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EFFECT OF DIETARY INTAKE OF VITAMIN D ON SERUM VITAMIN D LEVEL AND BONE MINERAL BIOMARKERS IN HEMODIALYSIS PATIENTS

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ABSTRACT

Background: Systemic mineral and bone metabolism disorders are frequently observed in patients with hemodialysis (HD). Patients undergoing hemodialysis have vitamin D deficiency; which can affect up to 90% of HD patients, and this is linked to higher risks, as well as increased all-cause mortality. **Objectives**: To examine the association between dietary intake of vitamin D and (vitamin D deficiency, bone mineral biomarker) in hemodialysis patients. **Methods:** From January to May 2024, 100 hemodialysis patients at Dialysis Centre in Medical City, Baghdad-Iraq participated in a cross-sectional research. A questionnaire filled out by the researcher with a direct interview gathered demographic, clinical, anthropometric, laboratory, and vitamin D consumption data. Arab Board for Health Specialisations committee approved ethics. All data were obtained using Excel for Windows and analysed using SPSS 26. A p-value under 0.05 was significant. **Results:** The study reports that the mean age and BMI of patients were 53.38±13.69 years and 27.44±4.86 kg/m^2 respectively, with a male to female ratio of 1.2:1. Among HD patients, 79% had inadequate Vitamin D3 levels, with eggs and fats being the strongest predictors of adequate levels at specific consumption thresholds. Milk, yogurt, and fish also significantly predicted adequate Vitamin D levels at defined weekly servings. **Conclusions:** S. Vit D3 was Adequate among 21.0% of patients and Inadequate among 79.0%. Low levels of Hb and dietary intake of milk, yogurt, cheese, egg, fish, grains, fat, and legumes were determinants of inadequate S. Vit D3 level among HD patients. Dietary intake of egg, fat, milk, yogurt, and fish can be used as predictors for adequate vitamin D level in HD patients.

KEYWORDS: Effect, Dietary Intake, Vitamin D, Serum Vitamin D, Bone Mineral, Biomarkers, Hemodialysis.

INTRODUCTION

1,25-Dihydroxyvitamin D (1,25[OH]2D) is the main steroid hormone that regulates mineral ion homeostasis. Since vitamin D and its metabolites can be generated endogenously in the right physiologic context, they are better classified as hormones and hormone precursors than vitamins. 7-dehydrocholesterol undergoes a photochemical cleavage in reaction to UV rays on the skin, forming vitamin D. Vitamin D2 is the type of vitamin D that comes from plants, whereas vitamin D3 is the form that comes from animals. These two variants are equally activated by human vitamin D hydroxylases and have comparable biological action.[1] The active hormone, calcitriol (1,25-dihydroxy- vitamin D), is produced by 25-hydroxylation of vitamin D in the liver and 1-hydroxylation of vitamin D in the kidney. Promoting intestinal calcium absorption is 1,25(OH)2D3's primary biological function. Furthermore, it improves the net renal reabsorption of calcium and phosphorus and promotes the absorption of other important minerals via the gut, including phosphorus, zinc, and manganese. Thus, 1,25(OH)2D3 has a significant modulatory role in maintaining calcium homeostasis. It also plays a large modulatory role in other organ systems, such as the immune system, endocrine glands, cardiovascular system, reproductive system, and neurological system.[2] The most popular type of renal replacement therapy in end-stage renal disease and acute kidney injury is hemodialysis. In order to do hemodialysis, the circulation must be opened either by a central venous catheter, an arteriovenous fistula, or an arteriovenous shunt like the Scribner shunt. Hemodialysis (HD) patients have a high mortality rate and a growing patient population. The primary cause of this high rate is cardiovascular disease, which cannot be fully explained by the existence of conventional risk factors. Systemic mineral and bone metabolism disorders, encompassing biochemical and bone abnormalities as well as vascular calcification, are frequently observed in patients with hemodialysis. These anomalies are common and signify non-conventional risk factors.[3,4] The majority of patients undergoing hemodialysis have vitamin D deficiency, which can be impacted by factors such as age, skin tone, length of sun exposure, obesity, sunscreen use, and the existence of certain illnesses like diabetes mellitus and chronic kidney disease (CKD). Vitamin D deficiency can affect up to 90% of hemodialysis patients, and this is linked to higher risks of stroke, vascular calcification, arterial stiffness, and left ventricular hypertrophy, as well as increased risks of cardiovascular and all-cause mortality.[4-6] The Aim of the Study to examine the association between dietary intake of vitamin D and (vitamin D deficiency, bone mineral biomarker) in hemodialysis patients.

