

Original Research Article

Evaluation of carotid intima media thickness and associated risk factors in patients with chronic kidney disease: a cross sectional study

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ABSTRACT

Background: Chronic kidney disease is distinguished by progressive loss of kidney function over a period of years in the end leading to irreversible kidney failure. CKD is a significant prognosticator of cardiovascular disease. Atherosclerosis is common in patients with risk factors associated with chronic kidney disease.

Methods: It was a cross sectional study on CKD patients in a tertiary care hospital. About 90 CKD stage 3-5 patients aged above 18 years were enrolled in the study. Serum lipid profile, RFT, serum calcium, phosphorous, and BP were estimated among all the patient. Patient risk factors were noted and CIMT levels were compared accordingly.

Results: Out of 90 patients, males were predominant. There was a significant positive correlation between stage 5 and CIMT (P value <0.001). Mean CIMT was higher in patients with type 2 Diabetes. Patients with higher phosphorous the mean CIMT was significantly higher.

Conclusions: The CIMT is early marker for atherosclerosis. Author observed it was significantly higher in patients with stage 3 and 5 CKD. CIMT is a non- invasive marker which should be done in all patients with CKD which is cost effective.

Keywords: Blood pressure, Chronic kidney disease, Carotid intima media thickness, Renal function tests

INTRODUCTION

Chronic kidney disease is distinguished by progressive loss of kidney function over a period of years in the end leading to irreversible kidney failure. Patients with chronic kidney disease (CKD) are at significantly increased risk for both morbidity and mortality from cardiovascular disease (CVD).¹

It is well documented that systemic inflammation plays a major role in the development of atherosclerosis as well as cardiovascular morbidity and mortality among Chronic

kidney disease (CKD) patients.² Dyslipidaemia is a common complication of progressive kidney disease which is characterized by high triglyceride and low high-density lipoprotein (HDL) cholesterol levels, accumulation of remnant particles, a predominance of small dense low-density lipoprotein (LDL) particles, and increased levels of lipoprotein A.

In patients with advanced chronic kidney disease (CKD), LDL and HDL particles undergo oxidative modification, resulting in the formation of small lipoproteins and enhances production of oxidized LDL.³

Risk factors for CKD

Family history

Family members of Chronic kidney disease (CKD) patients have higher prevalence of CKD and its risk factors.⁴

Gender

Studies have shown that Chronic kidney disease (CKD) is more common in men.⁵

Age

Renal function decreases with age its common in both men and women.⁵

Obesity

One of the strongest risk factors for end stage renal disease (ESRD) in twenty first century is obesity.⁶

Smoking

Smoking can increase the risk of CKD through pro-inflammatory state, oxidative stress, pro-thrombotic shift, endothelial dysfunction, glomerulosclerosis and atrophy of the tubules.⁷

Alcohol

Alcohol is commonest risk for CKD progression.⁶

Diabetes mellitus

Diabetes mellitus (DM) is the common cause of CKD and End stage renal disease (ESRD) in developing countries. Mechanism that lead to kidney disease in diabetes include hyperfiltration injury, advanced glycosylation and end products, and reactive oxygen species.⁸

Hypertension

Hypertension has been long time risk factor in patients with CKD and ESRD. It accounts for 27% of all ESRD patients and 28% of hemodialysis patients. Systemic hypertension is transmitted to intraglomerular capillary pressure leading to glomerulosclerosis and decrease renal function. The variable risk for impaired renal function is among patient with hypertension.⁶

Patients with CKD have higher prevalence of cardiovascular morbidity, but the risk of mortality is highest in patients with ESRD whose risk is thirty times greater than that of general population.⁹

Carotid intima media thickness (CIMT) is the non-invasive study that suggests presence of atherosclerosis and good indicator for presence of cardiovascular disease. The normal intima -media thickness of common carotid artery is evaluated by B mode ultrasound imaging was 0.74 ± 0.14 mm.¹⁰

METHODS

The study was conducted among the patients admitted in the General Medicine Ward of the Mahatma Gandhi Medical College and Research Institute with a diagnosis of Chronic Kidney Disease between October 2016 to March 2018. The patients were interviewed and enrolled for the study after fulfilling the following inclusion and exclusion criteria. Subjects were informed about the study and their consent was taken. Patients with CKD 3-5 above 18 years were taken into the study. 90 subjects were selected.

A questionnaire designed for the study was fulfilled by each candidate. BMI was calculated. BMI of 18-24.9 kg/m² was considered normal. BMI less than 18 kg/m² was considered malnourished. BMI more than 25 kg/m² was considered overweight. History of smoking, physical activity, diet and alcohol consumption was taken.

