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Medicine

A STUDY OF CAROTID INTIMA MEDIAL THICKNESS IN NON DIABETIC CHRONIC KIDNEY DISEASE

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ABSTRACT **INTRODUCTION:** Atherosclerosis is a disease of vascular intima in which all the vascular systems from aorta to coronary arteries can be involved and is characterized by intimal plaques. **AIMS AND OBJECTIVES:** To study and compare carotid intima medial thickness by carotid ultrasonography in non diabetic patients of chronic kidney disease on treatment other than dialysis and on dialysis. **MATERIAL AND METHOD:** The present study was conducted on non diabetic patients of chronic kidney disease presenting in the outpatient department (OPD) and inpatient department (IPD) in the Department of Medicine Guru Gobind Singh Medical College and Hospital, Faridkot. A total number of 90 CKD patients were included in the present study (45 patients on dialysis and 45 patients not on dialysis). **OBSERVATIONS:** The mean Glomerular filtration rate in patients on dialysis was 8.92 ±7.84ml/min/1.73m^2 and in non- dialysis patients was 16.41 ±10.62ml/min/1.73m^2. The mean carotid intimal thickness in both right and left carotids was around 0.72mm±0.13 in patients on dialysis and around 0.61mm±0.07 in patients not on dialysis. The carotid intima medial thickness was less than 0.8mm in 31(69%) of dialysis patients and in 44(98%) of non-dialysis patients and more than 0.8mm in 14(31%) of dialysis patients and in 1(2%) of non- dialysis patients. The CMD was diminished in 34(49%) of non- dialysis patients and 12(27%) of dialysis patients and lost in 13(29%) of both dialysis and non- dialysis patients. **CONCLUSION:** Chronic kidney disease is an independent risk factor for atherosclerosis. Thus, a direct causal relationship of CKD and atherosclerosis could be delineated from this study as other confounding causes of atherosclerosis such as diabetes mellitus, cigarette smoking have been eliminated. Carotid intima medial thickness is significantly increased in CKD patients on dialysis than in those not on dialysis. Carotid ultrasonography is an optimal non-invasive modality for assessing atherosclerosis in patients with CKD.

KEYWORDS : Atherosclerosis, CKD, Carotid Intimal Medial Thickness, Diabetes

INTRODUCTION

Atherosclerosis is a disease of vascular intima in which all the vascular systems from aorta to coronary arteries can be involved and is characterized by intimal plaques (1,2). Once endothelial dysfunction occurs, it results in changing the endothelial permeability and allowing the migration of low-density lipoprotein-cholesterol (LDL-c) into the vascular wall (3). Once LDL-c trapped within the vascular wall, it undergoes lipid peroxidation by locally secreted reactive oxygen species commonly called free radicals (4,5). The macrophage receptor recognition causes uptake of LDL by monocyte-derived macrophages via scavenger receptors and results in massive accumulation of lipids within the cytoplasm of macrophages giving picture of foamy appearance to these cells; Atherothrombotic disease is a progressive disorder resulting in acute myocardial infarction and stroke, which are responsible for the highest morbidity and mortality rates in the Western world (6)

The carotid bifurcation is one of the important sites of atherosclerotic plaque. Plaque development is thought to occur preferentially at geometrically predisposed areas such as arterial branch points. The biomechanical forces at arterial branching areas found to be the triggering factor of endothelial dysfunction creating barrier impairment (endothelial misalignment), proinflammatory process and prothrombotic function(7). Once endothelial dysfunction induced, fatty streaks develop results in atherosclerotic plaques at level of carotid bifurcation into external and internal carotid artery. The ostium of the internal carotid artery is mostly affected(8).

Carotid artery stenosis (CAS) occurring as a consequence of atherosclerosis and is considered symptomatic when ipsilateral retinal or cerebral ischemia occurs and asymptomatic when these symptoms are absent. A stenosis of the carotid artery greater than 50% is considered significant carotid artery disease. Differentiation between asymptomatic and symptomatic CAS is important for treatment of CAS(9).

CKD has been known as an independent risk factor for cardiovascular disease, including stroke(10). The pathophysiology of CKD is complex. Regardless of the method of renal injury (i.e., diabetes, hypertension, or glomerular disorders), once renal damage has occurred, a cascade of events ensues. In response to renal injury, there is thought to be an increase in intraglomerular pressure with glomerular hypertrophy, as the kidney attempts to adapt to nephron loss to maintain constant glomerular filtration(11). Patients with CKD have an up to 20-fold higher prevalence of premature arterial plaque formation and cardiovascular complications compared with the general population(12). Furthermore, atherosclerotic plaques of CKD patients are often calcified with markedly increased artery stiffness there is evidence that as the arterial stiffness increases, glomerular filtration rate decreases(13).

This evidence along with the high incidence rate of cardiovascular disease (CVD) among CKD patients, supports the use of new more sensitive tools for the early detection and prevention of CVD(14). Furthermore, the National Kidney Foundation recommends the use of carotid ultrasound for a more precise assessment of cardiovascular health in kidney disease(15).

