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Evaluation of atherosclerosis in patients with chronic kidney disease by measuring carotid intima media thickness: An observational study from a tertiary care center in India

Lamsaka Lyngdoh[1], Bodhibrata Banerjee[2], Sampurna Chowdhury[3], Rishav Mukherjee[4], Subhendu Bikash Naiya[5], Raja Bhattacharya[6]

[1,3,4,5]Senior Resident, [2]Post Graduate Trainee, [6]Associate Professor, Department of General Medicine, Medical College, Kolkata, West Bengal, India

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ABSTRACT

Background: Chronic kidney disease (CKD) is associated with a substantial cardiovascular mortality and morbidity. Besides other factors, accelerated atherosclerosis plays a significant role in this. Carotid intima media thickness (CIMT) is an index of systemic atherosclerosis. By measuring the CIMT with the help of B mode ultrasound at common carotid artery, the overall atherosclerotic burden in CKD patients can be estimated. Accordingly patients at increased risk of premature mortality can be identified so that timely intervention can be taken. **Aims and Objectives:** The aim of the study was to measure the CIMT at the level of common carotid artery by B mode ultrasound for estimation of atherosclerotic burden in patients with CKD. **Materials and Methods:** It is a hospital based observational cross-sectional study involving 70 patients carried out in the department of General Medicine of Medical College and Hospital, Kolkata for a period of 1 year. Patients were selected on the basis of certain inclusion and exclusion criteria. They were evaluated based on clinical history, disease duration, physical examination findings and certain investigation parameters such as complete hemogram, renal function tests, serum potassium, lipid profile, urinalysis, urine for albumin-creatinine ratio, ultrasonography of kidney-ureter-bladder, and CIMT value as measured by B mode ultrasound of carotid artery. The data collected were analyzed with a suitable statistical analysis software package. Range, frequencies, percentage, mean, standard deviation, and P value were calculated. $P<0.05$ was taken as significant. **Results:** The study showed a strong correlation between CIMT and BMI ($r=0.533$, $P<0.001$). CIMT for serum triglyceride levels (≥ 150 mg/dl) were significantly ($P<0.001$) high in patients (mean $\pm$ SD $= 1.45 \pm 0.559$) mg/dl in comparison with serum triglyceride levels (<150 mg/dl) (0.98 $\pm$ 0.380 mg/d). Patients with high cholesterol of ≥ 200 mg/dl have a higher CIMT of 1.56 ± 0.574 with $P<0.001$. There is statistically significant relation of LDL with respect to mean CIMT as $P<0.001$ at 1% level of significance. Hence, mean CIMT is more in LDL (≥ 130) than in LDL (<130). CIMT for HDL levels (<40 mg/dl) were high in CKD (mean $= 1.53 \pm 0.518$ mg/dl) patients compared to HDL levels (≥ 40 mg/dl) (mean $= 10.88 \pm 0.291$). It was found that mean CIMT was higher in the later stages of kidney disease (Stage 3B, 4 and Stage 5) as compared to early stages (Stages 1, 2, and 3). We also found that the Mean CIMT (1.214 ± 0.531 was higher in patients with CKD compared to sonographically defined normal value (<0.9 mm). Hence, CKD patients who have traditional risk factors for atherosclerosis such as higher BMI, higher serum total cholesterol level, higher serum triglyceride level, higher serum LDL level, and lower serum HDL level have a higher value of CIMT. **Conclusion:** B-mode ultrasound is a non-invasive sensitive tool for assessment of CIMT. Since CKD is associated with accelerated atherosclerosis and subsequent increased cardiovascular mortality, this modality may help us to identify patients with atherosclerotic burden so that timely intervention can be taken to reduce future cardiovascular complications in CKD patients.

