

ORIGINAL ARTICLE

Relationship Between Vitamin D Deficiency and Proteinuria in Patients with Ckd

ABDUL WARIS KHAN¹, GOHAR ALI KHAN², WAQAR AHMED KHAN³

¹Consultant Physician and Fellow Rheumatology Internal Medicine and Rheumatology Division of Rheumatology, Lady Reading Hospital Peshawar

²Assistant professor General Medicine Khalifa Gul Nawaz teaching Hospital/Bannu Medical college, Bannu

³Post Graduate Resident General Medicine Combined Military Hospital Peshawar Kpk Pakistan

Correspondence to: Gohar Ali Khan, Email: goharalikhan715@yahoo.com

ABSTRACT

Background: People with chronic kidney disease are at a higher risk of kidney failure and developing vitamin D deficiencies.

Objective: The aim of this study was to find out the association of vitamin D deficiency and proteinuria in patients with CKD

Materials and Method: The current study was conducted at the department of Medicine Khalifa Gul Nawaz teaching Hospital/Bannu Medical college, Bannu from January 2023 to April 2023 following approval from the ethical committee of the hospital. A total of 80 individuals were enrolled in our study. Written consent were taken from each participant. Clinical and demographic features including weight, sex, age height, marital status, income status, blood pressure were recorded. Laboratory factors such as 25 OH vitamin D3, electrolytes, urea, creatinine, hemogram, and parathormone, of each patient were assessed on specified forms. Data was analyzed using SPSS version 22 and the p value less than 0.005 was considered significant.

Results: In this study a total of 180 individuals were enrolled with chronic kidney disease, out of which 51(63.5%) were female and 29 (36.3%) were male. The mean age of the study participants' were 59.1±10.8 years. The deficiency of vitamin D was found in 15 (18.75%) cases. Participants with deficiency of vitamin D had 628.8 mg/g median UACR, those with sufficient vitamin D levels had 95 mg/g and with insufficient had 330.8 mg/g. So the prevalence of albuminuria increased with vitamin D deficiency

Conclusion: Our study concluded that individual with CKD had significantly high vitamin D deficiency and proteinuria was strongly associated with vitamin D deficiency. The prevalence of proteinuria increased with vitamin D deficiency.

Keywords: Relationship; Vitamin D deficiency; Proteinuria; CKD

INTRODUCTION

Damage to the kidney and reduction in the renal function is termed as chronic kidney disease (CKD). According to the Kidney Disease Outcomes Quality Initiative (KDOQI) recommendations it have been divided in to f stages¹. The worldwide frequency of CKD is 13.4%². People with disease are at a higher risk of kidney failure, cardiovascular disease and mortality, despite attempts to reduce risk factors. It has been underlined as one of the world's most vital health disasters, growing worldwide disease and death while exhausting limited health assets^{2,3}. As therefore, understanding its mechanism and developing novel management techniques that use non-traditional risk characteristics are crucial⁴. CKD increases the chance of developing vitamin D deficiencies. It is frequent in people with CKD, particularly those with transplanted kidneys and end-stage renal illness^{4,5}. The deficiency of occurs in all phases of CKD, although its incidence increases as renal function declines. Despite controlling for CKD stage & confounding parameters, persons with vitamin D concentrations below 15 ng/mL had a higher probability of all-cause death. Vitamin D insufficiency is a growing health concern in individuals with CKD⁶. It can cause severe osteoarthritis, rickets, gingivitis, bone loss, numbness, muscular pain, and sadness. Several studies have found a link between vitamin D depletion and lower glomerular filtration rate in individuals with CKD⁷. Vitamin D's role in Chronic kidney extends over its usual calcium and phosphorous balance effects, with possible effects on extra mineral metabolism processes such as immune system stimulation and renal function. According to several studies, vitamin D deficiency in patients receiving hemodialysis has been connected to muscle mass & strength⁸. In Pakistan, few research have been undertaken to evaluate the relationship of vitamin D deficiency and proteinuria in CKD individuals. Therefore the current study was carried out to determine the relationship between Vitamin D deficiency and proteinuria in patients with CKD

