

# Vitamin D Status in Patients with Renal Disorders at a Tertiary Care Hospital in Coimbatore, Tamil Nadu, India: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Patients with renal disorders often have insufficient levels of vitamin D. One of the key enzymes involved in activating vitamin D, 1- $\alpha$  hydroxylase, is present in the kidneys. As a result, patients with kidney diseases are more susceptible to developing vitamin D deficiency, which can increase mortality and morbidity in these patients. Additionally, variations in lifestyle and culture can contribute to geographical differences in baseline serum vitamin D levels.

**Aim:** To evaluate and compare serum vitamin D levels in patients with various renal disorders.

**Materials and Methods:** This retrospective cross-sectional study was conducted in the Department of Biochemistry at the KMCH Institute of Health Sciences and Research Centre in Coimbatore, Tamil Nadu, India from August 2018 to August 2019. Data from 269 patients were collected from the Medical Records Department (MRD) using a predefined data collection tool. All patients with renal disease, regardless of disease severity, who had serum vitamin D levels measured during the study period were included. The collected data included age, gender, height, weight, Body Mass Index (BMI), dietary history, diagnosis, serum vitamin D<sub>3</sub> levels,

and serum creatinine levels. The data were statistically analysed using Analysis of Variance (ANOVA) and Pearson's correlation coefficient.

**Results:** Among the study participants, 148 were males and 121 were females, with a mean age of 54.12 $\pm$ 17.43 years. The mean vitamin D<sub>3</sub> level in the study population was 20.8 ng/mL. The mean serum creatinine and urea levels were 2.2 $\pm$ 1.1 mg/dL and 63.2 $\pm$ 42.1 mg/dL, respectively. The mean estimated Glomerular Filtration Rate (eGFR) was 41.4 $\pm$ 25.34 mL/min/1.73 m<sup>2</sup>. The mean serum calcium, phosphate, and uric acid levels were 5.8 $\pm$ 2.65 mg/dL, 2.16 $\pm$ 0.87 mg/dL, and 3.6 $\pm$ 2.3 mg/dL, respectively. One-way ANOVA showed no significant difference in serum vitamin D<sub>3</sub> levels among patients with different renal diseases (F=0.473, p=0.854). Pearson's correlation analysis revealed no significant correlation between serum vitamin D<sub>3</sub> levels and any other parameters.

**Conclusion:** In present study, only 23% of patients had vitamin D levels within the normal reference range, 22% had insufficient vitamin D levels, and 55% had vitamin D deficiency. No significant difference in vitamin D levels was observed among patients with different renal diseases.

**Keywords:** Chronic kidney disease, Lifestyle variation, Nephrotic syndrome, Serum creatinine

## INTRODUCTION

Vitamin D, a fat-soluble prohormone, controls the levels of calcium and phosphate in the body [1]. The two primary forms of vitamin D are ergocalciferol (Vitamin D<sub>2</sub>) and cholecalciferol (Vitamin D<sub>3</sub>). When sunlight interacts with the precursor 7-dehydrocholesterol in the skin, vitamin D<sub>3</sub> is produced [2]. The liver's 25- $\alpha$  hydroxylase enzyme converts 7-dehydrocholesterol into 25(OH) vitamin D<sub>3</sub> by hydroxylating it. The kidney produces 1,25-dihydroxy Vitamin D<sub>3</sub> (1,25(OH)<sub>2</sub>D<sub>3</sub>) through the action of the enzyme 1 $\alpha$  hydroxylase [3]. The active form of vitamin D is 1,25-dihydroxyvitamin D, while the significant circulating form of vitamin D is 25(OH)D. Reduced renal mass will result in less 1- $\alpha$  hydroxylase available for the synthesis of active vitamin D metabolites, leading to lower 1,25-dihydroxyvitamin D levels in individuals with chronic renal diseases [4]. Decreased levels of vitamin D are associated with increased morbidity and mortality in patients with Chronic Kidney Disease (CKD) undergoing haemodialysis [5]. The major circulating form of vitamin D is 25-hydroxy vitamin D. Vitamin D insufficiency is defined as 25-hydroxy vitamin D levels between 15-30 ng/mL, while vitamin D deficiency is defined as 25-hydroxy vitamin D levels below 15 ng/mL [6].