Key words: Atherosclerosis; Carotid intima media thickness; Chronic kidney disease; Dyslipidemia; Ultrasonography

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Address for Correspondence:
Dr. Raja Bhattacharya, Associate Professor, Department of General Medicine, Medical College, Kolkata, West Bengal, India.
Mobile: +91-8777079509. **E-mail:** rbrbhattacharya@gmail.com

INTRODUCTION

Chronic kidney disease (CKD) is a serious condition associated with premature mortality, decreased quality of life, and increased health-care expenditures.[1] Many patients with CKD have cardiovascular disease. They die prematurely from this condition instead of surviving long enough to face dialysis or transplantation. Patients with CKD tend to have an excess of traditional risk factors for cardiovascular disease, such as hypertension, diabetes, and hyperlipidaemia.[2-4] Renal disease also promotes cardiovascular injury by different mechanisms. These include dysregulation of calcium and phosphate metabolism, vascular calcification, anemia, dyslipidemia, hyperhomocysteinemia, and endothelial dysfunction leading to accelerated atherosclerosis. The atherosclerosis is often asymptomatic. So a direct examination of vessel wall is necessary to detect affected individuals in early stages. According to International Atherosclerosis Project, the process occurs simultaneously in carotid, cerebral, and coronary artery.

Carotid intima-medial thickness (CIMT) is well-established index of systemic atherosclerosis.[5,6] Studies have shown that this is an independent predictor of cardiovascular mortality in CKD population.[7-11] Measurement CIMT of the common carotid artery by B-mode ultrasound is a suitable non-invasive method to visualize the arterial walls for monitoring the early stages of atherosclerotic process.[12-15] It is also helpful to decide the appropriate method of treatment, either surgical or medical in patients with carotid artery stenosis.[16-18]

Aims and objectives

The aim of the study was to identify the at risk population among CKD patients with regard to atherosclerotic burden by assessment of CIMT by B mode ultrasound of common carotid artery.

MATERIALS AND METHODS

This was an observational cross-sectional study conducted in the inpatient and outpatient department of General Medicine, Medical College and Hospital, Kolkata from January 2019 to August 2020. Permission was obtained from the Institutional Ethics Committee.

The study population was clinically stable adult patients of either sexes having CKD coming to Medical college within the stipulated time period (n=70). Focused history taking including the demographic profile of the patients, clinical history with duration of disease, medication history, disease specific therapy, and its duration along with clinical examination was done. Investigations were performed which included complete and clinical examination were done. Investigations including fasting lipid profile, urea, creatinine, potassium, urinalysis study, urine albumin-creatinine ratio (ACR), hemoglobin, USG whole abdomen with kidney, ureter, bladder, and CIMT as measured by USG Doppler study were carried out.

All ultrasound measurements were performed at the Dept. of Radiology, Medical College, Kolkata. CIMT was assessed at three levels on each side: Common carotid artery, bulb, and internal carotid artery. The mean CIMT was defined as the mean of the three CIMT measurements on each side, According to current sonographic criteria, a normal value is defined as CIMT <0.9 mm. In addition, the number and size of carotid atherosclerotic plaques were also assessed. The patients were categorized on the basis of age, sex, disease severity, and common risk factors. CIMT values obtained were correlated with the above parameters along with markers of atherosclerosis. The data collected were tabulated in a master chart.

Statistical analysis

Data analysis was performed with a commercially available statistical analysis software package (SPSS 27.0 for Windows; SPSS; Chicago, IL, USA). The Range, frequencies, percentage, mean, standard deviation, and P value were calculated. P<0.05 was taken as significant.

RESULTS

70 patients were included in the study. All of them had CKD (according to National kidney foundation). The patients were studied for CIMT in relation with the different stages of CKD and also with cardiovascular risk factor such as age, sex, BMI, and dyslipidemia.

Out of 70 CKD patients, 39 (55.7%) were males, and 31 (44.3%) were females. Baseline characteristics of cases are mentioned in Table 1. The mean value of these characteristics are shown in Figure 1. The distribution of age and sex of the patients are shown in Table 2 and Table 3 respectively. The same is shown in pictorial form in Figure 2 and Figure 3 respectively. The mean age of study population was 58.37±12.193 years (34–90 years). Mean CIMT level was 1.214±0.531mm.

