FACTORS AFFECTING NUTRITIONAL VITAMIN D LEVEL IN PATIENTS ON MAINTENANCE HEMODIALYSIS

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ABSTRACT

Objective: To determine which factors are affecting nutritional vitamin D levels in patients on maintenance hemodialysis.
Methods: It is a Cross sectional descriptive study conducted at DHQ hospital, Sheikhupura. All patients on maintenance hemodialysis for more than one month were included in this study. Patients with acute kidney injury and less than one month on hemodialysis were excluded from the study. Performa was designed for demographic (age, gender, education and address) and laboratory data (hemoglobin, urea, creatinine, albumin, bicarbonate, calcium, phosphate, intact parathyroid-PTH, vitamin D) of all the patients.
Results: One hundred and forty-six patients were enrolled in the study. Eighty-six (58.9%) were from more than fifty-years of age. Fifty-eight (39.7%) reported diabetes mellitus and Hypertension was the cause of End Stage Renal Disease (ESRD). All patients were on twice weekly dialysis. One hundred and ninety (81.5%) were started via double lumen catheter, sixty-nine (47.3%) had more than hundred total number of dialysis, one hundred and seven (73.3%) had need of transfusion. There was significant association observed of vitamin D3 levels with age, total number of dialysis and blood transfusions required. Vitamin D3 had significantly associated with intact parathyroid (iPTH) levels and albumin, 55.8% sample found with less than ten vitamin D3 level and iPTH between 100-600, whereas 88.4% sample found with less than four albumin levels (p-value < 0.05).
Conclusions: Vitamin D levels can be used as nutritional tool in dialysis patients. Age, albumin, PTH, total number of dialysis and blood transfusion had significant association with vitamin D level.

Key Words: vitamin D; hemodialysis; nutrition; end stage kidney disease; intact PTH.

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INTRODUCTION

Maintenance hemodialysis (HD) is one form of renal replacement therapy (RRT). It is provided twice or thrice weekly to the patients of end stage renal disease (ESRD) when these patients cannot sustain life without RRT[1]. Dialysis patients have to face the problem of malnutrition which might be due to the chronicity of the disease or inflammation secondary to dialysis process[2]. They have to face the deficiencies of both macronutrient and micronutrients. Variable deficiencies of fat-soluble vitamins have been observed but these do not need to be replaced except vitamin D[3].

Vitamin D is a fat-soluble vitamin, mainly stored in the liver and is important for bones and immune system. Skin and diet are two important sources of it[4]. There are mainly in two forms in the blood i.e., 25-hydroxy vitamin D (vit-D_3) and 1, 25 (OH) $_2$ vitamin D. vitamin D is used as nutritional marker in general population[5]. The metabolism and the mechanism of action of vit-D_3 is not fully understood up till now. Intra-cytosolic and

intra-nuclear mechanisms of action have been explained. This is more complicated in setting of chronic kidney disease (CKD) where patients have less sun exposure, poor diet, poor appetite, and mal absorption and less mobility, all are due to uremia[6]. Nutritional status is important and difficult to assess in CKD. Different nutritional markers like albumin, pre-albumin, hemoglobin, ferritin, serum iron, serum potassium, serum calcium, serum phosphate, parathyroid level (PTH), and vit-D3 have been used but no one is perfect[7]. Vit-D3 levels are used to estimate the malnutrition in patients on hemodialysis. Different factors can affect vitamin D3 level in this population but there is less evidence on this aspect. Demographic and clinical factors like age, gender, number of dialysis, duration of dialysis, blood transfusion, and adequacy of dialysis, have been discussed in different studies[8]. So, this study is performed to assess whether these factors can affect vitamin D level in our population or not.

METHODS

The study was conducted in dialysis center of DHQ hospital Sheikhupura, between March to April 2018. A total of one hundred and forty-six patients of ESRD were on maintenance dialysis were included in this study. Patients between ages of 18 to 80 were enrolled. Patients with acute kidney injury (AKI) and those who were on dialysis for less than one month, were excluded. Performa was designed for demographic (age, gender, education, employment status and address) and laboratory data (hemoglobin, urea, creatinine, albumin, bicarbonate, calcium, phosphate, intact parathyroid-PTH, vitamin D) of all the patients.

