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# TO STUDY THE PREVALENCE OF VITAMIN D3 DEFICIENCY IN NEPHROTIC SYNDROME

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**ABSTRACT** **Background:** Cross-sectional studies of children with Nephrotic Syndrome have shown deficiency of Vitamin D due to its loss in urine, bound to Vitamin D binding protein and through various other mechanisms. Therefore, this study was taken up to study the prevalence of Vitamin D deficiency in Children with Nephrotic syndrome. **Methods:** A prospective study of children with Nephrotic syndrome at the time of hospital admission to Department of Paediatrics, MMIMSR, Mullana, Ambala, was undertaken. 2ml venous blood of the child was collected for assessment of 25(OH)D. **Results:** A total of 50 children were enrolled in this study. Mean age was 6.4 years. Male to female ratio was 16:9. Vitamin D levels < 20ng/ml were seen in 76% children in the study population; with 28% patients having Vitamin D deficiency while 48% had insufficiency. Also, frequent relapsers and children with initial episode had lower levels of vitamin D as compared to infrequent relapsers. **Conclusion:** Children with Nephrotic Syndrome should have routine measurement of 25(OH)D and they will benefit from vitamin D supplementation, if having deficient/ insufficient levels. Individualized Vitamin D treatment strategy can be devised for each child.

**KEYWORDS :** Nephrotic Syndrome, Vitamin D, 25(OH)D, deficiency, bone mineral density.

## INTRODUCTION

Nephrotic syndrome (NS) is the spectrum of clinical manifestations of glomerulopathy that encompasses massive proteinuria/ nephrotic-range proteinuria (>3.5 g/24 hr.) or a urinary protein: creatinine ratio of >2. Clinical findings attributed to heavy protein losses are hypoalbuminaemia (< or = 2.5 gm/dl), generalized edema and hyperlipidemia (cholesterol >200mg/ dl)[1]. Worldwide incidence of NS is estimated to be 20-40 per million populations. In India, it is reported to be 90-100 per million populations[2]. Vitamin D can be both- either synthesized by the body or can be acquired from an outside source. It is normally synthesized in the skin(cholecalciferol) under sunlight in a non-enzymatic manner. In the liver, Vitamin D is hydroxylated to 25-hydroxyvitamin D (calcidiol) which is the best indicator of sufficiency of vitamin D. In the kidney, Calcidiol is hydroxylated to 1,25-dihydroxyvitamin D (calcitriol). Calcidiol deficiency can therefore occur as a result of decreased hepatic synthesis, increased hepatic catabolism, or renal loss of calcidiol, which is bound to vitamin D binding protein.Nephrotic patients excrete out the vitamin D-binding protein along with calcidiol bound to it, excessively so as to cause vitamin D deficiency[3].

## MATERIAL AND METHODS:

This study was a prospective cross sectional study that was conducted on children aged 1-12 years and suffering from Nephrotic syndrome in the department of Paediatrics. **Duration of study** was one and half years from November 2018 to August 2020 **Sample Size**: A total of 50 children were included.

### Inclusion criteria:

Children between 1 year and 12 years suffering from Nephrotic Syndrome

### Exclusion criteria:

1. Patients who were treated with vit D supplements.
2. Any patient who had taken medication that can cause vitamin D deficiency. (e.g.- Phenytoin)
3. Children with secondary Nephrotic Syndrome e.g. SLE, Malaria, drugs.
4. Congenital nephrotic syndrome.
5. Any known metabolic disorder that could alter vitamin D levels. E.g.- Hyperparathyroidism.

### Method Of Sampling:

All the relevant details were recorded in a pre-designed proforma. Informed written consent was obtained from the parents of the children, providing all the necessary information about the study.Venous blood sample of the child was collected. Minimum 2ml in 1 separate red cap vial (with clot activator) for 25(OH)D. After allowing it to settle for 10-15 minutes and later centrifugated, serum was separated and was used for serum Vit D estimation.The sample was stored at 4 degrees Celsius until analyzed if it had to be preserved for few days. Vitamin D was estimated by chemiluminescence immunoassay (CLIA) method. The method has been fully automated, high throughout immunoassay system. Machine used was SIEMENS ADVIA Centaur ®XP.

***Statistical analysis*:** All statistical calculations were done using (Statistical Package for the Social Science)SPSS 21version (SPSS Inc., Chicago, IL, USA )statistical program for Microsoft Windows. For comparing categorical data, Chi square ($\chi 2$) test was performed and exact test was used when the expected frequency is less than 5. A probability value ($p$ value)less than 0.05 was considered statistically significant.Comparison of quantitative variables between the study groups was done using Student t-test and Mann Whitney $U$ test for independent samples for parametric and non- parametric data respectively

## RESULTS:

A total of 50 nephrotic children were enrolled in the study. Out of all the nephrotic syndrome patients enrolled in the study, the maximum (46%) were seen in age band 4-8 years. 28% were in age group 9-12 years while 26% were in the age band of 1-3 years. There was a male preponderance with 64% boys and 36% girls, with male: female ratio being 16:9.

