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Original Research Article

Evaluation of Serum Vitamin D Level Before and After Haemodialysis in Chronic Kidney Disease Patients

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Abstract

Background: Chronic kidney disease (CKD) is a major global health concern, and vitamin D deficiency is frequently observed in patients undergoing maintenance haemodialysis due to impaired renal function and altered vitamin D metabolism. Vitamin D plays an essential role in calcium and phosphate homeostasis and bone health. Haemodialysis may induce short-term changes in circulating vitamin D levels through alterations in fluid balance and blood composition; however, these changes and their clinical significance remain insufficiently understood. Therefore, this study aims to compare serum 25-hydroxyvitamin D levels before and after haemodialysis in patients with CKD and assess their association with immediate post-dialysis outcomes within seven days.

Materials and Methods: This hospital-based prospective observational study was conducted among 100 CKD patients undergoing maintenance haemodialysis from June 2020 to December 2021. Serum 25-hydroxyvitamin D levels were measured 24 hours before and after haemodialysis and compared. Detailed clinical history, physical examination, and relevant investigations were performed to determine the aetiology of CKD. Patients with conditions or medications likely to affect vitamin D levels were excluded, and written informed consent was obtained from all participants.

Results: Among the 100 CKD patients, 54% were male, and diabetes with hypertension was the most common aetiology (30%). Vitamin D deficiency and insufficiency were observed in 69% and 24% of patients, respectively. Mean serum vitamin D levels significantly decreased after haemodialysis (19.08 ± 6.905 to 15.32 ± 7.134 ng/mL; $p < 0.0001$), with deficiency increasing to 75%. Vitamin D deficiency was significantly associated with cardiovascular events ($p < 0.0001$) and was observed in 94.7% of patients who died.

Conclusion: Vitamin D levels declined significantly after haemodialysis and were associated with increased cardiovascular morbidity and adverse outcomes, suggesting their potential role as a prognostic marker in CKD patients.

Keywords: Chronic Kidney Disease (CKD), Vitamin D, Haemodialysis, Serum 25-hydroxyvitamin D, End-stage renal disease.

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Introduction

Chronic Kidney Disease (CKD) refers to a group of pathophysiologic conditions characterized by impaired kidney function and a progressive decrease in glomerular filtration rate (GFR) [1]. End-stage kidney disease (ESRD) is defined as a glomerular filtration rate (GFR) of less than 15ml/min per 1.73m^2 in individuals who require renal replacement therapy (RRT) [1,2]. In 2017, the global prevalence of chronic kidney disease (CKD) was 9.1%, or roughly 700 million cases. According to the Global Burden of Disease Study 2017, CKD is the 12th leading cause of death [3] and India has 115.1 million patients of chronic kidney disease (CKD) out of 700 million worldwide [3]. Over 130,000 people in India are on dialysis, and the number is growing at a rate of about 232 per million people [4]. The principal primary cause of CKD globally is Diabetes Mellitus (DM) [5]. The rising prevalence of obesity and diabetes, [6,7] in addition to the ageing of the global population, is likely to lead to a rising burden of CKD [8]. Vitamin D is a fat-soluble vitamin that is primarily responsible for calcium and phosphorus homeostasis [9,10,11]. It also has immunomodulatory and antiproliferative properties in tissues such as the kidney, cardiovascular, and immune systems [9,11]. The skin is a major source of vitamin D, which is synthesized in response to

sunlight exposure (UV-B radiation). Other sources encompass nutritional supplements and fortified foods [12]. When exposed to sunlight, the skin produces vitamin D from its precursor 7-dehydrocholesterol. It is then converted to its active hormonal form, 1,25(OH)2D3, via a two-step hydroxylation reaction, which occurs first in the liver and then in the kidneys. Because the kidneys are involved in the formation of the active form of vitamin D3, vitamin D3 deficiency is seen in CKD patients with progressive glomerular function decline [11]. More recently, vitamin D deficiency has been associated with numerous events and conditions in the general population such as falls, fractures, diabetes, autoimmune diseases, cardiovascular and renal diseases, tuberculosis, depression, neurodegenerative diseases, and cancer [13,14]. Vitamin D deficiency is frequently observed in patients with chronic kidney disease (CKD), particularly those undergoing maintenance haemodialysis (HD). Although altered renal vitamin D metabolism is a major contributor to vitamin D abnormalities in these patients, the effect of an individual haemodialysis session on circulating vitamin D levels remains insufficiently understood. Haemodialysis induces changes in intravascular fluid volume and blood composition, which may influence measured serum vitamin D concentrations. Considering the important role of vitamin D in calcium and phosphate homeostasis, bone health, and the pathophysiology of CKD-related mineral and bone disorders, understanding these short-term changes may have clinical relevance. Therefore, the present study aims to evaluate and compare serum 25-hydroxyvitamin D levels before and after haemodialysis in patients with CKD to determine whether a significant change occurs during the dialysis session and to assess the effect of vitamin D level on the immediate outcome after haemodialysis within 7 days.

