

PREVALENCE OF VITAMIN D DEFICIENCY IN CHRONIC KIDNEY DISEASE: A SINGLE CENTERED STUDY FROM A RURAL TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

BACKGROUND

Vitamin D deficiency is highly prevalent among patients with chronic kidney disease (CKD). Accumulating evidence indicates the associations of vitamin D deficiency with morbidities and mortality in patients with CKD. The recent Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Bone Mineral Metabolism and Disease in Chronic Kidney Disease had recommended the measurements of 25-hydroxyvitamin D levels in patients with CKD who are not on dialysis. Little is known about the magnitude of vitamin D deficiency in patients with CKD living in rural South India.

AIM

To assess the prevalence of vitamin D deficiency among the patients with chronic kidney disease.

METHODOLOGY

The prevalence of 25-hydroxyvitamin D₃ (25OHD) deficiency (defined as a level <20 ng/ml) were examined in 100 patients with CKD. Patients on dialysis and those receiving medication known to influence vitamin D, were excluded. CKD was diagnosed based on history, clinical features, USG abdomen and renal function test and eGFR. We examined the levels of 25OHD in 100 patients with CKD stages 3 and 4. Patients were investigated for hemogram, renal function tests, serum vitamin D level, fasting blood sugar and ECG.

RESULTS

The overall prevalence of vitamin D deficiency among the CRF patients in our study was 69% and the insufficiency was present in 17% of the CRF patients and only 14% of the study subjects had normal vitamin D levels. Among the various factor influencing the prevalence of vitamin D deficiency in CRF patients, diabetes and hypertension are the most important factors. In our study the mean levels of vitamin D was much lower in patients with diabetes and hypertension when compared to patients without diabetes and hypertension and the difference was found to be statistically significant (p=0.003).

CONCLUSION

Our study concluded that vitamin D deficiency is highly prevalent among CKD patients. Diabetes and hypertension are the most important influencing factors in the development of hypovitaminosis D among the chronic renal failure patients.

KEYWORDS

Chronic renal failure, Vitamin D, Prevalence, Rural area.

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INTRODUCTION: Chronic kidney disease (CKD) is becoming a modern day epidemic worldwide and the fact is uniformly agreed that the presence of CKD is marked with poor outcomes¹ as it imposes a heavy burden of cardiovascular, metabolic, and infectious complications.² India is not exempted and there is a significant burden of

CKD, however exact figures vary.³ CKD is marked by low 25OH D (calcidiol), low 1, 25(OH)₂ vitamin D (calcitriol) as well as vitamin D resistance.⁴ Serum 25OH D levels begin to decline as early as stage 2 of CKD.⁵ And it is an important modifiable risk factor in this high-risk population, particularly cardiovascular events, and mortality increases as the estimated glomerular filtration rate (eGFR) decreases below 60 ml/min.⁶ Several mechanisms by which vitamin D deficiency occurs have been identified, like reduced exposure to sun light,⁷ defective skin synthesis of cholecalciferol in CKD,⁸ hyperpigmentation causing impaired response to sunlight mediated cholecalciferol synthesis seen in late CKD stages,⁹ and dietary restrictions prescribed to CKD patients, further, intestinal absorption of dietary and

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supplemental vitamin D (Vit. D) is impaired in uraemic conditions,¹⁰ and in a subset of CKD patients with severe proteinuria there is a significant urinary loss of Vit D binding protein leading to increased loss of Vit. D metabolites.¹¹

Similar to the general population, vitamin D deficiency in these patients is associated with elevated concentrations of parathyroid hormone and bone turnover markers as well as low bone mineral density.¹² Accumulating evidence indicates the associations of vitamin D deficiency with morbidities and mortality in patients with CKD. There is data that indicates Vitamin D treatment is an important factor that may mitigate the effects of hyperparathyroidism (HPTH) and hyperphosphatemia on cardiovascular mortality.¹³ These findings not only have practical applications to current dialysis treatment, but may also have important implications in the much larger population of CKD patients, who are in pre-dialysis segment.

Though hypovitaminosis D is common in patients with CKD many a times it goes undetected because of the cost of the investigation. If early diagnosis and treatment of vitamin D deficiency is done than 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 had recommended the measurements of 25-hydroxyvitamin D levels in patients with CKD who are not 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.¹⁴

Moreover, as of today only very few data are available regarding vitamin D levels among CKD patients in Indian population. So the present study was undertaken to assess the prevalence of vitamin D deficiency among CKD patients.

AIM: To assess the prevalence of vitamin D deficiency among the patients with chronic kidney disease.