MATERIALS AND METHOD

The current study was conducted at the department of Medicine

Khalifa Gul Nawaz teaching Hospital/Bannu Medical college, Bannu from January 2023 to April 2023 following approval from the ethical committee of the hospital. A total of 80 individuals of both genders and different age groups did not get hemodialysis (HD) therapy were enrolled. While individuals with malignancy, pregnant women and were on HD treatment were excluded. Written consent were taken from each participant. Clinical and demographic features including weight, sex, age height, marital status, income status, blood pressure were recorded. Laboratory factors such as 25 OH vitamin D3, electrolytes, urea, creatinine, hemogram, and parathormone, of each patient were assessed on specified forms. UACR was computed by dividing albumin (measured by radioimmunoassay) by creatinine (measured from a spot urine sample), expressed as mg/g. BMI was computed by dividing weight by height squared (kg/m²). The ratio of absolute neutrophil count to absolute lymphocyte count (NLR) was represented as a percentage. The product of calcium and phosphorus was calculated as Ca*P. The CKD-EPI formula was used to compute the estimated glomerular filtration rate (eGFR). Data was analyzed using SPSS version 22 and the p value less than 0.005 was considered significant. Descriptive statistics for biochemical and parameter data were provided using arithmetic mean (SD), percentages and frequencies. After demonstrating near normalcy by skewness and kurtosis analysis. Continuous variables were compared using one-way ANOVA for normal distribution data and the Kruskal-Wallis test for non-normally dispersed data.

RESULTS

In this study a total of 180 individuals were enrolled with chronic kidney disease, out of which 51(63.5%) were female and 29 (36.3%) were male. the mean age of the study participants were 59.1±10.8 years. 21 (26.3%) of the individuals were from high income families. Hypertension was found in 73 (91.3%) and Diabetes mellitus was reported in 46 (57.5%). 23 (28.8%) of the individuals ha coronary heart diseases as presented in table 1. Majority of the individuals were in the stage 3b of CKD 34 (42.5%), followed by stage 3a 23 (28.8%), stage 4 19 (23.8%) respectively as described in table 2. 14 (18. %)The deficiency of vitamin D was found in 15 (18.75%) cases as shown in table 2. Participants with deficiency of vitamin D had 628.8 mg/g median UACR, those with

Received on 23-05-2023

Accepted on 25-06-2023

sufficient vitamin D levels had 95 mg/g and with insufficient had 330.8 mg/g. So the prevalence of albuminuria increased with vitamin D deficiency as presented in table 3.

Table 1: Clinical and demographic features of the study population

Features	Frequency/percentage
Gender	
Male	51(63.5%)
Female	29 (36.3%)
Alcohol consumption	1 (1.3%)
Smoking	5 (6.3%)
High income	21 (26.3%)
Low income status	14 (17.5%)
Coronary heart disease	23 (28.8%)
Diabetes mellitus	46 (57.5%)
Mean age, years	59.1±10.8 years,
Hyperlipidemia	37 (46.3%)
Hypertension	73 (91.3%)

Table 2: Vitamin D deficiency and CKD phases.

Features	Frequency/percentage
Vitamin D status	
Deficient	15 (18.75%)
Sufficient	53 (66.25%)
Insufficient	12 (15.0%)
Stages of chronic kidney disease	
Stage 4	19 (23.8%)
Stage 3a	23 (28.8%)
Stage 3b	34 (42.5%)
Stage 2	4 (5.0%)

Vitamin D deficiency and its association with Albuminuria

Factors	N(%)
Median UACR with insufficient vitamin D	330.8 mg/g
Median UACR with deficient vitamin D	628.8 mg/g
Median UACR with sufficient vitamin D	95 mg/g
Mean UACR	340.8 ± 410.5 mg/g
Normoalbuminuria	21 (26.3%)
Microalbuminuria	27 (33.8%)
Macroalbuminuria	32 (40.0%)

DISCUSSION

Vitamin D is a steroid with cytosolic binding sites¹⁰. Up to 3% of the human genome is regulated by this vitamin. It has long played a crucial role in phosphorus and calcium metabolism. Its deficits have been linked to a variety of health issues, including falls, fractured bones, elevated blood sugar, immunological, cardiovascular, and renal illnesses, as well as TB, depression, neurological disorders, and malignancies¹¹. Vitamin D insufficiency has been linked to negative consequences on several organ systems in humans in recent years¹². Over 50% of older adults are vitamin D deficient, according to the Nutritional Standards consensus calculations¹³.

