ASSESSMENT OF 25-HYDROXY VITAMEN D IN PATIENTS ON REGULAR HEMODIALYSIS IN AIN SHAMS UNIVERSITY HOSPITAL

Thesis

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1,25(OH)2-19-nor-D2	**:**	Paricalcitol
1a-(OH)D2	**:**	Doxercalciferol
1a,25(OH)2D3	**:**	Calcitriol
25OHD	**:**	25 hydroxyvitamin D
BP	**:**	Blood pressure
CKD	**:**	Chronic kidney disease
CVD	**:**	Cardio vascular disease
DBP	**:**	Vitamin D-binding protein
EPO	**:**	Erythropoietin
ER	**:**	endoplasmic reticulum
ESRD	**:**	End stage renal disease
FGF-23	**:**	Fibroblast growth factor -23
GFR	**:**	Glomerular filtration rate
HD	**:**	Hemodialysis
IFN-γ	**:**	Interferon-γ
MBD	**:**	Mineral bone metabolism
NADPH	**:**	Nicotinamide adenine dinucleotide phosphate
PD	**:**	Peritoneal dialysis
PPAR	**:**	Peroxisome proliferator-activated receptor
PTH	**:**	Parathyroid hormone
RAAS	**:**	Renin-angiotensin-aldosterone system
SHPT	**:**	Secondary hyperparathyroidism
TNF-α	**:**	Tumor Necrosis factor-α

UVB	**:**	Ultraviolet radiation in the B-wavelength region
VDR	**:**	Vitamin D receptor
VDRA	**:**	Vitamin D receptor activator
VDREs	**:**	Vitamin D response elements
VEGF	**:**	Vascular endothelial growth factor

ABSTRACT

Background: Vitamin D deficiency (<20 ng/mL) and insufficiency (20–29 ng/mL) are common among patients with chronic kidney disease (CKD) or undergoing dialysis. Low 25(OH)D has been associated with high bone turnover, secondary hyperparathyroidism (SHPT), decreased bone mineral density (BMD), renal anemia , erythropoietin hypo responsiveness and sleep disturbance in CKD and dialysis patients

Methods: This cross sectional study was carried out on 100 End Stage Renal Disease patients on Maintenance Hemodialysis in the Hemodialysis unit of **Ain Shams University hospital, Cairo - Egypt**. Assessment of serum level of 25(OH) VIT D, and to identify if possible relation between vitamin D deficiency and other parameter like hemoglobin level, Parathyroid hormone, Calcium, Phosphorus, Iron profile, DM, HTN, medications

Results: Vitamin D deficiency is common in end stage renal disease patients on regular hemodialysis, in our study we found that 50% of patients have 25(OH) VIT D deficiency, 34% are insufficient and only 16% was sufficient. There was no significant correlation between the serum level of 25(OH) VIT D and hemoglobin level and iron profile also no significant relation between 25(OH) vitamin D and PTH, calcium, phosphorus.

Conclusion: Vitamin D deficiency and other disorders in calcium and phosphorus homeostasis are common in patient with end stage kidney disease on regular hemodialysis. We did not notice any significant relation between the levels of calcium, phosphorus, parathyroid hormone, serum albumin and vitamin D level. No significant relation between vitamin D level and hemoglobin level, iron profile. The National Kidney Foundation guidelines state that optimal 25(OH) D levels should be greater than 30 ng/ml.

Keywords: Vitamin D, end stage renal disease, parathyroid hormone, calcium, phosphorus

INTRODUCTION

End stage renal disease (ESRD) is characterized by decreased renal expression of 25- hydroxyvitamin D 1α-hydroxylase, the enzyme that catalyses the conversion of 25-hydroxyvitamin D (25(OH)D) the form synthesized in the liver by 25-hydroxylase following production of vitamin D in the skin, to the active form, 1,25-dihydroxyvitamin D (1,25(OH)2D). This is well appreciated in the clinical setting and the majority of haemodialysis patients require treatment with an active vitamin D or an analogue (calcitriol, alfacalcidol or paricalcitol) for the management of calcium and secondary hyperparathyroidism. UK guidelines changed in 2014 and now recommend the diagnosis and treatment of low serum 25(OH)D in all people with a glomerular filtration rate (GFR) less than 30ml/min/1.73m^2 however they make no recommendations for dosage or monitoring and as such recommendations have not widely translated into practice **(Huish et al., 2016)**.

However, recent data have shown that ESRD patients also have low serum 25(OH)D levels with vitamin D deficiency and insufficiency (serum 25(OH)D<30nmol/l and <75nmol/l respectively) seen in up to 95% of haemodialysis patients.

As early as stage 2 of CKD, serum 25(OH) vitamin D levels begin to decline. Reduced sun exposure, impaired skin synthesis of cholecalciferol due to renal disease, hyper pigmentation seen in late CKD stages and dietary restrictions that are commonly advised to CKD patients contribute to high prevalence of vitamin D deficiency. In addition, uremia impairs intestinal absorption of dietary and supplemental vitamin D, and in CKD patients with severe proteinuria there are high urinary losses of vitamin D binding protein (DBP) leading to increased renal loss of vitamin D metabolites **(Nigwekar et al., 2014).**

Sleep disturbance is extremely common in hemodialysis (HD) patients, with prevalence ranging from 41% to 83%.The presence of sleep disturbance has been associated with reduced quality of life and increased mortality in HD patients. Moreover, it has been reported to be involved in the development of cardiovascular diseases in patients undergoing maintenance HD. However, the pathogenesis of sleep disturbance in HD patients remains unclear. As a fundamental micronutrient, vitamin D is extremely essential for human health. A large body of preclinical studies has found the presence of vitamin D receptors in specific areas of the brainstem that are thought to regulate sleep. Furthermore, increasing clinical studies have shown that low serum levels of vitamin D are associated with poorer sleep,

including low sleep efficiency and short sleep duration, in non-HD subjects, suggesting a potential role for vitamin D in maintaining healthy sleep. Similarly, a significantly correlation between vitamin D levels and sleep quality has been found in patients with systemic lupus erythematosus (SLE). Recent uncontrolled clinical trials of vitamin D supplements in patients with sleep problems have reported improved sleep quality with higher levels of supplemental vitamin D **(Han et al., 2017).**

Nearly one tenth of hemodialysis (HD) patients exhibit erythropoietin (EPO) hypo responsiveness/resistance: inability to achieve or maintain target hemoglobin despite escalating EPO doses. An inverse association has been found between vitamin D levels and EPO requirements in chronic kidney disease patients. Vitamin D supplementation may improve response to EPO either by suppression of the chronic inflammatory status, control of hyperparathyroidism, or direct stimulation of erythroid progenitors **(Nand and Mittal, 2017).**

There is general consensus that serum 25(OH)D is the best biochemical marker for nutritional vitamin D status. Whether free 25(OH)D would be a better marker than total 25(OH)D is so far unclear. Free 25(OH)D can either be calculated based on the measurement of the serum concentrations of total 25(OH)D, vitamin D-binding protein (DBP), albumin, and the affinity