MATERIALS AND METHODS: This study was conducted on 100 adult pre-dialysis patients of CKD stage II-IV from September 2013 to June 2015 attending Govt. Medical College Hospital, Thanjavur, Tamil Nadu, South India, catering to a rural population of five districts. Diagnosis of CKD was based on history, clinical features, USG abdomen and renal function test and eGFR. Pre-informed, written consent for enrolment in the study was obtained. The study was duly approved by the institutional ethical committee. Patients on dialysis and those receiving medication known to influence Vit. D, such as Vit. D-containing drugs, corticosteroids, other immune suppressive agents, hormone

replacement therapy, anticoagulants, lithium, phosphate binders, and anticonvulsants, were excluded. Patients were investigated for hemogram, serum urea, creatinine and electrolytes, serum Vit. D level, USG abdomen, fasting blood sugar, ECG and urine analysis. Vit. D was measured with fully automated chemi luminescent immuno assay (CLIA) (LC-MS/MS) which employs non-immunological direct detection. The values were interpreted as deficiency: <20 ng/ml, Insufficiency: 20-30 ng/ml and Sufficiency: 30-100 ng/ml. All the data was entered in SPSS version 18 and the statistical significance were derived accordingly.

RESULTS: The overall prevalence of vitamin D deficiency among the CRF patients in our study was 69% and the insufficiency was present in 17% of the CRF patients and only 14% of the study subjects had normal vitamin D levels. The mean vitamin D levels among the males and females did not show a significant difference in the values ($p=0.592$) and also the prevalence of vitamin deficiency and insufficiency was almost similar among the males and females (table 1).

Age group comparison of the vitamin D levels among the study population had shown that as the age increases the mean level of vitamin D decreases and the difference was found to be statistically significant ($p=0.037$). The prevalence of vitamin D deficiency was more in the older age group than that of the younger age group patients of CRF.

Among the various factor influencing the prevalence of vitamin D deficiency in CRF patients, diabetes and hypertension are the most important factors. In our study the mean levels of vitamin D was much lower in patients with diabetes and hypertension when compared to patients without diabetes and hypertension and the difference was found to be statistically significant ($p=0.003$). In our study 54.5% of the study subjects without diabetes or hypertension had normal serum vitamin D levels, whereas only 3.7% and 5.8% of diabetes and hypertension patients with CRF had normal levels of vitamin D and among the patients having both diabetes and hypertension none of the patients had normal vitamin D levels, the prevalence of vitamin D deficiency was maximum in that group (91.1%).

The mean vitamin D levels are much lower among the patients with stage V CRF when compared to the patients in stage II CRF and this difference was found to be statistically significant ($p<.0001$). Similarly, the prevalence of vitamin D deficiency was much higher in stage IV (87.8%) and stage V (92.8%) CRF when compared to stage II and stage III CRF (table 4). So, as the severity of CRF increases the prevalence of vitamin D deficiency increases.

Gender	Deficiency	Insufficiency	Sufficiency	Mean	P value
Male (n=78)	55(70.5%)	12(15.3%)	11(14.1%)	19.73±5.4	0.592
Female (n=22)	14(63.6%)	5(22.7%)	3(13.6%)	20.04±6.5	
Total (n=100)	69(69%)	17(17%)	14(14%)		

Table 1: Gender and vitamin D levels among the study population

P value derived by applying T test.

Age group	Deficiency	Insufficiency	Sufficiency	Mean	P value
<30(n=4)	0	1(25%)	3(75%)	35.23±5.32	0.037
30–40(n=22)	11(50%)	4(18.1%)	7(31.8%)	28.34±7.16	
41–50(n=19)	12(63.1%)	6(31.5%)	1(5.2%)	19.78±6.72	
51–60(n=31)	27(87%)	3(9.6%)	1(3.2%)	18.74±7.06	
61–70(n=18)	15(83.3%)	2(11.1%)	1(5.5%)	17.31±5.85	
>70(n=6)	4(66.6%)	1(16.6%)	1(16.6%)	17.21±4.13	

Table 2: Age and Vitamin D levels among the study population

P value derived by applying T test.

Diabetes / Hypertension status	Deficiency	Insufficiency	Sufficiency	Mean	P value
Diabetes with CRF (n=27)	22(81.4%)	4(14.8%)	1(3.7%)	19.04±5.14	0.003
Hypertension with CRF (n=17)	12(70.5%)	4(23.5%)	1(5.8%)	19.36±5.74	
Patient with both diabetes and hypertension with CRF (n=34)	31(91.1%)	3(8.8%)	0	17.45±4.38	
Only CRF without diabetes and hypertension (n=22)	4(18.1%)	6(27.2%)	12(54.5%)	33.78±7.08	

Table 3: Vitamin D levels among the patients with diabetes and hypertension

P value derived by using ANOVA.

