Vitamin D Status in Hemodailysis Patients, A Single Center Study

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ABSTRACT:

BACKGROUND:

Vitamin D deficiency and insufficiency are common in patients with End Stage Renal Disease(ESRD). Vitamin D has been found to have beneficial effects on bone, cardiovascular and immune functions. There are little data about vitamin D levels in Iraqi patients on hemodalysis..

OBJECTIVE:

This study was conducted to determine the vitamin D status of Iraqi patients with ESRD on hemodialysis**.**

PATIENTS AND METHODS:

This study is a cross sectional study conducted at The Dialysis Center/ Baghdad Teaching Hospital . An eighty four patients with End Stage Renal Disease (ESRD) on regular Hemodialysis (HD) enrolled in the study from January to February 2013.

The basic data of the patients had been obtained (age ,weight ,duration on HD (months), infection with HCV, drugs doses for calcium and alphacalcidol . Blood samples were collected at the start of the HD session from the vascular access for calcium, phosphorus, albumin, cholesterol, uric acid and Vitamin 25(OH) D3 blood levels. These samples were sent for analysis to the Teaching Laboratories at Medical City.

Patients were considered as vitamin D3 insufficient if the levels were between 10 and 30 ng/ml , deficient if the levels were less than 10 ng/ml and sufficient if it was >30 ng/ml

We assess the correlation between vitamin D3 level and other variables tested in the study.

RESULTS:

The mean age of the patients was 49.8 ± 13.2 years, of these, 40 (47.6٪) were females and 44 (52.4٪) were males. Fifty five (65٪) patients were infected with hepatitis C virus and 29(35٪)were not . the median dose of calcium carbonate was 1086.1 ± 400 mg per day, The median dose of alphacalcidol was1.9 ± 1.1 mcg /week. Mean weight was 68.8 ± 17.5 kg. Median duration of HD was 24.8 ± 20.8 months (range 2–72 months).The patients were on twice a week (6-8 hours/week) HD sessions.

Mean of serum albumin, corrected calcium, phosphorus, Uric acid cholesterol were 3.0 ± 0.8 g/dl., 8.6 ± 1.4 mg/dl, 3.9 ± 1.4 mg/dl , 6.1 ± 2.4 mg/dl, 149.9 ± 39.2 mg/dl respectively .

Mean vitamin 25(OH) D3 level was 33.02 ± 7.2 ng/ml. 60(71.4٪) patients were vitamin D3 sufficient, 23(27.4٪) patients were vitamin D3 insufficient and only one (1.2٪) patient was vitamin D3 deficient.

There was a significant correlation between vitamin 25(OH)D3 levels and albumin , duration of HD, virology status while there was no correlation between weight, sex ,age , activity, calcium, cholesterol, uric acid , phosphorus ,dose of alphacalcidol or calcium carbonate and vitamin 25(OH)D3 level .

CONCLUSION:

The vitamin D insufficiency found in about one quarter of patients on hemodialysis while deficiency found only in 1.2% of patients and more than two third of patients had sufficient vitamin D3. There was a significant correlation between vitamin 25(OH)D3 levels and albumin , duration of HD, virology status.

KEYWORDS: vitamin D, haemodialysis**.**

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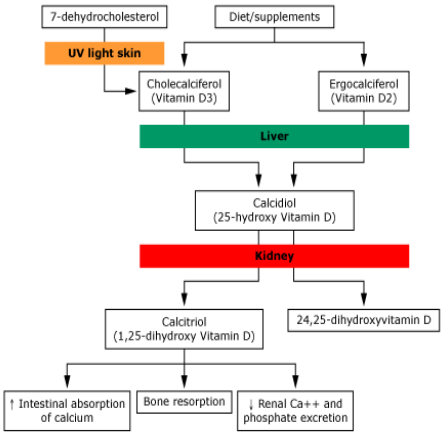
INTRODUCTION:

The vitamin D family includes the biologically inert fat-soluble prohormones vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol).

