showed no significant relationship between vitamin D levels and clinical outcomes.* **Conclusion:** *The study underscored a considerable frequency of vitamin D deficiency in children with nephrotic syndrome. Routine vitamin D screening and early management are crucial in addressing this deficiency and improving patient outcomes.*

**Keywords:** *Calcium metabolism, Clinical outcomes, Nephrotic syndrome, Pediatric, Vitamin D deficiency*

## INTRODUCTION

Primary nephrotic syndrome is a common pediatric disease. The annual incidence is estimated to be 2-4 cases per 100,000 children. The majority of the patients are younger than 6 years of age i-e 80% with male predominance. There is a clear geographical variety with children from Southeast Asia more affected (1). The occurrence of nephrotic syndrome is correlated with T-cell immune disorders and abnormal glomerular podocyte proteins; however, the exact etiology and pathogenesis of nephrotic syndrome remain poorly understood (2).

A number of studies have suggested that the permeability factors underlying glomerular filtration barrier dysfunction are associated with the pathophysiology of nephrotic syndrome, but these factors have not yet been identified (3). About 90% of children with nephrotic syndrome are in the idiopathic nephrotic syndrome group. The idiopathic nephrotic syndrome is accompanied by primary glomerular disease (4).

Vitamin D, a group of fat-soluble secosteroids, with two primary forms, D2 and D3, plays a vital role in human health. Its structure involves a steroid nucleus and a side chain, with D3 being more biologically active due to an additional methyl group. Once metabolized into its active form, calcitriol, vitamin D regulates calcium and phosphate homeostasis, influencing skeletal health. Beyond its classic role, vitamin D is now recognized for its involvement in immune function, cardiovascular health, and potential therapeutic applications in various medical conditions. Understanding its structure, metabolism, and wide-ranging utility is essential in harnessing its potential for improving human well-being. Vitamin D has been shown to exert immunomodulatory effects (5). The immune cell phenotype can be influenced by multiple natural and chemical compounds (6). One of these molecules is vitamin D3 and its active hormonal

metabolite 1,25-dihydroxyvitamin D3 (1, 25 (OH)2 D3) (7). Vitamin D deficiency is determined by a practical definition based on the measurement of serum 25-hydroxyvitamin D levels, categorized as follows: severe deficiency (<12 ng/ml), insufficiency (12-20 ng/ml), and sufficiency (20-100 ng/ml).

Children with nephrotic syndrome often display a number of calcium homeostasis disturbances causing abnormal bone histology, including hypocalcemia, reduced serum vitamin D metabolites, impaired intestinal absorption of calcium, and elevated levels of immunoreactive Parathyroid Hormone. These are mainly attributed to the loss of a variety of plasma proteins and minerals in the urine as well as steroid therapy (8).

It has been reported in a study that frequency of vitamin D deficiency was 47.05% in children with nephrotic syndrome (9). While another study reported that frequency of vitamin D deficiency was 100% in children with nephrotic syndrome (10).

Rationale of this study was to determine the frequency of vitamin D deficiency in children with nephrotic syndrome. Literature showed varied frequency of vitamin D deficiency in children with nephrotic syndrome. Through this study we want to confirm that whether the results of previous study are also applicable on local population. Furthermore, through this study we will also get local evidence which in future will help us to implement the screening of children with nephrotic syndrome for vitamin D level and apply early preventive or management protocols to prevent or treat the vitamin D deficiency and improve the outcome of patients of nephrotic syndrome. This will also help us improve our practice and guidelines for management of children with nephrotic syndrome.

# MATERIALS AND METHODS

This study utilized a cross-sectional research design to investigate the prevalence and extent of vitamin D deficiency among pediatric patients diagnosed with nephrotic syndrome. The research was conducted within the premises of the indoor and outdoor departments of Pediatrics Medicine at Children Hospital, PIMS Islamabad. The study encompassed a period of 6 months, initiated subsequent to the acquisition of ethical clearance from the institutional review board to ensure compliance with ethical standards and regulations.

