AlQalam
Alq J Med App Sci
https://journal.utripoli.edu.ly/index.php/Alqalam/index eISSN 2707-7179

Original article

Vitamin D Insufficiency and Deficiency in Chronic Kidney Disease Patients on Hemodialysis

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ARTICLE INFO

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***Received**: 26-05-2024*
***Accepted**: 04-07-2024*
***Published**: 08-07-2024*

***Keywords**. Vitamin D, Vitamin D deficiency, Vitamin D Insufficiency, Chronic Kidney Disease.*

ABSTRACT

About one billion people in the world suffer from vitamin D deficiency or insufficiency. Moreover, many data points indicate that vitamin D insufficiency and deficiency are highly prevalent among patients with chronic kidney disease (CKD) or undergoing dialysis. This study aimed to evaluate the level of vitamin D for dialysis patients at the Tripoli dialysis and treatment center. In this single center observational study, hospitalized dialysis patients who were diagnosed of Stage 5 CKD and healthy (control) groups had taken measurement of serum 25(OH)D in the Tripoli dialysis and treatment center. In this regard, One hundred and four patients were included in this study, of which (37%) were in Vitamin D insufficiency state while (30%) were in Vitamin D deficiency state. For the comparison between vitamin D levels among dialysis patients and control group which revealed that there were no significant differences between them with a p-value of 0.094. Furthermore, the correlation between serum 25 (OH) vitamin D, creatinine, PTH, and urea showed that there was a weak negative correlation between serum vitamin D and creatinine ($r = -0.364$, $p = 0.255$), between vitamin D and PTH ($r = -0.378$, $p = 0.226$), and between vitamin D and urea ($r = -0.347$, $p = 0.269$). Obviously, although vitamin D deficiency is strongly linked to kidney failure, the tests that work for this disease are limited, so introducing vitamin D for dialysis patients with CKD helps in understanding the patient's condition and helps in disease management.

***Cite this article.** Elahjal M, Elhaji F, Rhoma A, Muna E, Ferrara N, AshourA. Vitamin D Insufficiency and Deficiency in Chronic Kidney Disease Patients on Hemodialysis. Alq J Med App Sci. 2024;7(3):484-488. https://doi.org/10.54361/ajmas.247309*

INTRODUCTION

Vitamin D is an essential fat-soluble vitamin called calciferol [1]. It is found in some types of food, such as fish liver oils, fatty fish, mushrooms, egg yolks, and liver, and is produced endogenously in the skin by a photochemical reaction upon exposure to ultraviolet (UV) sunlight on 7-dehydrocholesterol to form previtamin D3 and subsequently VD3 [2, 3]. There are two main physiological forms of VD: ergocalciferol (VD2) from plant sources and cholecalciferol (VD3) from animal sources. [2,4,5]. Regardless of their source, VD2 and VD3 are transported to the liver by a VD-binding protein (VDBP), where they undergo hydroxylation and become 25-hydroxyvitamin D [25(OH)-VD]. This compound is the most commonly circulating form of VD, and its plasma levels are routinely measured as a marker of VD status [3,6,7].

The kidney is the primary site of synthesis of 1,25(OH)2D, the active, hormonal form of vitamin D [8]. The role of vitamin D is no longer limited to maintaining blood calcium and phosphate homeostasis within the normal physiological

range for healthy bones and muscles. Recent research has shown that it also plays an important role as a cell-differentiating and anti-proliferative factor with effects on a variety of tissues, such as the immune, cardiovascular, and renal systems [8] [9]. Vitamin D deficiency (VDD) was measured as 25 (OH) D less than 20 ng/mL, vitamin D insufficiency (VDI) as 20–29 ng/mL, vitamin D sufficiency of 30 ng/mL, and defined as having a vitamin D toxicity greater than 100 ng/mL. Vitamin D levels below 10 ng/mL were considered severe deficiency [2,10].

Vitamin D deficiency (VDD) is a recognized risk factor for all-cause mortality in normal individuals and in patients with chronic kidney disease (CKD); A disease is defined as a structural and functional abnormality of the kidneys that has been present for more than 3 months and has health consequences [2,11]. Possible causes of this vitamin D deficiency are a lack of exposure of renal patients to UV radiation, insufficient vitamin D intake, proteinuria, and the inability of the kidneys to produce the active form of vitamin D for its vital functions in the body [12].