Patients with renal problems frequently lack sufficient amounts of vitamin D [7]. In a study by Diniz HF et al., it was found that 21.5% of patients with CKD had vitamin D insufficiency [8]. Satirapoj B et al.,

and Rozita M et al., observed in their studies that serum vitamin D levels were lower in patients with CKD and varied according to the severity of the renal disease [9,10].

The present study was designed to evaluate the levels of serum vitamin D in patients with renal disorders and to study any association with alterations in other biochemical parameters, if present, in a tertiary care centre in South India. This was done due to the possible persistence of geographical variation in serum vitamin D levels [7]. In the available literature, vitamin D was mainly measured in patients with CKD [8-10]. Therefore, current study was aimed to assess vitamin D levels in patients with all types of renal disorders.

## MATERIALS AND METHODS

This retrospective cross-sectional study was conducted in the Department of Biochemistry at KMCH Institute of Health Sciences and Research, a tertiary care hospital in Coimbatore, Tamil Nadu, India, for a period of one year between August 2018 and August 2019. The study was approved by the Institutional Human Ethics Committee (EC/AP/640/10/2018), and data were collected from the Medical Records Department (MRD) of the Institution.

**Inclusion criteria:** All patients with renal disease, regardless of disease severity, who had serum vitamin D levels measured during the study period were included.

**Exclusion criteria:** Patients with CKD who had undergone renal transplantation and those on vitamin D supplementation were excluded from the study.

**Sample size calculation:** The sample size for the study was calculated to be 134. In the study by Diniz HF et al., [8], 73% of the study population had decreased vitamin D levels. The sample size was calculated using the formula:

$$n = (z_{\alpha/2})^2 \times pq / d^2$$

where n=sample size, p=percentage, q=1-p, d=desired degree of precision, and z=standard normal value at 95% confidence interval (Z score=1.96). Given p=73% and d=7.5%, the calculated sample size was found to be 134. Convenient sampling was done, and data from 269 patients were collected based on the inclusion and exclusion criteria.

## Study Procedure

Data were collected from the MRD using a predefined data collection tool. The collected data included age, gender, height, weight, diagnosis, serum vitamin D<sub>3</sub> levels, serum creatinine levels, serum uric acid, serum urea, calcium, phosphorus, estimated glomerular filtration rate (eGFR) and Body Mass Index (BMI). Based on the BMI, the patients were classified as underweight, normal weight, overweight, Class-1 obese, and Class-2 obese [11]. Serum Vitamin D<sub>3</sub> levels were estimated using an electrochemiluminescence assay in the Roche Cobas e411 immunoanalyzer. Serum creatinine was estimated using the modified Jaffe's method in the Roche Cobas 6000 analyser. The reference intervals for these parameters are assessed [Table/Fig-1].

Parameters	Method	Reference ranges of parameters studied
Serum creatinine	Modified Jaffe's method	0.7-1.4 mg/dL (males) 0.6-1.2 mg/dL (females)
Serum vitamin D <sub>3</sub>	Electrochemiluminescence	< 20 ng/mL (deficiency) 20-29 ng/mL (insufficiency) 30-100 ng/mL (sufficient) >100 ng/mL (potential toxicity)
Serum urea	Urease- glutamate dehydrogenase method	15-40 mg/dL
Serum uric acid	Uricase method	Males:3.1-7 mg/dL Females:2.5-5.6 mg/dL
Serum calcium	5-nitro-5'-methyl-(1,2-bis (o-aminophenoxy) ethan-N,N,N',N'-tetraacetic acid (NM-BAPTA) method	9-11 mg/dL
Serum phosphate	Molybdate UV/ Phosphomolybdate complex method	2.5-4.3 mg/dL
eGFR	Chronic Kidney Disease- Epidemiological Study equation (CKD-EPI equation)	GFR >90 without risk factor- Stage 0 CKD GFR >90 with demonstrated kidney damage-Stage 1 CKD GFR- 60-89 Stage 2 CKD GFR- 30-59 Stage 3 CKD GFR-15-29 Stage 4 CKD GFR <15 Stage 5 CKD

[Table/Fig-1]: Reference ranges.

