RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Carotid Intima-Media Thickness in Patients With Chronic Kidney Disease

KEYWORDS

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ABSTRACT *Background:*

Chronic kidney disease is a worldwide public health problem and is now recognized as a common condition that is associated with an increased risk of cardiovascular disease. Atherosclerosis is the most common cause of cardiovascular morbidity in ESRD patients. Atherosclerotic changes in carotid arteries are assumed to be indicative of atherosclerosis throughout the body and peripheral arteries . Carotid Intima-media thickness(CIMT) serves as an independent predictor of cardiovascular events and all-cause mortality in these patients. Measurement of carotid intima media thickness by B mode ultrasound was found to be suitable non-invasive method to visualise the arterial walls and to monitor the early stages of atherosclerotic process.

The Aim of the study is to evaluate Carotid intimal media thickness in patients with Chronic Kidney disease, the method used in the study is cross sectional study and Convenient non random sampling was used , the location selected for survey is Mediciti institute of medical sciences, Hyderabad.

Results:

In our study CIMT was increased in all stages of CKD. CIMT was significantly increased with each stage of CKD. The mean CIMT was high in stage 3, 4 and 5 and is significantly higher than stage 1 and 2. Significantly high CIMT was seen in patients with high levels of serum TC, TG and low levels of serum HDLC. The CIMT was significantly higher in patients with diabetes mellitus and hypertension .

Conclusion:

Thus the use of carotid ultrasound can aid the detection of the cardiovascular disease and as a marker of early subclinical atherosclerosis in early CKD patients with high cardiovascular risk factor.

INTRODUCTION

Chronic kidney disease (CKD) is emerging to be an important chronic disease globally. One reason is the rapidly increasing worldwide incidence of diabetes and hypertension. In India, given its population more than 1 billion, the rising incidence of CKD is likely to pose major problems for both healthcare and the economy in future years. Indeed, it has been recently estimated that the age-adjusted incidence rate of ESRD in India to be 229 per million population and more than 100,000 new patients enter renal replacement programs annually in India.[1]

Chronic kidney disease is a worldwide public health problem and is now recognized as a common condition that is associated with an increased risk of cardiovascular disease. Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in patients with chronic kidney disease. The spectrum of CVDs in patients with chronic kidney disease involves 3 main pathological forms: altered cardiac geometry and mechanics (left ventricular hypertrophy), accelerated atherosclerosis of both large arteries and coronaries, and arteriosclerosis.[1]

Atherosclerosis is the most common cause of cardiovascular morbidity in ESRD patients. Atherosclerotic changes in carotid arteries are assumed to be indicative of atherosclerosis throughout the body and peripheral arteries.[3] Increased arterial stiffness in renal patients may be a consequence of chronic volume overload, vascular calcification, inflammation, endothelial dysfunction, oxidative stress and several other factors. Increased arterial stiffness has significant clinical consequences: Isolated systolic hypertension, left ventricular hypertrophy and failure, and reduced myocardial perfusion. Arterial stiffness is measured by carotid intima media thickness.[4]

One of the factors currently considered as a risk factor for coronary artery disease in adults is the increase in intima-media thickness (IMT) of the carotid and femoral arteries. This factor serves as an independent predictor of coronary artery disease and is itself connected with other risk factors[4]. Intima-media thickness is linked with concentric left ventricular hypertrophy in dialysis patients and serves as an independent predictor of cardiovascular events and cardiovascular and all-cause mortality in these patients.

Measurement of carotid intima media thickness by B mode ultrasound was found to be suitable non-invasive method to visualise the arterial walls and to monitor the early stages of atherosclerotic process. Measurement of carotid intima media thickness is also helpful in clinical decision making , it is the best method of treatment for patients (either medical or surgical) with carotid artery stenosis and also can be used to assess the effects of medical therapy of atherosclerosis[5].

