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Prevalence of Vitamin D Deficiency in Children with Nephrotic Syndrome in a Tertiary Care Hospital in Eastern India

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Abstract **Original Research Article**

Background: Nephrotic syndrome is associated with loss of vitamin D binding protein in urine, leading to vitamin D deficiency. Corticosteroids used in the management of this illness is also known to have deleterious effects on bone health. This study was done to assess the prevalence of vitamin D deficiency in children with nephrotic syndrome. ***Methods:*** It is a cross sectional study conducted at the department of Pediatrics, R.G.Kar medical college and hospital, Kolkata, over a period of 18 months. Patient particulars and history were obtained from 100 children with nephrotic syndrome aged 2-12 years, admitted in the hospital or presented to the outpatient department. Samples were collected for the estimation of 25-hydroxy vitamin D. Data were analysed using standard statistical parameters. ***Results:*** Mean age of the population under study was 6.82±3.37 years with a male to female ratio of 1.6:1. First episode, frequent relapse and infrequent relapse nephrotic syndrome were present in 36, 24 and 40 children, respectively. Three fifth of them were having active disease. Vitamin D deficiency was seen in 66% of the study population (mean vitamin D level- 11.53±6.31 ng/dL). Children in remission had higher vitamin D levels than those with active disease (p=0.001). ***Conclusion:*** Vitamin D deficiency is present in a significant proportion of children with nephrotic syndrome. Those with active disease have lower levels of vitamin D than those in remission.

Keywords: Nephrotic syndrome, Vitamin D deficiency, Corticosteroids.

INTRODUCTION

Nephrotic syndrome is characterised by nephrotic range proteinuria, edema, hypoalbuminemia (serum albumin <2.5 g/dL) and hypercholesterolemia (cholesterol >200mg/dL). Proteinuria of >3.5g/day or urine protein creatinine ratio >2 defines nephrotic range proteinuria [1, 2]. It is known to affect 1-3 per 1 lakh children under the age of 16 years [2]. Incidence in the Indian subcontinent is 90-100 per million population [3].

Among the various metabolic effects of this renal disorder on growing children, vitamin D deficiency need special emphasis. It is found to stem from the loss of vitamin D binding protein, which is structurally similar to albumin, in urine [4, 5]. Changes in bone morphology following this has been documented previously [6, 7]. Corticosteroids, the mainstay of management of nephrotic syndrome is also known to have deleterious effects on bones [8].

This study was conducted to estimate the prevalence of vitamin D deficiency in children with nephrotic syndrome in a tertiary care hospital. Studies done previously from east India was centred on children in remission [9]. This study attempts to assess the magnitude of deficiency in active phase as well as remission of nephrotic syndrome.

MATERIALS AND METHODS

This was a cross sectional study on patients with nephrotic syndrome admitted in the pediatric ward or attending the biweekly conducted pediatric nephrology clinic of R.G.Kar medical college and hospital, Kolkata from January 2018 to June 2019.Children aged 2 to 12 years with newly diagnosed nephrotic syndrome, nephrotic syndrome on treatment and nephrotic syndrome relapse were included in the study. Those who were already on vitamin D supplementation or those with renal insufficiency were excluded.

Study population included first episode of nephrotic syndrome, FRNS (frequent relapse nephrotic syndrome, defined as 2 or more relapses in first 6 months or 4 or more relapses in any 12 months period) and IRNS (infrequent relapse nephrotic syndrome , including all cases of relapses not fulfilling criteria for FRNS) [10] . Remission in a case of nephrotic syndrome is defined as urine albumin nil or trace or urinary excretion of protein <4mg/m^2/hour for 3 consecutive early morning samples. Response to therapy is attainment of remission within the initial 4 weeks of corticosteroid therapy. Absence of remission despite therapy with daily prednisolone at a dose of 60mg/m^2/day for 4 weeks defines steroid resistance [10].

Informed consent was taken from the parents prior to enrolment for the study. Institutional ethical clearance was obtained before initiation of study. It was conducted over a period of 18 months.

After collecting relevant history and performing physical examination, samples were obtained for serum vitamin D estimation. Samples were sent to laboratory on the same day. Vitamin D status was assessed using 25- hydroxy vitamin D, which is unaffected by serum PTH levels (unlike, 1, 25-dihydroxy vitamin D) [11]. Levels of 25-hydroxy vitamin D was done by two step competitive binding immunoenzymatic assay using Beckman Coulter Access 2.

Serum level of 25- hydroxy vitamin D < 15 ng/mL was considered deficient, while levels <5ng/mL as severely deficient and 15-20 ng/mL as insufficient, in accordance with AAP guidelines [12].

Sample size was calculated based on the prevalence obtained by Cicilie *et al*., in their study [13]. Calculations with the precision of 5% and type 1 error of 5% gave the sample size of 100. Details of the patients and reports of investigation were entered on excel sheets and analysed using standard statistical tools. A p value < 0.05 was considered statistically significant.

