ABSTRACT

Background: Chronic kidney disease (CKD) is an emerging public health problem. Though hypovitaminosis D is common in CKD but it goes undetected because of cost of the investigation. In view of the association of hypovitaminosis D with disease and its implications, the present study was planned with a objective of estimating serum 25(OH)D3 level in patients of CKD and comparing it with non-CKD patients.

Material and Method: In the present observational study, 25(OH)D3 level was estimated in blood samples of 18 CKD patients and compared it with vitamin D3 level of non-CKD patients after obtaining approval from institutional ethics committee. Results: All subjects regardless of renal status had hypovitaminosis D (< 30ng/mL). There was significant difference in mean serum vitamin D3 level among CKD and non-CKD patients. Mean Vitamin D3 level was significantly low and also less than normal range in CKD patients though 13 patients with CKD were on supplementation of active vitamin D3. In CKD group, there was no difference in vitamin D3 level among those who were taking active vitamin D3 and those who were not on vitamin D3 supplementation. Conclusion: CKD group had severe degree of vitamin D deficiency which were not improved with vitamin D3 supplementation. However because of small sample size, it is difficult to come to any
conclusion. So further studies should be conducted to identify predictive variables that could be used for prognostic guidance in CKD patients.

**KEY WORDS:** Cholecalciferol, Chronic kidney disease, HPLC.

**INTRODUCTION**

Chronic kidney disease (CKD) is an emerging public health problem and one of the most powerful predictors of premature cardiovascular disease. Vitamin D deficiency is highly prevalent among patients with CKD.\[^1\] There is slow progressive decrease in the level of 1,25(OH)2 vitamin D in CKD as kidney function declines because of decrease in 1-α hydroxylase which is needed for generation of active form of vit D.\[^2,3\]

Vitamin D plays a central role in calcium and phosphorus homeostasis. Vitamin D deficiency is associated with higher prevalence of cardiovascular disease, hypertension, insulin resistance, diabetes, and dyslipidemia.\[^4\] Some studies have shown an association between mortality and vitamin D deficiency in dialysis- and nondialysis-dependent CKD.\[^5\] In a study by wolf et al correlation between levels of vitamin D and mortality was examined in patients of haemodialysis. Low levels were associated with increased mortality. Intervention with Vitamin D may be associated with improved outcome.\[^6\]

Vitamin D is proven to prevent nephrosclerosis and retard CKD progression through its anti-inflammatory and anti proliferative properties and inhibition of renin production.\[^7\] In patients with established CKD, treatment with calcitriol was associated with a trend towards a lower incidence of dialysis initiation and a decrease in overall mortality rates.

Although failure of 1, 25(OH) 2D3 synthesis is the cause of vitamin D deficiency in patients with CKD, studies on vitamin D levels are based on measurements of serum 25(OH)D. Many extra-renal cells are able to convert the circulating form of vitamin D, 25-hydroxy vitamin D (25(OH)D), into the active form.\[^8\] This has focused research on the autocrine function of vitamin D, and serum 25(OH)D deficiency has emerged as an important independent risk factor for morbidity and mortality, and a potential therapeutic target in CKD.\[^9\] At the same time, level of 1,25(OH)2D3 which is active form of vitamin D is difficult to measure because of its short half life compared to 25(OH)D which is the most stable and plentiful metabolite of vitamin D in humans and has a half-life of about 3 weeks, making it the most suitable indicator of vitamin D status.\[^10\]
The National Kidney Foundation (NKF) guidelines state that optimal 25(OH) D levels should be greater than 30 ng/mL, levels of 21 to 29 ng/mL are defined as insufficient, while levels below 20 ng/mL are considered deficient.\textsuperscript{[11,12]} Though hypovitaminosis D is common in patients with CKD but it goes undetected because of cost of the investigation. If deficiency of vit D is detected and treated it may improve the outcome in patients of CKD. The recent Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Bone Mineral Metabolism and Disease in Chronic Kidney Disease recommend the measurements of 25-hydroxyvitamin D levels in patients with CKD not yet on dialysis. Vitamin D has garnered much research and debate about supplementation in recent years, not only as it pertains to patients with kidney disease but also to those in the general population.

Moreover, there is paucity of data regarding vitamin D level in Indian population with CKD. In view of the association of hypovitaminosis D with diseases and its implications, the present study was planned with a objective of estimating serum 25(OH) D3 level in patients of CKD and comparing it with non-CKD patients.

**MATERIAL AND METHOD**

The present study was an observational study carried out in the department of pharmacology of tertiary care teaching hospital. In the present study, 25(OH)D3 level was estimated in blood samples of 18 CKD patients received in department of pharmacology after obtaining approval from institutional ethics committee. Level of 25(OH)D3 was estimated from serum by HPLC with UV detection. Demographic characteristics, details of other laboratory investigations was recorded from requisition form received along with sample. Prescription of CKD patients were analyzed to know whether the patient was on active Vitamin D supplementation. The levels of 25(OH)D3 in CKD patients was compared with those of control group which included sample of patients with diseases other than CKD (Non-CKD).

