Original Article

Proportion of insufficient, deficient and severely deficient level of 25 hydroxy Vitamin D in patients on hemodialysis

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Objective: To assess the proportion of insufficient, deficient and severely deficient level of 25 hydroxy Vitamin D in patients on hemodialysis.

Methodology: This cross sectional study was conducted from February to December 2020. A total of 196 patients who were between 18 – 80 years of age on maintenance hemodialysis for at least one month were selected using non probability consecutive sampling technique. Data were analyzed by SPSS version 22.

Results: Out of 196 patients, 112 (57.14%) were males and 84 (42.86%) females. 151 (77%) were diabetic and 157 (80.1%) hypertensive. Low level of vitamin D was observed in 187 (95.41%) patients. In these, 64 (32.7%) were severely deficient (25(OH) D < 10 ng/ml), 102(52.0%) had deficiency (25(OH) D 10 – 20 ng/ml) and 21(10.7%) hadinsufficient levels of vitamin D (25(OH)D 21 to 30 ng/ml).The relationship between severity of deficient levels had no correlation with age, gender, BMI and hypertension (p>0.05), while a statistically significant correlation was found with duration of CKD, duration of hemodialysis, number of hemodialysis sessions/week and diabetes.

Conclusion: Low level of vitamin D was observed in 95.41% patients on hemodialysis.

Keywords: Chronic kidney disease (CKD), 25 hydroxy Vitamin D, hemodialysis.

INTRODUCTION

In Pakistan,Chronic kidney disease (CKD) prevalence is around 21%.Impairments in the vitamin D metabolism is a well-known consequence of CKD.[1] 25hydroxy vitamin [25(OH)D] is the best indicator of vitamin D levels in the human body. 25(OH)D is hydroxylated in kidneys by the enzyme 1-α-hydroxylase to form the active analyte of vitamin D which is, 1,25 hydroxy vitamin D [1,25(OH) 2D].[2] Impairment in renal function is often associated with diminished conversion of 25(OH)D to 1,25(OH)2D. Extra renal conversion of 25(OH) D to 1, 25(OH)2D has been reported in organs such as prostate, breast, colon and macrophages.[3]

25(OH) 2D deficiency plays an empirical part in variety of common diseases including cardiovascular, autoimmune, neurological diseases, inflammations, gestational complications and carcinomas.[4] Low levels of serum 25(OH) D, may exacerbate secondary hyperparathyroidism (SHPT) in patients with early CKD. Decreased levels has been linked with reduced bone mineral density (BMD), muscle weakness, obesity and metabolic syndrome in dialysis patients.[5-7] Therefore circulating levels of 25(OH)D assume significance even when patients are being supplemented with active doses of vitamin D.[8]

Replenishing diminished levels of 25(OH)D in CKD patients may have beneficial effects on clinical outcomes.[9] Endocrine society guidelines with serum 25(OH)D levels >30 ng/ml as sufficient, levels, ranging from 21-30 ng/ml pointing to insufficient levels while values 20 – 10 ng/ml point towards vitamin D deficiency and levels less than 10 ng/ml are labeled as severe deficiency.

Kidney Disease Improving global outcomes (KDIGO) has established that 25(OH) D levels must be maintained above 30ng/dl in CKD patients.[10] However inadequate data is available regarding patients with CKD who are on dialysis. Deficiency of vitamin D is fairly common in Pakistan despite being a sun drenched country lying close to equator; this may be attributed to skin pigmentation, dressing habits and lifestyles.[11] In a study from India found that 64.44% patients were severely deficient and only 4.44%had sufficient amount of vitamin D.[12]

Proper vitamin D supplementation may lead to enhanced outcomes in diabetes, malignancies, immune system and cardiovascular diseases (CVD) in patients on hemodialysis.[13,14] The aim of this study was to assess the level of 25(OH)D in patients on hemodialysis.

METHODOLOGY

This cross sectional study was conducted from February to December 2020.WHO software for samples size calculation was used, with prevalence of vitamin D

deficiency in CKD patients taken as 6.67%.[12] A total of 196 patients who were between 18 – 80 years of age on maintenance hemodialysis for at least one month were includein the study using non probability consecutive sampling technique. Patients taking vitamin D supplements or drugs like glucocorticoids and phenytoin (ascertained through history and accompanied prescription) and known cases of malignancy were excluded from the study.Institutional approval was obtained and all patients gave an informed consent.

The weight of the participant was measured in kilograms. Standing body height was taken by height scale and Body Mass Index (BMI) was calculated (weight in kg/height in m^2) Questionnaire regarding age, gender, duration of chronic kidney disease, duration of hemodialysis, number of hemodialysis sessions per week, hypertension and diabetes was filled by the patient or principle investigator in case of illiterate patients.

Blood samples were collected at the start of hemodialysis session. Total 25(OH)D was measured on automated immunoassay analyzer (Abbott Architect i1000 based on Chemiluminesence)using Microparticle Immunoassay (CMIA) technique.

