Original Article

Vitamin D deficiency in hemodialysis patients

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ABSTRACT

Background: Vitamin D [(25(OH)D] deficiency and insufficiency is common in patients with chronic kidney disease (CKD). 25(OH)D has been found to have beneficial effects on bone, cardiovascular and immune functions. There are little data about vitamin D levels in Indian patients on dialysis. This study was undertaken to determine the vitamin D status of Indian CKD patients on hemodialysis. **Materials and Methods:** We included 45 patients on maintenance hemodialysis coming to Medanta, Medicity, Gurgaon. 25(OH) D levels were measured with radioimmunoassay (Diasorin) method and parathyroid hormone (PTH) was measured using electrochemiluminiscence immunoassay (ECLIA). **Results:** The mean age of patients was 55 ± 13 years. 32/45 (71%) were males. 23/45 (51%) were diabetics. The median duration of hemodialysis was 5.5 months (range 1–74 months). 33/45 (74%) patients were on thrice weekly hemodialysis. The mean level of vitamin D was 10.14 ± 8.7 ng/ml. Majority of the patients [43/45 (95.5%)] were either vitamin D deficient or had insufficient levels. 40/45 (88.9%) were vitamin D deficient (levels <20 ng/ml); of these, 29/40 (64.4%) had severe vitamin D deficiency (levels <10 ng/ml) and 3/45 (6.7%) had insufficient levels (20–30 ng/ml) of vitamin D. Only 2/45 (4.4%) patients had normal levels of vitamin D. 23/45 (51%) of patients were receiving calcitriol. The mean levels of serum calcium, phosphorus, alkaline phosphatase, and albumin were 8.8 ± 0.64 mg/dl, 5.0 ± 0.7 mg/dl, 126 ± 10.3 IU/l and 3.6 ± 0.62 g/dl, respectively. PTH levels ranged from 37 to 1066 pg/ml, and the median was 195.8 pg/ml. There was a weak correlation between 25(OH)D levels and weight, sex, hemoglobin, albumin, alkaline phosphatase, and presence of diabetes. There was, however, no correlation with duration of dialysis or PTH levels. **Conclusion:** Vitamin D deficiency and insufficiency are universal in our hemodialysis patients, with severe vitamin D deficiency in two-third of patients.

Key words: Chronic kidney disease, hemodialysis, vitamin D

Background

Impaired metabolism of vitamin D is a common feature of chronic kidney disease (CKD).[1,2] In healthy individuals, vitamin D is initially synthesized in the skin or acquired via the diet. This provitamin D is then hydroxylated to 25-hydroxyvitamin D [25(OH)D] in the liver. This is further converted by 1-alpha-hydroxylase in the kidney to 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], which is the active form of vitamin D and is responsible for calcium absorption from the intestine. Renal dysfunction is associated with impaired conversion of 25(OH)D to 1,25$(OH)_2$D. Therefore, supplementation with active vitamin D [1,25$(OH)_2$D] is commonly practised in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). However, recently it has been shown that 25(OH)D can be converted to 1,25$(OH)_2$D at sites other than the kidney, including the prostate, breast, colon, and macrophages.[3,4] Local production of 1,25$(OH)_2$D may be important for several biologic functions in these tissues; thus, circulating 25(OH)D levels may be relevant even when supplementation with active vitamin D is carried out, as in patients with CKD with low renal production of 1,25$(OH)_2$D.[1,2] Levels of 25(OH)D below 30 ng/ml are associated with increased parathyroid hormone (PTH) levels, low bone mineral density (BMD), and increased risk of hip fractures. According to the latest Endocrine Society

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guidelines, serum levels of 25(OH)D between 20 and 30 ng/ml indicate vitamin D insufficiency and levels less than 20 ng/ml indicate vitamin D deficiency.[5] Severe deficiency is defined as a 25(OH)D level less than 10 ng/ml. The recently published KDIGO (Kidney disease: Improving global outcomes) guidelines recommend that the serum level of 25(OH)D should be maintained over 30 ng/ml in patients of all stages of CKD.[6] An Indian study done in patients with newly diagnosed CKD revealed high prevalence of vitamin D deficiency.[7] However, limited data are available in patients with CKD stage 5 on dialysis.