These are obtained from mainly sun exposure (by photochemical conversion of 7-dehydrocholesterol in the skin), food (especially fatty fish), or nutritional supplements. These prohormones are converted by hydroxylation in the liver to 25-hydroxyvitamin D and, by a second hydroxylation step (performed by 1α-hydroxylase), to its active form, 1,25-dihydroxyvitamin D (calcitriol). The kidneys are the most abundant source (but not exclusive) of 1α-hydroxylase in the body, and therefore chronic kidney disease (CKD) is associated with deficiencies in calcitriol. (1,2)



In normal conditions, the renal production of calcitriol is tightly regulated by parathyroid hormone and by serum calcium and phosphorus levels. Calcitrol synthesis is also suppressed by both fibroblast growth factor 23(FGF23), secreted from bone, and conditions of metabolic acidosis. Extrarenal calcitriol conversion occurs in other tissues, such as those of the skin, colon, prostate, macrophages, and other organs, but the regulatory processes for this conversion are not well understood. Calcitriol has a half-life of only 4 to 6 hours, and the circulating levels are low. Calcitriol, which is transported to various target organs by vitamin D–binding protein, mobilizes calcium into the bloodstream by promoting absorption of calcium and phosphorus from food in the intestines and reabsorption of calcium in the kidneys. Calcitriol also promotes bone mineralization, bone growth, and bone remodeling by osteoblasts and osteoclasts, and it prevents hypocalcemia. (2)

Vitamin D deficiency has been linked to multiple disorders, including growth retardation, skeletal abnormalities (osteopenia, osteoporosis, and increased risk of fractures), muscle weakness, and left ventricular hypertrophy and to increased susceptibility to cancer, diabetes, autoimmune diseases, and infectious diseases.(3,4)

In the kidneys, vitamin D may be important for maintaining podocyte function, preventing epithelial-to-mesenchymal transformation, and suppressing renin gene expression and inflammation.(5)

Parathyroid hormone has a key role in calcium and phosphate homeostasis. It stimulates excretion of phosphate by the renal tubule and indirectly modulates intestinal calcium absorption by stimulating the activation of calcitriol synthesis. As vitamin D deficiency progresses, the parathyroid glands are maximally stimulated, causing secondary hyperparathyroidism. Thus, levels of 25-hydroxyvitamin D are inversely associated with parathyroid hormone levels, and calcitriol inhibits parathyroid hormone expression. Parathyroid hormone increases the metabolism of 25-hydroxyvitamin D to calcitriol, which further exacerbates the vitamin D deficiency. Elevated levels of parathyroid hormone have been implicated in left ventricular hypertrophy and in the metabolic syndrome, in which they contribute to impairments in glucose tolerance and to dyslipidemia$_5$

Insufficient to deficient levels of 25-hydroxyvitamin D have been reported in the majority of individuals with CKD, including patients not dependent on dialysis and those receiving maintenance dialysis.Deficiency seems to be more pronounced in black individuals.(6)

The circulating levels of 25-hydroxyvitamin D and calcitriol decrease with diminishing renal function across worsening stages of CKD.(3,5,6)

Because 25-hydroxyvitamin D has a longer half-life than does calcitriol (approximately 3 weeks), it is considered the best measure of vitamin D status.

On these premises, vitamin D insufficiency is commonly defined as 25-hydroxyvitamin D levels lower than 30 ng/mL, whereas deficiency is defined at levels lower than 15 ng/mL. Although there are known seasonal, geographic, ethnic, and age-related variations, and although the desirable level of vitamin D in patients with CKD has not yet been defined, it is recommended that serum levels of 25-hydroxyvitamin D be maintained higher than 30 ng/mL in patients with CKD.[7]

recently it has been shown that 25(OH)D can be converted to $1,25(OH)_2D$ at sites other than the kidney, including the prostate, breast, colon, and macrophages.