Personal and family medical history of obesity, hypertension, diabetes mellitus and renal disease was recorded. Blood pressure of each patient was recorded by sphygmomanometer. Fasting lipid profile, serum urea, serum creatinine, serum calcium, phosphorous was taken for all patients.

Fasting lipid profile was measured in MGMCRI Biochemistry laboratory. Total cholesterol was measured by CHOD-PAP method. Serum triglyceride level was measured by GPO method. HDL Cholesterol was measured by DIRECT method. Hitachi 902 auto-analyzer was used for estimation of fasting lipid profile.

Any patient having abnormal triglycerides or any of the cholesterol parameters which was above or below the normal range in the laboratory was considered dyslipidemia. Serum urea was measured by GLDH method in Hitachi 902 auto-analyzer in the Biochemistry Laboratory, MGMCRI, Pilliyarkuppam, Pondicherry, India.

Serum creatinine was estimated by JAFFE KINETIC method in Hitachi 902 auto-analyzer in hospital. Patients with CKD had raised renal parameters. Creatinine clearance was calculated by Cockcroft-Gault Equation and staging was done accordingly for all patients. All patients are screened for carotid intima media thickness bilaterally by using B-Mode ultrasonography. Individuals with atheromatous plaques and increased CIMT levels were started on stains.

Statistical method

Statistical analysis was carried out using SPSS version 19.0 (IBM SPSS, US) software with Regression Modules installed.

Descriptive analyses were reported as mean and standard deviation of continuous variables. Independent sample t test was used to compare the age, BMI, pulse rate, BP (systolic and diastolic), Lipid profile, RFT (urea, creatinine), serum calcium, serum phosphorous, B mode ultrasonography.

The frequencies, mean and standard deviation were generated. A p value less than 0.05 was taken as statistically significant.

RESULTS

Demographic data

A total 90 patients with chronic kidney disease were evaluated from November 2016 to May 2018. All non-critically ill patients who were admitted in the General Medicine Ward in Mahatma Gandhi Medical College and Research Institute, Pondicherry, India and who had consented for the study after fulfilling the inclusion and exclusion criteria.

All of them had a complete evaluation for co-morbidities and complications. All data were collected and tabulated. The baseline characteristics of all patients are given in the following tables.

All 90 patients had a complete evaluation for co-morbidities and complications. All data were collected and tabulated. The study population consisted of 90 patients which shows baseline features single group on gender with 53 males (58.%) and 37 females (41.%) (Figure 1).

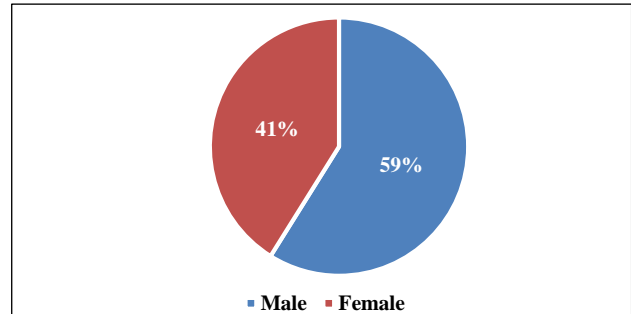


Figure 1: Gender distribution.

Table 1 shows the height and weight of all the patients was calculated for each subject and Basal Metabolic Index (BMI) was calculated. The mean BMI for patients was 23.1 ± 2.7 kg/m².

Table 1: Baseline features of both groups on age and BMI.

Features	(N=90)
	Mean (SD)
Age in years	60.6 (12.9)
BMI in kg/m ²	23.1 (2.7)

Table 2: Baseline features of all 3 stages on pulse and BP.

Features	Stage 3, N=26 (28.9)	Stage 4, N=26 (29.9)	Stage 5, N=38(42.2)	p value#
	Mean (SD)			
Pulse rate in bpm	85.5 (9.5)	83.5 (9.3)	83.9 (12.1)	0.56
SBP in mm of Hg	156.3 (19.1)	157.3 (20.1)	156.1 (17.3)	0.17
DBP in mm of Hg	96.4 (11.8)	93.4 (11.7)	94.6 (8.8)	0.25

Table 2 shows various stages of CKD in which 26 (28.9) patients belong to stage 3, 26 (29.9) patients belong to stage 4 and 38 (42.2) patients belong to stage 5. Patients with baseline pulse rate and blood pressure. The patients with stage 3 (N=26) had baseline mean pulse rate 85.5 ± 9.5 bpm, stage 4 had baseline mean pulse rate 83.5 ± 9.3 bpm and stage 5 patients had baseline mean pulse rate 83.9 ± 12.1 bpm respectively which showed no statistical significance (p value 0.56).

