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The relation between vitamin D status and anemia in patients with end stage renal disease on regular hemodialysis

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Abstract

Introduction: Anemia is a common complication in end-stage renal disease (ESRD) patients on regular hemodialysis (HD). There has been a lot of interest recently in the non-classical effects of 25(OH) vitamin D (calcidiol), including its association with erythropoiesis and anemia pathogenesis.

Objectives: To study the relation between anemia and vitamin D status in patients on regular HD

Results: This study is a cross-sectional study that included 90 patients on regular HD. Vitamin D status was classified into deficient (<20 ng/mL), insufficient (20-30 ng/mL) and sufficient (>30 ng/mL). The level of vitamin D measured in the patients ranged between 3.5 to 66 ng/mL with median of 16.35 ng/mL. There were statistically significant positive correlations between vitamin D levels and the level of hemoglobin ($P<0.001$), serum calcium levels ($P<0.001$) and serum PO4 levels ($P=0.023$). Higher hemoglobin levels were statistically related to both higher vitamin D values ($P<0.001$) and higher serum calcium concentration $P<0.001$). Meanwhile, a significant negative correlation was found between hemoglobin levels and serum PTH values ($P<0.001$).

Conclusion: There was a significant association between the status of vitamin D and the level of hemoglobin in dialysis population who were studied, independent from iron status. other associations with hemoglobin levels included PTH level and calcium.

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Introduction

Anemia is a complication that is commonly encountered when caring for patients with chronic kidney disease (CKD). Moreover, the severity of the anemia worsens as the glomerular filtration rate (GFR) declines, with a prevalence reaching approximately 90% in patients with a GFR less than 30 mL/min (1).

Previous studies have found anemia to be associated with significant morbidity and mortality in end-stage renal disease (ESRD) patients on hemodialysis (HD). Anemia leads to progression of left ventricular hypertrophy with increased risk of myocardial infarction and heart failure (2,3). Anemia has also been associated with depression, cerebrovascular stroke, and fatigue and reduced exercise tolerance (4).

The pathogenesis of anemia in CKD is multifactorial. The fall in GFR is typically accompanied by a decrease in erythropoietin production. However, several other factors contribute including absolute and functional iron deficiency, folate and vitamin B_{12}deficiencies and suppression of erythropoiesis by uremia (5).

Among patients with CKD or those on dialysis, vitamin D deficiency and insufficiency are increasingly common (6). Diet restrictions and decreased sunlight exposure are factors that affect vitamin D levels in dialysis patients. Del Valle et al reported inadequate sunlight exposure in approximately 84% of HD patients with vitamin D deficiency (7). Furthermore, uremia has a negative effect on the activation of plasma vitamin D in response to ultraviolet B (UVB) irradiation (8). One of the most common cutaneous manifestations in patients undergoing HD is hyperpigmentation, which too can impair the activation of vitamin D (9). Understanding vitamin D physiology has sparked interest in recent studies searching for other functions beyond its role in mineral and bone metabolism (10). It has been proven that activation of vitamin D can occur in several tissues, in addition to the kidneys (11). Several studies have shown that an increased risk of cardiovascular, musculoskeletal and autoimmune diseases, cancer and increased risk of infections can be associated with vitamin D deficiency (12,13). The study to evaluate early kidney disease and the third national health

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Implication for health policy/practice/research/ medical education

In a cross-sectional study that included 90 patients on regular hemodialysis, we found a statistically significant positive correlation between vitamin D levels and the level of hemoglobin.

and nutrition examination survey showed that vitamin D deficiency was significantly and independently associated with anemia in patients with CKD who do not require dialysis (14,15).

Objectives

This study aimed to evaluate the relation between anemia and vitamin D status in patients on regular HD

Patients and Methods

Study design

This is a cross-sectional study involving 90 patients in El Agouza hospital, Giza, Egypt, with ESRD on regular HD treatment for more than six months with age over 18 years. This study excluded patients with hepatitis B or hepatitis C infection, patients with malignancies, patient with hemolytic anemia, patients with malabsorption syndromes (Celiac disease and inflammatory bowel disease), patients with active or chronic infections, patients with active bleeding and renal transplant recipients. All patients were on fixed dose of erythropoietin 4000 units twice weekly, except those with hemoglobin more than or equal to 11 g/dL. The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines (2012) recommended that Hb targets should be in the range of 10.0–11.5 g/dL, regardless of whether the patients were receiving dialysis (16). Therefore, we defined anemia as an Hb level of <11 g/dL.