Local production of $1,25(OH)_2D$ may be important for several biologic functions in these tissues; thus, circulating 25(OH)D levels may be relevant even when supplementation with active vitamin D is carried out, as in patients with CKD with low renal production of $1,25(OH)_2D$. Levels of 25(OH)D below 30 ng/ml are associated with increased parathyroid hormone (PTH) levels, low bone mineral density (BMD), and increased risk of hip fractures.The recently published KDIGO (Kidney disease improving global outcomes) guidelines recommend that the serum level of 25(OH)D should be maintained over 30 ng/ml in patients of all stages of CKD.

Studies have also indicated that calcidiol deficiency and insufficiency are common in CKD, with only 29% and 17% of stage 3 and 4 CKD subjects, respectively, with sufficient levels

Most commercial assays for 25-hydroxyvitamin D are thought to be acceptable for detecting vitamin D deficiency. However, there are considerable variations between laboratories and between assays for measurement of circulating levels of 25-hydroxyvitamin D and parathyroid hormone. The 1,25-dihydroxyvitamin D assay should not be used for detecting vitamin D deficiency in patients with CKD because the results indicate that levels are normal or even elevated as a result of secondary hyperparathyroidism.

Studies associating active vitamin D treatment with improved survival in dialysis and predialysis CKD are now numerous [8.9.10] In HD patients, 25-hydroxyvitamin D levels have been shown to correlate with all-cause and cardiovascular mortality [11].

Treatment should replete and then maintain adequate stores. Vitamin D stores are assessed by measuring 25-OH vitamin D in the blood. Levels of >30 ng/mL are desirable.

PATIENTS AND METHOD:

This study is a cross section study conducted in The Dialysis Center /Baghdad Teaching Hospital, Medical City Complex, Iraq ., An eighty four patients with End Stage Renal Disease (ESRD) on regular Hemodialysis (HD) for more than three months enrolled in the study . The period of study was from January to February 2013.The basic data of the patients were collected (age, sex ,weight ,duration on HD (months),virology status) , drugs doses for calcium and alphacalcidol and blood sample was collected at the start of the mid-week HD session from the vascular access for calcium, phosphorus, albumin, cholesterol, uric acid and these samples were sent to the local laboratory of the dialysis unit for analysis. 25(OH) D3 samples were taken in a separate tube and centrifuged immediately and stored at cold storage. These samples were sent for analysis to the Teaching Laboratories in Baghdad Medical City. Dialysate calcium concentration was 1.75meq|dl

Patients were considered vitamin D3 insufficient if the levels were between 10 and 30 ng/ml and deficient if the levels were less than 10 ng/ml and >30 ng/ml considered as sufficient vitamin D3,> than 100 ng/ml considered toxic level .[12]

Inclusion criteria ,ESRD patients on HD for more than three months

We looked for any correlation between vitamin D3 level and other variable tested in those patients.

Analytical methods:- measurements of calcium, phosphorus, cholesterol, albumin, uric acid by spectrophotometer method .These assays are done on instruments (DECIL .CE 1011).

Vitamin 25(OH) D3 levels were measured by competitive inhibition enzyme immunoassay technique by ELISA Kit from Cusabio biotech co. China.

Statistical analysis:

Data of the 84 ESRD patients were transferred into computerized database form and checked for errors or inconsistency with the aid of Microsoft excel 2007, program for windows.

Data management and statistical analysis were performed by SPSS (statistical package for social sciences) version 20, for windows software.

Descriptive statistics for continuous variables; age, weight, Calcium level, PO4, uric acid,

cholesterol, Albumin, Calcium dose, 1 alpha and vitD3 level, were presented as mean and standard deviation (SD), while for categorical variables; sex, virology, exercise, and vitD3 categories (sufficient, insufficient and deficient), were presented as frequencies and percentages (%).

ANOVA test (F) test was used to assess the significance of association between vitD3 and the continuous variables, distributed by three categories of vit. D3 level. Student's t test was used to compare sufficient and insufficient groups.

Chi square test was used to assess the significance of association of VitD3 categories with other categorical variables, Fisher exact test was used alternatively when chi square couldn't be applied.