Normal value of the carotid intimal medial thickness:

Although reports were from different populations and though differing techniques and equipment were used, the reported CIMT measurements showed a consistent

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progression with age and greater values among men. Studies comparing the CIMT between abnormal and normal groups show that most of the abnormal CIMT measurements are above the 75th percentile of the mean common carotid artery IMT in normal subjects. Studies relating CIMT measurements to the risk of coronary and cerebro vascular events show that the risk of first myocardial infarction increases with an CIMT of 0.822mm or more and the risk of stroke with an CIMT of 0.75 mm or more. Despite this continuous relationship between CIMT and risk, there is no clear cut-off point for the definition of an abnormally high CIMT. The progression rate of the far-wall common carotid artery IMT of 0.034 mm per year or greater increases the risk of future events significantly. For younger age groups (20 to 30 years) mean CIMT values of 0.5 mm have been reported, while CIMT values of 0.9 mm have been found for older subjects (60 to 70 years) [6]. Because CIMT reflects global cardiovascular risk, its normal value might be better defined in terms of increased risk rather than statistical distribution within healthy population.

Inter-relationship between IMT and cardiovascular incidents

Study	No of subjects	Study population Findings
Finnish[7]	1257 healthy men	Increase in IMT of 0.1 mm resulted in an 11% increase of risk for AMI
ARIC[8]	13870 patient with cardio-vascular disease	IMT 1.0mm is associated with an increased risk ratio of 5 over 7 years
KIHD[9]	2150 healthy men	IMT > 1.0mm twofold greater increase for AMI over 3 years
CHS[10]	5116 older adults	IMT > 1.18 is associated with a fourfold greater risk for AMI and stroke over 6 year
CLAS[11]	162 men with coronary bypass surgery	Each increase in IMT of 0.03 mm per year is related to a relative risk of 3.1
Rotterdam[12]	1870 elderly subjects	Increase in IMT of 0.16 minis accompanied by a risk ratio of 1, for AMI or stroke over 3 years

ARIC, Atherosclerosis Risk in Communities: K1HD, Kuopio Ischemic Heart Disease Risk Factor Study; CHS. The Cardiovascular Health Study; CLAS, Cholesterol Lowering Atherosclerosis Study.

AIM OF THE STUDY
The study of Carotid intimal media thickness in patients with Chronic Kidney disease.

OBJECTIVES
To study the relation of carotid intimal media thickness in different stages of Chronic kidney disease

To study the relation of carotid intimal media thickness in chronic kidney disease with different co-morbid conditions such as hypertension, diabetes, smoking.

To study the relation of carotid intimal media thickness with fasting lipid profile.

MATERIALS AND METHODS
The method used in the study is cross sectional study and the location selected for survey is Mediciti Institute of Medical Sciences, Hyderabad

SUBJECTS:
100 patients (n) from nephrology unit were included in the study of age more than 18 yrs, from Mediciti Institute of Medical Sciences, Hyderabad

SAMPLING:
Convenient non random sampling.

INCLUSION CRITERIA
All patients admitted, fulfilled the criteria of CKD

1. Patients fulfilled the criteria of CKD
2. Serum creatinine > 2 mg/dl for > 3 months
3. Contracted Kidney on imaging
4. All patients >18 yr , both male and Female

EXCLUSION CRITERIA:
1. Age less than 18 yrs
2. ARF Patients
3. Pregnancy
4. Patients in ICU
5. History of stroke , myocardial infarction
6. Patients on hypolipidmic drugs

METHODS OF COLLECTION OF DATA:
A prospective study was performed in nephrology unit for 100 patients whose age is more than 18 years and the time period is 18months i.e, October 2014 to March 2016.

Comprehensive history was taken, detailed clinical examination was done and informed consent was taken for every patient.

INVESTIGATIONS:
CBC, Peripheral Smear Study, RFT, S.Electrolytes, S.Uric Acid, S.Calcium, S.Phosphorus, serum albumin, and urinalysis, HbsAg, optional Anti-HCV Abs, fasting lipid profile, CRP and USG abdomen, Chest X-Ray, ECG, Echocardiography, GFR estimation by cockroft gault Formula, Optional Renal Biopsy, Carotid intimal media thickness by B mode USG.