There has been renewed interest in studying the effects of supplementation with native vitamin D (cholecalciferol) in CKD patients with low 25(OH)D levels[8-11] and this interest has been fanned by studies that have demonstrated several potential nonskeletal benefits of vitamin D.[12,13] These benefits include effect of vitamin D on immune system, cardiovascular disease, diabetes, and some cancers.

In India, there is a paradox that despite adequate sunlight, deficiency of vitamin D is quite prevalent in the general population. This may be explained by clothing habits of Indian population, their pigmented skin, and changing lifestyle with limited outdoor activities.[14,15] Considering that most "free living" Indians are vitamin D insufficient or deficient, it stands to reason that patients with CKD on hemodialysis will be even more so. Yet, routine supplementation of these patients with vitamin D is not practised.

This study was undertaken to determine the vitamin D status of Indian CKD patients on hemodialysis.

Materials and Methods

The study was conducted in the departments of nephrology and endocrinology at Medanta, the Medicity, Gurgaon between July 2010 and September 2010. We included patients of CKD stage 5 who were on maintenance hemodialysis for more than 1 month at our center and were willing to participate in the study.

Blood sample was collected at the start of the hemodialysis session from the vascular access for calcium, phosphorus, albumin, and alkaline phosphatase. These samples were sent to Medanta laboratory for analysis. 25(OH)D and intact PTH samples were taken in a separate tube and centrifuged immediately; two aliquots were made and stored at-80°C cold storage. These samples were sent for analysis to Institute of Nuclear Medicine and Allied Sciences (INMAS), New Delhi, ensuring a cold chain. Patients were labeled vitamin D insufficient if the levels were between 20 and 30 ng/ml, and deficient if the levels were less than 20 ng/ml. We also subcategorized these patients to severe vitamin D deficiency if the level was less than 10 ng/ml.

Analytical methods

Measurement of calcium was done with aresanzo dye, phosphorus by phoshomolybdate reduction, alkaline phosphatase by 4-nitrophenyl phosphate method, hemoglobin by cyan-methemoglobin, and albumin by bromocresol green dye binding. These assays are done on Jhonson and Jhonson instruments (vitros 5600 and 5.1). 25(OH)D levels were measured with radioimmunoassay (Diasorin) method and PTH was measured using electrochemiluminiscence immunoassay (ECLIA, Roche diagnostics, Mannheim, Germany).

Results

Forty-five hemodialysis patients were analyzed for their vitamin D status. The characteristics of these patients are as shown in Table 1. Mean age was 55 ± 13 years. Of these, 13 were females and 32 were males. Median duration of dialysis was 5.5 months (range 1–74 months). Mean weight was 59 ± 6.7 kg. Mean hemoglobin was 10.4 ± 0.45 g/dl and albumin was 3.6 ± 0.62 g/dl. Twenty-three (51%) patients had diabetic nephropathy and 33 (74%) patients were on thrice a week hemodialysis.

Mean calcium, phosphorus, and alkaline phosphatase were 8.8 ± 0.64 mg/dl, 5.0 ± 0.7 mg/dl, and 126 ± 10.3 IU/l, respectively.

Mean 25(OH)D level was 10.14 ± 8.7 ng/ml. Only 2 (4.4%) patients were vitamin D sufficient and 3 (6.7%) were vitamin D insufficient. The remaining 40 (88.9%) were vitamin D deficient [Table 2 and Figure 1]. Of these, 29 (64.4%) had severe vitamin D deficiency with 25(OH)D less than 10 ng/ml. Majority of these patients were on usual calcium supplements and 23/45 (51%) patients were on calcitriol. PTH levels ranged from 37 to 1066 pg/ml and the median was 195.8 pg/ml.

There was a weak correlation between 25(OH)D levels and weight, sex, hemoglobin, albumin, alkaline phosphatase, and presence of diabetes. There was, however, no correlation with duration of dialysis or PTH levels [Table 3].