Materials and Methods

This Hospital-based prospective observational study was conducted in the Department of Medicine, Silchar Medical College and Hospital from 1st June 2020 to 30th December 2021 on 100 CKD patients who were on maintenance Haemodialysis. Patients who were unwilling to participate, patients less than 18 years of age, patients on drugs like OCPs, Phenobarbital, phenytoin, isoniazid, rifampicin, Sevelamer, glucocorticoids, sodium valproate, gabapentin, carbamazepine, calcitonin or on Vitamin D supplementation, Post renal transplant patients, Pregnant women, diagnosed cases of rickets and osteomalacia, patients with protein losing enteropathy, chronic liver disease, parathyroid disorders or Cushing's disease were excluded from the study. Informed written consent were taken from all patients. Detail history and relevant physical examination was done. The diagnosis of diabetic nephropathy was made when there was a long history of DM with diabetic retinopathy with slowly progressive oedema, albuminuria and hypertension. Hypertensive nephropathy was diagnosed with history of hypertension and evidence of hypertensive retinopathy on fundoscopy. ADPKD (Adult polycystic kidney disease) and obstructive uropathy were diagnosed based on Ultrasonography (USG) findings. The renal biopsy diagnosed cases were included where available. 5 ml of venous blood were drawn from median cubital vein 24 hour before the scheduled time of initiating 1st HD session and 24 hours after completion of the same. The Vitamin D test was performed using the VITROS 25-OH Vitamin D Total reagent pack and the VITROS 25-OH Vitamin D Total calibrators on the VITROS ECi/ECiQ Immunodiagnostic System and the VITROS 5600 Integrated System using Intellicheck Technology.

Statistical Analysis: Categorical data were expressed as frequencies and percentages, while continuous data were presented as mean ± standard deviation (SD). The Student's t-test was used to compare continuous variables, and the chi-square (χ^2) test was used to assess associations between categorical variables. A p-value <0.05 was considered statistically significant. Statistical analyses and graphical representations were performed using Microsoft Excel 2007 and SPSS version 24.0.

Results

The study is a single centered hospital based prospective observational study of 100 patients with CKD on haemodialysis. In this study, there were 54 male and 46 female participants. Most of the study subjects belonged to the age group of 41-60 years comprising of 46 study subjects out of which 20 patients (43.5%) were male and 26 patients (56.5%) were females (Table 1) with overall mean age of male study subject was 51.76±14.88 years whereas the mean age of the female study subject was 52.74±12.84 years. On etiological distribution, most of the study population had hypertension (11%), Diabetes Mellitus (20%) or both (30%), 10% had ADPKD, 8% had SLE, 7% had obstructive uropathy (OU) and in 14% of the subjects the cause was found to be undetermined (U).

Table 1: Age and Sex distribution among study subjects

Age (In Years)	Sex		Total	p Value
	Male(M)	Female(F)		
≤20	0	1	1	0.08
21-40	16(72.7 %)	16(27.3%)	22	
41-60	20(43.5%)	26(56.5%)	46	
>60	18(58.06%)	13(41.94%)	31	
Total	54	46	100	

On echocardiographic evaluation, LVH was the most common abnormality (42%), followed by diastolic dysfunction (18%), systolic dysfunction (17%), CAD (12%), and pericardial effusion (4%), while 7% of subjects had normal findings. Majority of the study subjects presented in stage V CKD (94%) and rest were in stage IV (6%). Out of the total population, 81 subjects were discharged and 19 subjects expired during the hospital stay, out of expired patients 57.9% (11 subjects) had Diabetes and Hypertension, 4 subjects (21.05%) had only Diabetes Mellitus (Table 2).