STUDY PERIOD:
The study was carried for 18 months from October 2014 to March 2016

STATISTICAL ANALYSIS:
Collected data was analyzed using SPS version 17.0 for qualitative data. For statistical analysis, Chi Square test was used. For quantitative data, student t test was used. P value <0.05 was considered significant.

RESULTS
Age Distribution of the Subjects

		Frequency	Percent
Age	25 – 30	19	19.0
	31 – 40	23	23.0
	41- 50	17	17.0
	51 – 60	20	20.0
	61 – 70	15	15.0
	Above 70	6	6.0
	Total	100	100.0

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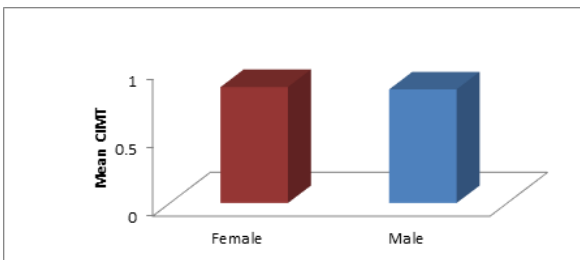
The age range was from 20-75 years in CKD patients. Maximum number of patients were in age group 30-50 years. The mean age was 46.57 years. Relation between the mean CIMT with age was not significant. The p value= 0.141.

Gender Distribution of the subjects

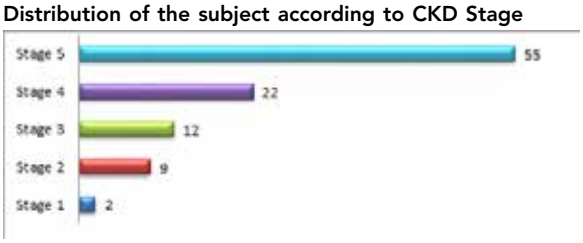
	Frequency	Percent
Female	42	42.0
Male	58	58.0
Total	100	100.0

Distribution of mean CIMT in relation to gender

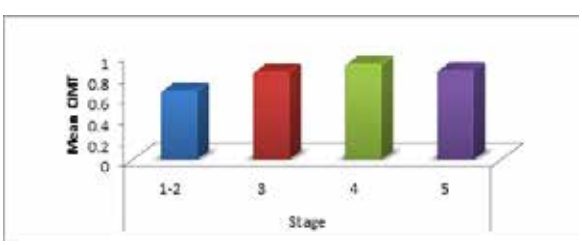


In our study, among 100 subjects 58 are males and 42 are females. The mean CIMT in females is 0.85mm and in males is 0.83mm.

Distribution of the subject according to CKD Stage



Distribution of mean CIMT according to (eGFR) stage of CKD

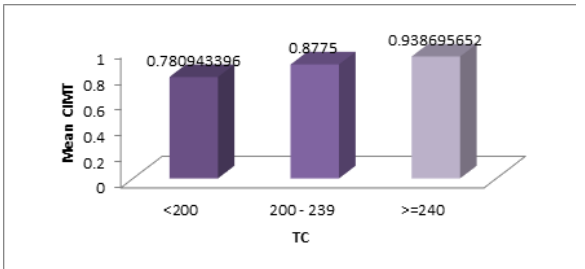


In my study, 55% of subjects were in stage 5 of CKD. The mean CIMT in subjects was 0.84 mm. The mean CIMT in different stages of CKD is shown in above graph. The mean CIMT was high in stage 3, 4 and 5 and it is significantly higher than stage 1 and 2. (p value < 0.001)

