ORIGINAL RESEARCH

Trend of Vitamin D deficiency in Chronic Kidney Disease patients

[1]Dr. Bavneet Kaur, [2]Dr. Jaswinder Kaur, [3]Dr. Vinshu

[1]Associate Professor, Department of Medicine, PIMS, Jalandhar.
[2]Associate Professor, Department of Medicine, PIMS, Jalandhar
[3]Junior Resident, Department of Medicine, PIMS, Jalandhar

Corresponding Author
Dr. Jaswinder Kaur
Associate Professor, Department of Medicine, PIMS, Jalandhar

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ABSTRACT
Introduction: Patients suffering from Chronic Kidney Disease (CKD) commonly have a high frequency of anomalies in their metabolite levels. Patients with a decreased Glomerular Filtration Rate (GFR) are more prone to experiencing severe vitamin D insufficiency in comparison to those with regular renal function. The aim of present study was to examine the correlation between vitamin D levels and disease severity among CKD patients at a tertiary care hospital.
Material and methods: The present cross- sectional study was conducted at a tertiary care center among 52 patients of chronic kidney disease who visited the department during the study period of one year. All the essential laboratory tests were done and clinical and demographic history was taken. Results were analyzed using SPSS version 25.0.
Results- Maximum patients were in the age group of 61 to 70 years (28.8%) and least were between the age of 18 to 30 years (3.8%). Number of male (69.3%) subjects was higher in number as compared to female (30.7%). Vitamin D level was assessed for all patients 1 patient had normal level, 39 patients had insufficiency of vitamin D level and 12 patients had deficiency of vitamin D level. Out of all the patients 1 had stage 3a, 2 had stage 3b, 8 had stage 4 and 41 had stage 5. In stage 5 there were 29 patients who had insufficient vitamin D where as 12 patients had deficient level of vitamin, results were significant with p value less than 0.001.
Conclusion: CKD patients had a deficiency in Vitamin D, with a more significant occurrence observed in the later stages of CKD.
Keywords: Chronic Kidney Disease, Glomerular Filtration Rate, Prevalence, Renal Disease, Vitamin D

INTRODUCTION

Chronic kidney disease (CKD) is characterized by structural or functional abnormalities in the kidney, along with or without a reduced estimated glomerular filtration rate (eGFR < 60 mL/min/1.73m^2), persisting for a duration of at least three months [1]. It is recognized as a substantial global health issue 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]
Vitamin D, a steroid hormone that plays a crucial role in bone metabolism, can be obtained through dietary sources, supplements, or synthesized in the body through the skin using UV radiation from a precursor [4]. Vitamin D insufficiency has been associated with a wide range of illnesses including increased risk of fractures, diabetes, renal disease, cardiovascular disease, auto-immune disease, depression, and cancer [5,6]. Various studies conducted in India have shown a high prevalence of vitamin D deficiency, ranging from 50-94% and 37-99%, respectively [7,8]
The kidneys have a crucial involvement in the metabolism and regulation of vitamin D. Consequently, individuals with impaired kidney function, such as those with chronic kidney disease (CKD), may have a shortage in vitamin D levels. Individuals suffering from chronic kidney disease (CKD) exhibit a significant occurrence of anomalies in their metabolites. Levels of serum 25OH D start to decrease as early as stage 2 of chronic kidney disease (CKD).[9] It is a significant risk factor that can be changed in this population at high risk, especially for cardiovascular events. The risk of death increases as the estimated glomerular filtration rate (eGFR) falls below 60 ml/min.[10]
Previous research studies [11,12] have demonstrated that patients with lower glomerular filtration rate (GFR) experience a more severe deficit of vitamin D in comparison to individuals with normal renal function. It is crucial to establish this correlation as it can differ depending on local factors. Given that CKD is a significant public health issue, there is a lack of information addressing the correlation between vitamin D insufficiency and the extent of CKD . Therefore, further research is important to elucidate this matter in order to implement appropriate measures to tackle it.[13]

Hence, this study was done to examine the correlation between vitamin D levels and disease severity among CKD patients at a tertiary care hospital.

MATERIAL AND METHODS

The present cross- sectional study was conducted at a tertiary care center among patients of chronic kidney disease who visited the department during the study period of one year. Patients were asked to sign an informed consent form after explaining them the complete procedure. Ethical clearance was taken from institutional ethics committee before commencement of study.

A total of 52 patients diagnosed with chronic kidney disease were selected through consecutive sampling on the basis of inclusion and exclusion criteria.