## STATISTICAL ANALYSIS

The data were statistically analysed using Statistical Package for the Social Sciences (SPSS) software version 28.0. The distribution of categorical variables is expressed in terms of mean and Standard Deviation (SD), while the distribution of non categorical variables is expressed in terms of percentages and frequencies. Comparison of means among patients with renal diseases was performed using ANOVA. The correlation between serum vitamin D levels and other parameters was determined using the Pearson's correlation coefficient.

## RESULTS

In the present study, out of 269 study participants, 148 were males and 121 were females. The age range of the study population

was 14 to 75 years, with a mean age of 54.12±17.43 years. In the present study, the majority of patients (109, 40.5%) were in the normal weight category, while the least number of subjects (10, 3.7%) were in Class-1 obesity. The mean vitamin D<sub>3</sub> level in the study population was 20.8 ng/mL. Among the study population, 148 (55%) had vitamin D deficiency, and 59 (22%) had vitamin D insufficiency [Table/Fig-2].

BMI classification (kg/m <sup>2</sup> )	Frequency	Percentage (%)
Underweight (<19)	98	36.4
Normal Weight (19-24.9)	109	40.5
Overweight (25-29.9)	41	15.2
Class-1 Obesity (30-34.9)	10	3.7
Class-2 Obesity (>35)	11	4.2
Vitamin D (ng/mL)	Frequency	Percentage (%)
Normal (>30)	62	23.0
Insufficiency (20-29.9)	59	22.0
Deficiency (<20)	148	55.0
<b>Total</b>	<b>269</b>	<b>100.0</b>

[Table/Fig-2]: Distribution of study population according to BMI classification and Vitamin D level.

The mean serum creatinine and urea levels of the population were 2.25±1.1 mg/dL and 63.2±42.1 mg/dL, respectively. The mean eGFR of the population was 41.44±25.34 mL/min/1.73 m<sup>2</sup>. The mean serum calcium, phosphate, and uric acid levels were 5.88±2.65 mg/dL, 2.16±0.87 mg/dL, and 3.69±2.3 mg/dL, respectively [Table/Fig-3].

Parameters	Mean±SD
Serum urea	63.2±42.1 mg/dL
Serum creatinine	2.25±1.1 mg/dL
Serum uric acid	3.69±2.3 mg/dL
Serum calcium	5.88±2.65 mg/dL
Serum phosphate	2.16±0.87 mg/dL
eGFR	41.44±25.34 mL/min/1.73 m <sup>2</sup>

[Table/Fig-3]: Mean serum levels of different parameters studied.

There was a positive correlation between the following serum parameters: urea and creatinine levels, creatinine and phosphate levels, urea and phosphate levels, calcium and phosphate levels. There was a negative correlation between serum creatinine and eGFR, serum urea and eGFR, and serum phosphate and eGFR. However, there was no significant correlation between serum vitamin D<sub>3</sub> levels and any other parameters, as shown by Pearson's correlation [Table/Fig-4]. In the present study, the majority of the study population (137, 50.9%) had CKD, followed by 51 (19%) with acute kidney injury and 40 (14.9%) with nephrotic syndrome [Table/Fig-5].

Among the patients with CKD, 73 (53.3%) had vitamin D deficiency, and among the patients with pyelonephritis, 10 (83.4%) had vitamin D deficiency. One (1%) of the patients with renal stones and 10 (83.4%) of the patients with pyelonephritis had vitamin D deficiency [Table/Fig-6]. There was no significant difference in serum vitamin D<sub>3</sub> levels among patients with different renal diseases, as shown by one-way ANOVA (F=0.473, p=0.854).

## DISCUSSION

A hospital-based retrospective cross-sectional study was conducted to determine the prevalence of vitamin D insufficiency and deficiency among patients with renal disorders. In present study, it was found that 66% of individuals in the age group of 55-65 years had vitamin D deficiency. This finding is consistent with a study by Kim C et al., where 58% of the population above 50 years of age had vitamin D deficiency [12]. This may be attributed to the higher prevalence of CKD in this age group, as diabetes and hypertension, which are major causes of CKD, often manifest around the age of 60 years.