Distribution of subjects by Serum Cholesterol Levels

	Frequency	Percent
<200	53	53.0
200 - 239	24	24.0
>=240	23	23.0
Total	100	100.0

Relation of mean CIMT with serum cholesterol

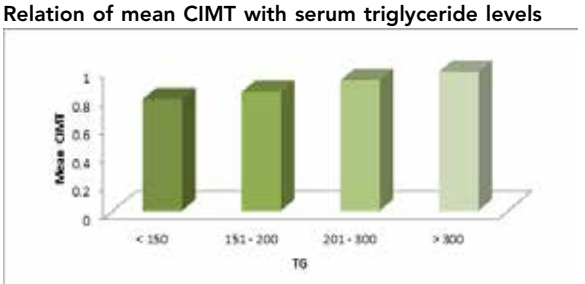


The mean serum cholesterol was 211.04 mg/dl. The mean CIMT was highest (0.93mm) in subjects with serum cholesterol levels >240mg/dl. The relation of mean CIMT with serum cholesterol levels was found to be highly significant (p value <0.001)

Distribution of subjects by Serum Triglyceride Levels

	Frequency	Percent
< 150	40	40.0
151 - 200	33	33.0
201 - 300	21	21.0
> 300	6	6.0
Total	100	100.0

Relation of mean CIMT with serum triglyceride levels



The mean serum triglyceride levels in subjects was 185.84mg/dl. The mean CIMT was high (0.97mm) in subjects with high serum triglyceride levels. There was highly significant correlation between serum triglyceride levels and mean CIMT. p value <0.001.

Distribution of subjects by serum HDL

	Frequency	Percent
< 30	34	34.0
30 - 59	66	66.0
Total	100	100.0

Relation of mean CIMT with serum HDL levels

CIMT

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		t test p value	
				Lower Bound	Upper Bound		
< 30	34	.9218	.08455	.8923	.9513	.000	< 0.001, HS
30 - 59	66	.7985	.10976	.7715	.8255		
Total	100	.8404	.11721	.8171	.8637		

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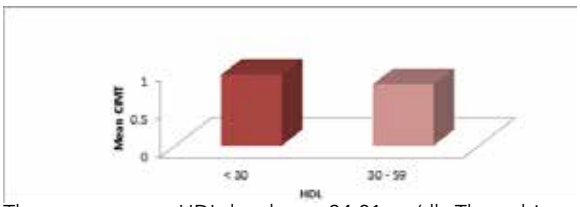
Relation of mean CIMT with serum HDL levels



The mean serum HDL level was 34.01mg/dl. The subjects with low serum HDL levels have high mean CIMT (0.921mm). The relation between mean CIMT and serum HDL levels was highly significant. The p value is <0.001.

Relation of mean CIMT in CKD patients with diabetes
In our study, 49% of subjects were diabetic patients .The mean CIMT in diabetic patients was high (0.89mm) compared to non diabetics(0.78mm). The p value is <0.001.

Relation of mean CIMT and smoking
In our study, 35% of subjects were smokers. The mean CIMT in these subjects was 0.87mm higher than non-smokers (0.82mm). The p value is 0.04.

Relation of mean CIMT with hypertension
In our study, 59% of subjects were hypertensive and mean CIMT was higher in hypertensive group (0.87mm) the p value is <0.001.

Distribution of mean CIMT in subjects on hemodialysis
In our study, 50% of subjects were on hemodialysis. The mean CIMT in dialysis group was 0.87 which higher than in non hemodialysis group. (0.804mm).the p value is 0.001

DISCUSSION

CKD encompasses a spectrum of different patho physiological process associated with abnormal kidney function and progressive decline in eGFR. Cardiovascular disease is the leading cause of morbidity and mortality in patients at any stage of CKD. The presence of any stage of CKD is a major risk factor for coronary, cerebrovascular and peripheral vascular disease. The prevalence of dyslipidemia in patients with CKD is greater than in general population, the disorder of lipoprotein metabolism increase in frequency severity as renal insufficiency advances.[6]

In my study, i took CIMT as a marker of atherosclerosis and measured it in different stages of CKD. And also traditional risk factors such as hypertension, smoking, and diabetes mellitus which show effect on CIMT as proven by previous studies are correlated with CIMT in CKD patients. In my study mean CIMT in CKD patients was 0.84mm, which is consistent with study done by Shoji et al[13] who studied CIMT in 110 patient pre-dialysis patients(0.889 ±0.035 mm) with normal healthy controls (0.685±0.010mm) , in which CIMT was significantly raised.

