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Original Research Article

Study of carotid intima media thickness as surrogate marker of endothelial dysfunction in early chronic kidney disease patients

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ABSTRACT

Background: Micro-albuminuria has been extensively regarded as a marker of generalized vascular endothelial impairment. Endothelial dysfunction is an early marker for atherosclerosis and can be detected before structural changes to the vessel wall.
Methods: This case control study was carried out in the Department of Medicine, MGM Medical College and MY Hospital, Indore, India, from December 2017 to February 2019, with sample size of 100 including 50 cases and 50 controls.
Results: In our study, mean CIMT of cases and controls was 0.83±0.10mm and 0.63±0.14mm in right respectively. Mean CIMT of cases and controls was 0.83±0.10 and 0.64±0.07mm in left side respectively. These results are suggestive that mean CIMT are significantly higher (p values <0.05 in each) in cases than controls. 90% of cases were in stage II of CKD and their mean CIMT was 0.83±0.09mm and 10% of cases were in stage I of CKD and their mean CIMT was 0.80±0.09mm and there were no significant difference in mean CIMT between CKD stage I and CKD stage II in cases. There were significant positive correlation between Mean CIMT and Age of cases (Pearson correlation=0.382, p-value 0.006).
Conclusions: Increased CIMT was found in all the cases as compare to controls so, increased CIMT can be used as an early marker of atherosclerosis in early CKD patients. Further study in large number of subjects may help to confirm or exclude the findings.

Keywords: Carotid intima media thickness, Chronic kidney disease, Endothelial dysfunction, Microalbinuria

INTRODUCTION

Micro-albuminuria has been extensively regarded as a marker of generalized vascular endothelial impairment.[1] Functions of endothelium are vasodilation, suppression of smooth muscle cell growth, and inhibition of inflammatory responses. Many of these effects are largely mediated by nitric oxide (NO), the most potent endogenous vasodilator. NO opposes the effects of endothelium-derived vasoconstrictors and inhibits oxidation of low-density lipoprotein (LDL). A defect in the production or activity of NO leads to endothelial dysfunction. Endothelial dysfunction is an early marker for atherosclerosis and can be detected before structural changes to the vessel wall are apparent on ultrasound or angiography.[2]

Atherosclerosis unless in a severe form is often asymptomatic, so that a direct examination of the vessel wall is necessary to detect affected individuals in the early stages.[3,4] Atherosclerosis is the most common risk factors of cardiovascular morbidity and mortality in CKD patients. Ischemic heart disease and ischemic stroke are common entities that share in many cases a similar pathophysiology, based on atherosclerosis. Its pathogenesis deals with inflammation in the vessel wall

which is well documented in literature.[5] Atherosclerotic changes in carotid arteries are assumed to be indicative of atherosclerosis throughout the body. It has been suggested by the International Atherosclerosis Project that the atherosclerotic process occurs at the same time in carotid, cerebral and coronary arteries. Carotid Artery Intimal Medial Thickness (CIMT) is well-established index of systemic atherosclerosis that correlate well with the incidence of coronary heart disease and stroke in non-uremic population as well as uremic population.[4,6,7]

Measurement of CIMT of the common carotid artery by B-mode ultrasound is found to be suitable non-invasive method to visualize the arterial walls and to monitor the early stages of the atherosclerotis.[8-10] Annuk et al reported that CRP and endothelial functions could provide complementary prognostic information regarding future cardiovascular disorders in renal patients.[11] So, this study was done in early CKD patients to look for CIMT as surrogate marker of endothelial dysfunction in these patients.

METHODS

This case control study was planned and carried out in the Department of Medicine, MGM Medical College and MY Hospital, Indore with sample size of 100 including 50 cases and 50 controls. Duration of study was from December 2017 to February 2019.

Inclusion criteria

Patients with age between 15 to 45 years with CKD Stage I and II.

Exclusion criteria

- Patients having eGFR<60ml/min/1.73m^2.
- Patients on hemodialysis.
- Patients age <15 or >45 years.
- Patient having acute kidney injury.
- Patients having Diabetes.
- Patient not giving consent.

Data collection

Early young CKD patients with age group of 15-45 years and their caregivers were explained about the study in detail verbally and by utilizing a patient information sheet written in simple understandable language.

After applying inclusion and exclusion criteria, selected patients were enrolled after taking consent to take part in the study and controls were also selected after obtaining their consent. A brief history was taken and the patient's vitals and weight were taken. Blood investigations like RFT, Lipid profiles, serum phosphorus, serum calcium, serum PTH, CRP (qualitative),serum Uric acid were done. Urinary micro albuminuria was tested. Finally bilateral CIMT thickness was measured. eGFR was calculated by Cockcroft Gault equation.

Measurement of CIMT

CIMT as a surrogate marker of atherosclerosis are measure for both cases and controls by B Mode Gray-scale on USG machine using linear probe of 7.5 to 12 MHz. to assess vascular endothelial dysfunction. Assessment of CIMT was done by Department of Radiology MYH and MGMMC Indore. Intimal-medial thickness is defined as the distance between the leading edge of the first echogenic line (Lumen-intima interface) and the second echogenic line (Media-adventitia interface) of the far wall over the area devoid of atherosclerotic plaque.

Microalbuminuria

A micro albumin specific urine dipstick test was used for the detection of micro albuminuria. These dip stick (QDX URINE TEST 11 MAU) used to detect various compound in the urine including micro albumin. Spot urine sample was collected from the cases and controls and micro-albuminuria was interpreted (positive or negative) on the basis of color developed on dipstick after matching with label on the dipstick container.

Data analysis

Data entered in the excel sheet and analysed by using SPSS 20 Software. Appropriate statistical tests were applied to analyze data. Unpaired ‘t’ test was used to calculate ‘p value’ and value less than 0.05 was considered statistically significant.