Research suggests that vitamin D deficiency affects both older and younger populations, even in nations with adequate sun exposure¹⁴. Maintaining appropriate vitamin D levels relies heavily on renal function. Humans require physiological activity to function properly. Low GFR increased the likelihood of vitamin D insufficiency by 32% compared to those with normal GFR¹⁵. It deficiency is common in chronic kidney disease individuals, especially those with end-stage renal dysfunction (ESRD) and recipients of kidney transplants¹⁶. One study found a greater prevalence of vitamin D deficiency among CKD patients. In the research, 42% of individuals with low GFR had insufficiency, whereas 41% had vitamin D deficiency¹⁷, individuals on (HD) have a much greater proportion of deficit compared to the general population, with rates ranging from 76-94%¹⁸. As renal function declines, CKD patients develop resistance to vitamin D replacement therapy¹⁹. The current study was carried out to determine the relationship between Vitamin D deficiency and proteinuria in patients with CKD. In this study a total of 180 individuals were enrolled with chronic kidney disease were enrolled

out of which 51(63.5%) were female and 29 (36.3%) were male. Similar study was carried out by Özgür in which female more than male which support our study²⁰. In our study the prevalence of deficiency of vitamin D was found in 15 (18.75%) cases. These findings are similar to the previous study²⁰, but our study results are not comparable to the study of Muhammad et al in which the prevalence of deficiency was much higher²¹. This difference in the frequency is to the fact that they only included advanced stage of patients and most of the patients were from rural areas in their study. Our study findings were not similar to another study²¹. Participants in our study with deficiency of vitamin D had 628.8 mg/g median UACR, those with sufficient vitamin D levels had 95 mg/g and with insufficient had 330.8 mg/g. So the prevalence of albuminuria increased with vitamin D deficiency. These findings are similar to the study conducted by Özgür²⁰. In their study individual with vitamin D had significantly high albuminuria. Another study revealed the association of albuminuria with deficiency of vitamin D (55% risk in increase)²². Albuminuria occurs with vitamin D deficit because the active component of vitamin D is essential for kidney function. The key molecular processes linking vitamin D deficiency to increased albuminuria is that podocytes are specialized cells in the kidney's filtration glomeruli that act as a tightly closed net (slit diaphragm) to retain protein in the circulation. Active vitamin D connects to the Vitamin D receptors on podocytes. Vitamin D deficiency reduces VDR activity. This affects essential structural & slit-diaphragm proteins such as nephrin and podocin, resulting in podocyte damage or foot processes efficacy. As a consequence, the filtration layer becomes "leaky," which allows albumin to enter into the urine²³.

CONCLUSION

Our study concluded that individual with CKD had significantly high vitamin D deficiency and proteinuria was strongly associated with vitamin D deficiency. The prevalence of proteinuria increased with vitamin D deficiency.

REFERENCES

1. Chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Levey AS, Atkins R, Coresh J, et al. *Kidney Int.* 2007;72:247-259. doi: 10.1038/sj.ki.5002343. [DOI] [PubMed] [Google Scholar]
2. Global prevalence of chronic kidney disease - a systematic review and meta-analysis. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FD. *PLoS One.* 2016;11:0. doi: 10.1371/journal.pone.0158765. [DOI] [PMC free article] [PubMed] [Google Scholar]
3. Prevalence of chronic kidney disease in China: a cross-sectional survey. Zhang L, Wang F, Wang L, et al. *Lancet.* 2012;3:815-822. doi: 10.1016/S0140-6736(12)60033-6. [DOI] [PubMed] [Google Scholar]
4. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. *N Engl J Med.* 2004;351:1296-1305. doi: 10.1056/NEJMoa041031. [DOI] [PubMed] [Google Scholar]
5. Relationship between vitamin D status and immunosuppressive therapy in kidney transplant recipients. Filipov JJ, Zlatkov BK, Dimitrov EP, Svinarov D. *Biotechnol Biotechnol Equip.* 2015;29:331-335. doi: 10.1080/13102818.2014.995415. [DOI] [PMC free article] [PubMed] [Google Scholar]
6. Chronic kidney disease, hypovitaminosis D, and mortality in the United States. Mehrotra R, Kermah DA, Salusky IB, et al. *Kidney Int.* 2009;76:977-983. doi: 10.1038/ki.2009.288. [DOI] [PMC free article] [PubMed] [Google Scholar]
7. Vitamin D deficiency. Holick MF. *N Engl J Med.* 2007;357:266-281. doi: 10.1056/NEJMra070553. [DOI] [PubMed] [Google Scholar]
8. Osteoporosis and periodontitis. Wang CJ, McCauley LK. <https://link.springer.com/article/10.1007/s11914-016-0330-3>. *Curr Osteoporos Rep.* 2016;14:284-291. doi: 10.1007/s11914-016-0330-3. [DOI] [PMC free article] [PubMed] [Google Scholar]
9. Association of kidney function, vitamin D deficiency, and circulating markers of mineral and bone disorders in CKD. Ureña-Torres P, Metzger M, Haymann JP, et al. *Am J Kidney Dis.* 2011;58:544-553. doi: 10.1053/j.ajkd.2011.04.029. [DOI] [PubMed] [Google Scholar]