The mean systolic blood pressure (SBP) in stage 3 CKD was 156.3 ± 19.1 , stage 4 = 157.3 ± 20.1 and stage 5 = 156.1 ± 17.3 mmHg respectively which showed no statistical significance (p value 0.17). The mean diastolic

blood pressure (DBP) with stage 3 = 96.4 ± 11.8 , stage 4 = 93.4 ± 11.7 and stage 5 = 94.6 ± 8.8 mmHg respectively which showed no statistical significance (p value 0.25).

Table 3: Distribution of risk factors among patient with Stage 3-5 CKD.

Features	(N=90) N (%)
Diabetes	45 (50)
Hypertension	78 (86.6)
Diabetes + Hypertension	40 (44.4)
Alcoholic	23 (25.6)
Smokers	25 (27.2)

Table 3 shows risk factors of CKD shows patients with diabetic 45 (50%) , hypertensive 78 (86.6%) and 40 (44.4%) patients had both. Patients with alcohol consumption were 23 (25.6) and smokers 25 (27.2).

Table 4 shows the mean variables of cholesterol, triglycerides, HDL, LDL, Serum creatinine, serum calcium, phosphorous, CMT (right/left), eGFR. The mean cholesterol in stage 3 was 143.6±35.5, stage

4=155.7±36.9, stage 5=168.3±47.4 mg/dl and was statistically insignificant (p value 0.067).

The mean triglycerides in stage 3 was 108.5±122, stage 4=119.5±136 and stage 5=121±178 mg/dl was statistically insignificant (p value 0.16). The mean HDL in stage 3 were 49.4±7.2, stage 4=46.2±8 and stage 5=48.4±6.7 mg/dl was statistically insignificant (p value 0.26).

Table 4: Relation between parameters and staging.

Mean (SD)				
Parameters	Stage 3	Stage 4	Stage 5	P value
Cholesterol	143.6 (35.5)	155.7 (36.9)	168.3 (47.4)	0.067
Triglycerides	108.5 (79-122)	119.5 (84-136)	121 (103-178)	0.16
HDL	49.4 (7.2)	46.2 (8)	48.4 (6.7)	0.26
LDL	77.8 (21.9)	86.8 (36.9)	93.9 (43.1)	0.23
EGFR	35.7 (33.3-45)	20.5 (17.7-27.1)	8.4 (6.8-11.9)	<0.001*
Serum creatinine	1.9 (1.6-2.2)	2.7 (2.1-3.1)	6.7 (5.1-9.1)	<0.001
Serum calcium	7.3 (0.7)	7.8 (1)	7.3 (1.1)	0.09
Magnesium	1.7 (1.5-2)	1.5 (1.4-1.8)	1.8 (1.6-2.1)	0.01
Phosphorous	4.4 (1.8)	3.6 (1.2)	5.4 (2.3)	0.002
CIMT Right	0.8 (0.08)	0.9 (0.07)	0.9 (0.1)	<0.001
CIMT Left	0.8 (0.08)	0.9 (0.09)	0.9 (0.1)	<0.001

The mean LDL in stage 3 was 77.8±21.9, stage 4 was 46.2±8 and stage 5 was 93.9±43.1 mg/dl is statistically insignificant (p value 0.23). The mean eGFR using Cockcroft-Gault equation in stage 3 was 35.7±45, stage 4 was 20.5±27.1 and stage 5 was 8.4±11.9 ml/min is statistically significant (p value <0.001). The mean serum creatinine in stage 3 was 1.9±2.2, stage 4=2.7±3.1 and stage 5=6.7±9.1 mg/dl is statistically significant (p value <0.001).

The mean serum calcium in stage 3 was 7.3±0.7, stage 4 was 7.8±1 and stage 5 was 7.3±1.1 mg/dl is statistically insignificant (p value 0.09). The mean phosphorous in stage 3 was 4.4±1.8, stage 4=3.6±1.2 and stage 5=5.4±2.3 mg/dl is statically significant (p value 0.002).

The mean magnesium in stage 3 was 1.7±2, stage 4=1.5±1.8 and stage 5=1.8±2.1 mg/dl is statistically significant (p value 0.01). The mean CMT (right) was 0.8±0.08 in stage 3 is 0.9±0.07 in stage 4 is and 0.9±0.1 in stage 5 which is statistically significant (p value <0.001). The mean CMT (left) in stage 3 CKD is 0.8±0.08, stage is 4, 0.9±0.009 and stage 5 is 0.9±0.1 mm and is statistically significant (<0.001).