Several previous studies by Kawagishi et al [14], Bevc et al[15](P = 0.0001),and Brzosko et al[16] shown significant correlation of mean CIMT with age and BMI in CKD patients. I found a negative correlation between CIMT in CKD patients and age, BMI of patients. Though my study has shown increase in mean CIMT with age and BMI , significant increase was not seen. My study compared CIMT in males and females, which showed that CIMT is slightly higher in females than in males. A significant correlation with gender was not seen.

In my study eGFR was calculated by Cockeroft Gault equation and correlated with mean CIMT. Mean CIMT was found to be higher in the late stages of kidney (stage 3, 4 and stage 5) as compared to mean CIMT in early stages (stage 1 and 2). Mean CIMT in stage 3, 4 and 5 is 0.834mm, 0.903mm and 0.85mm respectively and mean CIMT in stage 1 and 2 is 0.656mm.

Preston et al[17], Cheuk-Chun Szeto et al[18], Nakashima et al[19], Brzosko et al[16], shown a mean CIMT of 0.79MM, 0.746mm, 0.76mm, 0.808mm respectively, an significant high CIMT was seen in all stages of CKD. Lu Xia Zhang et al[20] in their study on stage 2-3 CKD patients (i.e., mild and moderate renal insufficiency) found significantly increased CIMT in those patients and concluded that arterial change might occur in course of CKD earlier than previously believed.

Similarly in our study CIMT increased in all the stages of CKD. CIMT had significantly increased with each stage of CKD. The mean CIMT in stage 3, 4 and 5 was significantly higher than stage 1 and 2.

Association between CIMT and lipid density levels is been inconsistently reported in CKD patients. In my study, the mean CIMT in patients with serum triglycerides levels <150mg/dl , 150-200mg/dl and >200mg/dl was 0.78mm, 0.83 mm and 0.91 mm respectively which shows statistically significant difference between the groups and the mean CIMT in CKD patients of serum cholesterol levels <200mg/dl, 200-240mg/dl and >240mg/dl is 0.78, 0.87 and 0.93 respectively. My study showed a positive correlation between serum TC,TG, HDLC levels with CIMT in CKD patients. Significantly high mean CIMT was seen in patients with high levels of serum TC, TG and low levels of serum HDLC. Attmann et al[21] showed significant decrease in serum HDLC in CKD patients. Similar decrease in serum HDLC levels was seen in my study. A highly significant correlation was seen between Serum levels of TC, TG with CIMT.

Previous studies by Kawagashi et al[13] suggests that beta cell dysfunction increases as renal function detoriates and also significantly contributes to accelerated atherosclerosis especially among diabetic CKD patients. In my study, the mean CIMT in diabetic CKD patients and non-diabetic CKD patients was 0.89mm and 0.78mm respectively and a significant correlation has been seen among diabetic and non-daibetic CKD patients.

Previous studies did not show the role of hypertension as determinant for CIMT in CKD patients. I found an significant association between hypertension and mean CIMT. There is significant difference in mean CIMT in dialysis group (0.87mm) compared to non dialysis group (0.81 mm) and similar results seen in Shahrzad O[3] study. I found positive correlation between smoking and mean CIMT. Kawagashi et al.[13] found an association between CIMT and smoking in CKD patients.

CONCLUSION

CIMT was increased in all stages of CKD. CIMT was significantly increased with each stage of CKD.

The data support that the high prevalence of atheromatous disease in the CKD population, which is higher in advanced stages of CKD and suggest the existence of specific risk factors that favour the atheromatous process.

The fact that patients in the early CKD stages had a higher prevalence of atheromatous changes demonstrates the

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need for the early detection of atheromatous disease in this population.

The different risk factors such as lipid abnormalities, diabetes mellitus, hypertension and smoking associated with CKD hasten the atheromatous process and so suggest the need of specific preventive measures depending on the severity of CKD.

The use of carotid ultrasound can aid the detection of the disease and as a marker of early subclinical atherosclerosis in early CKD patients with high cardiovascular risk factor.

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