## SAMPLE SIZE

A meticulous sample size determination was conducted to ensure the representation of the target population. Specifically, a sample size of 180 cases was calculated, aiming for a 95% confidence level with an 8% margin of error, while factoring in the expected prevalence of vitamin D deficiency, established at 47.05% within the population of children diagnosed with nephrotic syndrome. The sampling strategy employed was non-probability consecutive sampling, allowing for a systematic selection of eligible participants who met the predefined inclusion criteria.

## INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria comprised children aged between 1-13 years of both genders, presenting clinical manifestations consistent with nephrotic syndrome as per operational definitions. Conversely, exclusion criteria were established to eliminate potential confounding factors, including children with a recurrent history of vitamin D deficiency or those currently undergoing vitamin supplementations based on documented medical records. Additionally, children with a glomerular filtration rate (GFR) below 70 and those on anti-epileptics, as indicated by their medical history, were excluded from the study.

## DATA COLLECTION AND ANALYSIS

The data collection procedure adhered to a structured approach to ensure accuracy and comprehensiveness. A total of 180 eligible children meeting the inclusion criteria were enrolled from either the outpatient or inpatient sections of the Department of Pediatrics Medicine at PIMS, Islamabad. Informed consent was obtained from the parents or guardians of the participating children, after which relevant demographic information, encompassing name, age, gender, weight, and duration of nephrotic syndrome,

was meticulously recorded. Subsequently, venous blood samples were collected using a 3cc disposable syringe under aseptic conditions, and these were sent to the hospital laboratory for vitamin D level assessments. The laboratory reports were thoroughly reviewed, and vitamin D deficiency was confirmed for levels below 20 ng/ml. For children identified with a deficiency, standardized protocols for vitamin D deficiency management were implemented and documented using a dedicated proforma.

Following the data collection phase, the amassed data was accurately entered into SPSS version 20 for thorough analysis. Quantitative variables, encompassing age, weight, duration of nephrotic syndrome, and vitamin D levels, were characterized by mean and standard deviation (SD). Qualitative variables, such as gender and vitamin D deficiency status, were represented by frequencies and percentages. The data was further stratified based on age, gender, weight, and duration of nephrotic syndrome. Subsequently, chi-square tests were utilized for post-stratification comparisons, considering a significance level of $p \leq 0.05$. This analytical approach facilitated a nuanced understanding of the association between vitamin D deficiency and specific demographic or clinical parameters among pediatric patients afflicted with nephrotic syndrome.

# RESULTS

## CHARACTERISTICS OF STUDY PARTICIPANTS

The study included a sample of 180 participants, with an average age of 9.4 months and a standard deviation of 4.8 months (age demographic of participants is shown in Fig. 1a). In terms of weight, the mean weight was 16.4 kg with a standard deviation of 4.7 kg. The gender distribution indicated that 55% of the participants were male, while 45% were female (gender demographic of participants is shown in Fig. 1b). Regarding the duration of nephrotic syndrome, the data showed that 21.1% of the participants had a duration of 6 months, 38.3% had a duration of 1 year, and the majority, 40.6%, had been dealing with the syndrome for 2 years. In terms of vitamin D levels, 26.7% of the participants had vitamin D levels below 12 ng/ml, 36.1% fell within the range of 12-20 ng/ml, and 37.2% had levels between 20-100 ng/ml (Vitamin D in children with nephrotic syndrome graph is shown in Fig. 2). Furthermore, calcium levels were analyzed, revealing that 53.3% of the participants had hypocalcemia, while 46.7% had normal calcium levels. The post-follow-up status after 6 months showed promising results, with 34.4% of participants being cured, 46.1% experiencing improvement, and 19.4% remaining in a stationary condition (Table I).