Relation between CKD stages and CMT. In stage 3, CKD the mean CMT was 0.8 mm where stage 4 CKD had 0.9 mm and stage 5 CKD had 0.9 mm (Figure 2).

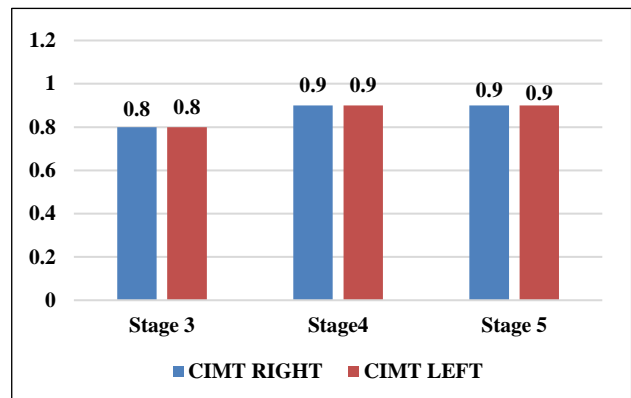


Figure 2: Relation between CMT and CKD stage.

The relation between smokers and non-smokers with CMT. The mean Right CMT in smokers is 0.86 mm compared to non-smokers 0.85 mm which is statistically insignificant (P value 0.8). The mean left CMT in smokers is 0.85 mm compared to non-smokers 0.84 mm which is statistically insignificant (P value 0.77).

The mean CMT in patients with 3-5 stages of CKD with and without hypertension in which (right CMT) is 0.9 mm in hypertensive individuals compared with non-hypertensive individuals it is 0.8 mm which is statistically insignificant (P value 0.8).

The mean Left CIMT in hypertensive individuals is 0.8 mm compared to non-hypertensive individuals it is 0.9 mm which is insignificant (P value 0.002).

The mean CIMT is 0.9 mm on right side in both alcoholics and non-alcoholics (P value 0.6). The mean CIMT on left side 0.8 mm in alcoholics and 0.9 mm in non-alcoholics which is insignificant (P value 0.4).

The relation between type 2 diabetic patients and CIMT. The mean right CIMT in diabetes is 0.8 mm and non-diabetes is 0.9 mm which is statistically insignificant (P value=0.47). The mean left CIMT in diabetes is 0.9 mm and non-diabetes is 0.8 mm which is insignificant (P value 0.5).

The mean female in stage 3 are 9 ± 24.3 , stage 4 are 12 ± 32.4 and stage 5 16 ± 43.2 . Mean Males in stage 3 are 17 ± 32.1 , stage 4 are 14 ± 26.4 and stage 5, 22 ± 41.5 in which p value is insignificant (P value 0.69).

The mean alcohol use in stage 3 are 4 ± 17.4 stage 4 are 7 ± 30 and stage 5 are 12 ± 52.2 where p value is insignificant (P value 0.34). The mean smokers in stage 3 are 6 ± 24 , stage 4 are 7 ± 28 , and stage 5 are 12 ± 48 . P value is insignificant (P value 0.75).

The mean diabetes in stage 3 are 13 ± 28.9 , stage 4 are 16 ± 35.6 and stage 5 are 16 ± 35.6 . P value is insignificant (P value 0.31).

DISCUSSION

Ninety patients with chronic kidney disease were taken up for the study. Present study population had more male population compared to females with male forming 53 out of 90 study subjects (58.9%). Another similar study done on CKD patients in Kumar VS et al, revealed high male population prevalence with 26 male out of 30 (96%) which was almost similar to this study. This may be attributed to the fact that male patients seek more medical attention compared to women in India.¹¹

In this study, population the mean BMI for patients is 23.1 ± 2.7 kg/m². A Study done by Lokesh S et al, on hemodialysis patients in a tertiary care hospital in South India showed BMI of 20.76 ± 4.249 kg/m². Low BMI in Indian population can be because of nutritional deficiency.¹²

The mean age in this study, population was 60 ± 12.9 . In this study, the mean age in stage 3 CKD was 58.3 ± 12.9 , stage 4 was 62.7 ± 12.1 and stage 5 was 60.7 ± 13.5 . The mean age in CKD stage 3 was 58 and in stage 5 it was 60.3. A similar study done by Macros AG et al, showed that mean in age CKD stage 3 was 56 ± 9 and Stage 5 was 58 ± 11 .

