



To Study Vitamin-D Insufficiency and Deficiency in Patients of Chronic Kidney Disease

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Abstract

Background: CKD is an emerging public health problem and one of the most powerful predictors of premature cardiovascular disease. Emerging evidence suggests that the progression of CKD and many of the cardiovascular complications may be linked to hypovitaminosis D. It appears that adequate replacement of vitamin-D in deficiency populations could potentially reduce premature morbidity and mortality.

Objectives: To study prevalence of Vitamin-D insufficiency and deficiency in patients of CKD and its association in different stages of CKD patients.

Methods: A prospective observational study was conducted on 100 patients of CKD attending indoor and outdoor unit in a tertiary care hospital who fulfilled the inclusion criteria.

Results: Suboptimal level of Vitamin-D observed in 90% of the patients with 25(OH) Vitamin-D level < 30 ng/ml in 58% of the patients and Vitamin-D level < 15 ng/ml in 32% of the patients. The proportions of patients with 25(OH) Vitamin-D < 30 ng/ml and < 15 ng/ml by CKD stage were 30% (3 of 10), 46.15% (6 of 13), 54.54% (6 of 11), 70.59% (24 of 34), and 50% (16 of 32), 0, 7.69%(1 of 13), 18.18% (2 of 11), 26.47% (9 of 34) and 50% (16 of 32).

Keywords: Vitamin- D, Chronic Kidney Disease, Insufficiency, Deficiency.

Introduction

Chronic Kidney Disease (CKD) is identified as a risk factor for Vitamin-D deficiency, and many papers show that the frequency of deficiency is high among these patients.¹⁻⁷ Even though little attention has been given to this association up until recently.⁸⁻⁹ CKD is an emerging public health problem and one of the most powerful predictors of premature cardiovascular disease. Emerging evidence suggests that the progression of CKD and many of the cardiovascular complications may be linked to hypovitaminosis D. Patients with CKD have an exceptionally high rate of severe vitamin D

deficiency that is further exacerbated by the reduced ability to convert 25-(OH) Vitamin- D into the active form, 1,25 dihydroxy-Vitamin- D. New evidence has now established that the role of vitamin-D is no longer solely restricted to classical function of maintaining calcium and phosphate homeostasis.^{10,11,12} Vitamin-D appears to play a more extensive role as a cell differentiating and anti-proliferative factor with actions in a variety of tissues^{10,11,13} including the renal, cardiovascular and immune system.^{11,13} In patients with CKD, the new non-classical role of vitamin-D also encompasses regulation of renin-angiotensin system (RAS)^{11,13} and the nuclear factor (NF) KB pathway,¹¹ two

pathways involved in a broad range of pathological processes.¹¹ It appears that adequate replacement of vitamin-D in deficiency populations could potentially reduce premature morbidity and mortality.

Aims and Objectives

1. To study prevalence of Vitamin-D insufficiency and deficiency in patients of CKD.
2. Association of Vitamin-D insufficiency and deficiency in different stages of CKD patients.

Material and Methods

Study was carried out on 100 patients of CKD attending indoor and outdoor unit in a tertiary care hospital.

Type of study- Prospective observational study.

Statistics- descriptive data were examined for all variables. For continuous variables results are presented as mean \pm SD, statistical difference in variables was compared using one-way analysis of variance ANOVA. Categorical variables were recorded as frequency counts and intergroup comparisons were analysed by Chi-square test. Statistical significance was accepted if p value < 0.05.

Inclusion Criteria

1. Patients of CKD with signs / symptoms suggestive of CKD.
2. Age: 15-60 yrs.

Exclusion Criteria

1. Patients not giving consent.
2. Patients with altered sensorium or distributed mental state.
3. Patients having primary or nutritional Vitamin- D deficiency.
4. Patients on drugs known to cause Vitamin-D deficiency.
5. Patients having co morbid conditions like coronary artery disease, CVA, and chronic liver disease.

