

# 25 Hydroxy Vitamin D Insufficiency and Deficiency in Stages of Chronic Kidney Disease Patients in Nepal

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**Abstract:** *Background:* Vitamin D is a sunshine vitamin. Vitamin D insufficiency and deficiency in chronic kidney disease (CKD) patients and also in normal renal functions in tropical regions<sup>3,4,5</sup>. The aim of this study was to determine the relation between the 25 (OH) vitamin D insufficiency and deficiency with the Nepalese patients of chronic kidney disease. *Materials and Methods:* A cross sectional descriptive study was designed from April to September 2018. Total 216 Chronic Kidney Patients were involved in this study. After taking consent from the patients and hospitals, we were collected blood samples from the patients and were analysed the Variables like 25 OH Vitamin D, Calcium, Phosphorus, Urea, Creatinine and Albumin. Data were analysed by using SPSS for Windows for different variables. *Result:* 216 chronic kidney Disease (CKD) patients were enrolled, 42% male and 58% female with mean age was 48.21± 15.45 and mean 25 (OH) Vitamin D was 20.54± 12.12. 25 (OH) Vitamin D deficiency (<10 ng/ml) and Insufficiency (10-30 ng/ml) were diagnosed as 18% and 66% of CKD patients. Out of 216 CKD patients, 10.2%, 21.3%, 25.8%, 13%, 13% and 16.7% patients were in CKD stage 1, 2, 3a, 3b, 4 and 5 respectively. CKD stages were significantly correlate with Sex, eGFR, Corrected Calcium, Phosphorus, Creatinine, Blood Urea Nitrogen (BUN) P<0.0001 but not with 25 (OH) Vitamin D (P>0.05). 25 (OH) Vitamin D levels were not correlated with Age and sex (P>0.05). Vitamin D deficiency and Insufficiency were also insignificant differences in CKD stages. (P>0.05). Phosphorous is negative correlation to 25 (OH) Vitamin D (r value -0.025 and P >0.927), whereas corrected Calcium is significant (r value 0.156 and P 0.023). *Conclusion:* Result of our present study indicated that vitamin D levels below the recommended values observed in stages of CKD

**Keywords:** Chronic Kidney Disease (CKD), 25 (OH) Vitamin D, Vitamin D deficiency

## 1. Background

Vitamin D is mainly taken from dietary sources or synthesised endogenously during the UVB light exposure to skin and then formation of 25 hydroxy Vitamin D in the liver. 1  $\alpha$ -hydroxylation change 25 hydroxy Vitamin D to active form of vitamin D known as calcitriol (1, 25 (OH) 2D3)<sup>[1]</sup>. Calcitriol promotes the intestinal and distal tubular absorption of calcium and by negative feedback on the parathyroid gland, lowering the Parathyroid hormone (PTH)<sup>[2]</sup>.

25 hydroxy vitamin D levels are negative relation with patients with chronic kidney disease (CKD)<sup>[3]</sup> and in those without this disease<sup>[4]</sup>. Deficiency and Insufficiency of vitamin D are widely in tropical regions with chronic kidney disease and in normal kidney functions<sup>[5]</sup>. 25 (OH) D deficiency are strongly associated with albuminuria but not impaired eGFR<sup>[6]</sup>.

As the production of 25 (OH) vitamin D is greater in high sun exposure, Nepal have a tropical and subtropical regions and Nepalese population with CKD are more likely to have high sun exposure; however no study in Nepalese population

has been done to prove this assertion. Therefore purpose of this investigation was to determine the correlation between 25 OH vitamin D and chronic kidney disease in Nepalese population.

## 2. Methods

A cross sectional multicentre study enrolled two hundred and sixteen chronic kidney disease patients from National Kidney centre, Sumeru Hospital and Golden Hospital from April to September 2018 in Nepal. This study was approved by Nepal Health Research Council (NHRC) Nepal and all centres.

Convenience sampling technique was adopted. We excluded the patients taken vitamin D supplement before being enrolled, acute kidney injury, history of thyroidectomy, malignancy and refusing written ethical consent. Prepared questionnaires were used to obtain demographic characteristics.