10. Borel, P., D. Caillaud, and N.J. Cano, Vitamin D bioavailability: state of the art. *Crit Rev Food Sci Nutr*, 2015. 55(9): p. 1193-205.
11. Autier, P., et al., Vitamin D status and ill health: a systematic review. *Lancet Diabetes Endocrinol*, 2014. 2(1): p. 76- 89.
12. Plum, L.A. and H.F. DeLuca, Vitamin D, disease and therapeutic opportunities. *Nat Rev Drug Discov*, 2010. 9(12): p. 941-55.
13. Manson, J.E., et al., Vitamin D Deficiency - Is There Really a Pandemic? *N Engl J Med*, 2016. 375(19): p. 1817-1820.
14. Palacios, C. and L. Gonzalez, Is vitamin D deficiency a major global public health problem? *J Steroid Biochem Mol Biol*, 2014. 144 Pt A: p. 138-45.
15. Friedl, C. and E. Zitt, Vitamin D prohormone in the treatment of secondary hyperparathyroidism in patients with chronic kidney disease. *International journal of nephrology and renovascular disease*, 2017. 10: p. 109-122.
16. Stavroulopoulos, A., et al., Vitamin D status in renal transplant recipients. *Am J Transplant*, 2007. 7(11): p. 2546-52.
17. Stefíková, K., et al., Insulin resistance and vitamin D deficiency in patients with chronic kidney disease stage 2-3. *Physiol Res*, 2011. 60(1): p. 149-55.
18. Drechsler, C., et al., Vitamin D status and clinical outcomes in incident dialysis patients: results from the NECOSAD study. *Nephrol Dial Transplant*, 2011. 26(3): p. 1024-32
19. Parikh, C., et al., Vitamin D and Clinical Outcomes in Dialysis. *Semin Dial*, 2015. 28(6): p. 604-9
20. Özgür, Y. (2021). Relationship between vitamin D deficiency, albuminuria, peripheral artery disease and 5-year mortality in chronic kidney disease. *J Coll Physicians Surg Pak*, 31(6), 644-650.
21. Muhammad, I., Khursheed, M., Muhammad, S., Muhammad, N., Ghulam, S., & ur Rehman, Z. (2022). PREVALENCE OF VITAMIN D DEFICIENCY AMONG PATIENTS WITH NEWLY DIAGNOSED CHRONIC KIDNEY DISEASE. *Khyber Journal of Medical Sciences*, 15(2), 78-80.
22. Damasiewicz MJ, Magliano DJ, Daly RM, Gagnon C, Lu ZX, beling PR, et al. 25-hydroxyvitamin D Levels and chronic kidney disease in the AusDiab (Australian Diabetes, Obesity and Lifestyle) study. *BMC Nephrol* 2012; 13:55. doi:10.1186/1471-2369-13-55
23. Nykjaer A, Dragun D, Walther D, et al. An endocytic pathway essential for renal uptake and activation of steroid 25-(OH) vitamin D3. *Cell*. 1999;96:507-15

This article may be cited as: Khan A.W., Khan G.A., Khan W.A., Relationship Between Vitamin D Deficiency and Proteinuria in Patients with Ckd. *Pak J Med Health Sci*, 2023; 17(7): 225-227.