Inclusion criteria- All CKD patients with stage 3, 4, 5, and GFR less than 60 mL/min/1.72 m^2 who were attending the hospital for dialysis were included in the study.

Exclusion criteria- The study excluded patients who were previously using Vitamin D supplements, patients with chronic disabling diseases and terminally ill patients, as well as patients on drugs such as steroids, anticonvulsants, and theophylline, which can impact the absorption of vitamin D.

A proforma was created to gather fundamental demographic information, including age, gender, addiction history, and pertinent medical history. Vitamin D levels were assessed using Chemiluminescence immunoassay in the laboratory. Vitamin D deficiency is characterized by 25-OH vitamin D levels below 10 ng/mL. Insufficiency is defined as values between 10 and less than 30 ng/mL. Normal range or sufficiency is indicated by levels between 30-100ng/mL[14].

The GFR was calculated using the Modification of Diet in Renal Disease (MDRD) algorithm. The estimated glomerular filtration rate (GFR) can be calculated using the formula: GFR = 175 × (Scr)-1.154 × (Age)-0.203 × 0.742 (if female). End-stage CKD patients were classified into four categories according to the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice recommendations of 2012 [15].

- CKD stage 3a (GFR 45-59 mL/min/1.72 m^2)
- CKD stage 3b (GFR 30-44 mL/min/1.72 m^2)
- CKD stage 4 (GFR 15-29 mL/min/1.72 m^2)
- CKD stage 5 (GFR< 15 mL/min/1.72 m^2)

The data was entered into Microsoft Excel and analyzed using SPSS version 25.0. The numerical data were represented by the mean and standard deviation (SD), whereas the categorical variables were represented by percentages. The ANOVA test and Pearson's Correlation were utilized, with a significance level of $p<0.05$.

RESULTS

In the present study maximum patients were in the age group of 61 to 70 years (28.8%) and least were between the age of 18 to 30 years (3.8%). Number of male (69.3%) subjects was higher in number as compared to female (30.7%). Out of all the patients 34.6% were smokers and 36.5% had habit of smoking. 57.6% had hypertension, 53.8% had diabetes and 48% had CVD as shown in table 1.

Table : 1 Demographic data of patients

Variable		Frequency (percentage)
Age	18-30	2 (3.8)
	31-40	5 (9.6)
	41-50	9 (17.3)
	51-60	10 (19.2)
	61-70	15 (28.8)
	Above 70 years	11 (21.1)
Gender	Male	36 (69.3)
	Female	16 (30.7)
Addictions	Smokers	18 (34.6)
	Alcohol	19 (36.5)
	None	15 (28.8)
Co-morbidities	Hypertension	30 (57.6)
	Diabetes	28 (53.8)
	CVD	25 (48.0)

Out of all the patients 1 had stage 3a, 2 had stage 3b, 8 had stage 4 and 41 had stage 5 with mean GFR value as 45.0±0.0; 34.2±3.7; 19.1±4.9 &7.48±3.4 respectively as shown in table 2.

Table: 2 Distribution of patients on the basis of CKD staging

CKD staging	Frequency (percentage)	Mean GFR
Stage 3a	1 (1.9)	45.0±0.0
Stage 3b	2 (3.8)	34.2±3.7
Stage 4	8 (15.3)	19.1±4.9
Stage 5	41 (78.8)	7.48±3.4

Vitamin D level was assessed for all patients 1 patient had normal level, 39 patients had insufficiency of vitamin D level and 12 patients had deficiency of vitamin D level with mean values as 31.2±0.0; 18.5±3.8 and 6.1±2.0 respectively as shown in table 3.

Table: 3 Distribution of patients on the basis of vitamin D level

Vitamin D level	Frequency (percentage)	Mean vitamin D level
Normal	1 (1.9)	31.2±0.0
Insufficient	39 (75)	18.5±3.8
Deficient	12 (23.1)	6.1±2.0

In stage 3a there was only one patient who had normal vitamin D level, in stage 3b there were 2 patients who had insufficient level, in stage 4 there were 8 patients who had insufficient level of vitamin D, in stage 5 there were 29 patients who had insufficient vitamin D where as 12 patients had deficient level of vitamin , results were significant with p value less than 0.001 as shown in table 4.