Table 2: Distribution of outcome of study subjects based on aetiology

Aetiology	Outcome		Total	P Value
	Discharged(D)	Expired(E)		
DM+HTN	19	11	30	0.106
DM	16	4	20	
HTN	10	1	11	
SLE	7	1	8	
ADPKD	9	1	10	
OU	7	0	7	
UN	13	1	14	
TOTAL	81	19	100	

Vitamin D deficiency was observed in 69% of the study population, while 24% had insufficient levels and only 7% had sufficient vitamin D levels. In the present study, vitamin D deficiency was most prevalent among subjects aged 41–60 years (46.4%) (Table-3). Among the 69 subjects who were vitamin D deficient, 35 were male (50.7%) and 34 female (49.3%) (Figure 1). Vitamin D insufficiency was also most common in the 41–60-year age group (54.17%), with equal proportions of males and females; overall, males had significantly lower vitamin D levels than females (p = 0.04).

Table 3: Distribution of serum Vitamin D based on Age

Age (In Years)	Vitamin D (ng/ml)			Total	p Value
	≤20	>20-30	>30		
≤20	1	0	0	1	0.301
21-40	15	6	1	22	
41-60	32	13	1	46	
>60	21	5	5	31	
Total	69	24	7	100	

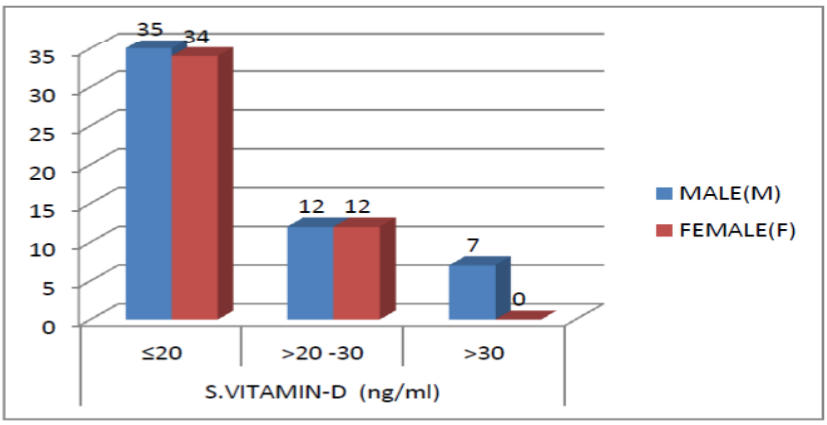


Figure 1: Distribution of S. Vitamin D based on gender

It was observed that among the study population, more subjects i.e., 79.7% with deficient vitamin D levels had increased incidence of vascular events compared to the insufficient group. Among the subjects having serum vitamin D levels in the insufficient range, 41.6% (10 out of 24 subjects) had vascular events (Table 4). Hence a significant number of subjects who had deficient levels of serum Vitamin D had more CVS events (p value<0.0001).

Table 4: Serum Vitamin D level among study subject based on vascular events

CVS Events	S. Vitamin D (ng/ml)			Total	P Value
	≤20	>20-30	>30		
Present(Y)	55	10	0	65	**<0.0001**
Absent(N)	14	14	7	35	
Total	69	24	7	100	

All subjects with vitamin D deficiency (69 subjects) had stage V CKD, while 20 subjects (83.4%) with vitamin D insufficiency had stage V CKD and 4 subjects (16.6%) had stage IV CKD, indicating a highly significant association between vitamin D deficiency and stage V CKD (p < 0.0001)(Table-5).

Table 5: Serum Vitamin D level in various stages of CKD

Stages Of CKD	S. Vitamin D (ng/ml)			Total	p Value
	≤20	>20-30	>30		
Stage I	0	0	0	0	**<0.0001**
Stage II	0	0	0	0	
Stage IIIA	0	0	0	0	
Stage IIIB	0	0	0	0	
Stage IV	0	4	2	6	
Stage V	69	20	5	94	
Total	69	24	7	100	

The mean serum vitamin D level 24 hour before HD was 19.015 ng/ml and serum vitamin D level 24 hour after HD was 15.32 ng/ml with increase in patients with Vitamin D deficiency from 69 to 75, 24 hrs after HD (Table 6). There was significant reduction of mean serum vitamin D level after 24 hour of haemodialysis with p value <0.0001. Out of the 19 expired patients 18 subjects were vitamin D deficient whereas only 1 subject expired from the insufficient group (Figure 2).