Patients were classified according to the severity of the CKD and estimated glomerular filtration rate

into 5 stages (Stage – 1 to Stage – 5). All subjects did not use Vitamin- D supplement before being enrolled in the study. All biochemical analysis of blood sample were conducted, like creatinine, total and ionic calcium, phosphorus, sodium, potassium, serum albumin, iPTH, Vit. D level, 24 hour urinary protein, USG abdomen for renal size and echotexture of all the patients were performed.

CKD is defined as the estimated creatinine clearance $C_{cr} < 90$ ml/min and signs of renal lesion.

Classification of CKD-

Stage	GFR ml/min per 1.73 m ²
0	>90 (with risk factor)
1	>90 (with demonstrated kidney damage)
2	60-89
3	30-59
4	15-29
5	<15

Vitamin-D deficiency and insufficiency are defined according to the guidelines proposed by kidney disease improving global outcomes. (KDIGO).

Serum levels of Vitamin-D are considered adequate when the concentration of 25(OH)D higher than 30 ng/ml. Levels between 16-30 ng/ml are considered as insufficient and the values that are equal or lower than 15 ng/ml defined the diagnosis of Vitamin-D deficiency.

Results

In our study out of 100 patients analysed, suboptimal levels of Vit. D is observed in 90% of the patients with 25-Hydroxy Vitamin-D level <30ng/ml in 58% of the patients and Vit. D level <15 ng/ml in 32% of the patients. Stage wise prevalence of Vit.D insufficiency- out of 10 patients stage-I of CKD Vit D. insufficiency is observed in 3 patients with prevalence of 30%. out of 13 patients belong to stage-II of CKD Vit. D. insufficiency is observed in 6 patients with prevalence of 46.15%, out of 11 patients belong to stage-III of CKD Vit. D. insufficiency observed in 6 patients with prevalence of 54.54% out of 34 patients belongs to stage-IV of CKD Vit.D insufficiency is observed in 24 patients with prevalence of 70.59% while out of 32 patients belong to stage-V of CKD Vit. D. insufficiency observed in 16 patients with prevalence of 50.00%.

Out of 10 patients stage -I of CKD Vit D. deficiency is not observed in any of the patient. Out of the 13 patients belong to stage-II of CKD Vit. D. deficiency observed in 1 patient with prevalence of 7.69%, out of 11 patients belong to stage-III of CKD Vit. D. deficiency observed in 2 patients with prevalence of 18.18%, out of 34 patients belongs to stage-IV of CKD Vit. D. deficiency observed in 9 patients with prevalence of 26.47% while out of 32 patients belong to stage-V of CKD Vit. D. deficiency observed in 16 patients with prevalence of 50.00%

Increasing prevalence of Vit. D deficiency with increasing severity of CKD was found.

Table 1 S. Vitamin- D level

stages	No.	Vit. D level		p-value	SEm	CD at 5%
		Mean	SD			
I	10	31.89	7.72	0<0.0001	0.68	1.89
II	13	27.75	7.02			
III	11	23.85	9.26			
IV	34	19.12	6.75			
V	32	14.55	5.22			

Table 2 Association of Normal Vitamin D in different stages of CKD patients

stages	No.	Vit. D level		F-value	p-value
		Mean	SD		
I	7	35.90	5.05	0.500	0.689
II	5	33.92	2.53		
III	4	33.64	4.21		
IV	1	31.60			
V	0				

Table 3 Association of Vitamin D insufficiency in different stages of CKD patients

stages	No.	Vit. D level		p-value	SEm	CD at 5%
		Mean	SD			
I	3	22.54	2.02	0.014	0.53	1.50
II	7	25.57	4.11			
III	5	21.12	3.71			
IV	24	21.84	4.49			
V	16	19.06	3.25			

Table 4 Association of Vitamin D deficiency in different stages of CKD patients

stages	No.	Vit. D level		F-value	p-value
		Mean	SD		
I	0	0	0	0.675	0.576
II	1	12.20			
III	2	11.09	1.31		
IV	9	10.48	2.14		
V	16	10.04	1.53		

Table 5 Prevalence of Vitamin D deficiency in patients of CKD

CKD stages	No.	No. of Vitamin D deficient patients	Prevalence of Vitamin D deficiency (%)
I	10	0	0
II	13	1	7.69
III	11	2	18.18
IV	34	9	26.47
V	32	16	50.00

Table 6 Prevalence of Vitamin D insufficiency in patients of CKD.

