DOI: 10.7860/NJLM/2024/59460.2821

Original Article

Biochemistry Section

Vitamin D Levels among Chronic Kidney Disease Patients at a Tertiary Care Hospital: A Cross-sectional Study

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ABSTRACT

Introduction: In patients with Chronic Kidney Disease (CKD), a high prevalence of metabolite abnormalities has been observed. Numerous studies have demonstrated that individuals with reduced Glomerular Filtration Rate (GFR) are more susceptible to severe vitamin D deficiency compared to those with normal kidney function.

Aim: To investigate the association between vitamin D levels and the severity of CKD among patients at Siddhartha Medical College, GGH in Vijayawada, Andhra Pradesh, India.

Materials and Methods: The present hospital-based cross-sectional study was conducted at Siddhartha Medical College, GGH, Vijayawada, Andhra Pradesh, India from December 2021 to February 2022. A total of 100 CKD patients with a GFR of less than 60 mL/min/1.72 m^2 were included in the study. Vitamin D levels were assessed using Chemiluminescence immunoassay (Access 2, Beckman Coulter), and vitamin D deficiency was defined as 25-OH vitamin D levels of less than 10 ng/mL, while insufficiency was defined as levels between 10 to 30 ng/mL. Statistical analysis was performed using Analysis of Variance (ANOVA) test and Pearson's correlation test.

Results: The mean age of the study population was 53.25±7.6 years, with the majority (32%) belonging to the 51-60 years age group. In terms of gender distribution, approximately three-fourths (72%) of the subjects were male. Hypertension was present in 44% of CKD patients, diabetes in 38%, and cardiovascular disease in 38%. Total 53% of CKD patients were classified as stage 4 on the Kidney Disease: Improving Global Outcome (KDIGO) CKD staging. Vitamin D deficiency was observed in 26% of patients, while 39% had insufficiency. A statistically significant association was found between the severity of CKD staging and mean vitamin D levels, with lower mean levels observed in stages 4 and 5.

Conclusion: Vitamin D deficiency was present in one-fourth of the CKD patients, and it was more pronounced in advanced stages of CKD.

Keywords: Glomerular filtration rate, Hypertension, Metabolite abnormalities, Renal disease

INTRODUCTION

With the epidemiological transition and the increasing burden of chronic diseases, non communicable diseases contribute to a high proportion of mortality and morbidity in India [1]. CKD, which arises due to abnormalities of kidney structure or function, leads to a reduction in kidney function. CKD is characterised by increased markers of kidney damage or urine sediment abnormalities, electrolyte abnormalities, and structural abnormalities [1]. Approximately, 195 million women are affected by kidney diseases worldwide. During 2001 to 2013, more than one-third (38%) of deaths in India were attributable to kidney failure. CKD is also an important risk factor for cardiovascular disease [2,3]. Approximately 2.2 lakh new patients of end-stage renal disease are added in India, and there is a growing concern about treatment facilities [4]. Accordingly, the Government of India launched the National Dialysis Program under the National Health Mission to provide dialysis for CKD patients, which is an important life-saving procedure and reduces expenditures for patients [5].

Vitamin D, also known as calciferol, is a fat-soluble vitamin primarily obtained from sun exposure, foods, and supplements. It promotes calcium absorption in the gut to enable bone mineralisation. It also plays a role in reducing inflammation, neuromuscular and immune function, and glucose metabolism [6,7]. The prevalence of vitamin D deficiency is reported worldwide, but it is often the most underdiagnosed and undertreated nutritional deficiency. Various studies conducted in India have shown a high prevalence of vitamin D deficiency, ranging from 50-94% and 37-99%, respectively [8-11].