Discussion

Vitamin D deficiency and insufficiency were seen in 88.9 and 6.7%, respectively, of our patients on hemodialysis as compared to 91.2 and 6.8%, respectively, in "normal" adult population from North India.[16] The reason for a better

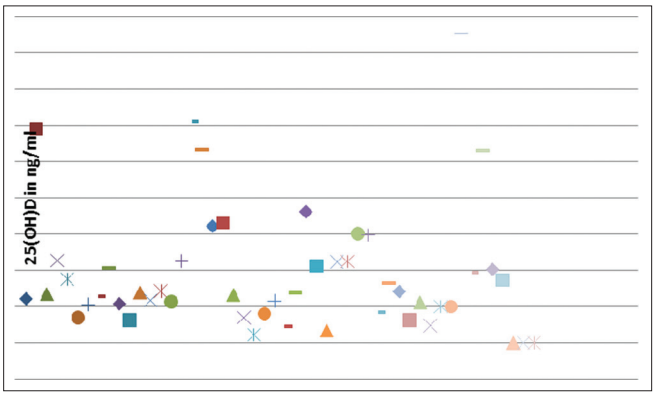

Figure 1: Distribution of 25(OH)D levels

Table 1: Clinical and biochemical characteristics of patients

Characteristic	Value (%)
Age (mean ± SD) (years)	55 ± 13
Male:female	32:13
Median duration of dialysis in months (minimum to maximum)	5.5 (1–74)
Weight (in kg) (mean ± SD)	59 ± 6.7 kg
Basic diagnosis	
Diabetic nephropathy	23/45 (51)
Glomerulonephritis	9/45 (20)
Hypertension	4/45 (9)
Interstitial nephritis	5/45 (11)
Others	4/45 (9)
Albumin (mean ± SD)	3.6 ± 0.62
Calcium (mean ± SD)	8.8 ± 0.64
Phosphorus (mean ± SD)	5.0 ± 0.7
Alkaline phosphatase (mean ± SD)	126 ± 10.3
25(OH)D (mean ± SD) (ng/ml)	10.14 ± 8.7
PTH (median and range) (pg/ml)	195.8 (37–1066)

Table 2: Vitamin D status of patients

Vitamin D status	Numbers
Severe vitamin D deficiency [25(OH)D < 10 ng/ml]	29
Vitamin D deficient [25(OH)D < 20 ng/ml]	40
Vitamin D insufficient [25(OH)D 21–30 ng/ml]	3
Vitamin D sufficient [25(OH)D > 30 ng/ml]	2

vitamin D status can be the calcium supplements being prescribed to most of these patients.

Severe deficiency was also very common, with as many as 64.4% patients showing serum 25(OH)D values below 10 ng/ml.

Our findings are consistent with previous data from Chandigarh which reported 77% prevalence of vitamin D deficiency and 22% insufficiency in male patients with newly diagnosed CKD patients.[7]

In CKD 4–5 stages, NHANES III data report vitamin D deficiency to be 17% and insufficiency to be 27%.[2] Other data from various countries report vitamin D deficiency or insufficiency to be 70–90%.

Table 3: Correlation between 25(OH)D levels and various clinical and biochemical parameters

Parameter	Correlation coefficient	Type of correlation
Weight	0.28	Mild
Sex	0.16	Mild
Duration of dialysis	0.059	None
Hemoglobin	0.28	Mild
Corrected calcium	0.097	None
Phosphorus	0.021	None
Albumin	0.21	Mild
Serum alkaline phosphatase	0.23	Mild
PTH	–0.089	None
Age	0.022	None
DM	0.25	Mild

There is evidence suggesting that vitamin D deficiency in CKD patients is associated with higher cardiovascular disease and mortality.[12-14]

Of note, most of these patients were on calcium carbonate or acetate preparations two to three times a day, each tablet containing 200 IU cholecalciferol. Despite taking about 400 to 600 IU cholecalciferol, the usual recommended daily intake for adults, 25(OH)D levels were low in most patients.

We found female sex, hemoglobin, and albumin to be correlating weakly with vitamin D levels. Also, presence of diabetes was negatively correlated with vitamin D levels. In a previous study,[17] female sex and hypoalbuminemia were found to be correlated with vitamin D deficiency in hemodialysis patients. The correlation of vitamin D levels with presence of diabetes is interesting. There is evidence of effect of vitamin D deficiency on glucose metabolism, but vitamin D deficiency being more common in CKD patients with diabetic nephropathy as the basic disease is not commonly reported.

We did not find any correlation between PTH levels and 25(OH)D, although an inverse correlation has been shown in previous studies which were done in earlier stages of CKD (Stages 3 and 4).[7,18]

Our findings suggest that vitamin D deficiency is universal in our hemodialysis patients and they probably require routine supplementation with higher doses of cholecalciferol. Further studies on supplementation are being carried out to define optimum dose schedules.

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