**Table I**. General characteristics of the patients with Nephrotic Syndrome(n=180)

| Variables | Categories | Mean (n=180) | S.D |
|---|---|---|---|
| Age (months) (mean± SD) | - | 9.4 | 4.8 |
| Weight (kg) (mean± SD) | - | 16.4 | 4.7 |
| **Variables** | **Categories** | **Frequency (n=180)** | **Percentage** |
| Gender | Male | 99 | 55% |
| | Female | 81 | 45% |
| Nephrotic Syndrome Duration | 6 months | 38 | 21.1 |
| | 1 year | 69 | 38.3 |
| | 2 years | 73 | 40.6 |
| Vitamin D levels | <12ng/ml | 48 | 26.7 |
| | 12-20 ng/ml | 65 | 36.1 |
| | 20-100 ng/ml | 67 | 37.2 |
| Calcium levels | Hypocalcemia | 96 | 53.3 |
| | Normal | 84 | 46.7 |
| 6-month post follow up status | Cured | 62 | 34.4 |
| | Improved | 83 | 46.1 |
| | Stationary | 35 | 19.4 |

## VITAMIN D STATUS IN STUDY PARTICIPANTS WITH NEPHROTIC SYNDROME

Among the male participants, 25.3% had vitamin D levels below 12 ng/ml, 36.4% fell within the range of 12-20 ng/ml, and 38.4% had levels between 20-100 ng/ml. In comparison, for female participants, 25.4% had vitamin D levels below 12 ng/ml, 35.8% were within the 12-20 ng/ml range, and 35.8% were in the

20-100 ng/ml range. The p-value for this comparison was 0.88, indicating no statistically significant gender-based difference in vitamin D levels.

When analyzing vitamin D levels based on the duration of nephrotic syndrome, it was found that the distribution across the three categories (below 12 ng/ml, 12-20 ng/ml, and 20-100 ng/ml) varied with the duration. For participants with a nephrotic syndrome duration of 6 months, none had vitamin D levels below 12 ng/ml, 47.4% were in the 12-20 ng/ml range, and 52.6% were in the 20-100 ng/ml range. For those with a duration of 1 year, 24.6% fell below 12 ng/ml, 24.6% were in the 12-20 ng/ml range, and the majority, 50.7%, were in the 20-100 ng/ml range. Participants with a 2-year duration showed a different distribution, with 42.5% below 12 ng/ml, 41.1% in the 12-20 ng/ml range, and 16.4% in the 20-100 ng/ml range. The p-values for these comparisons were 0.26 and 0.29, suggesting no statistically significant differences in vitamin D levels based on nephrotic syndrome duration.

Furthermore, vitamin D levels were examined in relation to calcium levels. Among participants with hypocalcemia, 27.1% had vitamin D levels below 12 ng/ml, 31.3% were in the 12-20 ng/ml range, and 41.7% were in the 20-100 ng/ml range. Conversely, among those with normal calcium levels, 26.2% had vitamin D levels below 12 ng/ml, 41.7% were in the 12-20 ng/ml range, and 32.1% were in the 20-100 ng/ml range.

Finally, the analysis of vitamin D levels concerning the 6-month post-follow-up status showed intriguing insights. Among participants categorized as "cured," 21% had vitamin D levels below 12 ng/ml, 30.6% were in the 12-20 ng/ml range, and 48.4% were in the 20-100 ng/ml range. For those classified as "improved," 26.5% had vitamin D levels below 12 ng/ml, 43.4% were in the 12-20 ng/ml range, and 30.1% were in the 20-100 ng/ml range. Participants categorized as "stationary" had 37.1% with vitamin D levels below 12 ng/ml, 28.6% in the 12-20 ng/ml range, and 34.3% in the 20-100 ng/ml range. The p-value for this comparison was 0.10, suggesting no statistically significant relationship between vitamin D levels and the 6-month post-follow-up status (Table II).

**Table II.** Correlation of Vitamin D Status with general variables of study participants (n=180) *Chi-square test

| Variables | Categories | Vitamin D levels | | | |
|---|---|---|---|---|---|
| | | <12ng/ml | 12-20 ng/ml | 20-100 ng/ml | P-value* |
| Gender | Male | 25 (25.3%) | 36 (36.4%) | 38 (38.4%) | 0.88 |
| | Female | 23 (25.4%) | 29 (35.8%) | 29 (35.8%) | |
| Nephrotic Syndrome Duration | 6 months | 0 (0%) | 18 (47.4%) | 20 (52.6%) | 0.26 |
| | 1 year | 17 (24.6%) | 17 (24.6%) | 35 (50.7%) | 0.29 |
| | 2 years | 31 (42.5%) | 30 (41.1%) | 12 (16.4%) | |
| Calcium levels | Hypocalcemia | 26 (27.1%) | 30 (31.3%) | 40 (41.7%) | |
| | Normal | 22 (26.2%) | 35 (41.7%) | 27 (32.1%) | |
| 6-month post follow up status | Cured | 13 (21%) | 19 (30.6%) | 30 (48.4%) | 0.10 |
| | Improved | 22 (26.5%) | 36 (43.4%) | 25 (30.1%) | |
| | Stationary | 13 (37.1%) | 10 (28.6%) | 12 (34.3%) | |