Data were stored and analyzed using IBM-SPSS version 23.0, count and percentages were reported for baseline samples characteristics and clinical characteristics. Correlation analysis was also done for vitamin D3 and different quantitative outcomes. P-values less than 0.05 were considered significant.

RESULTS

Table 1 reports the baseline characteristics of studied samples. Chi square association was applied. Eighty-six (58.9%) data were from age more than fifty-years old, seventy (52.1%) were female, eighty-six (58.9%) were literate, one hundred and twenty (82.2%) were unemployed and seventy-three (50%) data were received from rural samples. Table 2 reports the clinical Parameters fifty-eight (39.7%) reported diabetes mellitus and Hypertension was the cause of ESKD, one hundred and forty-six (100%) samples received two session of dialysis per week, one hundred and ninety (81.5%) were started via double lumen catheter, sixty-nine (47.3%) had more than hundred total number of dialysis, one hundred and seven (73.3%) had need of transfusion, and 79.5% required at least two-times blood transfusion per month.

Table 3 gives the association of vitamin D3 levels with different studied parameters, results showed that, vitamin D3 significantly associated with ipth levels and albumin, 55.8% sample found with less than ten vitamin D3 level and ipth between 100-600, whereas 88.4% sample found with less than four albumin levels. In the present study there was no significant association of Hb, Ca+, PO4- and bicarbonate with vitamin D3 levels. There was significant association observed of vitamin D3 levels with age group. Forty-three (29.45%) were severe vitamin D deficient, out of which majority (29.45%) were above fifty years of age. Gender, education, employment status and address did not give any significant association with vitamin D3 levels. There was significant association of vitamin D3 levels with total number of dialysis and blood transfusions required with p-value less than 0.05.

Table 1: Chi Square association of Vitamin D3 levels with Baseline Parameters

Characteristics		Vitamin D3 Levels								p-value
		<10		11-20		21-30		>30		
		n	%	n	%	n	%	n	%	
Age	16-30	4	9.3	5	7.1	1	5.9	5	31.3	0.035*
	30-50	10	23.3	21	30.0	8	47.1	6	37.5	
	>50	29	67.4	44	62.9	8	47.1	5	31.3	
Gender	Male	22	51.2	35	50.0	8	47.1	11	68.8	0.55
	Female	21	48.8	35	50.0	9	52.9	5	31.3	
Education	Literate	29	67.4	37	52.9	10	58.8	10	62.5	0.48
	Illiterate	14	32.6	33	47.1	7	41.2	6	37.5	
Employment status	Employed	9	20.9	10	14.3	2	11.8	5	31.3	0.35
	Unemployed	34	79.1	60	85.7	15	88.2	11	68.8	
Address	Urban	21	48.8	33	47.1	11	64.7	8	50.0	0.62
	Rural	22	51.2	37	52.9	6	35.3	8	50.0	