Vitamin D insufficiency (VDI) has attracted attention as a major public health problem worldwide, with an estimated incidence of more than 1 billion people. In people with CKD, the prevalence of VDD has been reported to be as high as 80% [3]. VDD, or VDI, is common in patients with CKD, and serum vitamin D levels appear to be inversely correlated with renal function. In addition, there is growing evidence that VDD can contribute to worsening kidney function and increased morbidity and mortality in patients with CKD, leading to serious problems such as rickets, gingivitis, osteoporosis, myalgia, and depression [13,14]. Although 25(OH)-VD levels begin to decline in individuals with CKD stage 2 (not yet on dialysis), deficient levels can be seen at all stages of CKD [15,16]. Several studies have shown that individuals with CKD are at high risk of VDD. Studies by Gonzalez et al. showed that 97% of hemodialysis patients had insufficient 25OH-VD levels [17]. This study was conducted to evaluate the prevalence of 25(OH)-vitamin D deficiency and insufficiency in patients with CKD undergoing dialysis at the Tripoli Dialysis and Treatment Center.

METHODS

Study area and design

This single-center study adopted an observational design. Patients presented to the study center were identified from medical records at the Tripoli Dialysis and Treatment Center. A simple random sample of those patients was chosen to determine vitamin D levels (25-hydroxy vitamin D). All aspects of the study protocol have been reviewed and authorized by the local ethics committee of the Tripoli Dialysis and Treatment Centre.

Sampling techniques and laboratory investigation

A total of 104 blood samples were collected from dialysis patients, and 34 blood samples of healthy candidates were used as a control sample. Vitamin D levels (25-hydroxy vitamin D) were measured for all candidates on Cobas e411 Analyzer (Germany, Roche). Another group of 30 dialysis patients were subjected to vitamin D, PTH, urea, and creatinine analyses to measure strength and the type of correlation between vitamin D and some biochemical indicators.

Data analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 27. Proportions were generated to demonstrate the distribution of VIT D in the studied participants. The Shapiro - Wilk test was used to evaluate the normal distribution of the data. A statistical procedure was implemented to compare the means of two independent groups (dialysis patients and healthy control groups) to determine if there was a significant difference between them, which was carried out using an independent T test. The correlation analysis between the various parameters (Vit.D., PTH, Urea, and Creatinine) was carried out by Spearman`s correlation. Results were considered statistically significant if the P-value was less than or equal to 0.05.

RESULTS

Demographic data

A total of one hundred forty candidates were collected to analyze their vitamin D status, divided into two groups: the dialysis group (CKD) at 74.3% (n = 104) and healthy control group at 25.7% (n = 36). Both genders were included, with ages ranging from 1-76 years.

Data analysis and interpretation

The results of blood vitamin D level among studied dialysis patients (CKD) showed that the participants with an optimum insufficient level (20–29 ng/mL) (37%) recorded the highest percentage, followed by those with a low level

of vitamin or deficiency (< 20 ng/L) (30%), while those with a high level or adequate level (> 30 ng/mL) were the third (28%), and those with severe deficiency (< 10 ng/mL) were found to have the lowest percentage (5%) (Figure 1).

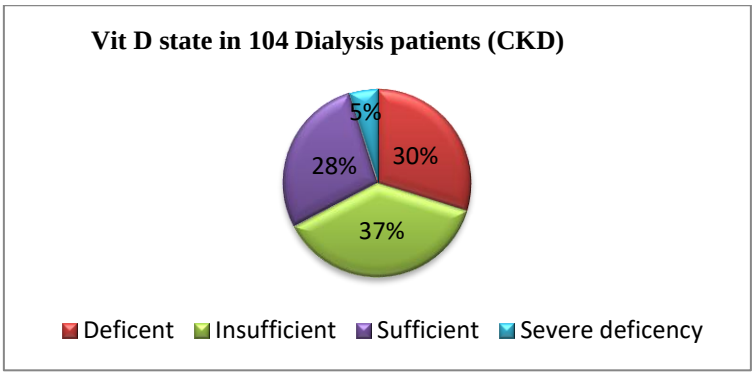

Figure 1. Vitamin D state among dialysis patients.

For study cases, table 1 shows the result of an independent sample (T) test that was performed to compare vitamin D levels in blood between dialysis patients and healthy controls. The data were expressed as mean ± SD, which revealed that there were no significant differences between vitamin D concentration in blood between dialysis patients (M = 25.03, SD = 11.10) and healthy controls (M = 21.06, SD = 14.94); T (df) = 1.686, P value = 0.094.