In present study, when CKD patients were staged, then 14 (20.0%) of the patients were in the Stage 5, 11 (15.7%) were in Stage 4. About 64.3% of the patients were in early stage of kidney disease (Stages 1, 2, and 3A and 3B) (Table 4 and Figure 4).

Table 1: Baseline characteristics of different parameters

Baseline parameters	Mean±SD
Age (years)	58.37±12.193
BMI	26.46±2.376
Total Cholesterol (mg/dl)	207.10±50.632
Triglycerides (mg/dl)	164.57±42.732
LDL (mg/dl)	132.01±46.519
HDL (mg/dl)	40.91±9.270
VLDL (mg/dl)	32.94±8.551
Carotid intima media thickness (mm)	1.214±0.531
UREA (mg/dl)	72.97±58.567
CREA (mg/dl)	2.83±3.511
Urine albumin-creatinine ratio (mcg/mg)	185.24±137.315
K+ (mmol/L)	4.16±0.766
Hb (g/dl)	10.75±1.749
GFR value (ml/min/1.73 m)	42.74±29.269

Table 2: The distribution of age of chronic kidney disease patients

Age	Frequency	Percent
≤40 years	4	5.7
41–60 years	42	60.0
61–80 years	20	28.6
>80 years	4	5.7
Total	70	100.0

Table 3: The distribution of sex of chronic kidney disease patients

Sex distribution	Number of patients	Percent
Female	31	44.3
Male	39	55.7
Total	70	100.0

Table 4: Distribution of the subject according to stages of CKD

CKD stages	Number of patients	Percentage
Stage1	6	8.6
Stage 2	16	22.9
Stage 3A	5	7.1
Stage 3B	18	25.7
Stage 4	11	15.7
Stage 5	14	20.0
Total	70	100.0

CKD: chronic kidney disease

Table 5: Distribution of mean CIMT according to (eGFR) stage of CKD

Stages of CKD	Mean CIMT
Stage1	1.026 mm
Stage 2	1.15 mm
Stage 3A	0.92 mm
Stage 3B	1.27 mm
Stage 4	1.19 mm
Stage 5	1.42 mm
Correlation coefficient (−0.169)	

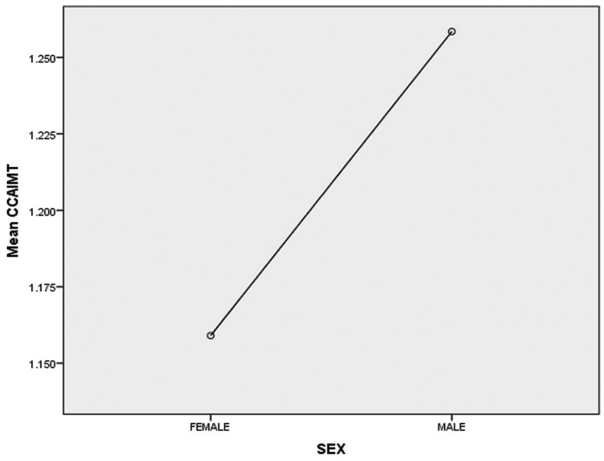
P-value (0.163) (NS) (P<0.05→significance). CKD: chronic kidney disease, CMIT: Carotid intima media thickness

Table 6: Significance of different parameters (AGE) with respect to mean carotid intima media thickness

Parameter	Category	Mean±SD	P-value
AGE	≤40 years	1.21±0.187	0.639
	41–60 years	1.23±0.546	
	61–80 years	1.21±0.563	
	>80 years	1.50±0.463	

Table 7: Significance of different parameters (SEX) with respect to mean carotid intima media thickness

Parameter	Category	Mean±SD	P-value
SEX	Male	1.26±0.543	0.441
	Female	1.16±0.519	



From Table 5, it is observed that there is no direct co-relation of the CIMT and eGFR (CC=−0.169 [P=0.163]). However, CIMT values are more in later stages of CKD (Stage 3B, 4, and 5) compared to early stages (Stages 1, 2, and 3A) (Figure 5).