28% of the patients showed deficiency (<12 ng/ml) of Vitamin D, 48% had insufficiency(12-20 ng/ ml). The remaining 24% had normal Vitamin D levels. In our study, 36% of the patients presented with nephrotic syndrome for the first time. Of the remaining, 34% were frequent relapsers and 30% had infrequent relapses. Maximum deficiency/insufficiency was noted in age group 4-8 years with a percentage of 42.1%. 9-12 years' category showed deficiency/ insufficiency in 31.6% cases. In the age group of 1-3 years, only 26.3 % had deficiency /insufficiency of Vitamin D.

Out of all Nephrotic cases who had Vitamin D deficiency/ insufficiency, boys had a representation of 57.9%. Major fraction of deficiency/insufficiency group is taken up by frequent relapsers (42.1%), closely followed by initial episode of Nephrotics (39.5%) and (18.4%) is accounted by the infrequent relapsers.

**Table 1: Profile Of Subjects In The Study**

| Catagory | Parameter | Number | Percentage |
|---|---|---|---|
| Gender | Male | 32 | 64% |
| | Female | 18 | 36% |
| Age group | 1-3y | 13 | 26.0% |
| | 4-8y | 23 | 46.0% |
| | 9-12y | 14 | 28.0% |
| Vitamin D levels | Deficiency (<12ng/ml) | 14 | 28.0% |
| | Insufficiency (12-20 ng/ml) | 24 | 48.0% |
| | Sufficiency (20-100 ng/ml) | 12 | 24.0% |

**Table 2: Correlation Of Vitamin D Levels With Frequency Of Relapses**

| | | Vit D | | | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| | | Deficiency/ Insufficiency | | Sufficiency | | | | |
| Nephrotic type | 1st episode NS | 15 | 39.5% | 3 | 25.0% | 18 | 10.66 | 0.005 |
| | Frequent relapser | 16 | 42.1% | 1 | 8.3% | 17 | | |
| | Infrequent relapser | 7 | 18.4% | 8 | 66.7% | 15 | | |

## DISCUSSION

This was a hospital based descriptive time bound study. In the Index study, a mean age of 6.3 years was noted. In a similar study, Banerjee et al (2013)[4] mean age was 6.25 years, Banerjee et al(2019)[5] - 5.45 years, Nielsen et al[6] -3.4 years and Solanki et al (2)- 5.7 years. Ignorance, late referrals, and financial crises can be thought of as important factors that contribute to delayed diagnosis of Nephrotic Syndrome and Vitamin D deficiency as a result of untreated long-standing Nephrotic syndrome. Many studies have shown males to be more prone to Nephrotic syndrome.This could be due to gender preference as most of my patients are from a rural setting. Parents tend to seek better healthcare and attention for their male offsprings. In this study, there was a male preponderance ( 64% ) , with male: female ratio being 16:9. In Concordant studies, like Banerjee et al (2013), 65% males; ratio was 26:14. Banerjee S et al (2019) also 62.5%. Som S et al showed 62% males and 38% females; with ratio 31:14[7]. A discordant study, Haldimann B et al (1980) showed female preponderance with 71.42 % females with ratio 18:7[8].

Nephrotic children receive multiple courses of steroids at various intervals, and so they are prone to reduction in serum Vitamin D levels, especially in the longer duration of steroid therapy. In this study, 28% of the nephrotic patients showed deficiency of Vitamin D(<12 ng/ml), while 48% had insufficiency. Illalu S et al demonstrated deficiency in 47% nephrotic subjects and insufficiency in 32.35%(9). Banerjee S et al (2019) showed deficiency(<12ng/ml) of total 25(OH)D in 72% children with NS[5]. Nielsen CA et al showed 92.8% children with vitamin D deficiency[6].

Repeated events of proteinuria may be the most probable cause of lower vitamin D levels in nephrotic children with multiple relapses. The current study showed mean Vitamin D value of 17.42 ng/ml (range: 4.2-43.91 ng/ml). The studies consistent with present study include Banerjee S et al (2013) with mean 16.91 ng/ml ( 12.4 ng/ml to 22.4 ng/ml)[4]. Another study, Banerjee S et al (2019) depicted mean of 4.6 ng/ml (1 ng/ml to 8.6 ng/ml)[5]. In a study by Zhang X et al, mean of 1.68 ng/ml was noted (1.62-36.08 ng/ml)[10].

Limitation of our study was a small sample size. We recommend that more studies with larger sample size should be done to make guidelines for assessment and supplementation of Vitamin D to prevent adverse effects of Vitamin D deficiency.

## CONCLUSION

This study was undertaken to ascertain Vitamin D levels in Nephrotic syndrome children in a rural tertiary care hospital. Serum Vitamin D levels were reduced below the normal level in majority of cases, even more so, in frequent relapsers. Therefore, it seems prudent to treat these children with Vitamin D at the time of presentation. Treatment with vitamin D may be individualized from case to case so as to avoid potential ill effects of Vitamin D deficiency.

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**CONFLICT OF INTERTEST:** None

**ETHICAL APPROVAL:** The study was approved by the Institutional Ethics Committee.

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