Table 1. Average vitamin D level for study cases

Parameter	State	N	Mean ± SD	T	P value
Vit D	Dialysis	104	25.03 ±11.1	1.686	0.094
	Control	36	21.0 ±14.9		

Use the Spearman's test to measure strength and the type of relationship between vitamin D and some biochemical indicators in sample of 30 dialysis patients. A weak reverse (negative) correlation was observed between vitamin D and (Urea, Creatinine, and PTH hormone). Table 2 shows that there was a weak reverse (negative) correlation between serum vitamin D and creatinine (r = -0.364, p = 0.255), between vitamin D and PTH (r = -0.378, p = 0.226), and between vitamin D and urea (r = -0.347, p = 0.269), which means that when vitamin D levels increase, the levels of PTH, creatinine, and urea decrease, and vice versa (Table 2).

Table 2. The correlation between vitamin D and different biochemical parameters

Spearman's rho Vit D	Urea	Creatinin	PTH
Correlation Coefficient	-0.347-	-0.364-	-0.378-
Sig. (2-tailed)	0.269	0.245	0.226

DISCUSSION

The association of kidney disease with vitamin D deficiency emerges from the fact that healthy kidneys play an important role in metabolizing vitamin D [18]. This study was conducted to evaluate the level of vitamin D in patients with CKD-5 undergoing HD. The current findings of this study showed that the dialysis participants with an insufficient level were (37%), followed by those with a those with a deficient level (30%), while those with an adequate and severe deficiency level were (28% and 5%, respectively). Different results were observed in many studies worldwide, as in an American study conducted at 1056 dialysis centers in the United States, it was shown that 79% and 57% of 908 people on chronic hemodialysis (HD) had 25(OH)-VD values <30 ng/ml and <20 ng/ml, respectively [16]. Moreover, a study by Del Valle E et al. showed that vitamin D insufficiency was found in 53.5% of the patients and vitamin D deficiency in 22.6% [19]. In addition, a Korean study implemented on pediatric patients on chronic dialysis revealed that vitamin D deficiency was found in 32.2% of the patients and VDI in 50.8% [20]. An Egyptian study revealed that the optimal level of vitamin D was encountered in only 1.4% of CKD patients; 68.2% of CKD patients had vitamin D deficiency [21]. Despite the differences in terms of vitamin D state sequences and percentages, it was still obvious that CKD and dialysis patients were suffering from vitamin D insufficiency and deficiency, which, as recommended by many experts, should be avoided by using supplementation. Many different factors, such as nutritional and sunlight exposure deficits, race, sex, age, and different diseases, could be responsible for this variation, as the studies conducted in different

countries under different circumstances indicate. As in this research, the majority of dialysis participants were on vitamin D supplementation regimens using either ergocalciferol or cholecalciferol daily, weekly, or monthly.

The result obtained from this research comparing vitamin D levels in blood between dialysis patients and healthy controls revealed that there were no significant differences between the two groups, with a P value of 0.094. Possible causes of this result are that dialysis patients take vitamin D pills or have injectable vitamin D during their dialysis treatment. Healthy kidneys are rich with vitamin D receptors and play a major role in turning vitamin D into its active form. When kidneys fail, their ability to activate vitamin D is lost [12].

As presented in this study, a weak reverse (negative) correlation was observed between vitamin D and (Urea, creatinine, and PTH hormone (Table 2). Concerning the correlation between serum vitamin D and PTH, there was a weak reverse (negative) correlation ($r = -0.378$, $p = 0.226$). The current result agreed with an Egyptian study that showed a similar result: serum PTH correlated negatively with serum 25(OH)D, with a correlation coefficient ($r = -0.69$, $P < 0.001$) [21]. As it is known, together with decreased kidney function, a decrease in 1,25(OH)2D leads to secondary hyperparathyroidism (SHPT) [4].

The findings of the current study, as shown in Table 2, revealed that a weak negative correlation between serum vitamin D and creatinine was found ($r = -0.364$, $p = 0.255$). In accordance with this study, the data of 96 patients who visited the kidney unit in Saudi Arabia showed a statistically significant negative correlation between creatinine and vitamin D ($r = -0.373$, $p = 0.001$) [18]. On the contrary, a study conducted by Del Valle E et al. showed that there was a statistically significant positive correlation between serum 25(OH)D levels and serum creatinine ($r = 0.38$; $p<0.001$) [19]. As shown in table 2, a weak reverse (negative) correlation was observed between vitamin D and urea ($r = -0.347$, $p = 0.269$).