From Table 6, it is observed that there is statistically no significant relation of categories of age with respect to mean CIMT as the P>0.05, at 5% level of significance. Mean CIMT is maximum in the age group more than 80 years and minimum in the age group of 61–80 years.

From Table 7, it is observed that there is statistically no significant relation of Sex with respect to mean CIMT as the P>0.05, at 5% level of significance. Mean CIMT is more in male than in female.

From Table 8, it is observed that there is statistically significant relation of BMI with respect to mean CIMT

Table 8: Significance of different parameters (BMI) with respect to mean carotid intima media thickness

Parameter	Category	Mean±SD	P-value
BMI	Non-obese	1.18±0.484	0.044*
	Obese	1.67±0.915	

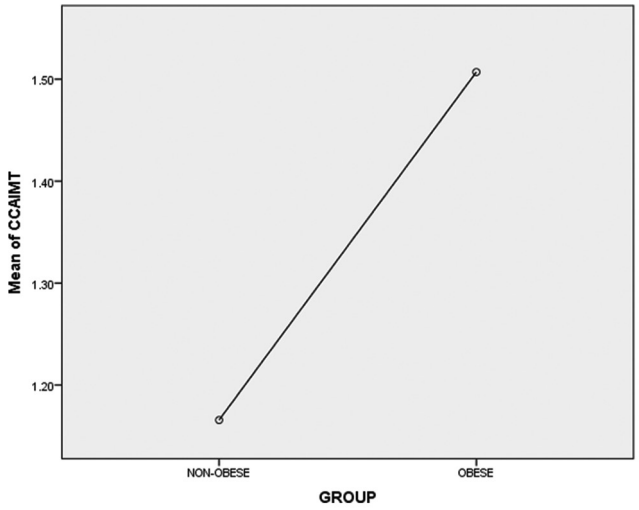
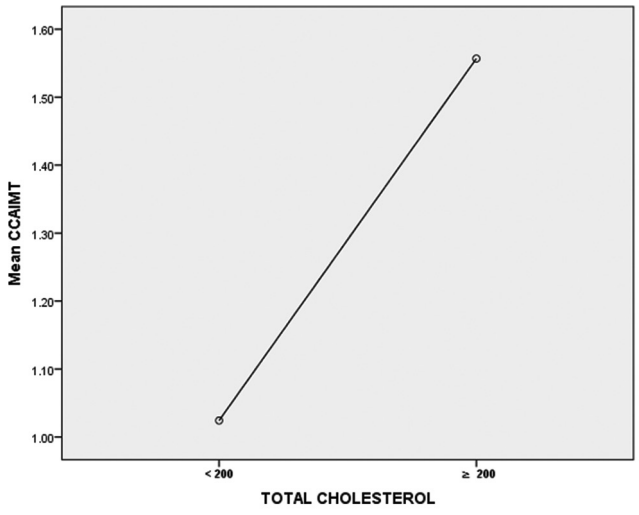


Table 9: Significance of different parameters (TC) with respect to mean carotid intima media thickness

Parameter	Category	Mean ± SD	P-value
TOTAL CHOLESTEROL	<200	1.02 ± 0.399	P < 0.001
	≥200	1.56 ± 0.574	

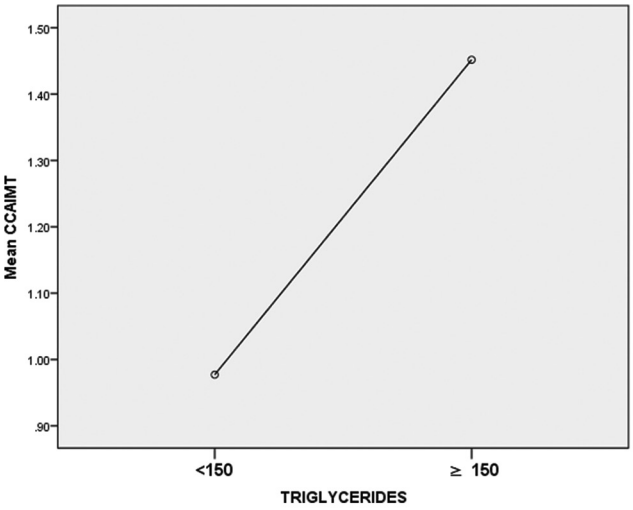


as the p<0.05, at 5% level of significance. Mean CIMT is more in obese than in non-obese.