Statistical Analysis: Data were analyzed on SPSS version 22. Post stratification chi-square test was applied keeping p-value < 0.05 as significant.

RESULTS

Out of 196 CKD patients, 112 (57.14%) were males and 84 (42.86%) females; 151 (77%) were diabetic and 157 (80.1%) were hypertensive. Descriptive statistics of age, BMI, vitamin D levels, duration of CKD, duration of hemodialysis are reported in Table 1. Low level of 25(OH)D was found in 187 (95.41%)patients. Out of these, 64 (32.7%) were severely deficient, 102 (52.0%) had deficiency and 21 (10.7%) had insufficient levels of 25(OH)D.

Stratification analysis showed that there was no association vitamin deficiency within all age groups (p = 0.425). Similarly, vitamin D deficiency was also not statistically significant with respect to gender (p = 0.897), BMI (p = 0.653) and hypertension (p = 0.415) while it was statistically significant with duration of CKD (p = 0.001), duration of hemodialysis (p = < 0.001), number of hemodialysis sessions per week (p = < 0.001) and diabetes (p = 0.001) as presented in (Table 2).

Table 1: Descriptive statistics study patients.

Variable	Mean	SD	95% Confidence Interval for Mean	
			Lower	Upper
Age (Years)	58.53	12.60	56.75	60.30
BMI (kg/m^2)	20.72	3.23	20.27	21.18
Vitamin D levels	14.40	8.34	13.22	15.57
Duration of CKD (months)	29.96	11.14	28.39	31.53
Duration of Hemodialysis (months)	18.36	8.62	17.15	19.58
Number of Hemodialysis sessions (Per Week)	2.21	0.67	2.11	2.30

DISCUSSION

Hemodialysis intensifies vitamin D deficiency. It is likely related with poor outcomes, including increased mortality.[14] In our study, 95.41% patients were found to have low levels of vitamin D as compared to 85.71% in a study carried out by Mittal et al.[15] In this study, vitamin D insufficiency was found in 10.7% patients which is higher than a study by Bansal et al (6.7%).[12]

The mean age of patients in this study was 58.53+12.60 years. Other studies reported mean age of 55 + 13 years[8] and 58.9 + 16.6 years.[16] The mean duration of hemodialysis in our study was 18.36 months, which was significantly higher as compared to findings reported by Bansal et al (5.5 months).[12] In our study, 77% were diabetic and 80.1% were hypertensive. However another study reported 51% cases to be diabetic and 9% hypertensive patients.[12]

When evaluating the relationship between severity of deficient levels of 25(OH)D, no correlation was found with age, gender, BMI and hypertension (p > 0.05), while a statistically significant correlation was found in case of duration of CKD, duration of hemodialysis ,number of hemodialysis sessions/week and diabetes (p < 0.05) (Table 2). However, another study found a weak positive correlation between 25(OH)D levels and gender and diabetes.[12] There is a strong need for longer duration, multi centric RCTs with emphasis on patient outcomes so that better clinical correlation is achieved and optimal dosing regimens can be suggested.

Table 2: Association of age, gender, BMI, duration of CKD, duration of hemodialysis, number of hemodialysis sessions per week, hypertension and diabetes with low levels of vitamin D.

Variable	Level of Vitamin D			Total	p-Value
	Insufficient	Deficient	Severe Deficient		
Age Groups (Years)					
≤ 40	2 (12.5%)	8 (50.0%)	6 (37.5%)	16	0.425
41 – 50	2 (8.3%)	16 (66.7%)	6 (25.0%)	24	
51 – 60	11 (17.5%)	33 (52.4%)	19 (30.2%)	63	
> 60	6 (7.1%)	45 (53.6%)	33 (39.3%)	58	
Gender					
Male	13 (12.1%)	58 (54.2%)	36 (33.6%)	107	0.897
Female	8 (10.0%)	44 (55.0%)	28 (35.0%)	80	
Body Mass Index					
Under Weight (BMI < 18.5)	3 (10%)	14 (46.7%)	13 (43.3%)	30	0.653
Normal (BMI 18.5 – 24.9)	15 (10.6%)	79 (56.0%)	47 (33.3%)	141	
Over weight (BMI 25 – 29.9)	3 (18.8%)	9 (56.3%)	4 (25%)	16	
Duration of CKD (Months)					
≤ 24	7 (17.1%)	25 (61.0%)	9 (22.0%)	41	**0.001***
25 – 36	9 (7.8%)	70 (60.9%)	36 (31.3%)	115	
> 36	4 (11.8%)	21 (61.8%)	9 (26.5%)	31	
Duration of Hemodialysis (Months)					
< 12	19 (6.9%)	95 (56.9%)	12 (36.2%)	126	**< 0.001***
13 – 24	1 (1.7%)	6 (10.3%)	51 (87.9%)	58	
> 24	1 (33.3%)	1 (33.3%)	1 (33.3%)	3	
Number of Hemodialysis Sessions Per Week					
1	14 (63.6%)	6 (27.3%)	2 (9.1%)	22	**< 0.001***
2	6 (6.2%)	78 (80.4%)	13 (13.4%)	97	
3	1 (1.5%)	18 (26.5%)	49 (72.0%)	68	
Hypertension					
Yes	15 (10.0%)	81 (54.0%)	54 (36.0%)	150	0.415
No	6 (16.2%)	21 (56.8%)	10 (27.0%)	37	
Diabetic Mellitus					
Yes	7 (6.9%)	78 (54.2%)	56 (38.9%)	144	**0.001***
No	11 (25.6%)	24 (55.8%)	8 (18.6%)	43	

