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The Relationship between 25(OH) Vitamin D and Pulmonary Hypertension in CKD Patients on conservative treatment and on hemodialysis

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ABSTRACT

Vitamin D has long been known to be an essential part of bone metabolism, although recent evidence suggests that vitamin D plays a key role in the pathophysiology of other diseases, including CVD, as well. Vitamin D deficiency activates renin-angiotensin-aldosterone system (RAAS) which affects cardiovascular system. Activation of RAAS is associated with pulmonary hypertension, relation between vitamin D deficiency and pulmonary hypertension could be therefore suggested. Pulmonary hypertension is a prevalent cardiovascular complication in CKD patients.

KEY WORDS: vitamin D, pulmonary hypertension

INTRODUCTION

Vitamin D deficiency has been implicated as a risk factor for cardiovascular disease and overall mortality in the general population [1]. Endothelial cell vitamin D receptors are up-regulated under stress, and its binding with the hormonal vitamin D ligand modulates response elements in the vascular endothelial growth factor promoter [2]. Vitamin D also affects the vascular wall by regulating the renin-angiotensin aldosterone axis and exerts anti-proliferative effects on vascular smooth muscle [3]. Elevated pulmonary vascular resistance and pulmonary remodeling by RAAS are main pathogenetic mechanisms of pulmonary hypertension [4]. For this reason, it could be suggested that a relation exists between vitamin D deficiency and pulmonary hypertension [5].

PATIENTS AND METHODS

The aim of this work was to study the relationship between pulmonary hypertension in CKD patients both on conservative treatment and on regular hemodialysis, and plasma 25(OH) vitamin D levels. This study was conducted on ninety persons, they were divided into three groups:

Group I: formed of thirty CKD patients on conservative treatment.

Group II: formed of thirty patients with end-stage renal disease receiving maintenance hemodialysis (for a period of more than six months) via AVF three times weekly.

Group III: thirty age-matched persons were selected to be the control group.

All Patients were subjected to detailed history taking and complete physical examination. Serum samples are collected from all patients of the three groups to assess level of vitamin D. They also subjected to Trans-thoracic two-dimensional and M-mode doppler echocardiography (TTE) to estimate PASP (pulmonary hypertension is defined as calculated PASP > 35 mm Hg).

Results

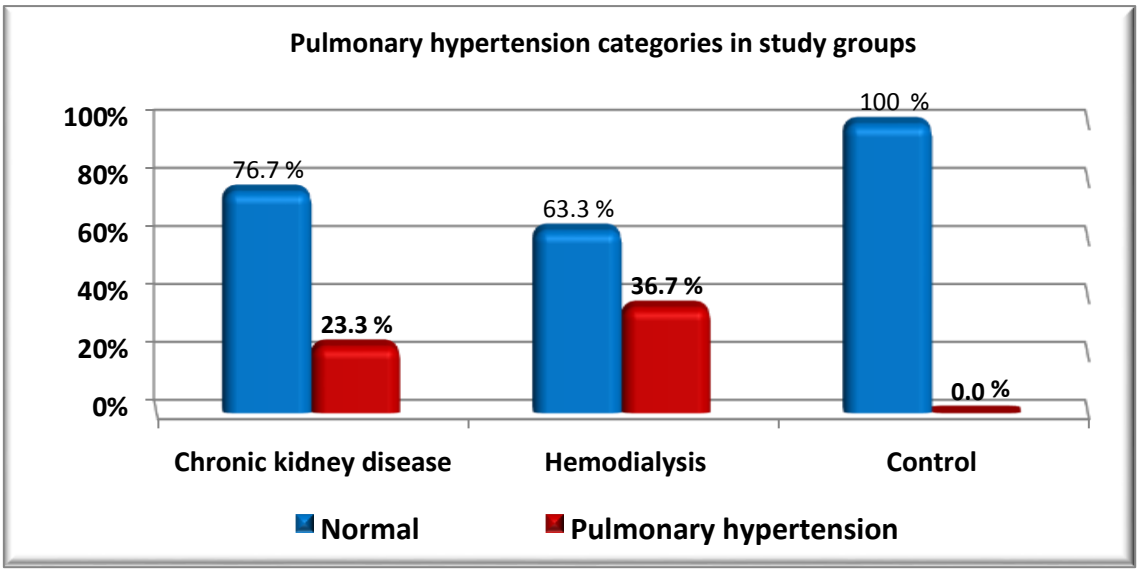
1-This study revealed that there is no statistically significant difference with p-value >0.05 between different study groups as regards to vitamin D categories.