From Table 9, it is observed that there is statistically significant relation of total cholesterol with respect to mean CIMT as the P<0.001 at 1% level of significance. Mean CIMT is more in TC (≥200) than in TC (<200).

Table 10: Significance of different parameters (TG) with respect to mean carotid intima media thickness

Parameter	Category	Mean±SD	P-value
Triglycerides	<150	0.98±0.380	P<0.001
	≥150	1.45±0.559	



From Table 10, it is observed that there is statistically significant relation of triglycerides with respect to mean CIMT as the P<0.001 at 1% level of significance. Mean CIMT is more in TG (≥150) than in TC (<150).

From Table 11 it is observed that there is statistically significant relation of HDL with respect to mean CIMT as the P<0.001 at 1% level of significance. Mean CIMT is more in HDL (<40) than in HDL (≥40).

From Table 12, it is observed that there is statistically significant relation of LDL with respect to mean CIMT as the P<0.001 at 1% level of significance. Mean CIMT is more in LDL (≥130) than in LDL (<130).

From Table 13, it is observed that there is statistically significant relation of VLDL with respect to mean CIMT as the P<0.01 at 1% level of significance. Mean CIMT is more in VLDL (≥130) than in VLDL (<130).

When univariate correlation analysis between CIMT and study parameters of age, BMI, serum total cholesterol levels, serum triglyceride levels, serum HDL-C levels LDL-C and VLDL-C, urine ACR, etc., was performed in CKD patients in Table 14, significant correlation (P<0.05) of CIMT was found with BMI, serum cholesterol and serum triglyceride levels, and serum HDL-C levels LDL-C and VLDL-C.

Table 11: Significance of different parameters (HDL) with respect to mean carotid intima media thickness

Parameter	Category	Mean±SD	P-value
HDL	<40	1.53±0.518	P<0.001
	≥40	0.88±0.291	

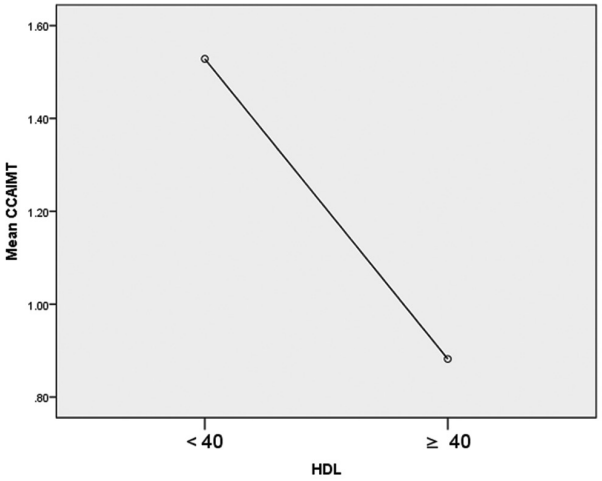


Table 12: Significance of different parameters (LDL) with respect to mean carotid intima media thickness

Parameter	Category	Mean ± SD	P-value
LDL	<130	0.97 ± 0.378	P < 0.001
	≥130	1.60 ± 0.517	