*p<0.05 was considered significant using Pearson chi square test

Table 2: Chi Square association of Vitamin D3 levels with clinical Parameters

Characteristics		Vitamin D3 Levels								p-value
		<10		11-20		21-30		>30		
		n	%	n	%	n	%	n	%	
Cause of ESRD	DM	9	20.9	10	14.3	1	5.9	3	18.8	0.76
	HTN	12	27.9	28	40.0	9	52.9	8	50.0	
	Stone disease	0	0.0	1	1.4	0	0.0	0	0.0	
	chronic GN	1	2.3	2	2.9	0	0.0	1	6.3	
	Cystic disease	0	0.0	1	1.4	0	0.0	0	0.0	
	both DM and HTN	20	46.5	28	40.0	6	35.3	4	25.0	
	other	1	2.3	0	0.0	1	5.9	0	0.0	
Dialysis sessions per week	2	43	100.0	70	100.0	17	100.0	16	100.0	N.A
	3	0	0.0	0	0.0	0	0.0	0	0.0	
	4 or more	0	0.0	0	0.0	0	0.0	0	0.0	
Dialysis start via	AVF	9	20.9	11	15.7	3	17.6	4	25.0	0.80
	double lumen catheter	34	79.1	59	84.3	14	82.4	12	75.0	
Total number of dialysis	<50	15	34.9	26	37.1	3	17.6	0	0.0	0.029*
	50-100	12	27.9	14	20.0	2	11.8	5	31.3	
	>100	16	37.2	30	42.9	12	70.6	11	68.8	
need for transfusion	yes	29	67.4	50	71.4	15	88.2	13	81.3	0.343
	no	14	32.6	20	28.6	2	11.8	3	18.8	
blood transfusion required	<2 times per month	36	83.7	59	84.3	10	58.8	11	68.8	0.046*
	2-4 times per month	7	16.3	8	11.4	7	41.2	5	31.3	
	> 4 times per month	0	0.0	3	4.3	0	0.0	0	0.0	

*p<0.05 was considered significant using Pearson chi square test

Table 3: Chi Square association of Vitamin D3 levels with other study Parameters

Parameters		Vitamin D3 Levels								p-value
		<10		11-20		21-30		>30		
		n	%	n	%	n	%	n	%	
Hb	≤11	40	93.0	63	90.0	15	88.2	12	75.0	0.261
	>11	3	7.0	7	10.0	2	11.8	4	25.0	
Ca+	<8.5	23	53.5	37	52.9	9	52.9	9	56.3	0.59
	8.5-10.5	18	41.9	33	47.1	7	41.2	7	43.8	
	>10.5	2	4.7	0	0.0	1	5.9	0	0.0	
PO4-	<2.5	4	9.3	7	10.0	1	5.9	2	12.5	0.25
	2.5-5.5	15	34.9	37	52.9	12	70.6	8	50.0	
	>5.5	24	55.8	26	37.1	4	23.5	6	37.5	
iPTH	<100	2	4.7	5	7.2	6	35.3	3	18.8	<0.01*
	100-600	24	55.8	54	78.3	10	58.8	10	62.5	
	>600	17	39.5	10	14.5	1	5.9	3	18.8	
Albumin	≤4	38	88.4	56	80.0	10	58.8	9	56.3	0.014*
	>4	5	11.6	14	20.0	7	41.2	7	43.8	
Bicarbonate	≤24	37	86.0	57	81.4	13	76.5	15	93.8	0.521
	>24	6	14.0	13	18.6	4	23.5	1	6.3	

*p<0.05 was considered significant using Pearson chi square test

DISCUSSION

Vitamin D have multiple functions besides bone health like have role in muscles, immune, endocrine and central nervous system. It is synthesized in the skin under the effect of sunlight. The capacity of the skin decreases with aging. Studies show decrease synthesis of Vitamin D in the skin is in the elderly population9. The severity of Vitamin D is deficiency is more in elderly patients[10] Vitamin D. Same findings were noted in this study. Twenty-nine (67.4 %) of the patients who were more than fifty years, were having severe deficiency. Vitamin D deficiency is a major public health problem worldwide having its high prevalence, particularly among elderly people. Skin pigmentation, sedentary life style, central obesity are known causes of vitamin D deficiency. Is gender being important in vitamin d metabolism? This question has been answered in different studies where it is shown men has more deficiencies as compared to