All patients were subjected to full history and physical examination with emphasis on demographic data age, gender, duration of HD, cause of renal failure, comorbidities, and medications. Laboratory tests included serum calcium, phosphorus, 25(OH) D and intact parathyroid hormone (iPTH) levels, hemoglobin level, ferritin level, serum iron, total iron binding capacity (TIBC) and calculation of transferrin saturation (TSAT). Serum 25(OH) vitamin D level was measured by ELISA (Cal biotech. USA, REF: VD2208), serum samples were collected and centrifuged and separated as soon as possible, stored at -20°C, all specimens were allowed to come to room temperature before use. Vitamin D deficiency was defined as serum levels < 20 ng/dL, insufficiency 20-30 ng/dL and sufficiency >30 ng/dL.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study was approved by Ain Shams University ethical committee (Ref# FWA000017585). Informed consent was taken from all participants.

Statistical analysis

IBM SPSS statistics (V. 25.0, IBM Corp., USA, 2017-2018) was used for data analysis. Data were expressed as median and percentiles for quantitative non-parametric measures. The following tests were conducted: (*a*) Comparison between two independent groups for non-parametric data using Wilcoxon rank sum test; (*b*) Comparison between more than 2 patient groups for non-parametric data using Kruskal-Wallis test; and (*c*) Ranked Spearman's correlation test to study the possible association between each two variables among each group for non-parametric data. The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 are highly significant.

Results

This study recruited 90 patients with ESRD, maintained on regular HD in El Agouza hospital HD unit. Table 1 shows the demographics of the study population with the mean age of 51.13 ± 10.44 years consisted of 68 males and 22 females with median duration of HD of 9.50 (6-2) years. Around 32 (35.6%) of patients were diabetic while 86 (95.6%) of them were hypertensive. As regards the etiology of ESRD the majority of the patients listed hypertension and diabetes 37 (41.1%) and 32 (35.6%) patients respectively.

The level of vitamin D measured in the patients ranged between 3.5 to 66 ng/mL with median of 16.35 ng/mL (8-34 ng/mL). About 24 patients had vitamin D deficiency (vitamin D levels <20 ng/dL) (Table 2). Accordingly, patients with insufficient levels (vitamin D levels 20-

Table 1. Demographic data of the study population

		N = 90
Gender	Female	22 (24.4%)
	Male	68 (75.6%)
Age (y)	Mean ± SD	51.13 ± 10.44
	Range	24–66
Dialysis duration (y)	Median (IQR)	9.50 (6–12)
	Range	1–21
Diabetic	No	58 (64.4%)
	Yes	32 (35.6%)
HTN	No	4 (4.4%)
	Yes	86 (95.6%)
Etiology of ESRD	Hypertension	37 (41.1%)
	Diabetic nephropathy	32 (35.6%)
	Lupus nephritis	4 (4.4%)
	Chronic glomerulonephritis	4 (4.4%)
	Chronic tubulointerstitial nephritis	2 (2.2%)
	ADPKD	1 (1.1%)
	Hereditary nephritis	1 (1.1%)
	Amyloidosis	1 (1.1%)
	Unknown	8 (8.9%)

ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease.

Table 2. Classification of the patients according to vitamin D3 levels (ng/dL)

Vitamin D3	No. (%)
Deficient	24 (26.7%)
Insufficient	32 (35.6%)
Sufficient	34 (37.8%)
Median (IQR)	16.35 (8–34)
Range	3.5–66.3

30 ng/dL) were 32 individuals, while patients with sufficient (>30 ng/dL) levels were 34 cases. Table 3 shows no statistically significant relations between vitamin D levels and the gender of the patients ($P=0.536$), their age ($P=0.973$), duration of HD ($P=0.600$), diabetes mellitus ($P=0.064$) and hypertension ($P=0.249$).