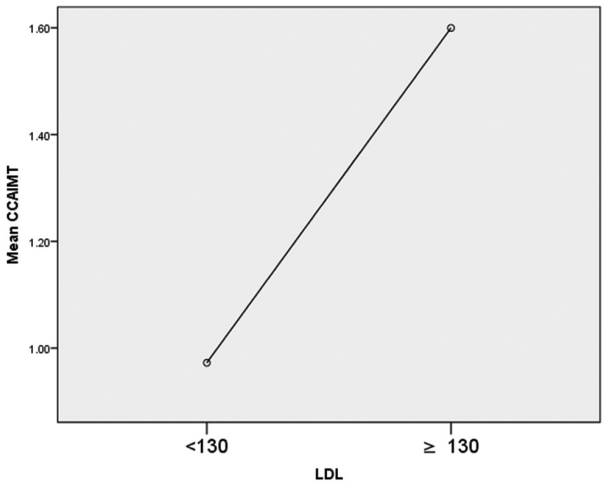


Table 13: Significance of different parameters (VLDL) with respect to mean carotid intima media thickness

Parameter	Category	Mean±SD	P-value
VLDL	<30	1.01±0.396	0.005*
	≥30	1.37±0.572	

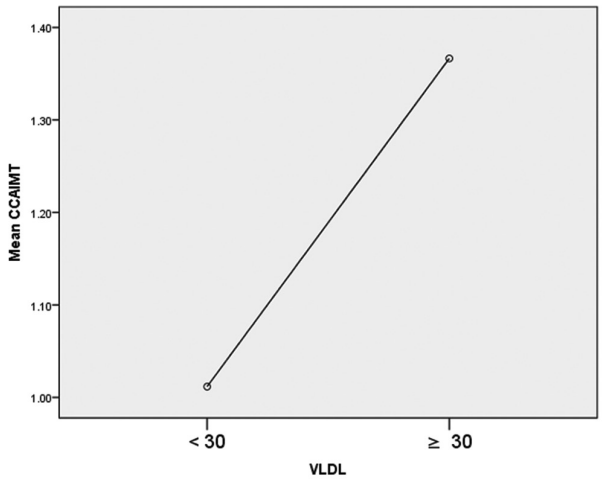


Table 14: Significance of correlation of parameters with carotid intima media thickness

Parameter	Correlation coeff (r)	P-value
Age (years)	0.096	0.431(NS)
BMI	0.533	P<0.001(HS)
Total Cholesterol (mg/dl)	0.564	P<0.001(HS)
Triglycerides (mg/dl)	0.419	P<0.001(HS)
LDL (mg/dl)	0.550	P<0.001(HS)
HDL (mg/dl)	−0.541	P<0.001(HS)
VLDL (mg/dl)	0.412	P<0.001(HS)
UREA (mmHg)	0.011	0.930 (NS)
CREA (mg/dl)	0.046	0.705 (NS)
Urine albumin-creatinine ratio (mcg/mg)	0.077	0.527 (NS)
K+ (mmol/L)	0.120	0.323 (NS)
Hb (gms/dl)	−0.035	0.777 (NS)
GFR value (ml/min/ 1.73 m)	−0.169	0.163 (NS)

DISCUSSION

70 patients were included in our study. All of them had CKD (according to National kidney foundation). The patients were studied for CIMT in relation with the different stages of CKD and also with cardiovascular risk factor such as age, sex, BMI, and dyslipidemia. In our study, the mean age of patients was 58.37±12.19 years (range 34–90 years). Maximum number of subject was 42 (60%) in age group of 41–60 years. Out of 70 CKD patients, 39 (55.7%) were males and 31 (44.3%) were females. Mean CIMT level was 1.214±0.531 mmHg. The present study showed strong correlation between CIMT and BMI (r=0.533, P<0.001). In relation to sex, this study showed that males had higher CIMT values than females. According to lipid profile, this present study observed that CIMT for serum triglyceride levels (≥150 mg/dl) were significantly (P<0.001) high in patients (mean±SD =1.45±0.559) mg/dl in comparison with serum triglyceride levels (<150 mg/dl) (0.98±0.380 mg/d). So also, patients with high cholesterol of