PATIENTS AND METHODS

A cross sectional study was carried out among 100 hemodialysis patients at Dialysis Center in Medical City, Baghdad-Iraq from 1 January 2024 till 30 May 2024.

The target population was represented by all patients that were admitted to the Dialysis Center for hemodialysis, with convenience sampling.

Inclusion criteria: (1) patients had been on HD for 1 year or more, (2) patients were over 18-years-old, (3) patients did not have active hepatitis or any other liver disease.

Exclusion criteria: (1) patients who had cancer (2) patients showed active inflammation or infection.

The data was collected for 3 consecutive months, about 3 days / week using a questionnaire paper which filled by researcher with direct interview. The questionnaire included:

a) Demographic and clinical data (age, gender, past medical history, dialysis duration)
b) Anthropometric measurements: weight (kg), height(cm), BMI
c) Laboratory findings (vitamin D3 and bone mineral biomarker): s. albumin, s. calcium, s. phosphorus, s. vit D3, s. PTH, Hb, and ALP
d) Dietary intake of vitamin D: milk, dairy products, grains, meat, fat, legumes, fruits, vegetables, chicken)

Vitamin D status was considered adequate (≥ 30 ng/ml), insufficient (15-< 30 ng/ml), or deficient (≤ 15 ng/ml). Vitamin D deficiency was further subdivided into moderate (10-≤ 15 ng/ml) or severe (< 10 ng/ml). Biological variables were assessed according to serum 25(OH)D level (30 ng/ml), which is a criterion of deficiency and insufficiency according to the Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines from the National Kidney Foundation.[7]

Dietary assessments

Dietary vitamin D and calcium intakes were collected by using 24-hour recall and 2-day food diaries. Dietary data for the first day were assessed by a dietitian using 24-hour recall with plastic food models, whereas data for the second and third days were completed using 2-day food diaries.

To analyze the association between serum 25(OH)D level and major vitamin D food sources, three food groups were selected based on previous studies as follows: total fish (50 g/serving), including anchovy, tuna, croaker, codfish, mackerel, and salmon; eggs (50 g/serving); and milk (200 ml/serving). All consumption frequencies were standardized into servings per week.[8]

Ethical approval was obtained from the committee of the Arab Board for Health Specializations. Verbal informed consent was obtained from all patients.

All data were collected using Excel for Windows and an analysis with the Scientific Package of the Social Sciences version 26 (SPSS) was performed. The chi-square test or Fisher's exact test was used for nominal variables, as appropriate. The independent *t*-test was used to compare continuous variables. ROC curve analysis for diagnostic indices was done. A *p*-value less than 0.05 was considered significant.

RESULTS

A total of 100 hemodialysis (HD) patients were included with mean age of 53.38±13.69 years and mean Body Mass Index (BMI) of 27.44±4.86 kg/m2. Male to female ratio was 1.2:1. Overweight was observed among 46.0% of patients, while obesity was found among 22%. Dialysis duration was mostly less than 5; 87.0%. Thirty four percent of patients were diabetics (DM), with duration of >10 years among 55.9%; and 75.0% were hypertensive (HTN), with duration of ≤10 years among 62.7%. Table 1

Table 1: Demographic and Clinical Data of HD Patients.