There were statistically significant positive correlations between vitamin D levels and the value of hemoglobin ($P<0.001$), serum calcium levels ($P<0.001$) and serum PO4 levels ($P=0.023$). However, significant negative correlations of vitamin D levels with serum iPTH levels ($P<0.001$), serum iron ($P=0.019$) and TSAT ($P=0.012$) were detected. There was no statistically significant relation between vitamin D levels and type of dialysis access ($P=0.437$), TIBC ($P=0.193$), serum ferritin levels ($P=0.125$) or serum albumin concentration ($P=0.541$) (Table 4).

In Table 5, using Spearman's correlation coefficient, highly significant positive correlation between vitamin D3 levels and both hemoglobin levels ($P<0.001$) and serum calcium levels ($P<0.001$) were detected. Meanwhile, there was highly significant negative correlation between vitamin D3 levels and serum iPTH (intact PTH) levels $P<0.001$) and TSAT ($P=0.003$).

There were no significant correlations between vitamin D3 levels in all three groups of patients and age of the patients, duration of HD, serum phosphorus levels, serum iron levels, TIBC, serum ferritin levels or serum albumin levels (Table 6).

Table 7 shows highly significant positive relation between hemoglobin levels of all patients and their vitamin D3 levels ($P<0.001$). Meanwhile, no significant relationship between hemoglobin level and presence of diabetes ($P=0.533$) or hypertension ($P=0.748$), etiology of ESRD ($P=0.302$) and type of dialysis access ($P=0.960$) was detected.

Additionally, highly significant positive correlations between plasma hemoglobin concentration with both vitamin D3 ($P<0.001$) and serum calcium levels ($P<0.001$) were seen. Meanwhile, a highly significant negative correlation between hemoglobin levels and serum iPTH levels was seen ($P<0.001$).

There were no statistically significant correlations between hemoglobin levels and age of the patients, duration of HD, serum phosphorus levels, serum iron, TIBC, serum ferritin levels, TSAT or serum albumin levels (Table 8).

Discussion

Observational studies have reported that vitamin D deficiency worsens with progression of CKD stage (17).

Table 3. Vitamin D levels in the 3 groups and demographic data

		Vitamin D3 levels (ng/dL)					
		Deficient n = 24	Insufficient n = 32	Sufficient n = 34	Test value	*P* value	Sig.
Gender	Female	5 (20.8%)	10 (31.2%)	7 (20.6%)	1.246	0.536	NS
	Male	19 (79.2%)	22 (68.8%)	27 (79.4%)			
Age	Mean ± SD	51.33 ± 10.18	50.78 ± 10.61	51.32 ± 10.76	0.028	0.973	NS
	Range	24–63	24–65	26–66			
Dialysis duration	Median (IQR)	9.5 (6.5–11.5)	10 (7–12)	8 (5–11)	1.021	0.600	NS
	Range	2–18	1–21	1–17			
Diabetic	No	14 (58.3%)	17 (53.1%)	27 (79.4%)	5.505	0.064	NS
	Yes	10 (41.7%)	15 (46.9%)	7 (20.6%)			
HTN	No	0 (0.0%)	1 (3.1%)	3 (8.8%)	2.783	0.249	NS
	Yes	24 (100.0%)	31 (96.9%)	31 (91.2%)			
Etiology of ESRD	Hypertension	11 (45.8%)	7 (21.9%)	19 (55.9%)	27.089	0.041	S
	Diabetic nephropathy	10 (41.7%)	15 (46.9%)	7 (20.6%)			
	Lupus nephritis	1 (4.2%)	2 (6.2%)	1 (2.9%)			
	Chronic glomerulonephritis	0 (0.0%)	0 (0.0%)	4 (11.8%)			
	Chronic tubulointerstitial nephritis	0 (0.0%)	2 (6.2%)	0 (0.0%)			
	ADPKD	0 (0.0%)	1 (3.1%)	0 (0.0%)			
	Hereditary nephritis	0 (0.0%)	0 (0.0%)	1 (2.9%)			
	Amyloidosis	0 (0.0%)	0 (0.0%)	1 (2.9%)			
	Unknown	2 (8.3%)	5 (15.6%)	1 (2.9%)			

ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease.
P value < 0.05: Significant; P-value < 0.01: Highly significant.