Stage of CRF	Deficiency	Insufficiency	Sufficiency	Mean	P value
Stage II (n=6)	0	1(16.6%)	5(83.3%)	35.34±4.21	<.0001
Stage III (n=19)	1(5.2%)	9(47.3%)	9(47.3%)	28.62±5.83	
Stage IV (n=33)	29(87.8%)	4(12.1%)	0	18.52±4.92	
Stage V (n=42)	39(92.8%)	3(7.1%)	0	17.38±6.36	

Table 4: Vitamin D levels among the different stages of CRF

P value derived by applying student T test.

DISCUSSIONS: The key finding of the present study was the prevalence of vitamin D deficiency was much higher among the patients with CRF particularly in the late stages of CRF, stage IV and stage V. Older age group patients, diabetes and hypertension patients were more prone to develop vitamin D deficiency. In the present study female gender did not had any independent risk in the development of vitamin D deficiency, whereas previous studies had shown more prevalence of hypovitaminosis D in females when compared to males.¹⁵ Since our study had a small female population (n=22) when compared to males the exact causal relationship between females and hypovitaminosis D was not been derived.

The older age group population in the present study was more prone to develop vitamin D deficiency when compared to the younger age group and similar type of results was shown by Adams J S et al and Autier P et al.^{16,17} The reason can be quoted as; the old age people are keeping indoors when compared to the younger age group population. The exact causal relationship is yet to be proved between hypovitaminosis D and CKD.

But several theories had been put forth by various authors for the deficiency of vitamin D in the CKD patients. The first one is the decrease protein and calorie intake leading on to low vitamin D levels. The second one is the CKD patients would be mostly restricted to indoors and so reduced exposure to sunlight and leading on to low vitamin D levels. The third one is the urinary loss of the metabolites of vitamin D due to overt proteinuria in the CRF patients.^{18,19}

In our study about 70% of the hypertensive patients had low vitamin D levels and the results are almost in par with the other studies.^{20,21,22} Essential hypertension can lead on to several disturbances in the systemic and cellular calcium metabolism. Studies have shown that the dietary calcium intake is often lower and the renal excretion of calcium is higher in hypertensive patients when compared to normotensive subjects. Epidemiologic studies have shown an inverse relationship between serum vitamin D levels and the diastolic blood pressure.²³

Whereas few clinical trials had shown that the daily administration of 5µg of vitamin D did not have any effects on blood pressure in normotensive subjects. However, few authors had proven that with 10 microgram of vitamin D /day had a shown a reduction of blood pressure among the hypertensive patients.²⁴ Another study had shown that reduction in the diastolic and systolic blood pressure was observed in mildly hypertensive patients after 6 wks. of UV-B exposure.²⁵

In our study about 81% of diabetic patients and 91% of patients with both diabetes and hypertension had deficiency of vitamin D levels. So diabetes is as such an independent risk factor in the development of hypovitaminosis D. Studies had shown that vitamin D deficiency has been implicated in decreased insulin secretion and increased insulin resistance which further lead on to the development of type 2 diabetes mellitus.²⁶ A recent study in Saudi Arabia had shown that 98.5% of diabetic patients had low vitamin D levels. A recent study in Finland had shown an inverse relationship between fasting insulin and Vitamin D levels.²⁷ In a recent nested

case-control study conducted among 608 women of newly diagnosed type 2 diabetes, higher plasma vitamin D concentration was associated with lower risk of type 2 diabetes.²⁸ In another longitudinal with a mean follow up of 2.7 years revealed that higher vitamin D levels had a lower risk of diabetes mellitus in high risk patients.²⁸ A similar type of results was also seen in a study done using Asian subjects.

In our study the vitamin D levels were decreasing as the stage of CKD increases. The vitamin D levels were much lower among the patients with stage IV and stage V CKD when compared to stage II and stage III and similar type of results were shown in studies done by Mohd. Rozita et al and Gal-Moscovici et al,²⁹ and the authors also quoted that overt proteinuria in the stage IV and stage V CRF could be the triggering factor for reduced vitamin D levels.

CONCLUSION: Vitamin D deficiency in CKD is more prone for vascular calcification leading on to coronary artery diseases. So early detection and adequate treatment of this entity must be a priority among physicians and nephrologists who treat CKD patients routinely. The present study concludes that Vitamin D deficiency is seen in most of the patients with CKD, as estimated by levels of 25 OH D3. In developing countries like India, where financial resources are limited, predialysis CKD patients may be screened using easily available methods, like CLIA and RIA, to reduce the morbidity and mortality by treating the condition accordingly.

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