**Statistics**

Data was analyzed using Graph pad prism software (version 5.1). Data was expressed as mean ± SD wherever applicable. Unpaired ‘t’ test was used to compare vitamin D3 level between CKD and non-CKD patients and between subgroups in CKD patients.

**RESULTS**

Among CKD patients, 15 were men and 3 were women with mean age 42.17±13.43 years. Table 1 shows serum levels of urea, creatinine, Na, K and uric acid in CKD patients. Table 2
shows serum vitamin D3 level among CKD and non-CKD patients. All subjects regardless of renal status had hypovitaminosis D (< 30ng/mL) There was significant difference in mean serum vitamin D3 level among CKD and non-CKD patients. Mean Vitamin D3 level was significantly low and also less than normal range in CKD patients though 13 patients with CKD were on supplementation of active vitamin D3. (Cholecalciferol) In CKD group, there was no difference in vitamin D3 level among those who were taking active vitamin D3 and those who were not on vitamin D3 supplementation. [Table 2]

Table 1: Demographic profile of chronic kidney disease patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>42.17±13.43</td>
</tr>
<tr>
<td>Blood Urea (mg/dl)</td>
<td>188.4±70.54</td>
</tr>
<tr>
<td>Sr creatinine (mg/dl)</td>
<td>12.36±4.01</td>
</tr>
<tr>
<td>Uric acid(mg/dl)</td>
<td>10.30±2.51</td>
</tr>
<tr>
<td>Na 2+ (mEq/l)</td>
<td>136.3±9.43</td>
</tr>
<tr>
<td>K+(mEq/l)</td>
<td>4.09±1.03</td>
</tr>
</tbody>
</table>

Table 2: Comparison of serum Vitamin D3 level between CKD and non CKD patients

<table>
<thead>
<tr>
<th>Serum vitamin D3 level (ng/ml)</th>
<th>CKD (n= 18)</th>
<th>Non-CKD (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>On active Vit D3 supplementation</td>
<td>No active Vit D3 supplementation</td>
</tr>
<tr>
<td>&gt;30ng/ml</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>20-30 ng/ml</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>10-20 ng/ml</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>≤ 10 ng/ml</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>19.78 ±15.27</td>
<td>28.49±9.40 *</td>
</tr>
</tbody>
</table>

Figure indicates no of patients, *p<0.05 (0.04)

**DISCUSSION**

Vitamin D insufficiency is highly prevalent in the CKD population. In the absence of published, definitive evidence based guidelines, present study was planned to demonstrate vitamin D status in CKD patients.

Patients with kidney disease have reduced activity of the enzyme 1-α hydroxylase (CYP27B1) in the kidneys, which converts 25-hydroxyvitamin D (25(OH)D) to its more active form, 1,25-dihydroxyvitamin D (1,25(OH)2D).\(^2,3\)

Since the prevalence of hypovitaminosis D (<30 ng/ml) in both of our groups was high, it raised the question of what were the common similar factors in both groups. The two main determinants of vitamin D levels are sunlight exposure and dietary intake. Dietary deficiency
is very common in countries like India with poor resources. Lack of sun exposure is also undeniably an important issue to discuss even though India is a tropical country with a hot and humid climate. Surprisingly, many other studies from India showed a similar prevalence of hypovitaminosis D.\[^{13,14}\]

Present study confirmed that CKD patients have low vitamin D levels. Several epidemiologic studies have reported patients with CKD and ESRD to have lower 25(OH) D concentrations than the general population. These findings are in accordance with our results.\[^{15,16,17}\] Many factors may account for low levels of 25(OH)D in kidney disease, including the loss of vitamin D binding protein in the urine, ineffective synthesis in the skin upon exposure to ultraviolet B radiation, and likely reduced nutritional intake and sun exposure.\[^{18}\] Low 25(OH)D levels in patients with CKD and ESRD have been associated with a higher risk of all-cause mortality and a faster progression of kidney disease.\[^{19}\]

In present study, out of 18 patients, 13 were on vitamin D3 supplementation but when measured, mean vitamin D3 value was below normal. Similar finding were noted by Parikh et al in CKD patients treated with cholecalciferol.\[^{11}\] Progressively worsening eGFR, Proteinuria with the loss of vitamin D binding protein, non-compliance, higher phosphorus level, wrong timing of administration or changes in intestinal absorption may account for both the low levels of vitamin D observed and the vitamin D resistance in CKD.\[^{20,21,22,23}\]

In contrast, One metaanalysis concluded that therapies with 1, 25-dihydroxyvitamin D and analogues are associated with reduced mortality in CKD patients suffering from secondary hyperparathyroidism. This metaanalysis supportive of prescribing vitamin D therapies to CKD patients, while respecting good practice guidelines.\[^{19}\] Finally to summarize, Although the vitamin D levels among the study subjects and their control are below normal range, CKD group had severe degree of vitamin D deficiency which were not improved with vitamin D3 supplementation. However because of small sample size, it is difficult to come to any conclusion. So further studies should be conducted to identify predictive variables that could be used for prognostic guidance in CKD patients.

REFERENCES
2. Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr 2003; 89: 552-72