Parameters		Correlations						
		Vitamin D	Creatinine	Urea	Calcium	Phosphate	Uric Acid	eGFR
Vitamin D	Pearson's correlation	1	-0.044	-0.066	-0.027	-0.057	-0.046	0.005
	Sig. (2-tailed)		0.470	0.282	0.664	0.349	0.449	0.936
	N	269	268 <sup>#</sup>	269	269	269	269	269
Creatinine	Pearson's correlation	-0.044	1	0.779**	0.128*	0.456**	0.084	-0.454**
	Sig. (2-tailed)	0.470		<0.001	0.037	<0.001	0.172	0.000
	N	268 <sup>#</sup>	268 <sup>#</sup>	268 <sup>#</sup>	268 <sup>#</sup>	268 <sup>#</sup>	268 <sup>#</sup>	268 <sup>#</sup>
Urea	Pearson's correlation	-0.066	0.779**	1	0.131*	0.356**	0.121*	-0.404**
	Sig. (2-tailed)	0.282	<0.001		0.032	<0.001	0.047	0.000
	N	269	268 <sup>#</sup>	269	269	269	269	269
Calcium	Pearson's correlation	-0.027	0.128*	0.131*	1	0.367**	0.065	-0.108
	Sig. (2-tailed)	0.664	0.037	0.032		<0.001	0.289	0.076
	N	269	268 <sup>#</sup>	269	269	269	269	269
Phosphate	Pearson's correlation	-0.057	0.456**	0.356**	0.367**	1	0.108	-0.250**
	Sig. (2-tailed)	0.349	<0.001	<0.001	<0.001		0.078	<0.001
	N	269	268 <sup>#</sup>	269	269	269	269	269
Uric acid	Pearson's correlation	-0.046	0.084	0.121*	0.065	0.108	1	-0.081
	Sig. (2-tailed)	0.449	0.172	0.047	0.289	0.078		0.188
	N	269	268 <sup>#</sup>	269	269	269	269	269
eGFR	Pearson's correlation	0.005	-0.454**	-0.404**	-0.108	-0.250**	-0.081	1
	Sig. (2-tailed)	0.936	<0.001	<0.001	<0.001	<0.001	0.188	
	N	269	268 <sup>#</sup>	269	269	269	269	269

**[Table/Fig-4]:** Correlation between serum Vitamin D levels and other parameters.

\*\*Correlation is significant at the 0.01 level (2-tailed)

\*Correlation is significant at the 0.05 level (2-tailed)

<sup>#</sup>missing data

Type of renal disease	Frequency	Percentage (%)
Chronic kidney disease	137	50.9
Glomerulonephritis	3	1
Acute kidney injury	51	19.0
Pyelonephritis	12	4.5
Renal calculus	5	1.9
Nephrotic syndrome	40	14.9
Others*	21	7.8
Total	269	100.0

**[Table/Fig-5]:** Distribution of study population according to their diagnosis (N=269).

\*Others- Polycystic kidney disease, Horse-shoe kidney, Systemic lupus erythematosus related kidney disease, Radiation nephropathy, Renal cancer, Renal tuberculosis

Diagnosis	Vitamin D <sub>3</sub> classification			p-value
	Normal (>30)	Insufficiency (20-29.0)	Deficiency (<20)	
Chronic kidney disease	31 (22.62%)	33 (24.08%)	73 (53.3%)	<0.001
Glomerulonephritis	0 0	0 0	3 (100%)	<0.001
Acute kidney injury	14 (27.45%)	12 (23.52%)	25 (49.03%)	<0.001
Pyelonephritis	1 (8.3%)	1 (8.3%)	10 (83.4%)	0.014
Renal calculus	1 (20%)	3 (60%)	1 (20%)	<0.001
Nephrotic syndrome	10 (25%)	6 (15%)	24 (60%)	<0.001
Others	5 (23.80%)	4 (19.04%)	12 (57.16%)	<0.001

**[Table/Fig-6]:** Distribution of study population according to their diagnosis and vitamin D levels.

p-value was calculated using student's t-test

Vitamin D deficiency was also observed in 54% of the population in the age group of 5-15 years. Aparna P et al., found that 53% of children in the age group of 5-15 years had vitamin D deficiency, which may be attributed to factors such as increased indoor time, pollution, and sunscreen usage [13]. In present study, among patients with renal disorders, 55% had vitamin D deficiency. Satirapoj B et al.,

also reported that 50% of patients with renal disorders had vitamin D deficiency [9]. The prevalence of vitamin D deficiency in these patients can vary depending on factors such as the duration and type of renal disorder, genetic susceptibility, geographic location, lifestyle, and presence of other risk factors.