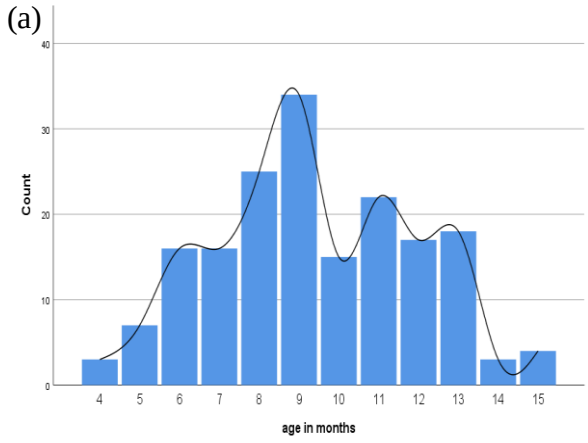


**Fig. 1a.** Age demographics of participants

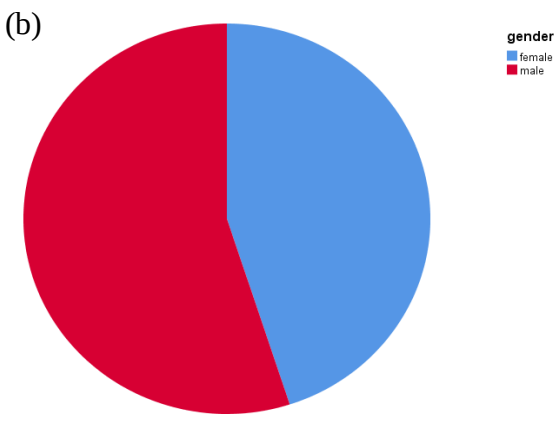


**Fig. 1b.** Gender demographics of participants

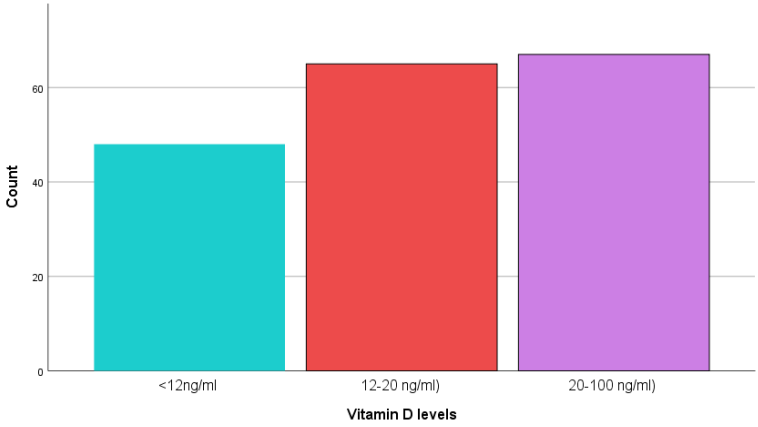


**Fig. 2.** Vitamin D status in children with Nephrotic Syndrome

# DISCUSSION

Nephrotic syndrome is a prevalent pediatric disorder, particularly affecting children below 6 years of age, with a notable male predominance (11). Its occurrence shows geographical variance, with a higher incidence observed in Southeast Asian children (12). While its association with T-cell immune disorders and abnormal glomerular podocyte proteins is recognized, the precise etiology and pathogenesis remain incompletely understood.

The study's primary focus was to investigate the prevalence of vitamin D deficiency in children diagnosed with nephrotic syndrome. Vitamin D, known for its immunomodulatory effects, including influence on immune cell phenotype, could be a significant factor in nephrotic syndrome management (13). Children with nephrotic syndrome often exhibit disturbances in calcium homeostasis, attributed to protein and mineral loss in urine, as well as steroid therapy. Numerous studies have shown varied degrees of vitamin D deficiency or insufficiency in children, including those with nephrotic syndrome, as a result of growing awareness of vitamin D deficiency across the world (14-17).