Variables		No.	%
Gender	Male	54	54.0%
	Female	46	46.0%
BMI kg/m2	Normal weight	32	32.0%
	Overweight	46	46.0%
	Obese	22	22.0%
Dialysis duration (years)	<5	87	87.0%

	≥5	13	13.0%
DM		34	34.0%
Duration of DM/ years (no.34)	≤10	15	44.1%
	>10	19	55.9%
HTN		75	75.0%
Duration of HTN/ years (no.75)	≤10	47	62.7%
	>10	28	37.3%
Total		100	100.0%

BMI = Body Mass Index, HD = hemodialysis, HTN=hypertension, DM=diabetes

Mean of S. Albumin was 3.97±0.59 g/dL, and that of S. Calcium was 8.64±0.98 mg/dL, S. Phosphorus was 5.16±1.55 mg/dL, S. Vit D3 was 20.78±11.11 ng/ml, S.PTH was 350.18±290.05 pg/mL, Hb was 9.07±1.71 g/dl, and that of ALP was 131.17±109.13 IU/L. Table 2.

Table 2: General Biochemical Results.

Variables	Mean±SD
S. Albumin g/dL	3.97±0.59
S. Calcium mg/dL	8.64±0.98
S. Phosphorus mg/dL	5.16±1.55
S. Vit D3 ng/ml	20.78±11.11
S.PTH pg/mL	350.18±290.05
Hb g/dl	9.07±1.71
ALP IU/L	131.17±109.13

S. Vit D3 was Adequate among 21.0% of patients and Inadequate among 79.0% [Insufficient 43.0%, Moderate deficiency 22.0%, and Severe deficiency 14.0%]; as shown in figure 1.

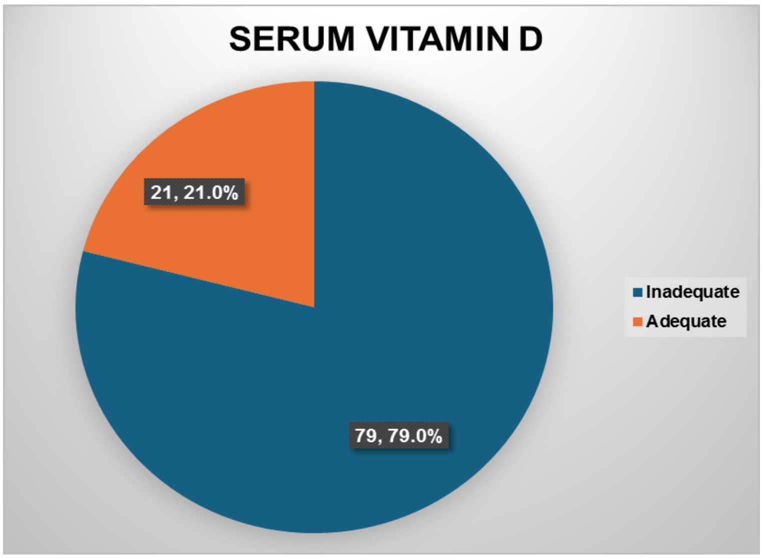

Figure 1: Serum Vit. D3 Level among HD Patients.

Mean Dietary intake of nutrients per serving/week among HD patients was as follows: Milk 1.67±2.72, Yogurt 4.72±3.61, Cheese 1.45±2.00, Egg 6.62±3.58, Fish 1.43±1.39, Grains 51.03±15.71, Meat 1.33±1.95, Fat 7.78±6.06, Legumes 2.05±1.52, Fruits 7.34±4.62, Vegetables 16.20±6.37, Chicken 6.75±4.78. Table 3.

Table 3: Mean Dietary Intake of Nutrients Per Serving/Week among HD Patients.

