Association between Serum 25-Hydroxyvitamin D Level and Cardiac Functions in Chronic kidney Disease Patients

Thesis

Submitted for Partial Fulfillment of Master Degree
In Internal Medicine

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2020

Thank to Allah for Accomplishment of this work

I wish to express my deepest gratitude to all those who assisted me to complete this work.

First and foremost, my thanks are directed to ***Professor Dr. Saeed Abdelwahab Saeed****, Professor of Internal Medicine and Nephrology,Faculty of Medicine, Ain Shams University, for his unlimited help and continuous insistence on perfection, without his constant supervision, this thesis could not have achieved its present form.*

Many thanks and appreciation to ***Dr. Ashraf Hassan Abd-elmobdy,*** *Lecturer of Internal Medicine and Nephrology, Faculty of Medicine, Ain shams University, for his supervision and encouragement and for his kindness throughout the work.*

I am greatly indebted to ***Dr. Waleed Mohammed Salam****, Lecturer of Cardiology, Faculty of Medicine,Ain shams University, for fruitful suggestions and wise guidance created this thesis.*

It is my pleasure to extend my obligation to all members of my family and my colleges.

LIST OF CONTENTS

LIST OF ABBREVIATIONS

ABD	:	Adynamic bone disease
ACE-2	:	Angiotension –converting enzyme 2
ACE-I	:	Angiotension –converting enzyme inhibitor
ACR	:	Albumin/creatinine ratio
AF	:	Atrial fibrillation
AKI	:	Acute Kidney injury
ARBs	:	Angiotensin receptors antagonist
BMI	:	Body mass index
BP	:	Blood pressure
BUN	:	Blood urea nitrogen
BWT	:	Body weight
CBC	:	Complete Blood Picture
CKD	:	Chronic kidney disease
CKD-MBD	:	Chronic kidney disease-mineral bonedisorder
COX2	:	Cyclooxygenase 2
CRP	:	C-reactive protein
CVD	:	Cardiovascular disease
DD	:	Diastolic Dysfunction
DHF	:	Diastolic heart failure

DM : Diabetes mellitus

DMSA : Dimercaptuosuccinic acid

DN : Diabetic nephropathy

e GFR : estimated glomerular filtration

EF : Ejection fraction

ESAs : Erythropoietin –stimulating agents

ESRD : End stage renal disease

ETRA : Endothelin receptor antagonist

FGF-23 : Fibroblastic growth factor 23

GFR : Glomerular filtration rate

GN : Glomerulonephritis

HD : Hemodialysis

HF : .Heart failure

HTN : Hypertension

IGFs : Insulin- like growth factors

IVSD : Inter ventricular septum diameter

JAK : Janus kinase

LAD : Left Atrial Diameter

LVEDD : Left Ventricular End Diastolic Diameter

LVESD : Left Ventricular End Systolic Diameter

LVH : Left Ventricular Hypertrophy

LVMI	:	Left Ventricular Mass Index
NO	:	Nitric oxide
PTH	:	Parathyroid hormone
RAAS	:	Renin-Angiotensin –Aldosterone system
RAS	:	Renin –Angiotensin system
RCT	:	Randomized clinical trial
ROD	:	Renal osteodystrophy
RRT	:	Renal replacement therapy
SHPT	:	Secondary hyerparathyrodism
STAT	:	Signal transducer and activators of transcription
TDI	:	Tissue Doppler Imaging
TNF	:	Tumor necrosis factor
UF	:	Ultrafiltration
US	:	Ultrasonography
VDR	:	Vitamin D receptor
VEGF	:	Vascular endothelial growth factor
VLDL	:	Very low density lipoprotein
VSMCs	:	Vascular smooth muscle cells

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Chronic kidney disease (CKD) is a major public health problem worldwide and is associated with a considerable increase in morbidity and mortality, cardiovascular disease is most common cause of death among chronic kidney disease patients.

There is an increasing interest in using vitamin D levels as a novel marker for CVD, because epidemiological data have shown a strong correlation between the risk of CVD and vitamin D deficiency.

The aim of study was to determine the association between serum vitamin D level and cardiac functions assessed by tissue Doppler imaging in chronic kidney disease patients.

Patients and methods: our study conducted on 90 patients from outpatient clinic or inpatient department of national institute of nephrology and urology.

All patients were subjected to full history , full clinical examination, laboratory investigations including : serum urea , serum albumin , complete blood picture, serum electrolytes (calcium and phosphorus), PTH, serum vitamin D , lipid profile and echocardiography and Tissue Doppler imaging .

Conclusion: serum vitamin D is positively correlated with diastolic function among CKD patients, increased incidence of left ventricular hypertrophy in CKD patients especially with vitamin D deficiency ,Tissue Doppler imaging is more accurate than echocardiography to estimate diastolic function.