The results indicated a considerable frequency of vitamin D deficiency in children with nephrotic syndrome, aligning with existing literature (18, 19). Children with nephrotic syndrome in remission were tested for levels of 25 OH vitamin D, and it was shown that 68 percent of children had levels below 20 ng/ml and 90 percent had levels over 30 ng/ml (20). In a study done by Aggarwal et al. in 2016, it was discovered that 26% of children with nephrotic syndrome and 74% of children with nephrotic syndrome had inadequate levels of 25 OH vitamin D (21). In the present study there was mi VD deficiency in 36.1% of study population, and severe VD deficiency was found in more than 26.7% cases. This could be due to overall low VD levels in all age groups with various conditions.

In a research by Goldstein et al., 12 individuals with nephrotic syndrome were included, and 11 (91.66%) of them had hypocalcaemia (22). In the current study hypocalcemia was present in 53.3% of the participants. However, all of the children with nephrotic syndrome in a research by Banerjee et al. had normal blood calcium and phosphate levels (23). Interestingly, the analysis showed no significant gender-based differences in vitamin D levels. Similarly, the duration of nephrotic syndrome did not significantly impact vitamin D levels. However, it is worth noting that participants with a longer duration tended to have higher rates of severe vitamin D deficiency. Calcium levels did not show a direct correlation with vitamin D levels, implying a multifaceted interplay of factors in calcium metabolism among these patients.

The 6-month post-follow-up status revealed that the majority of participants experienced either improvement or remained in a stationary condition. The association between this post-follow-up status and vitamin D levels was not statistically significant, indicating that vitamin D levels may not directly influence short-term outcomes.

The study's findings echo existing research that showcases a high prevalence of vitamin D deficiency in children with nephrotic syndrome. This emphasizes the necessity for routine monitoring of vitamin D levels and implementation of early preventive or management protocols to mitigate vitamin D deficiency's effects and improve patient outcomes.

By the end of this discussion, it is important to acknowledge the study's limitations. The cross-sectional design limits our capability to establish causation the direction of associations. Furthermore, some other factors that are not considered in this study could add to vitamin D deficiency and hypocalcemia. Such factors include such as differences in sunlight exposure, dietary and genetic factors. Future research could

delve deeper into the underlying reasons for the observed associations. Longitudinal studies could also provide valuable insight in assessing the effectiveness of diverse strategies for improving vitamin D status in this specific patient population along with studies relating whether childhood vitamin D deficiency has enduring effects on bone health and overall well-being.

# CONCLUSION

In conclusion, understanding the frequency of vitamin D deficiency in children with nephrotic syndrome is vital for appropriate clinical management. The study reinforces the need for continued research and emphasizes the potential benefits of routine vitamin D screening for this patient population. The insights gained from this study can inform future guidelines for the management of children with nephrotic syndrome, ultimately enhancing clinical practice and improving patient care.