vitamin D categories	**Chronic kidney disease** (n=30)	**Hemodialysis** (n=30)	**Control** (n=30)	**p-value**	**Sig**
	No. (%)	**No. (%)**	**No. (%)**		
Deficient (< 10 ng/ml)	11(36.7%)	11(36.7%)	7(23.3%)	0.2	NS
Insufficient (10-29 ng/ml)	7(23.3%)	5(16.7%)	7(23.3%)		
Sufficient (30-100 ng/ml)	8(26.7%)	13(43.3%)	16(53.4%)		
Potential toxicity >100 ng/ml	4(13.3%)	1(3.3%)	0(0%)		

2- This study revealed there is statistically significant difference with p-value <0.05 between different study groups as regards to presence of pulmonary hypertension with majority of both chronic kidney function (23.3%) and hemodialysis (36.7%) groups had pulmonary hypertension but controls all of them were normal pulmonary pressure.

PASP categories	**Chronic kidney disease** (n=30)	**Hemodialysis** (n=30)	**Control** (n=30)	**p-value**	**Sig.**
	No. (%)	**No. (%)**	**No. (%)**		
Normal	23(76.7%)	19(63.3%)	30(100%)	<0.0001[b,c]	**HS**
Pulmonary hypertension	7(23.3%)	11(36.7%)	0(0%)		

a: significance between CKD, and HD
b: significance between CKD, and control
c: significance between HD, and control



3-This study revealed that no statistically significant correlation with p-value >0.05 between Vitamin D level and PASP among each of chronic kidney disease, hemodialysis, and control groups.

Vitamin D (ng/ml)	PASP (mm/Hg)		
	r	p-value	Sig.
Chronic kidney disease (n=30)	-0.27	0.2	NS
Hemodialysis (n=30)	0.01	0.9	NS
Control (n=30)	0.34	0.07	NS

DISCUSSION

We could not find any significant difference between different study groups with respect to vitamin D categories. We could not find any direct correlation between Vitamin D levels and PASP, these data come in disagreement with other studies [6] that found significant correlation between PAP and Vitamin D in their patients, increased PAP correlated positively with PTH and negatively with 25-hydroxy vitamin D levels. However, it should be noticed that Demir M and co-workers have put CKD patients in their exclusion criteria.

We tried to establish a relationship between vitamin D levels and PHT in CKD and HD patients. First, we examined the relation between vitamin D and basic profiles of the study groups. No correlation could be established between Vitamin D level and age, BMI similar to others who reported that there was no statistically significant difference between their two groups (patients& controls) in terms of age, gender distribution, body mass index, and smoking status or other lab investigations (GFR, Albumin, Albuminuria) among chronic kidney disease group [7]. Likewise, no correlation could be established between lipid profile (Cholesterol, triglycerides, HDL, LDL) and vitamin D levels opposing data from Jorde R, et al who reported that high 25-hydroxyvitamin D [25(OH)D] levels were associated with a favorable serum lipid profile [8].To date, evidence from randomized, controlled trials indicated that vitamin D supplementation could increase LDL cholesterol concentrations, but does not appear to significantly affect total cholesterol, HDL cholesterol and triglycerides. The lipid modulating effects of vitamin D supplement should be further investigated through large-scale, randomized trials with adequate doses which can effectively elevated the active form of vitamin D in plasma and with proper population which has hyperlipemia as an inclusion criterion [9].

Our data established a clear definitive relationship between CDK/HD and ECHO abnormalities compared to controls, however unfortunately we could not establish a direct correlation between these findings and vitamin D levels, except for an isolated correlation between vitamin D levels and LVEDD in CKD but not in HD patients.

CONCLUSION

The failure to establish a definite relationship between pulmonary hypertension and vitamin D status in CKD & hemodialysis patients is mainly due to strict exclusion criteria which obliged us to work on a small number of patients (only 90 persons, 30 persons were CKD, 30 were HD patients and 30 persons were control) which may not be enough to establish such relation.

As regards PAP estimation it was done depending on echocardiographic evaluation which gives inaccurate results, the only accurate method is right heart catheterization, thus limiting the possibility of finding a correlation.

Concerning vitamin D status, all patients were marginal, almost no difference was found between groups, this may be due to their good nutritional status (their mean serum albumin was normal, the serum cholesterol of HD patients was high, also URR of them was about 65% thus denoting that they have adequate dialysis and with good appetite), they also have good sun exposure (the study was done in summer) which in turn will result in adequate synthesis of vitamin D by skin and most of them are of good body built (normal mean BMI value).

The novelty of our study is that we are the first who try to find a correlation between vitamin D status and pulmonary hypertension in CKD and ESRD patients.

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