

Original Research Article

Status of vitamin D, lipid profile and carotid artery intima media thickness in patients with chronic kidney disease stage III to V

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is characterized by irreversible sclerosis and loss of nephrons. The renal mass progressively declines over a prolonged period, depending on the underlying etiology. In CKD the most common feature is hypovitaminosis D which alter the vascular smooth muscle cell proliferation and reprogram the osteoblastic changes, finally leading to increase arterial wall thickness.

Methods: A cross sectional study carried out over a 2-year period in Department Nephrology and General Medicine OPD, MIMS, Vizianagaram, Andhra Pradesh, India. 120 in which 60 are normal healthy individuals and 60 are CKD patients with stage 3 to 5. In all the participants serum creatinine, blood urea, serum triglycerides serum total cholesterol, HDL cholesterol estimated and serum 25 OH vitamin D are estimated.

Results: The diagnostic criteria for CKD like blood urea, serum creatinine and eGFR were significantly higher in CKD when compared to control. In the present study, systolic and diastolic blood pressure was significantly increased in CKD compared with control. The Carotid Intima Media Thickness (CIMT) both left and right side were significant higher in CKD when compared with control. There is a significantly decreased levels of serum vitamin D in CKD (14.53 ng/mL±6.88) when compared with control (28.87 ng/mL±6.28).

Conclusions: Present study finding suggested that there is a raised value of CIMT in CKD patients. High triglycerides, cholesterol and decreased HDL and declined vitamin D low hemoglobin, decreased eGFR, increased systolic blood pressure, raised CIMT value were found to be significantly increased in CKD patients.

Keywords: Carotid intima media thickness, Chronic kidney disease, Vitamin D

INTRODUCTION

Chronic Kidney Disease (CKD) is characterized by irreversible sclerosis and loss of nephrons. The renal mass progressively declines over a prolonged period, depending on the underlying etiology.¹ CKD patients are classified five stages based on Glomerular Filtration Rate (GFR). Diabetes and hypertension could stand as the main etiology for the increased incidence of CKD. It

affects 10-16% of the adult population worldwide.² In India, the recent estimate is found to be 229 per million population.³ The National Kidney Foundation (NKF) Task Force on Cardiovascular Disease in CKD demonstrated the prevalence of cardiovascular disease in CKD and associated high death rate.⁴

Vitamin D is well known factor that regulates bone and mineral metabolism by promoting calcium, phosphate

absorption and suppressing Parathyroid hormone (PTH) secretion.^{5,6} Its downregulation of vascular smooth muscle cell proliferation and migration and suppression of inflammation triggered expression of endothelial adhesion molecules. Vitamin D also prevent vascular calcification by, inhibition of bone morphogenic protein-2 expression. Decreased vitamin D can cause low calcium and hyperparathyroidism. PTH normally causes absorption of calcium and excretion of phosphorous.⁷

In CKD, the most common feature is hypovitaminosis D leading to secondary hyperparathyroidism. This would have caused an increase in calcium and a decrease in phosphate levels. But due to the declined renal mass, this does not happen and PTH secretion is further stimulated.⁸ These may alter the vascular smooth muscle cell proliferation and reprogram the osteoblastic changes, finally leading to increase arterial wall thickness.⁹

The Chronic Kidney Disease there is a qualitative and quantitative metabolic abnormalities of plasma lipids. The most common abnormality is increased serum triglycerides, cholesterol and decreased HDL cholesterol. This factor may be increased risk factors for cardiovascular complications and further increases the mortality and morbidity of CKD.

Arterial wall thickness can be measured by carotid intima media thickness test (CIMT) and the extent of carotid atherosclerotic vascular disease may be estimated. The test measures the thickness of the inner two layers of the carotid artery, the intima and the media. Early detection of these changes may hint the need for a more aggressive approach towards heart disease and stroke.¹⁰

Though, CKD can have a deleterious consequence of CVD and increased mortality, estimation of vitamin D, serum triglycerides, cholesterol, HDL-cholesterol and measuring CIMT might throw a warning sign of the future risk. Early intervention could help the CKD patients for a better life and outcome.