## References:


1. Zolotas E, Krishnan RG. Nephrotic syndrome. Paediatrics and Child Health. 2016;26(8):349-52.
2. Kucukerdogan C, Oguz EG, Okyay GU, Sahin H, Selen T, Ayli MD. The Relationship of Vitamin D Level with Renal Prognosis in Focal Segmental Glomerulosclerosis Patients-A Retrospective Study. Journal of Clinical & Diagnostic Research. 2021;15(8).
3. Odaka J, Kanai T, Ito T, Saito T, Aoyagi J, Betsui H. Apolipoprotein CI Levels Are Associated with the Urinary Protein/Urinary Creatinine Ratio in Pediatric Idiopathic Steroid-Sensitive Nephrotic Syndrome: A Case Control Study. International journal of nephrology. 2017;2017.
4. Yousefichaijan P, Eghbali A, Khosrobeigi A, Taherahmadi H, Rafiei M, Tayebi S. Vitamin D status in children with nephrotic syndrome. Journal of Comprehensive Pediatrics. 2018;9(3).
5. Mazzaferro S, Goldsmith D, Larsson T, Massy Z, Cozzolino M. Vitamin D metabolites and/or analogs: which D for which patient? Current vascular pharmacology. 2014;12(2):339-49.
6. Lang C-L, Wang M-H, Chiang C-K, Lu K-C. Vitamin D and the Immune System from the Nephrologist's Viewpoint. ISRN endocrinology. 2014;2014.
7. Vanherwegen A-S, Gysemans C, Mathieu C. Vitamin D endocrinology on the cross-road between immunity and metabolism. Molecular and cellular endocrinology. 2017;453:52-67.
8. Esmaeeili M, Azarfar A, Hoseinalizadeh S. Calcium and vitamin D metabolism in pediatric nephrotic syndrome; an update on the existing literature. International Journal of Pediatrics. 2015;3(2.1):103-9.
9. Illalu S, Venkatareddy VS, Fattepur SR. Study of prevalence of vitamin D deficiency in nephrotic syndrome. International Journal of Contemporary Pediatrics. 2019;6(2):288.
10. Selewski DT, Chen A, Shatat IF, Pais P, Greenbaum LA, Geier P. Vitamin D in incident nephrotic syndrome: a Midwest Pediatric Nephrology Consortium study. Pediatric Nephrology. 2016;31(3):465-72.
11. Tamura H. Trends in pediatric nephrotic syndrome. World journal of nephrology. 2021;10(5):88.
12. Chanchlani R, Parekh RS. Ethnic differences in childhood nephrotic syndrome. Frontiers in pediatrics. 2016;4:39.
13. Athanassiou L, Mavragani CP, Koutsilieris M. The immunomodulatory properties of vitamin D. Mediterranean journal of rheumatology. 2022;33(1):7.
14. Mehlawat U, Singh P, Pande S. Current status of Vitamin-D deficiency in India. Innov Pharm Pharmacother. 2014;2(2):328-35.
15. Akhtar S. Prevalence and correlates of vitamin D deficiency-perspectives from Pakistan. Pakistan journal of pharmaceutical sciences. 2016;29(4).
16. Ali ST, Naqvi KZ, Maqsood M, Thontia S. Prevalence of Vitamin D Deficiency among Postpartum Women and their Newborns: a cross-sectional study in Karachi, Pakistan. Pak J Surg. 2013;29(1):41-5.
17. Khadilkar A, Khadilkar V, Chinnappa J, Rathi N, Khadgawat R, Balasubramanian S. Prevention and treatment of vitamin D and calcium deficiency in children and adolescents: Indian Academy of Pediatrics (IAP) guidelines. Indian pediatrics. 2017;54:567-73.
18. Tolppanen A-M, Sayers A, Granell R, Fraser WD, Henderson J, Lawlor DA. Prospective association of 25-hydroxyvitamin D 3 and D 2 with childhood lung function, asthma, wheezing, and flexural dermatitis. Epidemiology. 2013:310-9.
19. Fuleihan GE-H, Nabulsi M, Choucair M, Salamoun M, Shahine CH, Kizirian A. Hypovitaminosis D in healthy schoolchildren. Pediatrics. 2001;107(4):e53-e.

20. Weng FL, Shults J, Herskovitz RM, Zemel BS, Leonard MB. Vitamin D insufficiency in steroid-sensitive nephrotic syndrome in remission. Pediatric nephrology. 2005;20:56-63.
21. Aggarwal A, Yadav AK, Ramachandran R, Kumar V, Kumar V, Sachdeva N. Bioavailable vitamin D levels are reduced and correlate with bone mineral density and markers of mineral metabolism in adults with nephrotic syndrome. Nephrology. 2016;21(6):483-9.
22. Goldstein DA, Haldimann B, Sherman D, Norman AW, Massry SG. Vitamin D metabolites and calcium metabolism in patients with nephrotic syndrome and normal renal function. The Journal of Clinical Endocrinology & Metabolism. 1981;52(1):116-21.
23. Banerjee S, Basu S, Sengupta J. Vitamin D in nephrotic syndrome remission: a case–control study. Pediatric nephrology. 2013;28:1983-9.