In this study, 26 (28.9%) are stage 3, 26 (28.9%) are stage 4 and 38 (42.2%) are stage 5. In this study, in stage

5 CKD predominantly are male. Another study done by Macros AG et al, revealed more number of male predominance in stage 5 CKD which is similar to this study.¹³

Hypertension is one of the common cause of CKD. In this study, 78 patients (86.7) who are known hypertensive. The mean systolic BP in stage 3 CKD is 156.3 ± 19.1 mmHg and mean diastolic BP 96.4 ± 11.8 mmHg, in stage 4 CKD mean SBP 157.3 ± 20.1 mmHg and mean DBP 93.4 ± 11.7 mmHg and in stage 5 CKD mean SBP was 156.1 ± 17.4 mmHg and mean DBP was 94.6 ± 8.8 mmHg. In a study done by Dhivya et al, the mean systolic BP is 156 ± 22.152 mmHg and diastolic BP was 93.75 ± 13.90 mmHg.¹⁴ The values in both studies were similar.

In this study, the mean cholesterol levels in stage 3 CKD was 143 ± 35.5 , In stage 4, CKD 155.7 ± 36.9 and in stage 5 CKD 168.3 ± 47.4 . The mean HDL in stage 3 CKD was 49.4 ± 7.2 , stage 4 was 46.2 ± 8 and in stage 5 was 48.6 ± 6.7 . The mean LDL in stage 3 CKD was 77.8 ± 21.9 , stage 4 CKD was 86.8 ± 36.9 and stage 5 CKD was 93.9 ± 43.1 . This showed that patients in stage 5 CKD has increased LDL and decreased HDL which is the surrogate marker for atherosclerosis. A study done by Schreier L et al, was found that patients with stage 3-5 CKD had lower levels of HDL and higher triglyceride levels which is similar to this study.¹⁵

In this study, 50% of patients were type 2 DM and 44.45% patient were both hypertensive and Type 2 DM, 74.4% were alcoholics and 27.8% were smokers. Patients with these risk factors CIMT levels are differentiated.

The mean phosphorous in stage 3 CKD was 4.4 ± 1.8 mg/dl, in stage 4 CKD 3.6 ± 1.2 and in stage 5 CKD 5.4 ± 2.3 . Hyperphosphatemia is a significant risk factor for vascular complication. In this study, patient with CKD stage 5 had increased phosphorous levels which is independent factor associated with increased CIMT. In this study, patients with increased phosphorous had increased CIMT especially in stage 5 CKD. A study done by Dubey A et al, was found that greater phosphate level was one of the significant factors associated with increased CIMT which was similar to this study.¹⁶

In this study, CIMT was found to be higher in patients with CKD stage 4 and 5. The mean CIMT in stage 3 CKD was 0.8 ± 0.08 , in stage 4 CKD was 0.9 ± 0.1 and in stage 5 CKD 0.9 ± 0.1 . P value in Right CIMT is <0.001 and left CIMT <0.001 which is statistically significant. In this study, there was no difference of CIMT in stage 4 and 5 CKD. There was significant association between mean CIMT and age group of CKD patients. The older age groups had significantly higher CIMT than younger groups. A study done by Kumar VS et al, revealed that increased CIMT levels are in patients with stage 4 and 5 CKD compared with stage 3 CKD which is similar to this study.¹¹ In this study, author compared CIMT with

different parameters and risk factors. Serum phosphorous levels were high in patients with increased CIMT. A similar study done by Dubey A et al, revealed that hyperphosphatemia is marker for atherosclerosis.¹⁶

In this study, population CIMT was compared with smokers and non-smokers. There was no correlation between CIMT and smokers. A similar study done by Ishimura E et al, had positive relationship between CIMT and smoking which was not in this study.¹⁷

CIMT with or without hypertension: In this study, the mean CIMT in hypertensive patients is 0.9 mm and non-hypertensive patients mean CIMT is 0.8 mm which is not significant (P value 0.8).

CIMT with or without Diabetes: Diabetes is risk factor for CKD and atherosclerosis. In this study, the mean CIMT in diabetes is 0.9 mm and in patients without diabetes is 0.8mm. Present study showed a significant correlation between CIMT and diabetes. The similar study was done by Afolabi et al, revealed that patients with diabetes had increased CIMT.¹⁸

CONCLUSION

Based on the results and the methodology employed, author have concluded that chronic kidney disease with risk factors increases CIMT. Increase in CIMT is related to renal failure, but there was a significant increase in patients with increase in LDL and total cholesterol levels. CIMT was higher in patients with CKD stage 4 and 5. The patient with CKD and diabetes had an increase CIMT compared without diabetes. In this study, patient with CKD stage 5 had increased phosphate level which is one of the significant and independent factor associated with increased CIMT.

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