Level of significance was two tailed and set at $P \leq 0.05$ to be considered as significant

RESULT:

An eighty four HD patients were analyzed for their vitamin D status. The characteristics of these patients are as shown in (Table No -1). Mean age was 49.8 ± 13.2 Of these, 40 (47.6٪) were females and 44 (52.4٪) were males. Mean weight was 68.8 ± 17.5 kg. fifty five(65٪) were infected with hepatitis C virus and 29(35٪)were not . the median dose of calcium carbonate was 1086.1 ± 400 mg per day, the median dose of alphacalcidol was1.9 ± 1.1 mcg/week Median duration of dialysis was 24.8 ± 20.8 months (range 2–72 months).

The patients were on twice a week HD sessions (8 hours /week

Mean of serum albumin, corrected calcium, phosphorus, Uric acid cholesterol were 3.0 ± 0.8 g/dl., 8.6 ± 1.4 mg/dl, 3.9 ± 1.4 mg/dl , 6.1 ± 2.4 mg/dl, 149.9 ± 39.2 mg/dl respectively . (Table No-1) Mean 25(OH) D3 level was 33.02 ± 7.2 ng/ml. sixty (71.4٪) of patients were vitamin D3 sufficient, 23(27.4٪) of patients were vitamin D3 insufficient and one(1.2٪) of patient only was vitamin D3 deficient, zero patient with toxic level (table No -1 figure No-1).

In this study the results show only one patient with vitamin D3 deficiency so we exclude this result and make the comparison between the sufficient and insufficient groups .(figure No.1 and table No.2 and .3)

There was a significant correlation between vitamin 25(OH)D3 levels and serum albumin , duration of HD, virology status while there was no correlation between weight, sex ,age , calcium, cholesterol, uric acid , phosphorus ,dose of one alpha or calcium carbonate and vitamin 25(OH)D3 levels (table III-2 and table III-3)

DISCUSSION:

The mean vitamin 25(OH) D3 level was 33.02 ± 7.2 ng/ml in patients on HD (table 1) as compared to 31.4 ±22.98003 ng/ml, in "normal" adult population in Al-Jebouri et al study[13] from Tikrit governorate in Iraq.

Vitamin D deficiency, insufficiency and sufficiency were seen in (1.2%), (27.4%) and (71.4%) respectively (figure 1), of our patients on HD as compared to 52.8%, 37.7% and 9.4% respectively in Al-Jebouri et al study[13]. Its obvious that the normal population from Jebouri et al study are more deficient with vitamin D3 than our patients in Baghdad this may be due to that patients on HD had more medical care and more vitamin supplementation and this results are consistent with results from north India show that patients in HD has better vitamin D status than normal population.[14,15]

In Bhan I et al study [16] from North America the Result of Vitamin D deficiency, insufficiency and sufficiency were 20 %, 77% and 3% of patients on HD respectively[14,] and in Beena Bansal etal study[15] from north India were in 64.4%, 31.8% and 4.4% of patients respectively in comparison to (1.2%), (27.4%) and (71.4%) respectively (figure 1), of our patients on HD.

Our results are not consistent with this result from these different parts of the world as the results mentioned was from countries with cold climate as we did not find result for patients on HD in the nearby region to compare with it also the results taken In Bhan I etal study from North America was taken for the patients just starting HD as our results as we will discuss later shows that patients short duration on HD had lower level of vitamin D3

In this study results show low serum albumin levels were also associated with an increased risk of vitamin D deficiency(table 2), this results are consistent with Bhan I etal study.[16]

Albumin is likely to reflect level of nutrition, and low serum albumin might correlate with lower intake of dietary sources of vitamin D. alternatively, low albumin could represent reduced carrying capacity for vitamin D, which largely circulates in protein-bound form [17]. However, another possible explanation is that a common disorder predisposes to both hypoalbuminemia and vitamin D deficiency. This could represent chronic inflammation, an aspect of many co-morbid illnesses.

Also results of this study show that short duration on HD (table 2) associated with low vitamin D3 this may be explained by that patients in predialysis stage are with restricted diet including

diet rich in vitamin D3 another explanation could be predialysis patients are do not receive good medical care, or patients with longer duration on HD are with good compliance with their medical care. In Beena Bansal et al study [14] the duration of HD was not found to be correlated of with vitamin D3 level in HD patients.