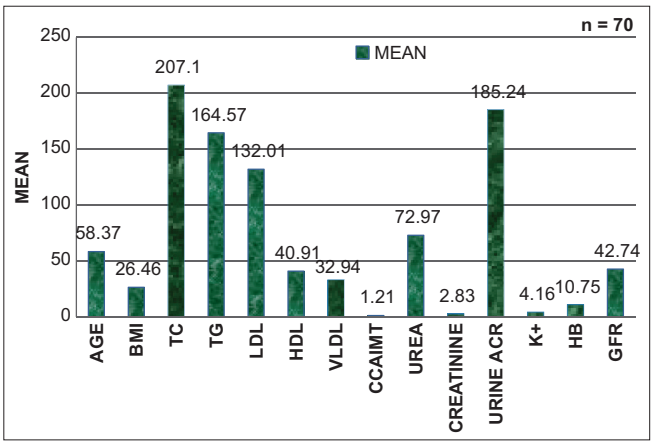


Figure 1: Mean value of baseline characteristics of different parameters

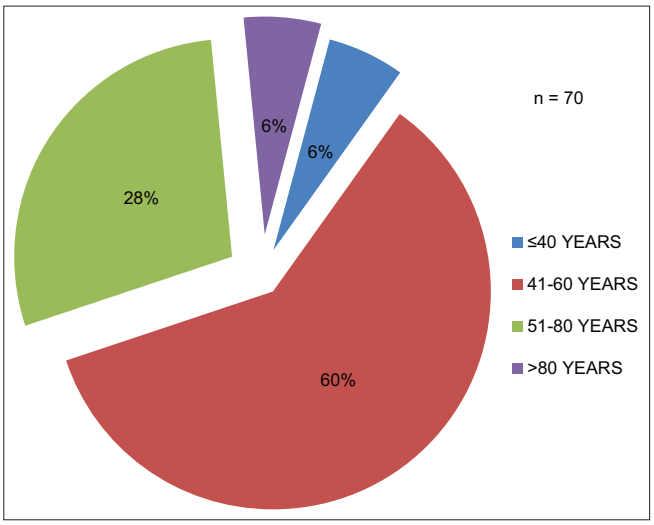


Figure 2: Age distribution among CKD patients. CKD: Chronic kidney disease

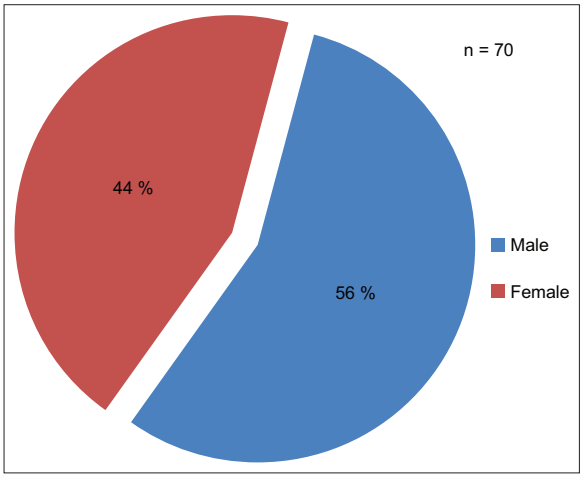


Figure 3: Sex distribution among CKD patients. CKD: Chronic kidney disease

≥200 mg/dl have a higher CIMT of 1.56±0.574 with P<0.001. There is statistically significant relation of LDL with respect to

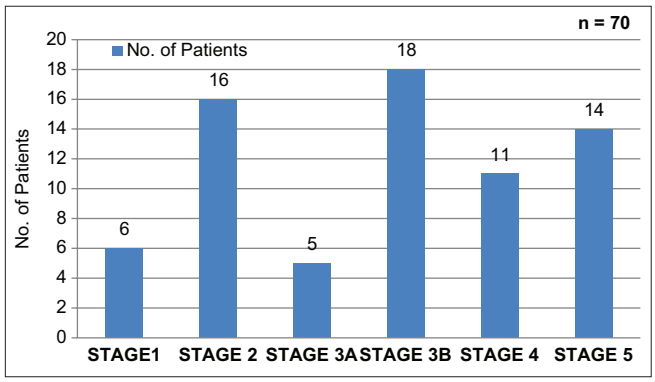


Figure 4: Distribution of the subject according to stages of CKD. CKD: Chronic kidney disease