CKD stages	No.	No. of Vitamin D insufficient patients	Prevalence of Vitamin D insufficiency (%)
I	10	3	30.00
II	13	6	46.15
III	11	6	54.54
IV	34	24	70.59
V	32	16	50.00

Discussion

Vitamin- D deficiency is common among patients with chronic kidney disease (CKD), presence of Vit. D both in general population and in patients in CKD is based mainly on the effects of Vitamin-D on the calcium homeostasis and bone health. Bone disorders, mineral abnormalities and vascular calcification in individuals with moderate to advanced CKD seem to be related to a progressive deficiency of active Vitamin-D and worsening secondary hyperparathyroidism. Serum levels of 25-Hydroxy Vitamin-D are also inversely associated with serum PTH level both in patients with CKD¹⁵ and in those without this disease¹⁶. Serum 25-Hydroxy Vitamin-D is also an inverse predictor of disease progression and death in patients with CKD.^{17,18}

Recent observation has indicated that serum 25-Hydroxy Vitamin -D is significantly lower in participant with a serum decrease in estimated glomerular filtration rate (GFR) compare with those with normal kidney function. In the study carried out by Herculano Ferreira Diniz et al (2012)¹⁵ out of the 125 patients analyzed 92 (73.6%) had low levels of serum 25-Hydroxy Vitamin-D i.e. serum concentration was <30ng/mL out of these 65 (52%) had insufficient level of Vit. D and 27 (21.6%) had level lower than 15 ng/ml considered as deficient. Del Valle E et al (2007)⁵ in this study, we considered adequate Vitamin-D levels those above

30ng/ml (U.S.A National Kidney Foundation DOQI Guidelines), Vitamin-D insufficiency when levels were between 15 and 30ng/ml, and Vitamin-D deficiency when levels were below 15ng/ml. The mean 25(OH) D levels were significantly higher in men than in women (28.6_{v.s.}18.9ng/mL; p=0.001). Vitamin-D insufficiency was found in 53.5% of the patients (n=45) and Vitamin-D deficiency in 22.6% (n=19).

In our study out of 100 patients analysed, suboptimal level of Vitamin-D observed in 90% of the patients with 25(OH) Vitamin-D level < 30 ng/ml in 58% of the patients and Vitamin-D level < 15 ng/ml in 32% the patients.

Pietro Ravani et al (2009)¹⁹ patient distribution by CKD stage was: 9.5% in stage 2; 40.5% in stage 3, 40.5% in stage 4; and 9.5% in stage 5. Over 60% of the study sample had parathyroid hormone (PTH) levels >65pg/mL. The median value of plasma levels of 25D was 18.1ng/mL (interquartile range: 13-26ng/mL), and that of 1,25D was 8.5pg/ml (13-27.5 pg/mL). The proportions of patients with 25D<30 and <15ng/mL (the thresholds for VD insufficiency and deficiency states²⁰) by CKD stage were: 62% (10 to 16) and 25% (4 of 16, stage 2); 79% (54 of 68) and 29% (20 of 68, stage 3); 85% (58 of 68) and 37% (25 of 68, stage 4); and 88% (14 of 16) and 56% (9 of 16, stage 5).

In our study the proportions of patients with 25(OH) Vitamin-D < 30 ng/ml and < 15 ng/ml by CKD stage were 30% (3 of 10), 46.15% (6 of 13), 54.54% (6 of 11), 70.59% (24 of 34), and 50% (16 of 32), 0, 7.69%(1 of 13), 18.18% (2 of 11), 26.47% (9 of 34) and 50% (16 of 32).

Conclusion

It can be concluded that increasing prevalence of Vitamin-D deficiency and insufficiency with increasing severity of CKD was found. The result of our study raise an important public health issue and need to be confirmed by large scale cohort study in the other populations.

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