CONCLUSION

According to our findings, the dialysis patients suffer from a significant decrease in the level of vitamin D in their blood. Moreover, since there is an inverse negative correlation between the level of vitamin D and urea, creatine, and PTH, it is critical that physicians consider requesting that serum vitamin D be tested routinely in kidney disease patients undergoing dialysis. These findings are useful for providing data that may assist with the management of CKD patients.

Acknowledgments

In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

Conflicts of Interest

The authors declare no conflicts of interest.

REFERENCES

1. Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Dietary Reference Intakes for Calcium and Vitamin D. Ross AC, Taylor CL, Yaktine AL, Del Valle HB, editors. Washington (DC): National Academies Press (US); 2011.
2. Inda Filho AJ, Melamed ML. Vitamin D and kidney disease: what we know and what we do not know. J Bras Nefrol. 2013 Oct-Dec;35(4):323-31.
3. Franca Gois PH, Wolley M, Ranganathan D, Seguro AC. Vitamin D Deficiency in Chronic Kidney Disease: Recent Evidence and Controversies. Int J Environ Res Public Health. 2018 Aug 17;15(8):1773.
4. Jean G, Souberbielle JC, Chazot C. Vitamin D in Chronic Kidney Disease and Dialysis Patients. Nutrients. 2017 Mar 25;9(4):328.
5. Deluca HF. History of the discovery of vitamin D and its active metabolites. Bonekey Rep. 2014 Jan 8;3:479.
6. Al-Badr W, Martin KJ. Vitamin D and kidney disease. Clin J Am Soc Nephrol. 2008 Sep;3(5):1555-60.
7. Abdul Razzaque MR, Tebha SS, Tukruna A, Arif A, Kogut LM, Afsar NA, Shabbir D, Zaidi ZA. 25-Hydroxyvitamin-D deficiency in chronic kidney disease stages III, IV, and V in South Asian population: a retrospective cohort. SAGE Open Med. 2023 Jan 19;11:20503121221148613.
8. Kumar R, Tebben PJ, Thompson JR. Vitamin D and the kidney. Arch Biochem Biophys. 2012 Jul 1;523(1):77-86.
9. Williams S, Malatesta K, Norris K. Vitamin D and chronic kidney disease. Ethn Dis. 2009 Autumn;19(4 Suppl 5):S5-8-11.
10. Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. Nutrients. 2014 Feb 21;6(2):729-75.
11. Dusso A. Kidney disease and vitamin D levels: 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, and VDR activation. Kidney Int Suppl (2011). 2011 Sep;1(4):136-141.

12. Çankaya E, Bilen Y, Keleş M, Uyanık A, Akbaş M, Güngör A, Arslan Ş, Aydınlı B. Comparison of Serum Vitamin D Levels Among Patients With Chronic Kidney Disease, Patients in Dialysis, and Renal Transplant Patients. Transplant Proc. 2015 Jun;47(5):1405-7.
13. Kim CS, Kim SW. Vitamin D and chronic kidney disease. Korean J Intern Med. 2014 Jul;29(4):416-27.
14. Kantas T, Avendaño Capriles C, Babor S, Tamdin T, Al-Rihani H, Thalla A, et al. Relationship Between Chronic Kidney Disease Staging and Vitamin D Deficiency: A Retrospective Study. Cureus. 2022 Jan 13;14(1):e21221.
15. LaClair RE, Hellman RN, Karp SL, Kraus M, Ofner S, Li Q, Graves KL, Moe SM. Prevalence of calcidiol deficiency in CKD: a cross-sectional study across latitudes in the United States. Am J Kidney Dis. 2005 Jun;45(6):1026-33.
16. Bhan I, Burnett-Bowie SA, Ye J, Tonelli M, Thadhani R. Clinical measures identify vitamin D deficiency in dialysis. Clin J Am Soc Nephrol. 2010 Mar;5(3):460-7.
17. González EA, Sachdeva A, Oliver DA, Martin KJ. Vitamin D insufficiency and deficiency in chronic kidney disease. A single center observational study. Am J Nephrol. 2004 Sep-Oct;24(5):503-10.
18. Abdel-Gayoum AA. Serum vitamin D and parathyroid hormone profiles in patients with various stages of renal disease. Australas Med J. 2015 Feb 28;8(2):33-40.
19. Del Valle E, 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 Jul;11(3):315-21.
20. Cho HY, Hyun HS, Kang HG, Ha IS, Cheong HI. Prevalence of 25(OH) vitamin D insufficiency and deficiency in pediatric patients on chronic dialysis. Perit Dial Int. 2013 Jul-Aug;33(4):398-404.
21. El Din US, Fayed A, El Nokeety MM, Abdulazim DO, Salem MM; Vascular Calcification Group. Vitamin-D deficiency is encountered in almost all egyptian stage 3-5 chronic kidney disease patients in spite of the sunny weather. Saudi J Kidney Dis Transpl. 2019 Nov-Dec;30(6):1389-1397.