Table 4. Vitamin D level in 3 groups in relation to clinical parameters including

		Vitamin D3			Test value	*P* value	Sig.
		Deficient n = 24	Insufficient n = 32	Sufficient n = 34			
Dialysis access	Arteriovenous fistula	23 (95.8%)	29 (90.6%)	33 (97.1%)	3.774[a]	0.437	NS
	Arteriovenous graft	1 (4.2%)	1 (3.1%)	1 (2.9%)			
	Permanent HD catheter	0 (0.0%)	2 (6.2%)	0 (0.0%)			
Serum calcium (mg/dL)	Mean ± SD	8.57 ± 1.07	8.43 ± 0.67	9.32 ± 0.68	11.646[b]	0.000	HS
	Range	7.6–11.9	6.9–9.7	8.6–12			
Serum phosphorus (mg/dL)	Mean ± SD	4.63 ± 0.81	4.52 ± 0.92	5.32 ± 1.67	3.935[b]	0.023	S
	Range	2.9–7.2	2.6–8.1	2.7–11			
PTH (pg/mL)	Median (IQR)	669.5 (468.5–782.5)	528.5 (380–666.5)	157.5 (112–213)	50.646[c]	0.000	HS
	Range	230–1197	46.7–1107	28–444			
Hemoglobin (g/dL)	Mean ± SD	8.73 ± 0.83	9.24 ± 1.43	11.24 ± 1.83	24.660[b]	0.000	HS
	Range	6.6–10.1	6.7–14.3	7–14.3			
Serum iron (µg/mL)	Mean ± SD	65.33 ± 20.36	66.38 ± 18.88	53.06 ± 22.16	4.159[b]	0.019	S
	Range	28–94	27–109	16–98			
TIBC	Mean ± SD	185.46 ± 47.19	204.94 ± 58.36	216.56 ± 77.32	1.676[b]	0.193	NS
	Range	105–303	112–311	112–390			
Ferritin (ng/mL)	Mean ± SD	471.54 ± 139.92	399.62 ± 158.78	374.94 ± 216.51	2.131[b]	0.125	NS
	Range	236–764	15.9–720	16–782			
TSAT (%)	Mean ± SD	35.16 ± 8.12	33.12 ± 7.90	26.87 ± 14.66	4.670[b]	0.012	S
	Range	9–47	8–46	5–56			
Serum albumin (g/dL)	Mean ± SD	3.93 ± 0.39	3.94 ± 0.31	3.84 ± 0.48	0.618[b]	0.541	NS
	Range	3.4–4.9	3.5–4.7	3.1–5.1			

P value > 0.05: Non-significant (NS); *P* value < 0.05: Significant (S); *P* value < 0.01: Highly significant (HS).
[a] Chi-square test; [b] One Way ANOVA test; [c] Kruskal-Wallis test.

However, there was no difference in prevalence of vitamin D deficiency between CKD patients and the general population in a cross sectional study by Guesseous et al (18). Low 25-hydroxy vitamin D levels have been associated with secondary hyperparathyroidism, decreased bone mineral density and high bone turnover in CKD and patients receiving chronic dialysis treatment (19,20). Moreover, it has been associated with a decrease in muscle power and an increased fall risk (21). It has been suggested in studies conducted on bone marrow red cell precursor cells that the active form of 25OH vitamin D, calcitriol is associated with upregulating erythropoietin-receptors. Additionally, the active form of 25OH vitamin D also increases cell membrane permeability to calcium stimulating and proliferation of pre-erythroid cell series along with erythropoietin (22).

Table 5. Correlation of vitamin D3 levels with the other studied parameters using spearman correlation coefficient

	Vitamin D3	
	R	*P* value
Age	-0.027	0.798
Disease duration	-0.064	0.550
Hemoglobin	**0.569****	**0.000**
Serum calcium	**0.537****	**0.000**
Serum phosphorus	0.173	0.103
Intact PTH	**-0.733****	**0.000**
Serum iron	-0.197	0.062
TIBC	0.184	0.082
Ferritin	-0.180	0.090
TSAT (%)	**-0.305****	**0.003**
Serum albumin	-0.129	0.226

P value < 0.05: Significant; *P* value < 0.01: Highly significant.

Our study is cross-sectional that recruited 90 ESRD patients on regular HD in Al Agouza hospital HD center.

In the current study, 66% of patients had vitamin D levels below 30 ng/mL. Several studies have shown a high prevalence of vitamin D deficiency and insufficiency in CKD patients sometimes reaching over 80% (23). There are various causes of 25(OH)vitamin D deficiency in dialysis and CKD population like deficient sunlight exposure (24), impaired vitamin D synthesis and metabolism (25), uremic gastritis and dietary restrictions (26).