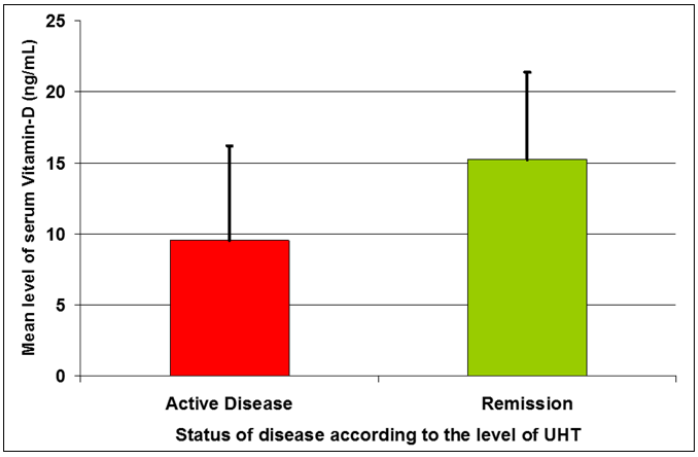
RESULTS

During the study period, 100 children were enrolled for the study. The population had a median age of 7 years (mean 6.82±3.37 years, range 2-12 years). They had a male: female ratio of 1.6:1. At study entry, 73% of the patients were on treatment. Maximum number of them were on standard dose of alternate day prednisolone (34%), followed by daily prednisolone (25%) and others (14%). 36% of the children were having first episode of nephrotic syndrome, while 24% and 40% were having frequent and infrequent relapse nephrotic syndrome, respectively. 60% of the children were having active disease while 40% were in remission.

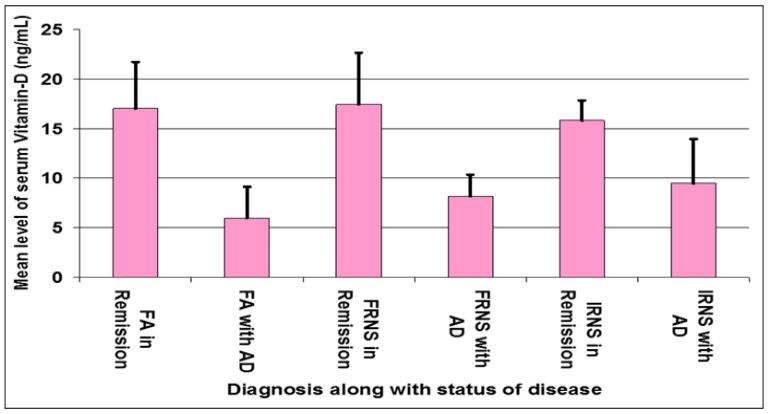
Table-1: Distribution of cases

Diagnosis	First episode	IRNS	FRNS
Active disease	10 (40%)	20 (80%)	10 (25%)
Remission	25 (60%)	5 (20%)	30 (75%)

Study population had a mean vitamin D level of 11.53±6.31 ng/mL and a median of 11.1 ng/mL. Among enrolled children, 66% were having deficiency of vitamin D. In our study, 48% had mild to moderate deficiency and 18% had severe deficiency. 28% had insufficient, but not deficient levels of vitamin D (p< 0.0001). Mean vitamin D among those with active disease and remission were 9.56±6.64 ng/dL and 15.23±6.16 ng/dL, respectively. Those in remission had higher values than those with active disease (p< 0.001). The same held true when individual diagnoses groups were analysed separately too.



Among various diagnoses groups, FRNS had higher values of vitamin D, followed by first episode and IRNS. When disease activity was added, first episode nephrotic syndrome in remission had highest levels of vitamin D and first episode with active disease having the lowest values (p< 0.0001).



DISCUSSION

Assessment of vitamin D deficiency in children with nephrotic syndrome, done previously by Cecilie *et al*., Sinha S *et al*., and D. Selewski *et al*., showed prevalence of vitamin D deficiency in 93%, 71.7% and 100% cases [13-15]. In our study, we found vitamin D deficiency in 66% of the children. A major explanation for this discrepancy is the difference in the cut off values used to define vitamin D deficiency. Cecilie *et al*., and D. Selewski considered values < 20ng/mL as deficient [13, 15], while Sinha S *et al*., considered values < 15ng/mL as deficient [14]. In our study, cut off of <15ng/mL was used.

In a study conducted by Basu S *et al*., median serum 25- hydroxyl vitamin D of children attending an OPD in a tertiary care hospital of east India was found to be 19ng/mL [16]. In our study involving children with nephrotic syndrome had lower median vitamin D levels.

Banerjee S *et al*., had documented increase in vitamin D in children in remission phase in their cross sectional study [9]. Our study showed higher levels of vitamin D among those in remission. Higher value of vitamin D among FRNS in our study was mainly due to increased proportion of children with remission in FRNS. Lowest value of vitamin D among children with active phase of first episode of nephrotic syndrome may be because of delay in identification of symptoms by parents, while in a relapsing child parents are more aware of the nature and presentation of the illness.

Studies done by Banaerjee S *et al*., and Ayi Dilla Septarini had shown improvement in vitamin D status following supplementation [17, 18]. Large group trials are required before making any recommendations in this direction.

Addressing this important concern in the vulnerable age group of growing children need special attention while dealing with children with nephrotic syndrome. For making accurate comments on the vitamin D metabolism in children with nephrotic syndrome, multi centre long duration follow up studies are required.

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