Key words: vitamin D, diastolic dysfunction, Tissue Doppler imaging.

INTRODUCTION

Chronic kidney disease (CKD) has been considered one of the risk factors of cardiovascular disease, and even minor to moderate renal insufficiency has been reported to be associated with adverse cardiovascular events. Furthermore, in CKD patients, cardiovascular disease is the major cause of death, which cannot be entirely explained by the clustering of the traditional cardiovascular risk ***(Rahman et al., 2015)***.

In patients suffering from chronic kidney disease (CKD), the prevalence of cardiovascular disease is much more common than in the general population.

Their high morbidity and mortality can't be explained by traditional cardiovascular risk factors, such as advanced age, the presence of diabetes, hypertension, hypertriglyceridemia and low levels of high-density lipoprotein (HDL) cholesterol ***(Fanari et al., 2015).***

Chronic kidney disease patients usually experienced several comorbid conditions including cardiovascular disorders and at final end-stage renal disease (ESRD) stage, cardiovascular mortality accounts for about 50% of total mortality.

.End-stage renal disease (ESRD) patients commonly have a higher risk of developing cardiovascular diseases than general

population. Chronic kidney disease is an independent risk factor for atrial fibrillation (AF) ***(chen et al., 2016).***

According to studies, also abnormalities of calcium, phosphorus, vitamin D, and parathyroid hormone (PTH) are associated with the occurrence of cardiovascular disease.Some of them also indicate a relationship between vitamin D deficiency and hypertension, insulin resistance, diabetes, and dyslipidaemia. Vitamin D deficiency is present even in the early stages of chronic kidney disease ***(Fanari et al., 2015).***

Vitamin D deficiency is more common in diabetic patients with nephropathy. When micro vascular complications were evaluated, vitamin D levels were found to be lower in patients in whom these complications were more severe. Vitamin D deficiency is therefore associated with microvascular complications in diabetic patients ***(Onut et al., 2016).***

Vitamin D deficiency is associated with a substantially increased risk of all-cause dementia and Alzheimer disease. This adds to the on-going debate about the role of vitamin D in non-skeletal conditions ***(Lee et al., 2015).***

Epidemiological studies have shown an inverse relationship between vitamin D levels and cardiovascular diseases. However, a causal relationship between both hasn't been investigated yet ***(chen et al., 2016).***

AIM OF THE WORK

To determine the association between serum 25-hydroxyvitamin D level and the myocardial function, assessed by tissue Doppler imaging in the CKD population.

CHAPTER (1)

CHRONIC KIDNEY DISEASE (CKD)

Chronic kidney disease (CKD)is a type of kidney disease in which there is gradual loss of kidney function over a period of months to years. Initially there are generally no symptoms; later, symptoms may include leg swelling, feeling tired, vomiting, loss of appetite, and confusion. Complications include an increased risk of heart disease, high blood pressure, bone disease, and anemia**(*Liao MT*.,2012).**

Signs and symptoms

CKD is initially without symptoms, and is usually detected on routine screening blood work by either an increase in serum creatinine, or protein in the urine. As the kidney function decreases***:***

- **Blood pressure** is increased due to fluid overload and production of vasoactive hormones created by the kidney via the renin–angiotensin system, increasing the risk of developing hypertension and heart failure**.**
- **Urea** accumulates, leading to azotemia and ultimately uremia (symptoms ranging from lethargy to pericarditis and encephalopathy). Due to its high systemic concentration, urea is

excreted in eccrine sweat at high concentrations and crystallizes on skin as the sweat evaporates (uremic frost).

- **Fluid overload** symptoms may range from mild edema to life-threatening pulmonary edema.
- **Hyperphosphatemia** results from poor phosphate elimination in the kidney. Hyperphosphatemia contributes to increased cardiovascular risk by causing vascular calcification**(*Hruska KA*.,2008).**
- ***H*ypocalcemia** results from 1,25 dihydroxyvitamin D_3 deficiency (caused by high FGF-23 and reduced kidney mass) and resistance to the action of parathyroid hormone **(*Bacchetta J et al.,2013).***

Osteocytes are responsible for the increased production of FGF-23, which is a potent inhibitor of the enzyme 1-alpha-hydroxylase responsible for the conversion of 25hydroxycholecalciferol into 1,25 dihydroxyvitamin D_3**(*Longo et al.,2018)***.

Later, this progresses to secondary hyperparathyroidism, kidney osteodystrophy, and vascular calcification that further impairs cardiac function. An extreme consequence is the occurrence of the rare condition named calciphylaxis **(*Brandenburg VM.,2011)***.