Kidneys play a vital role in the metabolism and regulation of vitamin D; therefore, impaired renal function, as seen in CKD patients, may lead to deficiency of vitamin D levels. Patients with CKD show a high prevalence of metabolite abnormalities, and previous studies [12,13] have shown that patients with reduced GFR have severe vitamin D deficiency compared to those with normal kidney function. It is imperative to determine this association as it can vary based on geographical aspects. With CKD being a public health problem, there is a paucity of data regarding the association of vitamin D deficiency with the severity of CKD in Andhra Pradesh. Therefore, more studies are required to shed light on this issue so that necessary steps can be taken to address it.

Hence, the present study was conducted with the objective of studying the association between vitamin D levels and the severity of the disease among CKD patients at a tertiary care hospital in Andhra Pradesh.

MATERIALS AND METHODS

The present hospital-based cross-sectional study was conducted at Siddhartha Medical College, GGH in Vijayawada, Andhra Pradesh, India for a duration of three months from December 2021 to February 2022. The study was approved by the Institutional Ethics Committee (Ethical Committee approval number: IEC/2022/010/SMC). All patients provided informed consent before being included in the study.

Inclusion criteria: All CKD patients with stage 3, 4, 5, and GFR less than 60 mL/min/1.72 m^2 [14,15] who were attending the hospital for dialysis were included in the study.

Exclusion criteria: Patients who were already on Vitamin D supplements prior to the start of the study, patients with chronic

debilitating conditions and terminally ill patients, and patients on medications such as steroids, anticonvulsants, theophylline, which affect vitamin D absorption, were excluded from the study.

Sample size: A total of 100 CKD patients were included in the study using a convenient sampling technique.

Study Procedure

A proforma was prepared to collect basic demographic data such as age, gender, addiction history, and relevant medical history. Assessment of Vitamin D levels was performed using Chemiluminescence immunoassay (Access 2, Beckman Coulter) in the Department of Biochemistry. Vitamin D deficiency was defined as 25-OH vitamin D levels below 10 ng/mL, insufficiency when the levels were between 10 and less than 30 ng/mL, and normal range or sufficiency when levels were between 30-100 [14].

The GFR was estimated using the Modification of Diet in Renal Disease (MDRD) equation. Estimated GFR=175×(Scr)-1.154×(Age)-0.203 × 0.742 (if female). End-stage CKD patients were categorised into four stages based on the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice 2012 guidelines [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)

STATISTICAL ANALYSIS

The data was entered in Microsoft Excel 2010 version and analysed using Epi Info software version 7.2 provided by the Centre for Disease Control and Prevention (CDC), Atlanta. Numerical data were presented as mean and Standard Deviation (SD), while categorical variables were presented as percentages. ANOVA test and Pearson's Correlation were applied, with $p<0.05$ considered statistically significant.

RESULTS

A total of 100 CKD patients were included, and their demographic information showed that the mean age of the study population was 53.25±7.6 years, with the majority (32%) belonging to the 51-60 years age group. The gender-wise distribution showed that about three-fourths (72%) were males and 28% were females, with a male-to-female ratio of 2.6:1. Regarding co-morbidities, hypertension was present in 44% of CKD patients, diabetes in 38%, and cardiovascular disease in 38%. The mean duration of kidney disease was 5.4±1.5 years, and the most common cause of CKD was diabetic kidney disease (38%), followed by chronic interstitial nephritis (28%). Nearly one-third admitted to being smokers (31%), and more than two-thirds (68%) mentioned having an occasional drinking habit [Table/Fig-1].

Based on the KDIGO clinical practice 2012 guidelines [15], more than half of the patients (53%) belonged to stage 4 (GFR 15-29 mL/min/1.72 m^2), and about one-third of them (32%) belonged to stage 5 (GFR<15 mL/min/1.72 m^2). The mean GFR among CKD patients in stage 3a was 55.3±4.7 mL/min/1.72 m^2, in stage 3b it was 38.1±3.8 mL/min/1.72 m^2, in stage 4 the mean GFR was 22.9±7.3 mL/min/1.72 m^2, and in stage 5 it was 10.6±2.8 mL/min/1.72 m^2. In stage 5 of CKD, 43.8% were vitamin D deficient compared to 20.7% and 9.1% in stage 4 and stage 3b, respectively. All four patients with stage 3a had normal levels of vitamin D [Table/Fig-2].