Results of this study show that infection with hepatitis C virus associated with higher level of vitamin D3(table 3), this may be explained by that patients with hepatitis C virus are those with longer duration on HD as observed in our patients and may be of good nutritional status and good compliance with medical care.

Table 1: Characteristics of patients in the study (84 patients).

Variable		mean ± SD	No.84 (100%)
Sex	Male		44 (52.4)
	Female		40 (47.6)
Age (years)		49.82 ± 12.94	
Weight(kg)		68.8 ± 17.5	
Duration(months)		24.8 ± 20.8	
Vit D3 level		33.02 ± 7.2	
Corrected Calcium (mg/dl)		8.6 ± 1.4	
Phosphorus(mg/dl) (mg/dl) (mg/dl)		3.9 ± 1.4	
Uric acid(mg/dl)		6.1 ± 2.4	
Cholesterol(mg/dl)		149.9 ± 39.2	
Albumin(g/L)		3.0 ± 0.8	
Calcium Dose mg		1082.1 ± 389	
Alphacalcidol dose		1.97 ± 1.01	
Hepatitis C	Negative		29 (34.5)
	Positive		55 (65.5)

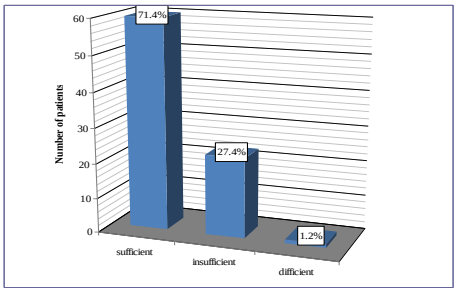


Figure 1: Frequency Distribution of Vitamin.D3 level Among the Patients.

Table 2:Correlation of vitamin D3 level with Gender and HCV Status.

Variables		Vit D3 categories						P sufficient vs. insufficient	P all groups
		Sufficient		Insufficient		Deficient			
		N	%	N	%	N	%		
Sex	Male	32	72.7	11	25.0	1	2.3	0.81	0.57
	Female	28	70.0	12	30.0	0	0.0		
HCV	Negativeee	17	58.6	12	41.4	0	0.0	0.041	0.043 [sig]
	Positive e	43	78.2	11	20.0	1	1.8		

Table 3: Correlation Between Patients' Parameters and Vitamin.D3 Level distributed by categories. (N=84).

Parameter (mean)	Vit. D3 categories			P value sufficient vs. insufficient	P.value comparison of 3 groups
	Sufficient	Insufficient	Deficient		
Age (years)	49.92	50.95	18.3	0.74	0.045 [sig]
Weight (kg)	69.9	66.7	56.1	0.43	0.54
Corrected Calcium mg/dl	8.55	8.66	9.30	0.75	0.83
Phosphorus mg/dl mg/dl	3.74	4.09	5.70	0.31	0.25
Uric acid mg/dl	6.00	6.19	7.30	0.76	0.83
Cholesterol mg/dl	148.5	153.3	151	0.62	0.88
Albumin g/L	3.12	2.80	3.0	0.034 [sig]	0.18
Duration months	28.0	16.3	24	0.022 [sig]	0.07
Calcium Dose mg	1120	978	1200	0.14	0.26
Alphacalcid dose Ug	1.93	1.96	3.00	0.91	0.59

CONCLUSION:

The vitamin D insufficiency found in about one quarter of patients on HD while deficiency found only in 1.2% of patients and more than two thirds of patients had sufficient vitamin D3 .

Higher level of vitamin D3 level found in patients with higher albumin level, longer duration of HD and in patient s with hepatitis C virus infection .

Recommendations

- Annually measurement of vitamin D3 especially for patients in predialysis stage with Vitamin D supplementation if need.
- Multicenter Studies for vitamin D level in normal population and ESRD in different region of the country.
- The practice and policy of physicians and nephrologists in prescription of vitamin D to the patients should be considered and appointed

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