RESULTS

This study was conducted in 100 subject (50 cases and age and gender matched 50 controls) at MGM Medical College and MY Hospital Indore, India.

Table 1: Distribution of cases and controls according to age.

Age group	Number of cases (%)	Number of controls (%)
< 25 Year	2 (4%)	2 (4%)
25 - 35 year	12 (24%)	13 (26%)
36-45 year	36 (72%)	35 (70%)
Total	50	50

As shown in table 1, there were 2 (4%) cases in the age group <25years, 12 (24%) cases in the age group 25-35years, 36 (72%) cases in the age group 36-45years. Majority of the cases were in the age group 36-45years.

As shown in table 2, mean CIMT of cases and controls was 0.83±0.10mm and 0.63±0.14mm in right

respectively. Mean CIMT of cases and controls was 0.83±0.10 and 0.64±0.07mm in left side respectively. These results are suggestive that mean CIMT are significantly higher (p values <0.05 in each) in cases than controls.

Table 2: Distribution of cases and controls according to CIMT.

CIMT	Subject	Number	Mean CIMT(mm)	SD	p value
Right CCA	Cases	50	0.83	0.10	p <0.05
	Controls	50	0.63	0.14	
Left CCA	Cases	50	0.83	0.10	p <0.05
	Controls	50	0.64	0.07	
Mean CIMT	Cases	50	0.83	0.10	p <0.05
	Controls	50	0.64	0.08	

CCA- Common Carotid Artery, Unpaired 't' test used to calculate 'p' value

Table 3: Distribution of mean CIMT according to stages of CKD.

Stage of CKD	Number of cases	Mean CIMT (in mm)	p value
Stage I	5	0.80±0.09	>0.05
Stage II	45	0.83±0.09	
Total	50	0.83±0.09	

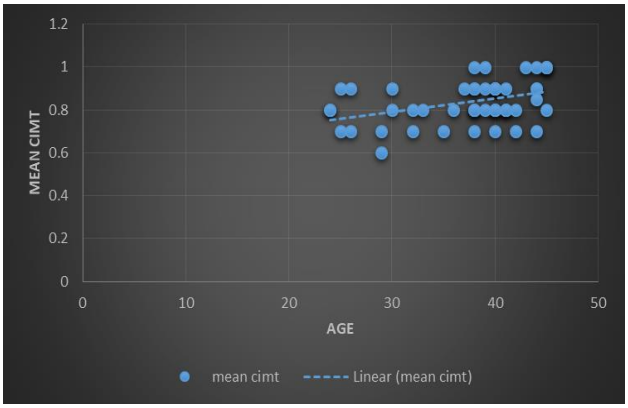

Figure 1: Correlation between mean CIMT and age of cases.

As shown in table 3, in present study, 90% of cases were in stage II of CKD and their mean CIMT were 0.83±0.09mm and 10% of cases were in stage I of CKD and their mean CIMT were 0.80±0.09mm. There were no significant difference of mean CIMT between CKD stage I and CKD stage II in cases.

As shown in figure 1, there were significant positive correlation between mean CIMT and age of cases. (Pearson correlation = 0.382, p-value 0.006).

DISCUSSION

This study was a case control study done in MYH Hospital Indore, India, with age and sex matched 50 cases and 50 controls, study title was "Study of Carotid Intima Media Thickness as Surrogate Marker of Endothelial Dysfunction in Early Chronic Kidney Disease Patients."

In present study, most of the cases 36 (72%) were age group of 36-45 years, 12 (24%) case were age group of 25-35 years and 2 (4%) cases were <25 years age of group.

In this study 36 (72%) cases were male and 14 (28%) cases were female, in the control group 37 (74%) were male and 13 (26%) were female. The mean age was 37.34±6.16 years and 37.44±5.65 years in cases and controls respectively. In current study mean CIMT (in mm) in cases were 0.83±0.10mm in right side and, 0.83±0.10mm in left side [mean (right and left both) CIMT= 0.83±0.10mm]. In control mean CIMT were 0.63±0.14 mm in right side, 0.64±0.07mm in left side [mean (right and left both) CIMT =0.64±0.08].

These results were suggestive that mean CIMT is significantly high in cases as compare to controls. On comparison of this study with study done by Sashiraj Lahoti et al, they found that CIMT in CKD patients was between 0.80±0.28mm and 0.64±0.16 in control (p=0.0001), they also conclude that mean CIMT was increased in all stages of CKD and another study done by Olutoyin Morenike Lawal et al and Arun Kumar Ponna et al, they also found that mean CIMT was higher in CKD population.[12-14] A study done by Lu Xia Zhang et al, concluded that arterial change might occur in the course of CKD earlier than previously believed.[15]

In current study 90% of cases were in stage II of CKD and their mean CIMT were 0.83±0.09mm and 10% of cases were in stage I of CKD and their mean CIMT were 0.80±0.09mm. There is no significant difference of mean CIMT between CKD stage I and CKD stage II in case. This finding was well correlated with findings of Sashiraj Lahoti et al.[12] In present study we found that 52% of

cases had atherosclerotic vascular disease [stroke in 28% cases and CAD in 24% cases] and Sashiraj Lahoti et al also found that Cardiovascular disease was more prevalent among patients with CKD as compared with controls.[12]

In current study found that CIMT was positively correlated with age and another study done by Sashiraj Lahoti et al they found similar result.[12]

CONCLUSION

Increased CIMT was found in all the cases as compare to controls so, increased CIMT can be used as an early marker of atherosclerosis in early CKD patients. Further study in large number of subjects may help to confirm or exclude the findings.

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