In our study, we divided our participants according to their vitamin D status into deficient, insufficient and sufficient groups. We found a highly significant relation between 25(OH) vitamin D levels and hemoglobin levels of our patients ($P<0.001$). The patients with sufficient 25(OH) vitamin D levels had higher mean hemoglobin levels than those with insufficient 25(OH) vitamin D levels and subsequently than those with deficient 25(OH) vitamin D levels (mean 11.24 ± 1.83, 9.24 ± 1.43, and 8.73 ± 0.83 ng/dL, respectively). Similarly, Patel et al, found

Table 6. Relationship between vitamin D3 levels in all patients and the other demographic parameters

		Vitamin D3		Test value	*P* value	Sig.
		Median (IQR)	Range			
Gender	Female	15.95 (11–32)	3.8–51	-0.521[a]	0.602	NS
	Male	16.85 (8–34.5)	3.5–66.3			
Diabetic	No	19.5 (10–36)	4–66.3	-1.691[a]	0.091	NS
	Yes	14.3 (6.8–24.5)	3.5–57			
HTN	No	35.2 (25.35–41.7)	17.7–46	-1.831[a]	0.067	NS
	Yes	16 (8–33.8)	3.5–66.3			
Etiology of ESRD	Hypertension	30.7 (8–37)	4–51	9.119[b]	0.332	NS
	Diabetic nephropathy	14.3 (6.8–24.5)	3.5–57.0			
	Lupus Nephritis	13.4 (9.25–24.9)	5.5–36			
	Chronic glomerulonephritis	32 (31.5–35.5)	31–39			
	Chronic tubulointerstitial nephritis	17.85 (17.7–18)	17.7–18			
	ADPKD	13 (13–13)	13–13			
	Hereditary nephritis	46 (46–46)	46–46			
	Amyloidosis	37.4 (37.4–37.4)	37.4–37.4			
	Unknown	12.65 (9–18.85)	6.7–66.3			
Dialysis access	Arteriovenous fistula	16 (8–34)	3.5–66.3	0.230[b]	0.891	NS
	Arteriovenous graft	22 (8.3–34)	8.3–34			
	Permanent HD catheter	20 (18–22)	18–22			

ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease; HD, hemodialysis.

P value > 0.05: Non-significant (NS); *P* value < 0.05: Significant (S); *P* value < 0.01: Highly significant (HS).

[a] Mann-Whitney test; [b] Kruskal-Wallis test.

Table 7. Hemoglobin level in relation to demographics data and vitamin D status

		Hemoglobin		Test value	*P* value	Sig.
		Mean ± SD	Range			
Gender	Female	9.38 ± 1.62	6.6–12.3	-1.431•	0.156	NS
	Male	10.02 ± 1.88	7–14.3			
Diabetic	No	9.95 ± 1.92	6.6–14	0.626•	0.533	NS
	Yes	9.7 ± 1.68	7.9–14.3			
HTN	No	10.15 ± 2.22	7.6–12.3	0.322•	0.748	NS
	Yes	9.85 ± 1.83	6.6–14.3			
Etiology of ESRD	Hypertension	10.19 ± 2.07	6.6–14	1.213••	0.302	NS
	Diabetic nephropathy	9.69 ± 1.68	7.9–14.3			
	Lupus nephritis	8.78 ± 1.44	6.7–10			
	Chronic glomerulonephritis	11 ± 1.73	8.4–11.9			
	Chronic tubulointerstitial nephritis	8 ± 0.57	7.6–8.4			
	ADPKD	8.5 ± 0	8.5–8.5			
	Hereditary nephritis	9 ± 0	9–9			
	Amyloidosis	12.3 ± 0	12.3–12.3			
	Unknown	9.4 ± 1.17	8.2–11.9			
Dialysis access	Av fistula	9.86 ± 1.86	6.6–14.3	0.041••	0.960	NS
	Av graft	9.67 ± 1	8.7–10.7			
	Permanent HD catheter	10.15 ± 2.47	8.4–11.9			
Vitamin D3 (ng/dL)	Deficient	8.73 ± 0.83	6.6–10.1	24.660	0.000	HS
	Insufficient	9.24 ± 1.43	6.7–14.3			
	Sufficient	11.24 ± 1.83	7–14.3			

ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease; HD, hemodialysis.