Dietary intake	Mean±SD (serving/ week)
Milk	1.67±2.72
Yogurt	4.72±3.61
Cheese	1.45±2.00
Egg	6.62±3.58
Fish	1.43±1.39
Grains	51.03±15.71
Meat	1.33±1.95

Fat	7.78±6.06
Legumes	2.05±1.52
Fruits	7.34±4.62
Vegetables	16.20±6.37
Chicken	6.75±4.78

Distribution of demographic and clinical data of HD patients regarding S. Vit D3 adequacy was shown in table 4 and revealed no significancy, P>0.05.

Table 4: Distribution of demographic and clinical data of HD patients regarding S. Vit D3 adequacy.

Variables		S. Vit D3				P* value
		Inadequate		Adequate		
		No.	%	No.	%	
Gender	Male	44	81.5%	10	18.5%	0.62
	Female	35	76.1%	11	23.9%	
Age/ years ***(mean/SD)***		53.65	13.18	52.38	15.76	0.71**
BMI kg/m2	Normal weight	25	78.1%	7	21.9%	0.27
	Overweight	34	73.9%	12	26.1%	
	Obese	20	90.9%	2	9.1%	
Dialysis duration (years)	<5	68	78.2%	19	21.8%	0.73
	≥5	11	84.6%	2	15.4%	
DM	Yes	30	88.2%	4	11.8%	0.12
	No	49	74.2%	17	25.8%	
Duration of DM (years)	≤10	14	93.3%	1	6.7%	0.61
	>10	16	84.2%	3	15.8%	
HTN	Yes	58	77.3%	17	22.7%	0.58
	No	21	84.0%	4	16.0%	
Duration of HTN (Years)	≤10	38	80.9%	9	19.1%	0.39
	>10	20	71.4%	8	28.6%	

****Chi*^{2} *test or fisher's exact test; **independent t test.***

Low levels of Hb and dietary intake of milk, yogurt, cheese, egg, fish, grains, fat, and legumes were determinants of inadequate S. Vit D3 level among HD patients, P<0.05, as shown in table 5.

Table 5: Distribution of Biochemical Results and Dietary Intake among HD Patients Regarding S. Vit D3 Adequacy.

Variables	S. Vit D3		P* value
	Inadequate	Adequate	
	Mean±SD	Mean±SD	
S. Albumin g/dL	3.94±0.63	4.09±0.39	0.28
S. Calcium mg/dL	8.55±0.98	8.96±0.95	0.09
S. Phosphorus mg/dL	5.19±1.56	5.06±1.54	0.74
S. PTH pg/mL	377.42±301.42	247.70219.44	0.06
Hb g/dl	8.86±1.57	9.84±2.04	0.019
ALP IU/L	130.32±115.27	134.39±84.38	0.88
Milk	0.67±1.51	5.43±2.98	<0.001
Yogurt	3.59±2.72	8.95±3.46	<0.001
Cheese	0.84±1.40	3.76±2.23	<0.001
Egg	5.28±2.00	11.67±3.73	<0.001
Fish	1.04±1.04	2.90±1.55	<0.001
Grains	48.91±15.79	59.00±12.83	0.008
Meat	1.18±1.91	1.90±2.02	0.12
Fat	5.48±3.93	16.43±4.70	<0.001
Legumes	1.81±1.44	2.95±1.50	0.004
Fruits	7.22±4.73	7.81±4.26	0.58
Vegetables	15.77±6.30	17.81±6.50	0.21
Chicken	6.48±4.68	7.76±5.15	0.31

Independent t test

ROC curve analysis for diagnostic indices of dietary intake for adequate vitamin D level was done**.** Comparison of the area under curve (AUC) revealed that egg and fat had the widest area under the curve, they were significantly **excellent** predictor (AUC=0.940, P<0.001, Sensitivity 95% and Specificity 70%) and (AUC=0.965, P<0.001), Sensitivity of 95% and Specificity 81%) respectively. Egg cut off point of 6.5 serving/week or more; and fat cut off point of 8.5 serving/week or more, predicted adequate vitamin D level in HD patients, as shown in table 6 & figure 2.

