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Original Article

Correlation of Carotid Artery Tunica Intima Medial Thickness in Different Stages of Chronic Kidney Disease as A Marker of Atherosclerosis

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Abstract

Introduction: Chronic kidney disease (CKD) is a significant predictor of cardiovascular mortality. Accelerated atherosclerosis is common in CKD patients and hence more prone to cardiovascular disease (CVD) mortality. Carotid artery tunica intima medial thickness (CIMT) is a direct marker of atherosclerosis which can be measured non-invasively using B-mode ultrasonography to detect early atherosclerosis.

Aim: To study the relationship between CIMT as a surrogate marker of atherosclerosis in CKD independent of classical risk factors and the relationship between CIMT of hemodialyzed CKD patients and CKD patients without hemodialysis.

Methods: Fifty patients were subjected to the following blood investigations: complete blood count, renal function test, serum electrolytes, urine albumin sugar, and deposits. Glomerular filtration rate (GFR) was calculated using the modification of diet in renal disease (MDRD) formula. CIMT was measured using B mode ultrasonography.

Results: In our study, we found that CIMT increased progressively with CKD disease progression and had an independent positive correlation. Compared to the normal population, the mean CIMT was higher in CKD patients. The mean CIMT correlated positively with traditional risk factors for atherosclerosis such as age, diabetes, hypertension, and smoking. The mean CIMT was significantly higher in patients undergoing hemodialysis than the patient not undergoing hemodialysis. There is no correlation between gender and CIMT.

Conclusion: Hemodialysis acts as a significant risk factor for accelerated atherosclerosis. Aggressive management of risk factors in these patients helps in reducing the incidence of vascular events.

Key words: Atherosclerosis, Carotid artery intimamedia thickness, Kidney disease, Risk factor

INTRODUCTION

Atherosclerosis is a systemic disease involving the deposition of lipids in tunica intima and infiltration of inflammatory cells predominantly in large and medium-sized arteries.[1] Cardiovascular events are the leading cause of death in patients with chronic kidney disease (CKD). Cardiovascular events are about twice as common in CKD patients compared to the general population.[2] In CKD patients undergoing hemodialysis, the risk increases up to 20–40 times. Apart from renal disease, hemodialysis is itself a risk factor for atherosclerosis. Conventionally, cardiovascular events such as myocardial infarction were diagnosed with an invasive procedure such as angiography. Detection by angiography requires complete occlusion of the vessel lumen. Early detection of partial occlusion of the vessel wall, particularly coronary arteries, can be made with computed tomography (CT) imaging techniques that rely on calcium deposition in the vessel wall.[3] More recently, the measurement of carotid artery tunica intima medial thickness (CIMT) evolved as an non-invasive tool in screening patients at risk of cardiovascular diseases (CVDs). The common carotid artery provides a convenient way to study elastic artery structure and function because of its size, location, and accessibility. CIMT measured by B-mode ultrasound imaging was safe and an independent

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predictor of vascular events.[4] Measurement of CIMT can also be used as an indicator of atherosclerosis in dialysis patients. In CKD patients, CVDs are the leading cause of death, and CIMT measurement can be used as a marker of early atherosclerosis. In this study, various proatherogenic risk factors, including hemodialysis, a risk factor in CKD were studied using CIMT.[5]

Aim

To study the relationship between CIMT as a surrogate marker of atherosclerosis in CKD patients independent of classical risk factors.

MATERIALS AND METHODS

This cross-sectional study was conducted in the department of General Medicine at Tirunelveli Medical College. About 50 CKD patients attended Nephrology and General Medicine OPD between December 2017 and October 2018.

Inclusion Criteria

Patients undergoing regular hemodialysis for at least 6 months were identified as hemodialysis patients. Patients with glomerular filtration rate (GFR) <60 ml/min per 1.73 m^2 for 3 months or more calculated using "modification of diet in renal disease (MDRD)".

Exclusion Criteria

Patients who are undergoing regular hemodialysis for <6 months. Patients with GFR more than 60 ml/min per 1.73 m^2 calculated using the MDRD formula. Patients who are not willing for the study after informed consent.

After getting informed consent, patients were subjected to detailed history taking, clinical and laboratory investigations. In addition, they were subjected to the following blood investigations: complete blood count, renal function test, serum electrolytes, urine albumin sugar, and deposits. GFR was calculated using the MDRD formula. CIMT was measured using B-mode ultrasonography. CIMT is measured from the leading edge of the first echogenic line and second echogenic line. A single radiologist measured CIMT at three sites on both sides. The average is taken as mean CIMT.

RESULTS

In our study, most of the individuals were <30 years of age, constituting 34% of the study population. In our study, out of 50 patients, about 66% were male, and 34% were female population. In our study, 34% of patients had serum creatinine less than the normal value of 1.2 mg/dl, while 66% had >1.2 mg/dl. In our study, ESRD patients with GFR <15 ml/1.73 m^2 occupy 40% of the study population. Only 6% of individuals belong to Stage I CKD. In our study, out of 50 patients, 29 patients were non-diabetic and 21 patients were diabetic. In our study, hypertension is present in an equal proportion of the study population. In our study, most individuals were undergoing hemodialysis, which is up to 60% of the study population. In our study, about 34% of individuals were smokers and 16% of individuals were non-smokers. In our study, CIMT mean was taken as 1 mm. About 62% of individuals had a mean CIMT of <1 mm and about 38% had a mean CIMT of more than 1 mm. In our study, with the mean CIMT of 1 mm, 60% had less than mean on the right side, and 40% had CIMT more than mean on the right side. In our study, about 60% had CIMT <1 mm on the left side, and 40% had CIMT >1 mm on the left side [Tables 1 and 2].