All patients were explained the importance of examinations of variables and were asked to sign the written

**Table 1:** Characteristics of Patients By chronic kidney Disease (CKD) stages

Numbers of Report	CKD stages						P value
	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 4	Stage 5	
216	(N=22)	(N=46)	(N=56)	(N=28)	(N= 28)	(N=36)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Male (N, %)	0(0.0%)	13(28.3%)	32(57.1%)	11(39.3%)	12(42.9%)	22(61.1%)	<i>P</i> < 0.001
Female (N, %)	22(100%)	33(71.7%)	24(42.9%)	17(60.7%)	16(57.1%)	14(38.9%)	
eGFR(ml/min/1.73m <sup>2</sup> )	99.36±33.39	85.76±27.49	57.91±12.96	39.14±4.57	21.25±3.45	7.81±3.33	<i>P</i> < 0.0001
Corrected Calcium mmol/L	2.30±0.20	2.30±0.21	2.30±0.20	2.26±0.16	2.21±0.23	2.19±0.20	<i>P</i> < 0.05
Phosphorus (mg/dL)	4.10±0.70	4.00±0.80	4.30±0.90	4.20±0.80	4.10±1.20	5.20±1.60	<i>P</i> < 0.0001
Albumin (g/dL)	4.10±0.40	4.10±0.60	4.10±0.30	4.10±0.40	3.80±0.50	3.90±0.60	<i>P</i> < 0.0001
BUN (mg/dL)	10.48±3.6	12.13±4.1	18.16±6.8	21.67±6.2	36.43±11.7	55.66±23.43	<i>P</i> < 0.0001
Creatinine (mg/dL)	0.70±0.11	0.91±0.15	1.29±0.19	1.58±0.20	2.81±0.70	8.04±4.00	<i>P</i> < 0.0001
25 (OH) Vitamin D (ng/ml)	21.54±11.95	21.91±11.64	22.69±10.94	23.36±14.94	15.36±9.26	17.15±12.30	<i>P</i> > 0.05

consent and taken blood samples and were analysed by cobass ECL analyser. Corrected calcium was calculated by using formula: corrected calcium (mmol/L) = Calcium measured (mmol/L) + 0.02 [40-albumin (g/L)]. Estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease equation, which includes four variables:  $eGFR (ml/min \text{ per } 1.73 \text{ m}^2) = 175 \times (P_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$ . Chronic kidney disease (CKD) classified as CKD stage 1 (eGFR = > 90 ml/min per 1.73 m<sup>2</sup>), CKD stage 2 (eGFR = 60 to 90 ml/min per 1.73 m<sup>2</sup>), stage 3a (eGFR = 45 to 59 ml/min per 1.73 m<sup>2</sup>) stage 3b (eGFR = 30 to 44 ml/min per 1.73 m<sup>2</sup>), stage 4 (eGFR = 15 to 29 ml/min per 1.73 m<sup>2</sup>) and stage 5 (eGFR = <15 ml/min per 1.73 m<sup>2</sup>). Serum analysis like Calcium, Phosphorus, Urea, Creatinine and Albumin were measured by ERBA XL 200. Serum 25-hydroxyl Vitamin D concentrations were analysed by cobass e411 ECL (electrochemiluminescence) analyser. A

25 hydroxy vitamin D deficiency was defined as less than 10ng/ml and insufficiency as 10 to 30 ng/ml.

### 3. Statistical Analysis

Created descriptive data were analysed for all variables. Results are presented as mean ± SD for continuous variables. An analysis of Variance (ANOVA) was used to compare Age, Sex, 25(OH)D level, Corrected Calcium, Creatinine, Blood Urea Nitrogen (BUN), Albumin and Phosphorus with stages of Chronic Kidney Disease (CKD) respectively.

Multivariate regression analysis was used to correlate 25(OH) vitamin D levels with corrected calcium and phosphorus. Threshold for statistical significance was set to *P* < 0.05. All statistical Analysis was completed with SPSS Ver. 16 for Windows.

**Table 2:** Vitamin D deficiency and Insufficiency by CKD stages.

25 (OH) Vitamin D		CKD stage						
		stage 1	stage 2	stage 3a	stage 3b	stage 4	stage 5	Total
<b>Deficiency</b>	Count:	3	5	6	3	10	11	38
<10 ng/mL	% within	7.90%	13.20%	15.80%	7.90%	26.30%	28.90%	100.00%
<b>Insufficiency</b>	Count:	15	34	39	19	14	21	142
10-30 ng/mL	% within	10.60%	23.90%	27.50%	13.40%	9.90%	14.80%	100.00%
<i>P value = P &gt; 0.05</i>								