Also; Milk, Yogurt, and Fish had the widest area under the curve, they were significantly **good** predictor (AUC=0.888, P<0.001, Sensitivity 85% and Specificity 78%), (AUC=0.896, P<0.001, Sensitivity 95% and Specificity 78%), and (AUC=0.834, P<0.001), Sensitivity of 85% and Specificity 74%) respectively. Milk cut off point of 5 serving/week or more; Yogurt cut off point of 6.5 serving/week or more, and Fish cut off point of 1.5 serving/week or more, predicted adequate vitamin D level in HD patients, as shown in table 6 & figure 2.

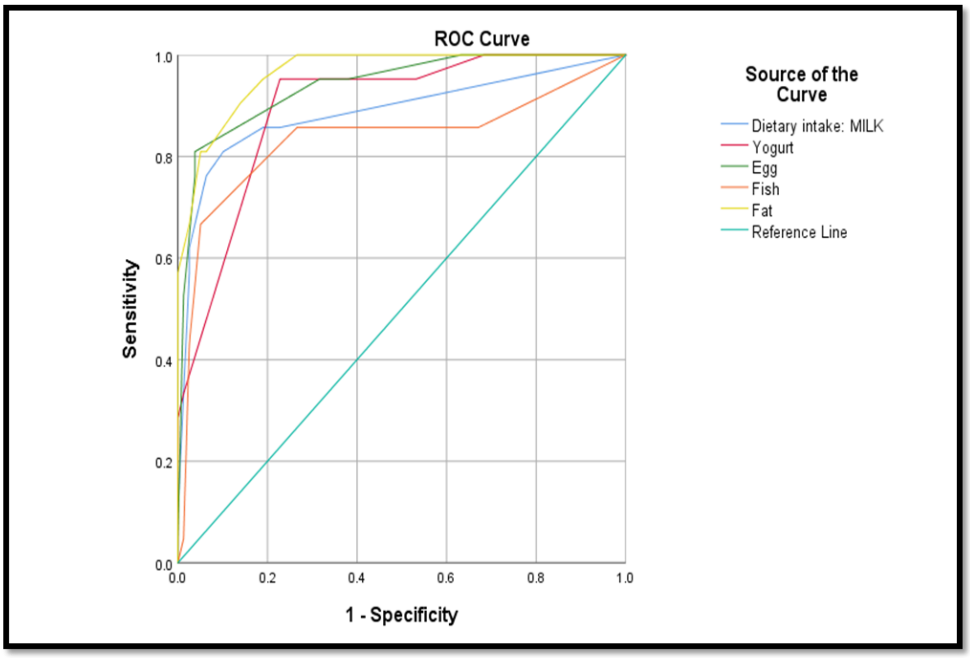

Figure 2: Diagnostic Value of Dietary Intake for Adequate Vitamin D Level in HD Patients.

Table 6: Diagnostic Value of Dietary Intake for Adequate Vitamin D Level in HD Patients.

Variables	AUC	P value	95% CI		Cut off point (serving/week)	Sn%	Sp%
			Lower Bound	Upper Bound			
Milk	0.888	<0.001	0.788	0.987	5	85	78
Yogurt	0.896	<0.001	0.826	0.966	6.5	95	78
Egg	0.940	<0.001	0.883	0.997	6.5	95	70
Fish	0.834	<0.001	0.709	0.959	1.5	85	74
Fat	0.965	<0.001	0.932	0.998	8.5	95	81

CI=Confidence Interval, AUC=Area Under the Curve, AUC ≥90≈ excellent; AUC ≥70≈ good; AUC<70≈inadequate