In our study population, there is an increase in CIMT as the age increases. There is a progressive increase in CIMT as a person ages, which indicates that the risk of atherosclerosis increases with age. There is a positive correlation between age and CIMT with a *P* value of 0.001, which is statistically significant. The mean CIMT in females is 0.95 and the mean CIMT in males is 0.99. There is no significant correlation between sex and CIMT with a *P* value of 0.567. Hence, there is no difference in risk of atherosclerosis in different sex [Table 3].

DISCUSSION

Multiple epidemiological studies have shown that traditional and emerging cardiovascular risk factors are associated with increased CIMT.[6-8] Age, hypertension, diabetes mellitus, dyslipidemia, and smoking all positively correlate with increased CIMT. Emerging risk factors, including lipoprotein (a), oxidized low-density lipoprotein, and homocysteine, correlate positively. Inflammatory markers are associated with atherosclerosis, and these markers do correlate with elevated CIMT values. Wang *et al.* showed elevated CIMT with C-reactive protein in women in Framingham Heart Study, even after adjusting traditional risk factors.[9] C-reactive protein was found to be associated with CIMT in the Rotterdam study and could predict the progression as well.[10] The constellation of cardiovascular risks with abdominal obesity, hypertension, hyperglycemia, hypertriglyceridemia, and insulin resistance, known as metabolic syndrome, has a different perspective on CIMT value and is a subject of research.[11]

As the person progresses from one stage to the next stage, there is an increase in CIMT. According to Kato *et al.*, there

Table 1: Patients characteristics

Characteristics	Frequency	Percentage
Age group		
<30	17	34.0
31–40	8	16.0
41–50	16	32.0
>50	9	18.0
Gender		
Male	33	66.0
Female	17	34.0
Blood Urea		
<40	11	66.0
>40	39	34.0
Serum Creatinine		
<1.2	33	66
>1.2	17	34
CKD Stage		
I	3	6
II	9	18
III	14	28
IV	4	8
V	20	40
CIMT-Mean		
>1	19	38
<1	31	62
CIMT-RT		
>1	20	40
<1	30	60
CIMT-LT		
>1	20	40
<1	30	60

CKD: Chronic kidney disease, CIMT: Carotid artery tunica intima medial thickness

Table 2: Patient comorbidities

Characteristics	Frequency	Percentage
Diabetes mellitus	21	42
Hypertension	25	50
Hemodialysis	20	40
Smoker	16	32

is a positive correlation between the stage of CKD and mean CIMT with a *P*-value of 0.001.[12]

Diabetes is a common cause of end-stage kidney disease. The mean CIMT in diabetic patients was 1.17, and the mean CIMT in nondiabetic patients was 0.84. There is a positive correlation between diabetes and CIMT with a *P*-value of 0.001, which is significant. According to Papagianni *et al.*, where they showed diabetic patients had increased CIMT.[13]

The mean CIMT in hemodialysis patients is 1.23, and the mean CIMT in non-dialysis patients was 0.81. This shows that patients undergoing hemodialysis have accelerated atherosclerosis hence HD itself can be considered as pro-atherogenic. This is in accordance with Zanchetti *et al.*, where they showed increased CIMT in patients undergoing hemodialysis. Our study is in accordance with Zanchetti *et al.* and Stenvinkel *et al.*[14,15]

Table 3: Comparison CIMT with patient characteristics

Characteristics	Mean	SD	*P*-value
Age group			
<30	0.75	0.1	0.001
31–40	0.92	0.19	
41–50	1.14	0.17	
>50	1.17	0.18	
Gender			
Male	0.99	0.26	0.567
Female	0.95	0.19	
CKD			
I	0.7	0.13	0.001
II	0.77	0.69	
III	0.85	0.09	
IV	0.97	0.03	
V	1.23	0.12	
Diabetes Mellitus			
Present	1.17	0.18	0.001
Absent	0.84	0.17	
Hypertension			
Present	1.17	0.16	0.001
Absent	0.79	0.29	
Hemodialysis			
Present	1.23	0.12	0.001
Absent	0.81	0.12	
Smoker			
Present	1.17	0.17	0.001
Absent	0.89	0.21	

CKD: Chronic kidney disease, CIMT: Carotid artery tunica intima medial thickness

The mean CIMT in smokers is 1.17, and the mean CIMT in non-smokers is 0.89. There is a positive correlation between CIMT and smoking with a *P*-value of 0.001, which is significant.

CONCLUSION

Compared to the normal population, the mean CIMT was higher in CKD patients. The mean CIMT increases as the person progresses from one stage to another stage. The mean CIMT correlated positively with traditional risk factors for atherosclerosis such as age, diabetes, hypertension, and smoking. The mean CIMT was significantly higher in patients undergoing hemodialysis than the patient not undergoing hemodialysis. There is no correlation between gender and CIMT.

LIMITATIONS

Only a smaller number of patients were enrolled. This study doesn't take into account other atherosclerotic markers such as serum lipoprotein, obesity, level of physical activity, hypercoagulable states such as serum homocysteine. This is a cross-sectional study; hence, follow-up of patients is not possible.

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