In terms of BMI, 40% of the study population fell within the normal range. 36% were underweight, 15% were overweight, and less than 5% were obese. According to a study by Lagunova Z et al., there is an inverse relationship between BMI and vitamin D levels, with higher BMI associated with lower vitamin D levels [14]. This is likely due to the sequestration of vitamin D in excess adipose tissue in obese patients [12].

The spectrum of renal disorders observed in our study included CKD, glomerulonephritis, acute kidney injury, pyelonephritis, renal calculus, and nephrotic syndrome. Among these, 85% of patients with pyelonephritis had vitamin D deficiency. A study by Shalaby SA et al., found that decreased vitamin D levels are associated with an increased frequency of urinary tract infections and progression to pyelonephritis in children [15]. Nseir W et al., also reported a similar association between vitamin D deficiency and pyelonephritis in premenopausal women [16]. Therefore, the higher prevalence of vitamin D deficiency observed in patients with pyelonephritis in our study may be a cause rather than an outcome.

In present study, it was found that 60% of patients with nephrotic syndrome had vitamin D deficiency. Illalu S et al., conducted a study to determine the prevalence of vitamin D deficiency in patients with nephrotic syndrome and found that 47% of them had deficiency [17]. Nephrotic syndrome is characterised by the loss of proteins in urine due to the effacement of podocytes in the glomerulus. Since vitamin D is transported in the blood by binding to vitamin D binding protein, which is also lost in urine, it leads to vitamin D deficiency. This explains the observed vitamin D deficiency in 60% of patients with nephrotic syndrome in our study [17].

In our study, 53% of patients with CKD were found to have vitamin D deficiency. Rozita M et al., also found that 40% of patients with CKD had vitamin D deficiency [10]. The active form of vitamin D, 1,25-dihydroxy cholecalciferol, is produced by the action of 1 $\alpha$  hydroxylase present in the kidney. In chronic renal failure, there is a reduction in the quantity of available 1- $\alpha$  hydroxylase due to decreased renal mass, leading to decreased 1,25-dihydroxy cholecalciferol production [18].

Metabolic and hormonal changes in CKD result in increased transcription of 24,25 hydroxylase and fibroblast growth factor-23, as well as decreased transcription of 1- $\alpha$  hydroxylase and megalin. Megalin, a cell surface receptor in the proximal convoluted tubule, is responsible for the reabsorption of vitamin D binding protein along with vitamin D [19,20]. The alteration in the transcription status of these proteins manifests as vitamin D deficiency in patients with CKD [18]. A comparison of present study with others is shown in [Table/Fig-7] [8-10,17].

Author	Study location/ year of the study	Sample size	Comparison with the current study
Diniz HF et al., [8]	Brazil/2012	125	52% of the patients with CKD had vitamin D insufficiency, 21.5% had vitamin D deficiency.
Satirapoj B et al., [9]	Thailand/2013	2895	Mean vitamin D levels were significantly lower according to the severity of the renal disease in patients with CKD.
Illalu S et al., [17]	Karnataka/2019	43	47.05 % of the paediatric nephrotic syndrome patients had vitamin D deficiency and 32.35% had vitamin D insufficiency.
Rozita M et al., [10]	Malaysia/2013	50	Vitamin D deficiency more prevalent among patients with CKD when compared to healthy controls.

[Table/Fig-7]: Comparison of the findings of the current study with others [8-10,17].

## Limitation(s)

This is a single centre retrospective study; therefore, the results cannot be generalised to the entire population. Multi centre, prospective studies are required to confirm the findings.

## CONCLUSION(S)

More than half of the patients with renal diseases had vitamin D deficiency. Regardless of the underlying cause, vitamin D levels were found to be decreased in the majority of the study population. There was no significant correlation between serum vitamin D<sub>3</sub> levels and other parameters, including serum urea, creatinine, uric acid, and eGFR. Therefore, further large population-based studies are

recommended to determine whether routine monitoring of vitamin D status and its supplementation are necessary to improve the quality of life in these patients.

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