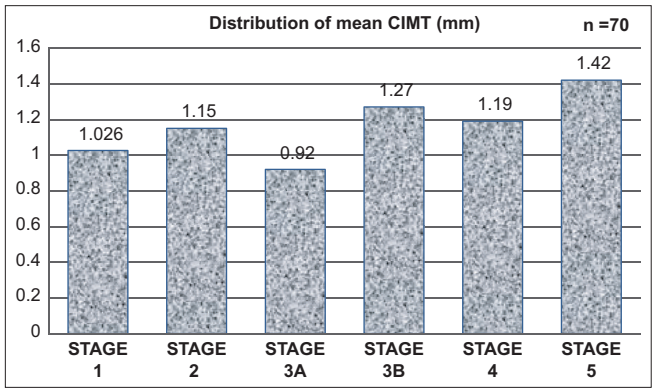


Figure 5: Distribution of the of mean CIMT according to stages of CKD. CIMT: Carotid intima media thickness, CKD: Chronic kidney disease

mean CIMT as the P<0.001 at 1% level of significance. Hence, mean CIMT is more in LDL (≥130) than in LDL (<130). In the present study, CIMT for HDL levels (<40 mg/dl) were high in CKD (mean=1.53±0.518 mg/dl) patients compared to HDL levels (≥40 mg/dl) (mean=10.88±0.291). It was found that mean CIMT was higher in the late stages of kidney disease (Stage 3B, 4 and Stage 5) as compared to early stages (Stage 1, 2, and 3A). According to age, our study showed that mean CIMT is higher in older patients with mean age of 58.37±12.93 years. In present study, the mean CIMT level was 1.214±0.531 mm. According to current sonographic criteria, a "normal" CIMT value is referred as <0.9 mm. Thus, the CIMT was higher in patients with CKD compared to sonographically define normal value.

Limitations of the study

A possible limitation of our study was the small sample size attributed to the stringent inclusion criterions of our study design. This was an institution based study and this could have introduced selection bias. The patients were followed up for the short term outcomes and this assessment may not represent the long-term therapeutic benefits. Extended follow-up period could have changed our outcomes. No blinding was done at any step in the study.

CONCLUSION

From this study, we can conclude that CKD patients who have traditional risk factors for atherosclerosis such as higher BMI, higher serum total cholesterol level, higher serum triglyceride level, higher serum LDL level, and lower serum HDL level have a higher value of CIMT. B-mode ultrasound is a non-invasive sensitive tool for assessment of CIMT. It can help us to identify patients with atherosclerotic burden so that timely intervention can be taken to reduce future cardiovascular complications in CKD patients.

ACKNOWLEDGMENT

Consent was taken from the patients for conducting the study after approval from the Institution Ethics Committee (IEC). We would like to express our gratitude to our patients for their cooperation. We would also like to thank the department of Radiodiagnosis, Pathology and Biochemistry for logistics support.

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Authors Contribution:
LL- Concept and design of the study, prepared first draft of manuscript; **RB**- Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript; **BB**- Interpreted the results; reviewed the literature and manuscript preparation; **SC**- Preparation and revision of the manuscript; **RM**- Preparation and revision of the manuscript; **SBN**- Preparation and revision of the manuscript.

Work attributed to:
Medical College, Kolkata - 700 073, West Bengal, India.

Orcid ID:
Dr. Lamsaka Lyngdoh - https://orcid.org/0000-0003-1639-5820
Dr. Bodhibrata Banerjee - https://orcid.org/0000-0002-1520-5258
Dr. Sampurna Chowdhury - https://orcid.org/0000-0002-5010-7565
Dr. Rishav Mukherjee - https://orcid.org/0000-0001-5883-2908
Dr. Subhendu Bikash Naiya - https://orcid.org/0000-0001-9759-7453
Dr. Raja Bhattacharya - https://orcid.org/0000-0002-2159-9708

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