Regarding vitamin D status, the present study found vitamin D deficiency in more than one-fourth of CKD patients (26%) with vitamin D levels being less than 10 ng/mL. Vitamin D insufficiency (10-30 ng/mL) was found in more than one-third (39%) of them [Table/Fig-3]. A statistically significant association was found between mean vitamin D levels and the severity of CKD stage. Lower mean vitamin D levels (12.36±3.43) were found in stage 5 CKD compared to other stages of CKD. Hence, it is clear that with increasing severity of CKD, the mean vitamin D values are getting lower, with the lowest mean vitamin D levels being observed in CKD stage 5 [Table/Fig-4].

A significant positive correlation was found between mean vitamin D levels and GFR (r-value=0.67 and p-value=0.002), indicating that mean vitamin D levels were higher in the earlier stages of CKD.

Demographic variables	Number
Age group (years)	
41-50	26
51-60	32
61-70	18
>70	24
Gender	
Male	72
Female	28
Addictions	
Smokers	31
Alcohol	68
Co-morbidities	
Hypertension	44
Diabetes	38
Cardiovascular disease	38
Cause of CKD	
Diabetic kidney disease	38
Chronic interstitial nephritis	28
Hypertensive nephropathy	15
Chronic glomerulonephritis	12
Obstructive uropathy	04
Autosomal dominant polycystic kidney disease	03

[Table/Fig-1]: Demographic data.

CKD stage	Mean GFR (mL/min/1.72 m^2)	Vitamin D status		
		Normal	Insufficient	Deficient
Stage 3a (n=4)	55.3±4.7	04 (100%)	-	-
Stage 3b (n=11)	38.1±3.8	08 (72.7%)	02 (18.2%)	01 (9.1%)
Stage 4 (n=53)	22.9±7.3	17 (32.1%)	25 (47.2%)	11 (20.7%)
Stage 5 (n=32)	10.6±2.8	06 (18.7%)	12 (37.5%)	14 (43.8%)

[Table/Fig-2]: Distribution according to categorisation of CKD stages.

Vitamin D	n	Mean±SD (vitamin D)
Normal (>30 ng/mL)	35	45.7±8.6
Insufficiency (10-30 ng/mL)	39	20.7±7.8
Deficiency (<10 ng/mL)	26	8.8±2.5

[Table/Fig-3]: Vitamin D status in CKD patients.

CKD subgroup	Vitamin D Mean±SD	p-value
Stage 3a (n=4)	33.53±6.24	0.00001*
Stage 3b (n=11)	25.71±3.94	
Stage 4 (n=53)	21.62±7.47	
Stage 5 (n=32)	12.36±3.43	

[Table/Fig-4]: Distribution of mean vitamin D levels according to CKD staging.
'ANOVA' test applied
*p<0.05 considered statistically significant

DISCUSSION

With the rise in non communicable diseases, the prevalence and incidence of CKD are increasing, making it a major public

health problem globally and in India. CKD not only has disease manifestations but also leads to potential complications that affect the quality of life. The present hospital-based study was conducted among 100 CKD patients to assess vitamin D levels in a tertiary care hospital. Demographic characteristics showed that the majority of the patients were fifty years and above, with a male preponderance. Similar findings were seen in a study by Sathyan S et al., (2016) who conducted a clinical and epidemiological study on CKD patients [1]. They found that nearly two-thirds of the patients were males and 47.45% belonged to the 41-60 years age group.