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

CKD stage	Normal	Insufficient	Deficient	P value
Stage 3a	1	0	0	<.001
Stage 3b	0	2	0	
Stage 4	0	8	0	
Stage 5	0	29	12	

DISCUSSION

The global and Indian public health sectors are facing a significant challenge due to the increasing prevalence and incidence of Chronic Kidney Disease (CKD), which is closely linked to the growth in non-communicable diseases. Chronic kidney disease (CKD) not only presents with disease symptoms, but also gives rise to potential consequences that impact standard of living. The present study was done in a hospital setting among 52 patients with chronic kidney disease (CKD) to evaluate the levels of vitamin D. The demographic data revealed that the majority of the patients were aged above 60 years, with a higher number of males. A study conducted by Sathyan S et al found similar results in a clinical and epidemiological investigation on individuals with chronic kidney disease (CKD) [16].

The study revealed that around 66% of the patients were male, while 47.45% fell within the age range of 41-60 years. The main discovery of this study was that the occurrence of vitamin D deficiency was much greater among individuals with CKD, especially in the advanced stages of the disease, specifically stage IV and stage V which was statistically significant ($p<0.001$) Patients in the older age group, as well as those with diabetes and hypertension, were more susceptible to developing vitamin D deficiency.

In a study conducted by Ghosh SK and Ghosh S in, it was shown that there is a substantial positive association ($r=0.665$, $p<0.0001$) between eGFR and vitamin D level. The study indicated that stage 3a CKD patients had higher average vitamin D levels (36.31) compared to stage 5 CKD patients, who had levels of 11.11. These findings were similar to the results of the current investigation. [17] Nevertheless, a study conducted by Kantas T et al. in Pakistan discovered a modest yet noteworthy association between eGFR and blood vitamin D ($r=0.018$, p-value=0.012) [18].

In a study conducted by Satirapoj B et al. in Thailand, it was found that vitamin D insufficiency and deficiency were associated with different stages of chronic kidney disease (CKD) in an Asian population. The study observed that the levels of 25-hydroxyvitamin D decreased significantly as the severity of renal impairment increased, which aligns with the findings of the current study [14].

Although the precise mechanism between vitamin D deficiency and the risk of renal events is not fully understood, numerous molecular pathways have been suggested. Vitamin D undergoes enzymatic conversion in the liver to

25(OH)D, which is the primary form found in the bloodstream. It is further changed in the kidney to 1,25(OH)2D, which is the biologically active form of vitamin D. Insufficient amounts of 1,25(OH)2D in the body can cause the RAS system to deteriorate by causing aberrant metabolic profiles, including elevated renin, proteinuria, blood pressure, insulin resistance, and renal damage. For instance, the administration of vitamin D reduces the levels of renin receptor and renin expression in rat models of chronic kidney disease (CKD). Another potential mechanism is that insufficient amounts of 25(OH)D may regulate inflammation and oxidative stress, leading to a decrease in fibroblast activation. Furthermore, the progression of chronic kidney disease (CKD) has been associated with a decrease in the reabsorption of 25-hydroxyvitamin D (25(OH)D) and a drop in the levels of 1,25-dihydroxyvitamin D (1,25(OH)2D) inside the renal proximal tubules (38). Furthermore, it is well-established that levels of 1,25(OH)2D have the ability to decrease the expression of nuclear factor kB and induce a transition in T-helper cell response from T-helper 1 cell to T-helper 2 cell. As a result, this decreases tissue damage caused by T-helper 1 cells and enhances the production of immunomodulatory cytokines by T-helper 2 cells. An inherent genetic tendency that impacts the functioning of vitamin D binding protein (DBP) has been proposed as a potential mechanism in the link between vitamin D levels and the likelihood of experiencing kidney-related issues. DBP is enabled through the process of receptor-mediated endocytosis. Cublin and megalin facilitate the absorption of extracellular ligands in the renal proximal tubule. Insufficient levels of these proteins lead to an elevated excretion of vitamin D in the urine. [19]

The study is limited by a small sample size, and the reliance on data from only one tertiary care center. These characteristics restrict the potential to apply the study findings to a broader population.

CONCLUSION

Patients with chronic kidney disease (CKD) were found to have a shortage in Vitamin D, with the deficiency being more prominent in the latter stages of CKD. The increasing prevalence of chronic kidney disease (CKD) as a public health concern and the rapid advancement of the disease have a negative impact on the overall well-being of CKD patients. The current study emphasizes the need of healthcare practitioners comprehending the challenges encountered by CKD patients and consistently conducting screenings to promptly treat concerns like vitamin D insufficiency. Additional multicentric research are necessary to establish further evidence that can assist policymakers in making informed decisions regarding the prevention of CKD and its long-term consequences.

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