### 4. Results

Patient's characteristics like Sex, Estimated glomerular filtration rate (eGFR), corrected calcium, phosphorus, albumin, Blood Urea Nitrogen (BUN), Creatinine and 25(OH) Vitamin D were demonstrated according to chronic kidney disease stages in table 1. All Nepalese two hundred sixteen patients were enrolled in this study whereas 90 (42%) male and 126 (58%) female. Mean of variables were calculated as: Patient age was 48.21 ± 15.45, Vitamin D was 20.54 ± 12.12, eGFR was 52.53 ± 35.63, Corrected Calcium was 3.08 ± 0.19, Phosphorus was 4.4 ± 1.1 Albumin was 4.03 ± 0.48. Out of 216 Chronic kidney disease (CKD) patients, 25 (OH) Vitamin D deficiency (<10 ng/ml) and Insufficiency (10-30 ng/ml) was diagnosed as 38 (18%) and 142 (66%) respectively. 22 (10.2%) patients were in CKD stage 1, 46 (21.3%) patients were in stage 2, 56 (25.8%) patients were in CKD stage 3a, 28 (13%) patients were in CKD stage 3b, 28 (13%) patients were in CKD stage 4 and 36 (16.7%) patients were in CKD stage 5. By Using ANOVA technique, CKD stages were significant with Sex, eGFR,

Corrected Calcium, Phosphorus, Creatinine, Blood Urea Nitrogen (BUN) *P* < 0.0001 but no difference observed with 25 (OH) Vitamin D (*P* > 0.05). 25 (OH) Vitamin D levels were insignificant difference in Age and sex (*P* > 0.05). 25 (OH) Vitamin D deficiency (<10 ng/ml) and Insufficiency (10-30 ng/ml) were also insignificant differences in CKD stages. (*P* > 0.05). Multivariate regression analysis was performed for dependent variable 25 (OH) Vitamin D with constant predictors corrected calcium and Phosphorus. Phosphorus is negative correlation to 25 (OH) Vitamin D (*r* value -0.025 and *P* > 0.927), whereas corrected Calcium is significant (*r* value 0.156 and *P* 0.023).

### 5. Discussion

This study revealed that despite Nepalese population live in atropical and subtropical regions, 25(OH) Vitamin D insufficiency and deficiency are common in chronic kidney disease of Nepalese patients this result is supported by the study in Brazilian population<sup>[7,8,9]</sup>. Average Serum 25(OH) Vitamin D level was 20.54 ± 12.12 in two hundred sixteen

Nepalese CKD patients. A study estimated that worldwide nearly 1 million people have deficiency of vitamin D<sup>[10]</sup>. Also a study Third National Health and Nutrition Examination Survey (NHANES III) showed that average 25(OH) Vitamin D was significant with Chronic Kidney Disease stages compare with those with normal<sup>[11]</sup>. However our output showed insignificant difference of 25(OH) Vitamin D with CKD stages. Beside low 25(OH) Vitamin D were associated with corrected calcium. A study showed > 80% having low 25(OH) Vitamin D and progressive vitamin deficiency deterioration from stage 3 to stage 5<sup>[19,20]</sup>. Further high prevalence of 25(OH) Vitamin D deficiency and insufficiency in this study according to study<sup>[12, 13]</sup>. In Nepalese CKD patients, our study showed serum 25(OH) Vitamin D levels were associated with hypo-albuminaemia, like study in 76 Japanese CKD patients<sup>[14]</sup>. It is unclear that Vitamin D deficiency in CKD patients although showed that renal problem is a risk factor for deficiency of Vitamin D<sup>[15,16]</sup>. One current survey reported that 86% of CKD patients (n=43) had 25(OH) Vitamin D inadequate (<30 ng/ml) which has been earlier explained by others<sup>[17,18]</sup> and in our study we found 84% of Nepalese CKD patients insufficient and deficient of 25(OH) Vitamin D where as 16% patients have sufficiency (>30 ng/ml). Finally the output of this study revealed associations. Limitation of our study as number of sample is limited. Despite these limitations, this study explored the knowledge on 25(OH) Vitamin D at different stage of chronic kidney disease in Nepalese patients, disdain of tropical region of Nepal.

## 6. Conclusion

In Summary, We found unselected CKD Nepalese patients that serum 25(OH) Vitamin D were insufficiency and deficiency. Even though Nepalese population live in tropical and sub-tropical region, most patients had low level of 25(OH) Vitamin D in stages of CKD. Future research in large population and cohort studies should be designed toward solving the reveal relationship between 25(OH) Vitamin D and different stage of chronic kidney disease to clinically meaningful outcome.

## 7. Competing interests

The authors state no conflict of interest

## 8. Acknowledgement

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