Regarding the cause of CKD, diabetic kidney disease and chronic interstitial nephritis were the most common causes in the present study, which was consistent with the findings of a study by Kumar V et al., [2]. They also found that diabetic kidney disease (24.9%) and chronic interstitial nephritis (23.2%) were the most common causes. However, in contrast, the study by Sathyan S et al., (2016) found that chronic glomerulonephritis was the most common etiological diagnosis (51%), which could be due to geographical variations and differences in the prevalence of diabetes between the two studies [1]. Hypertension and diabetes were the most common co-morbid conditions associated with CKD patients in the present study. The study found a high prevalence of vitamin D deficiency and insufficiency among chronic kidney patients, which accounted for nearly two-thirds (65%) of the study population. This was comparable to the findings of a study by Mittal SP et al., from Bangladesh, where pre-haemodialysis vitamin D levels were deficient in 58.73% of patients, but post-haemodialysis vitamin D levels were markedly low (85.71%) due to the washedout phenomenon in haemodialysis patients [16]. However, the present study did not assess the aspect of pre- and post-haemodialysis.

The KDIGO clinical practice 2012 guidelines were used to grade the severity of CKD based on GFR. The present study found that as the severity of CKD staging increased, the mean vitamin D levels significantly decreased, which was statistically significant (p=0.00001). A positive correlation was also found between mean vitamin D levels and GFR, with a Pearson's correlation value (r) of 0.67, which was statistically significant (p=0.002).

Similar findings were observed in a study by Ghosh SK and Ghosh S, from Kolkata, where a positive correlation was found between eGFR and vitamin D level, which was statistically significant (r=0.665, p<0.0001) [17]. In their study, higher mean vitamin D levels (36.31) were found in stage 3a CKD patients compared to 11.11 in CKD stage 5, which was comparable to the findings of the present study. However, a study by Kantas T et al., from Pakistan found a weak but significant correlation between eGFR and serum vitamin D (r=0.018, p-value=0.012) [18].

Another study by Satirapoj B et al., from Thailand on vitamin D insufficiency and deficiency with stages of CKD in an Asian population found that the mean 25-hydroxyvitamin D levels were significantly lower with the severity of renal impairment, which was similar to the observations of the present study [14]. The prevalence of vitamin D deficiency/insufficiency was 66.66% in CKD stage 3a, 70.9% in stage 3b, 74.6% in stage 4, and 84.7% in CKD stage 5.

A comparison of the findings in the present study with previous studies is shown in [Table/Fig-5] [14,16,17,19-21].

Name of the author, place and year of the study	Sample size	Vitamin D deficiency and insufficiency in CKD patients
		Percentage
Present study findings,Vijayawada, Andhra Pradesh, 2022	100	65%
Mittal SP et al., [16], Himachal Pradesh, 2018	69	58.73%
Ghosh SK and Ghosh S, [17], Kolkata, 2020	100	62%
Satirapoj B et al., [14], Bangkok, Thailand, 2013	2895	78%
Lee J et al., [19], Korea, 2023	2144	64.7%
Arulanantham R et al., [20], Tamil Nadu, 2016	100	86%
Mohamed MG et al., [21], Egypt, 2021	75	88%

[Table/Fig-5]: Comparison of present study findings with other studies [14,16,17,19-21].

Limitation(s)

The limitations of the study include a small sample size, the use of a convenient sampling technique, and the reliance on data from a single tertiary hospital centre. These factors limit the generalisability of the study findings.

CONCLUSION(S)

Vitamin D deficiency was found in one-fourth of the CKD patients, and it was more pronounced in advanced stages of CKD. The growing burden of CKD as a public health problem and the rapid progression of the disease affect the overall quality of life among CKD patients. The present study highlights the need for healthcare professionals to understand the complications faced by CKD patients and regularly screen them to address issues such as vitamin D deficiency at an early stage. Further multicentric studies are required to establish more evidence, which can help policymakers make appropriate decisions regarding the prevention of CKD and its long-term effects.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 04, 2023
- Manual Googling: Sep 25, 2023
- iThenticate Software: Sep 29, 2023 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 02, 2023**
Date of Peer Review: **Sep 14, 2023**
Date of Acceptance: **Sep 30, 2023**
Date of Publishing: **Apr 01, 2024**