females. Some studies depict statistically non-significant association of gender with Vitamin D deficiency[11]. Our study shows the same trend but the difference was not statically significant where twenty-two (51.2%) males were having severe deficiency as compared to twenty-one (48.8%) females. Rural residents have higher rates of smoking, obesity, as well as lower health and literacy which contribute to poor health outcomes[12]. Al though one might expect more exposure to ultraviolet light in a rural population and higher Vitamin D in rural population but studies show rural population when compared to their urban counterparts showed significantly lower vitamin D levels and were more Vitamin D deficient may be due to dietary intake habits[13]. In our study result are similar to the previous studies but are statistically non-significant as where twenty-one (51.2%) rural participants were having severe deficiency as compared to twenty-one (48.8%) urban participants. Growing scientific evidence has implicated Vitamin D deficiency in a multitude of chronic conditions, including DM, HTN, or both and other cardiovascular diseases[14]. The relationship between Vitamin D deficiency and diabetes has extensively studied, identified mechanism for this relationship include the presence of vitamin D receptors on the B-islet cells in the pancreas responsible for secreting insulin, as well as clinical improvement in diabetic patients who receive vitamin D[15]. The great majority of studies demonstrate that lower Vitamin D levels are associated with a higher prevalence of hypertension. Our study has also illustrated the same trend 9 (20.9%) participant having DM alone, 12 (27.9%) participants having HTN and 20(46.5%) participants having both DM and HTN show sever deficiency of Vitamin D and are leading causes of ESRD. Impact of other causes are non-significant.

Vitamin D deficiency in patients on dialysis is extensively seen due to reduced ingestion of foods rich in (fish, cream, milk, and butter) by patients. Kidney disease progression is associated with diminishing dietary intake. The patients on dialysis are advised to follow a phosphorus-restricted diet. Many patients on spend less time outdoors, leading to lower sunlight exposure and reduced endogenous synthesis of vitamin D3 in the skin but the impact of no of dialysis on severity of Vitamin D deficiency is not properly defined[16]. Our study also depicts deficiency of Vitamin D in patient on dialysis but shows mixed results as patients having <50 dialysis per year with sever Vitamin D deficiency are 15 (34.9%), 50-100 dialysis per year with sever Vitamin D deficiency are 12 (27.9%) and >100 dialysis per year with sever Vitamin D deficiency are 16 (37.2 %). The concurrent fluid removal and electrolyte correction during hemodialysis make hemodialysis the first choice for transfusing blood in population. The anemia in CKD is treated with iron infusions and the administration of erythropoietin, but blood transfusion need is still required and is on rise[17]. In previous studies adequate data about link of vitamin D deficiency with no of blood transfusions is not available. In our study patient requiring <2 blood transfusions per month having sever vitamin D deficiency are 36(83.7%). In hemodialysis patients' anemia has high prevalence, and insufficient erythropoietin production is a major contributor. Although erythropoietin is injected to treat anemia in patients with CKD but the optimal hemoglobin levels are still unclear[18]. Different studies have demonstrated that low level of hemoglobin is associated with sever Vitamin D deficiency in hemodialysis patients[19]. Our study also supports the previous studies as 40 (93%) patients having Hb level <11 presents sever Vitamin D deficiency. Increased serum parathyroid hormone (PTH) levels and Vitamin D in-sufficiency are mostly attributed to CKD and mineral-bone disorder (MBD). Studies have indicated that vitamin D deficiency or insufficiency significantly increased cardiovascular diseases in dialysis population. However, the relationship between serum PTH levels and Vitamin level is not consistent in major studies[20]. Our study reveals 2 (4.7%) patients having low vitamin D level have iPTH level <100, 24(55.8%) have iPTH level 100-600 and 17 (39.5%) patients have iPTH level >600. Vitamin D deficiency appears to be an important contributing factor to reduced serum albumin level in patients with ESRD, and lower level of vitamin D needs supplementation with Vitamin D to normalize low serum albumin concentrations[21]. Our study also supports this as albumin level is ≤4 in 38 (88.4%) severely Vitamin D deficient patients and this level is >4 in 5 (11.6%) severely Vitamin D deficient patients. Studies show raise in raises serum bicarbonates raises Vitamin D levels in vitamin D-deficient chronic renal failure patients and vice versa[22]. Our studies support these facts as bicarbonates level ≤24 in 37 (86%) severely Vitamin D deficient patients and >24 in 6 (14 %) severely deficient patients.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board of DHQ Hospital, Sheikhupura via Research No. 09 Dated: February 12, 2018.

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AUTHOR'S CONTRIBUTIONS

YS: Conception, Design
SA: Literature Review
NM: Data collection
QUA: Data analysis
RA: Critical review, Proof reading