CONCLUSION

It was concluded through our study that deficiency and insufficiency of 25(OH)D is rampant in patients on hemodialysis, with one-third patients showing a severe deficiency. This is a matter of grave concern and may cause adverse patient outcomes. These unfavorable

conditions can be easily prevented by timely and prompt replacement of 25(OH)D.

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REFERENCES

1. Hasan M, Sutradhar I, Gupta RD, Sarker M. Prevalence of chronic kidney disease in South Asia: a systematic review. BMC Nephrol. 2018; 19: 291-4.
2. Christakos S, Dhawan P, Verstuyf A, Verlinden L, Carmeliet G. Vitamin D: Metabolism, Molecular Mechanism of Action, and Pleiotropic Effects. Physiol Rev. 2016; 96: 365-408.
3. Jacobs ET, Kohler LN, Kunihiro AG, Jurutka PW. Vitamin D and Colorectal, Breast, and Prostate Cancers: A Review of the Epidemiological Evidence. J Cancer, 2016; 7: 232-40.
4. Di Somma C, Scarano E, Barrea L, Zhukouskaya VV, Savastano S, Mele C, et al. Vitamin D and Neurological Diseases: An Endocrine View. Int J Mol Sci. 2017; 18: 2482-5.
5. Lee YH, Kim JE, Roh YH, Choi HR, Rhee Y, Kang DR, et al. The combination of vitamin D deficiency and mild to moderate chronic kidney disease is associated with low bone mineral density and deteriorated femoral microarchitecture: results from the KNHANES 2008-2011. Clin Endocrinol Metab. 2014; 99: 3879-88.
6. D. Bataille S, Landrier JF, Astier J, Giaime P, Sampol J, Sichez H, et al. The "Dose-Effect" Relationship Between 25-Hydroxyvitamin D and Muscle Strength in Hemodialysis Patients Favors a Normal Threshold of 30 ng/mL for Plasma 25-Hydroxyvitamin. Ren Nutr. 2016; 26: 45-52.
7. Ahmadi F, Damghani S, Lessan-Pezeshki M, Razeghi E, Maziar S, Mahdavi-Mazdeh M. Association of low vitamin D levels with metabolic syndrome in hemodialysis patients. Hemodial Int. 2016; 20: 261-9.
8. Rosen CJ, Abrams SA, Aloia JF, Brannon PM, Clinton SK, Durazo-Arvizu RA, et al. IOM committee members respond to Endocrine Society vitamin D guideline. J Clin Endocrinol Metab. 2012; 97: 1146-52.
9. Jean G, Souberbielle JC, Chazot C. Vitamin D in Chronic Kidney Disease and Dialysis Patients. Nutrients, 2017; 9: 328-32.
10. Wheeler DC, Winkelmayer WC. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD) Forward. Kid Int Supplements, 2017; 7: 1-59.
11. Hassan S, Muzammil SM, Jafri L, Khan AH. An audit of clinical laboratory data of 25[OH]D at Aga Khan University as reflecting vitamin D deficiency in Pakistan. JPMA. 2015; 65: 1247-50.
12. Bansal B, Bansal S, Mithal A, Kher V, Marwaha R. Vitamin D deficiency in hemodialysis patients. Indian J Endocr Metab. 2012; 16: 270-3.
13. Nakashima A, Yokoyama K, Yokoo T, Urashima M. Role of vitamin D in diabetes mellitus and chronic kidney disease. World J Diabetes, 2016; 7: 89-100.
14. Wolf M, Shah A, Gutierrez O, Ankers E, Monroy M, Tamez H et al. Vitamin D levels and early mortality among incident hemodialysis patients. Kidney Int. 2007; 72: 1004-13.
15. Mittal S, Sandhu H, Singh, B. Study of Vitamin D levels in patients with Chronic Kidney Disease. Bangladesh J Med Sci. 2018; 17: 652-60.
16. Del Valle E1, Negri AL, Aguirre C, Fradinger E, Zanchetta JR. Prevalence of 25(OH) vitamin D insufficiency and deficiency in chronic kidney disease stage 5 patients on hemodialysis. Hemodial Int. 2007; 11: 315-21.