METHODS

Type of study was case-control study. Study population was patients and attendants who attended the Department of Nephrology. Study period was for 2 year that is from January 2017 to January 2019. Sample size was 120 in which 60 are normal healthy individuals and 60 are CKD patients with stage 3 to 5.

Inclusion criteria

The patients attending Nephrology Department diagnosed with CKD.

Exclusion criteria

Known Subjects with history of smoking, alcoholism and medicines which influence serum calcium and vitamin D

levels are excluded. Patients with any debilitating illness also excluded from this study. CKD patients who did not provide inform constant were excluded.

Study design

The study consists of 60 CKD patients divided into 3 groups based on eGFR and 60 normal healthy individuals, age and sex matched individuals. Informed consent will be taken from the patients and controls. Demographic data will be collected followed by history regarding current health status, history of medication, alcoholism and active smoking. A questionnaire was given to all patients and detailed clinical examination was performed.

In all the participants, blood pressure measured by using mercury sphygmomanometer both systolic and diastolic blood pressure was measured based on 1st and 5th korotkoff phase. An average of two readings was considered.

Carotid artery intima media thickness test

Carotid artery ultrasound scans recorded for each participant with a 10-MHz linear-array transducer to measure intima media thickness (IMT) in the far wall of the right and left common carotid arteries within 2 cm proximal to the carotid bulb. The region with the thickest IMT, excluding areas with focal lesions, was measured. The average IMT was calculated from the right and left IMT measurements. All focal plaques within the carotid tree (common, internal, and external carotid arteries and bulb) identified as wall thickness. The area of each plaque was calculated as the average lesion thickness (in mm) multiplied by the lesion length (in mm). In those participants with multiple plaques, plaque area is the sum of the areas of all plaques observed in the carotid tree.¹¹

Sample analysis

About 5 ml of venous blood was collected from all the subjects for biochemical analysis. Serum creatinine was estimated by alkaline picrate method, blood urea was estimated by urease method, serum total cholesterol and HDL cholesterol are estimated by cholesterol oxidase method.¹²⁻¹⁵ Serum triglycerides was estimated by glycerol kinase method.¹⁶ Serum 25 OH vitamin D was analysed on Siemens ADVIA Centaur by Chemiluminescence immunoassay (CLIA) method.

Estimated GFR (eGFR) was computed by employing Mayo Clinic Quadratic Equation (MCQE) based on serum creatinine and age in years.^{17,18}

The MCQE estimated GFR (ml/min /1.73 m²)

=exp [1.911+5.249 / SCr-2.114 / SCr2-(0.00686 x age (years)] (-0.205 if female).

Statistical analysis

Data will be expressed in Mean and Standard deviation (mean±SD). Z test was used for comparison of means between controls and cases. The statistical significance was determined at 5% (p <0.05) level.

RESULTS

The present study was conducted at Maharajah’s Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India. A total of 120 CKD subjects were included. They are further divided into CKD (60) and Normal healthy individual as control (60).

Table 1 shows the mean age of the CKD was 44.26 years±11.19 Control it was 44.18 years±11.67. As regards the sex distribution, the majority of subjects were male in CKD 60% and control 60%. The diagnostic criteria for CKD like blood urea, serum creatinine and eGFR were significantly higher in CKD when compared to control. In the present study systolic and diastolic blood pressure was significantly increased in CKD compared with control. There is a significantly decreased level of hemoglobin in CKD when compared with control.

Table 1: Profile of CKD and control.

Parameters	CKD	Control
Number	60	60
Age (mean±SD) (yrs)	44.26±11.19	44.18±11.67
Sex		
Males %	60	60
Females %	40	40
Blood urea (mg/dl)	89.12±21.69	26.72±8.01**
Serum creatinine (mg/dl)	6.72±2.32	1.01±0.12**
eGFR (mL/min)	28.67±9.89	100.67±8.73**
Blood pressure (mm Hg)		
Systolic	153.75±21.97	112.28±10.28**
Diastolic	93.12±7.83	70.21±8.83**
Hemoglobin (g/dl)	8.52±0.78	12.86±0.93**
Stages of CKD		
Stage III	2	-
Stage IV	28	-
Stage V	30	-