P value > 0.05: Non-significant (NS); *P* value < 0.05: Significant (S); *P* value < 0.01: Highly significant (HS).

that 25 (OH) vitamin D deficiencies were significantly associated with anemia in patients with early CKD (14). However, most patients in that study were CKD stage 3 and none were on dialysis.

Furthermore, it was clear that higher levels of vitamin D were significantly associated with lower PTH levels. Serum PTH levels in patients with deficient and insufficient 25(OH) vitamin D levels were higher than those with sufficient 25(OH) vitamin D levels with median values (669.5, 528.5 and 157.5 ρg/mL respectively;

Table 8. Correlation of hemoglobin level with the other parameters using Spearman's correlation coefficient

	Hemoglobin	
	R	*P* value
Vitamin D3	0.569**	0.000
Age	0.033	0.758
Disease duration	-0.171	0.107
Serum calcium (mg/dL)	0.410**	0.000
Serum phosphorus (mg/dL)	0.109	0.308
PTH (pg/mL)	-0.477**	0.000
Serum iron (µg/mL)	-0.004	0.972
TIBC	0.022	0.835
Ferritin (ng/mL)	0.047	0.663
T.SAT (%)	-0.005	0.962
Serum albumin (g/dL)	-0.198	0.061

$P < 0.001$). Similarly, several studies detected also negative correlation between 25(OH) vitamin D and serum PTH levels, establishing the role of vitamin D in suppressing secondary hyperparathyroidism along with calcitriol (19,20).

High PTH levels were significantly associated with lower hemoglobin levels in our study. Bone marrow fibrosis can occur in high PTH levels leading to both anemia and erythropoietin resistance in CKD and dialysis patients (27). However, in the studies that examined the relation between hyperparathyroidism and anemia, 25(OH) vitamin D levels were not routinely measured (28).

Vitamin D has an anti-inflammatory action, reducing interleukin 6 and hepcidin levels leading to improved erythropoietin hyporesponsiveness (29). In our study, ferritin levels were higher in patients with deficient levels of vitamin D, however, this was not found to be statistically significant. A significant negative relation between vitamin D level and serum iron ($P = 0.019$) and transferrin saturation (%) ($P = 0.012$) was clear in our study. Patients with vitamin D deficiency had higher serum iron level and higher transferrin saturation levels compared with those with sufficient vitamin D levels. This finding, together with higher levels of ferritin in patients with deficient vitamin D may suggest that inflammation may play a role in the pathogenesis of anemia in those patients. Our study also supports the findings of Patel et al who found no evidence of iron deficiency in vitamin D deficient CKD patients (14).

Anemia was defined as hemoglobin level less than 11 g/dL. Risk factors associated with lower hemoglobin levels in this study included deficient vitamin D levels, high parathyroid hormone levels and high calcium levels. There was no statistically significant association between hemoglobin and duration of dialysis, age of patients, original kidney disease and type of vascular access. However, several studies including Madore et al have found age, race, gender erythropoietin (EPO) dose and frequency that EPO was administered, iron status (serum iron, transferrin saturation and ferritin), serum albumin, and the efficiency of dialysis by urea reduction ratio , were all found to be significantly associated with hemoglobin concentration (30). In the current study, all patients were on erythropoietin twice weekly, except those with hemoglobin over 11 g/dL, during the time of the study.

Conclusion

This study has found a statistically significant relation between the patients' vitamin D status and hemoglobin concentration. There was a correlation between vitamin D deficiency and anemia in our studied population. Further studies are needed to establish a causal relationship between 25 hydroxy vitamin D deficiency and anemia.

Limitations of the study

A few limitations should be noted. First, this was a single-center study; hence, additional studies with larger numbers of participants are needed to further establish the relationship between vitamin D deficiency and anemia. Second, it is difficult to establish a causal relationship between vitamin D deficiency and anemia as the current cross-sectional study design. Lastly more factors related to anemia in ESRD were not available as C-reactive protein, hepcidin and dialysis adequacy.

Authors' contribution

EN and LK conceived the idea, AT and ER contributed to the data collection and analysis. LK wrote the manuscript. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Conflicts of interest

The authors declare that they have no competing interests.

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