DISCUSSION

This study involved 100 hemodialysis (HD) patients with a mean age of 53.38±13.69 years, aligning with findings by Sethi et al., who reported a mean age of 54.44 ± 14.19 years.[9] The average Body Mass Index (BMI) was 27.44±4.86 kg/m², comparable to studies by Ishtawi et al., (26.47±8.4)[10] and Krassilnikova et al., (26.95 ±8.3).[11] Male patients were predominant, mirroring the sex distribution in studies by Krassilnikova et al., and El-Arbagy et al., with males comprising around 58.6% of their samples.[11,12] Comorbid conditions such as diabetes and hypertension were prevalent in more than one-third and three-quarters of the sample, respectively, although these rates were lower compared to Nazzal et al.'s findings (50.9% diabetic and 87.7% hypertensive)[13] This discrepancy could be attributed to the younger demographic in the current study compared to Nazzal et al.'s study.[13] Vitamin D insufficiency was widespread among the patients, with only 21% having adequate serum Vitamin D3 (S. Vit D3) levels and the remaining showing various levels of deficiency—43.0% insufficient, 22.0% moderately deficient, and 14.0% severely deficient. This aligns with the high prevalence of vitamin D deficiency noted in other studies concerning chronic kidney disease (CKD) patients.[10, 12, 14] Factors contributing to this deficiency in CKD include loss of vitamin D and its binding protein via urine, reduced renal megalin levels affecting vitamin D metabolism, and increased fibroblast growth factor 23 (FGF-23) which degrades active vitamin D forms. Other contributing factors might include limited sun exposure, poor dietary vitamin D intake, and decreased renal activity of 1α-hydroxylase due to uremic toxins.[14] Despite the general vitamin D deficiency, the study found no significant correlation between serum vitamin D3 levels and the presence of diabetes or hypertension, consistent with findings from el-Din Afifi et al., and Nazzal et al. However, there was a notable association between hemoglobin (Hb) levels and S. Vit D3, where lower Hb was linked to inadequate vitamin D3 levels. This observation was supported by el-Din Afifi et al., where positive correlations between vitamin D levels and hemoglobin values were statistically significant ($P<0.001$).[13, 15] This relationship was also significant in multivariate analyses conducted by Kim et al., suggesting a direct influence of vitamin D on erythroid precursor cells in CKD patients and an indirect impact through inflammatory cytokines and secondary hyperparathyroidism affecting erythropoiesis.[16] Dietary intake also played a crucial role in determining serum vitamin D3 levels. Low consumption of milk, yogurt, cheese, eggs, fish, grains, fats, and legumes was associated with inadequate vitamin D levels. Eggs and fats were the most predictive, with high sensitivity and specificity in determining adequate vitamin D levels at consumption cut-offs of 6.5 servings/week and 8.5 servings/week, respectively. Milk, yogurt, and fish also significantly predicted adequate vitamin D levels with substantial area under the curve (AUC) values, delineating specific weekly consumption thresholds that could ensure sufficient serum vitamin D levels. Contrasting these results, a study by Lee et al., adjusted for BMI and gender, indicated that dietary intake of vitamin D-rich foods did not increase serum 25(OH)D levels in HD patients.[14] This discrepancy could potentially be explained by the dietary restrictions aimed at controlling phosphate intake in HD patients, as suggested by Krassilnikova et al., highlighting the complex interplay of dietary management in maintaining adequate vitamin D levels amidst the challenges posed by HD treatment.[11]

CONCLUSIONS

Serum Vit D3 was Adequate among 21.0% of patients and Inadequate among 79.0%. Low levels of Hb and dietary intake of milk, yogurt, cheese, egg, fish, grains, fat, and legumes were determinants of inadequate S. Vit D3 level among HD patients. Egg and fat were significantly **excellent** predictor for adequate vitamin D level in HD patients; with cutoff point of (6.5 and 8.5) serving/week or more respectively. Milk, Yogurt, and Fish were significantly **good** predictor for adequate vitamin D level in HD patients; with cutoff point of (5, 6.5, and 1.5) serving/week or more respectively.

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