**=p<0.001

Table 2 shows the Carotid Intima Media Thickness (CIMT) both Left and Right side were significant higher in CKD when compared with Control. The mean cholesterol was significantly higher in CKD (221.84 mg/dL±48.10) compared with control (154.23 mg/dL±18.66). In the present study serum triglycerides was significantly higher in CKD (168.20 mg/dL±38.24) when compared with control (110.28 mg/dL±12.28). The serum HDL was significantly decreased in CKD (37.15 mg/dL±10.72) when compared with control (44.63

mg/dL±7.88). There is also significantly decreased levels of serum vitamin D in CKD (14.53 ng/mL±6.88) when compared with control (28.87 ng/mL±6.28).

Table 2: CIMT and biochemical profile in CKD and control group.

Parameters	CKD	Control
CMIT left side (mm)	0.87±0.31	0.67±0.11
CMIT Right side (mm)	0.79±0.41	0.62±0.10
Total cholesterol (mg/dl)	221.84±48.10	154.23±18.66
HDL-C (mg/dL)	37.15±10.72	44.63±7.88
Triglycerides (mg/dL)	168.20±38.24	110.28±12.28
25-OH vit D (ng/ml)	14.53±6.88	28.87±6.28

DISCUSSION

In CKD, there is decreased glomerular filtration rate which causes increased blood urea and serum creatinine. In CKD due to hypervolemic and the uncontrolled hypertension causes raised blood pressure. In CKD anemia is cofounder and it is an independent risk factor for CVD due to anemia there is a poor oxygen delivery and raises stroke volume.

In the present study in CKD patients CIMT was higher in both left and right side compared to control. Previous studies done by Lu Xia Zhang et al, reported that in CKD stage II and III CIMT was significantly raised and concluded the progression CKD will causes arterial change.¹⁹ Preston et al, shown that Stage III and IV have raised CIMT compared with Normotensive.²⁰ Atherosclerotic changes in carotid arteries might be indicative of atherosclerosis of coronary arteries. CIMT is a non-invasive marker for generalized atherosclerosis and good indicator for coronary heart disease.

In this study, triglycerides are increased significantly Kawagishi et al, and Brzosko et al, also found same results.^{21,22} The cause for raised triglycerides is due to decreased lipoprotein lipase (LPL) activity, increased plasma apolipoprotein C-III and inhibition of lipase by uremic toxins all these factors contribute raised triglycerides.^{23,24}

The serum cholesterol level was higher in CKD patients previous study by Brzosko et al, and Arun Kumar et al, also showed increased cholesterol value.^{22,25} In CKD patients HDL was significantly decreased this is due to declined apolipoproteins AI and AII, Decreased LCAT activity which is responsible for esterification of free cholesterol in HDL particles and raised Cholesteryl Ester Transfer Protein (CETP) activity it causes transport of cholesterol from HDL triglyceride-rich lipoproteins.^{26,27} High triglyceride and low HDL contribute to plaque formation and CIMT was strongly associated with atherogenic lipids.²⁸ In this study, authors also found that significant decline of vitamin D when compared to control. Renal dysfunction leads to hypovitaminosis D.

Vitamin D inhibit cyclin-dependent kinase-2 activity and further causes suppression vascular smooth muscle cell proliferation.²⁹ In CKD decreased vitamin D associated with increased CIMT value.

From the findings of present study, it was concluded that there is a raised value of CIMT in CKD patients. High triglycerides, cholesterol and decreased HDL and declined Vitamin D Low hemoglobin, decreased eGFR, increased systolic blood pressure, raised CIMT value were found to be significantly increased in CKD patients. Using CIMT with ultrasonography is a cost effective, non-invasive, easy and reproducible. Early detection of CIMT and correction of Vitamin D and lipid abnormality assist in the reducing progression deleterious effects.

CONCLUSION

Morphometric features of transverse and sigmoid sinus with other superficial landmarks is essential during posterolateral approaches to the posterior cranial fossa. The measurements of asterion with other bony landmarks provide database for the clinical-surgical practice and also for forensic and anthropological application.

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