نقص فيتامين (د) وعدم كفايته في مرضى الكلى المزمن الذين يخضعون لغسيل الكلى

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المستخلص

الفشل الكلوي المزمن هو أحد الأسباب الرئيسية للوفاة بين الليبيين في مدينة طرابلس. يعاني حوالي مليار شخص في العالم من نقص فيتامين (د) أو نقصه الحاد. علاوة على ذلك ، تشير العديد من نقاط البيانات إلى أن نقص فيتامين (د) ونقصه منتشران بشكل كبير بين المرضى الذين يعانون من مرض الكلى المزمن (CKD) أو يخضعون لغسيل الكلى. تهدف هذه الدراسة إلى تقييم مستوى فيتامين (د) لمرضى غسيل الكلى في مركز طرابلس لغسيل وعلاج الكلى. تم تضمين عينات من 140 (المرضى والمجموعات الضابطة) ممثلة ب 53 من الذكور (37.9٪) و 87 من الإناث (62.1٪) في الدراسة. حيث تم تضمين عينات من 104 من مرضى الغسيل الكلوي و 36 مجموعة من الأصحاء في هذه الدراسة. تم جمع البيانات خلال شهرين من بداية يونيو 2023 إلى نهاية يوليو 2023 بمساعدة استبيان معد لذلك.حيث تم إجراء مقابلات مع مائة وأربعة مريضا يزورون مركز غسيل الكلى والعلاج في طرابلس. بعد ان تم جمع عينات الدم من المشاركين و اجرا مجموعة من التحاليل تضمنت قياس مستويات هرمون الغدة الجار درقية و فيتامين د واليوريا والكرياتينين. تم تحليل البيانات التي تم جمعها احصائيا باستخدام برنامج (SPSS) الإصدار 27. أظهرت النتائج الحالية لهذه الدراسة أن المصابين بأمراض الكلى المزمن و الخاضعين لغسيل الكلى ان الذين لديهم مستوى غير كاف من فيتامين (د) كان (37٪) ، يليهم مستوى القصور في فيتامين (د) بنسبة (30٪) بينما كان المستوى الكافي والنقص الحاد الشديد لفيتامين د (28٪) و (5٪) على التوالي. نتيجة اختبار العينة المستقلة (T) التي تم إجراؤها لمقارنة مستوى فيتامين (د) بين مرضى غسيل الكلى ومجموعة الاصحاء معبرا عنها (المتوسط =25.03 و الانحراف المعياري=11.10)(المتوسط =21.06و الانحراف المعياري=14.94) على التوالي؛ والتي كشفت انه لا توجد فروق ذات دلالة احصائية بينهما مع قيمة .(pvalue=0.094)علاوة على ذلك ، تم استخدام معامل ارتباط سبيرمان بشكل مناسب لاختبار العلاقة بين مصل الدم 25 (OH) فيتامين (د) والكرياتينين وهرمون الغدة الجار درقية واليوريا. كان هناك ارتباط سلبي ضعيف بين فيتامين (د) في الدم والكرياتينين (r = -0.364- ، p = 0.255و بين فيتامين (د) و هرمون الغدة جار درقية (r = -0.378-, p = 0.226)) و بين فيامين (د) و اليوريا.(r = -0.347-, p=0.269) : من الواضح أنه على الرغم من أن نقص فيتامين (د) يرتبط ارتباطا وثيقا بالفشل الكلوي ، إلا أن الاختبارات التي تعمل على هذا المرض محدودة ، لذا فإن إدخال التحليل الروتيني لفيتامين (د) لمرضى غسيل الكلى او المصابين بمرض الكلى المزمن يساعد في فهم حالة المريض ويساعد في إدارة المرض .

الكلمة الدالة: فيتامين د ، نقص فيتامين د الحاد، فيتامين د الغير كافئ ، مرض الكلى المزمن.