Table 6: Mean serum vitamin D levels 24 hour before and after haemodialysis

Serum Vitamin D Before HD(ng/ml) [Mean±SD]	Serum Vitamin D After HD(ng/ml) [Mean±SD]	P Value
19.015±6.905	15.320±7.134	**<0.0001**

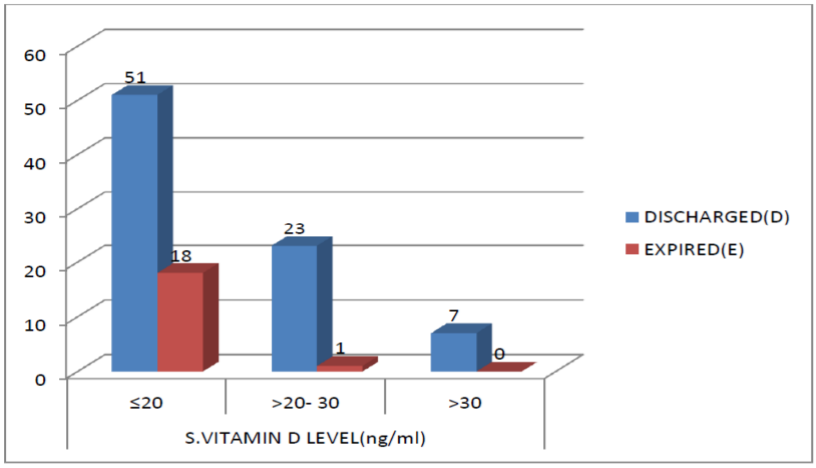


Figure 2: Serum vitamin D levels among the study subjects and its impact over outcome

Discussion

The present study was conducted on 100 CKD patients on maintenance haemodialysis, where 54% were male and 46% were female. Most of the study subjects belonged to 41-60 age group (Mean age Male: 51.76±14.88 & Female: 52.74±12.84 years). Among the aetiology, 30% of the study population

had both diabetes and hypertension, Diabetes Mellitus and hypertension alone accounted for 20% and 11% respectively. Similar results were found in C. Ramann et al study where out of 50 cases of CKD, 44% were due to the combined effect of both HTN and DM and the prevalence of diabetic nephropathy and hypertensive nephropathy among the study population were 18% and 16% respectively [15]. In this study, 94% of the study subjects were in Stage V CKD and only 6% in stage IV CKD. In studies conducted by Neha Sundhir et al [16] and Vidyasagar Sarpal [17], most of the study subjects presented in Stage V CKD (63% and 37% respectively).

In the present study, 69% of subjects had vitamin D deficiency, 24% had insufficiency, and 7% had sufficient levels, with no cases of vitamin D intoxication. Similar findings were reported by Bhan et al. [18], who observed vitamin D levels below 20 ng/mL in 57% of patients on chronic haemodialysis, and González A.E. et al. [19], who reported vitamin D deficiency in the majority of chronic haemodialysis patients (14% with severe Vitamin D deficient).

Cardiovascular events or ASCVD were observed in 79.7% of patients with vitamin D deficiency and 41.6% of those with insufficiency, showing a statistically significant association ($p < 0.0001$). Similarly, Wang T. J. et al. [20] reported a significantly higher risk of cardiovascular events among patients with vitamin D levels below 15 ng/mL during a 7-year follow-up. Drechsler C. et al. [21] also found that vitamin D deficiency was associated with a threefold higher risk of sudden cardiac death over a mean follow-up of 3.6 years. These findings suggest that vitamin D deficiency may be associated with increased cardiovascular risk through mechanisms involving insulin resistance, ventricular hypertrophy, atherosclerosis, and vascular calcification. In the present study, mean serum vitamin D levels significantly decreased after haemodialysis (19.08 ± 6.905 vs. 15.32 ± 7.134 ng/mL; $p < 0.0001$), with deficiency increasing from 69% to 75%. Similarly, Mittal SP et al. [22] reported an increase in vitamin D deficiency from 58.73% to 85.71% after haemodialysis, while Lee S. et al. [23] observed a decrease in mean vitamin D levels from 13.9 ± 7.2 to 10.6 ± 6.3 ng/mL.

Among the 19 expired patients in the study group, 18 of them (94.7%) had vitamin D deficiency. In other studies, conducted by Mayanne M et al. [24] and Wolf M et al. [25] also found similar results in their study i.e., vitamin D deficiency is associated with higher mortality in patients of HD.

Conclusion

Serum vitamin D levels were significantly lower in advanced stages of CKD and decreased further after haemodialysis. Vitamin D deficiency was significantly associated with increased cardiovascular morbidity and adverse outcomes, suggesting that serum vitamin D may serve as a potential prognostic marker for short-term mortality in patients with CKD.

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