CIMT (carotid intima media thickness) is a well recognized and accepted marker to predict cardiovascular disease(16). CIMT as measured by B-mode ultrasound is a surrogate marker for atherosclerosis and can be used to detect an accelerated and subclinical atherosclerotic disease process. Advantages of CIMT are that it is non invasive, relatively inexpensive, and can be repeatedly performed with no adverse effects on the patient.(17)

AIMS AND OBJECTIVES

- To study and compare carotid intima medial thickness by carotid ultrasonography in non diabetic patients of chronic kidney disease on treatment other than dialysis and on dialysis.

MATERIALS AND METHODS

The present study was conducted on non diabetic patients of chronic kidney disease presenting in the outpatient department (OPD) and inpatient department (IPD) in the Department of Medicine Guru Gobind Singh Medical College and Hospital, Faridkot. A total number of 90 CKD patients were included in the present study (45 patients on dialysis and 45 patients not on dialysis). The sample size was

calculated using two sided two sample t test and achieved to detect a difference of -0.5 between the null and alternative hypothesis. Written informed consent was obtained from all the participants. All patients underwent investigations like Hemoglobin, renal function test and ultrasound abdomen. Carotid Doppler was done in the Department of Radiodiagnosis on Philips Affinity 70 ultrasound system using a linear frequency probe of 12.5 MHz. Intima medial thickness of the both common carotid arteries was evaluated 1cm proximal to their bifurcation. IMT was calculated as the mean value of 3 individual measurements at different points within the region of interest. Doppler flow measurements and plaques in Internal Carotid Artery (ICA), External Carotid Artery (ECA) and Common Carotid Artery (CCA) were also evaluated.

Inclusion Criteria

- Age group 18 to 65 years.
- Patients with non diabetic chronic kidney disease on dialysis.
- Patients with non diabetic chronic kidney disease on treatment other than dialysis.

Exclusion Criteria

- Diabetes mellitus
- Underlying coronary artery disease
- Cigarette smokers

OBSERVATIONS

TABLE 1: MEAN GLOMERULAR FILTRATION RATE IN BOTH DIALYSIS / NON- DIALYSIS GROUP

	Dialysis (45 patients)		Non-Dialysis (45 patients)		Total	p-value
	Mean	SD	Mean	SD		
Glomerular filtration rate ml/min/1.73m2	8.92	7.84	16.41	10.62	-3.808	0.000

Table 1 shows that mean Glomerular filtration rate in patients on dialysis was 8.92 ±7.84ml/min/1.73m^2 and in non- dialysis patients was 16.41 ±10.62ml/min/1.73m^2. So, most of the patients on dialysis were end stage renal disease patients and non- dialysis patient were in stage 4 and also found that Glomerular filtration rate of dialysis patients was significantly less than patient not on dialysis (p=0.000).

TABLE 2: KIDNEY STATUS ON ULTRASOUND IN BOTH DIALYSIS / NON- DIALYSIS GROUP

	Dialysis/Non-Dialysis				Total
Ultrasound abdomen	Dialysis	Dialysis	Non-Dialysis	Non-Dialysis	
CMD lost	13	29%	13	29%	26
CMD diminished	12	27%	22	48%	34
Shrunken Kidney	9	20%	3	7%	12
Renal stones with HUN	9	20%	4	9%	13
PCKD	1	2%	3	7%	4
Single kidney	1	2%	0	0%	1

Table 2 shows that CMD was diminished in 34(49%) of non- dialysis patients and 12(27%) of dialysis patients, CMD lost in 13(29%) of both dialysis and non- dialysis patients. Shrunken kidneys were present in 9(20%) of the dialysis patients and 3(7%) of the non-dialysis patients. These were among the majority of ultrasound findings.

TABLE 3: RIGHT AND LEFT CAROTID INTIMA MEDIAL THICKNESS IN BOTH DIALYSIS / NON- DIALYSIS GROUP

	Dialysis (45 patients)		Non-Dialysis (45 patients)		T	p value
	Mean	SD	Mean	SD		
Right carotid intima medial thickness in mm	0.72	0.13	0.61	0.07	4.785	0.000
Left carotid intimal medial thickness in mm	0.71	0.13	0.61	0.07	4.591	0.000

Table 3 shows that mean carotid intimal thickness in both right and left carotids was around 0.72mm±0.13 in patients on dialysis and around 0.61mm±0.07 in patients not on dialysis. The difference between mean carotid intima media thickness in both groups was also statistically significant(p=0.000). It was more in patients on dialysis than patients not on dialysis.

TABLE 4: CAROTID INTIMA MEDIAL THICKNESS IN BOTH DIALYSIS / NON- DIALYSIS GROUP

	0.8mm has been taken as normal value for CIMT	Dialysis/Non-Dialysis				Total	chi-square value	p-value
		Dialysis (45 patients)		Non-Dialysis (45 patients)				
Carotid intima medial thickness	< 0.8	31	69%	44	98%	75	13.5	0.001
	> 0.8	14	31%	1	2%	15		

Table 4 shows that carotid intima medial thickness was less than 0.8mm in 31(69%) of dialysis patients and in 44(98%) of non-dialysis patients and more than 0.8mm in 14(31%) of dialysis patients and in 1(2%) of non- dialysis patients. It was found that carotid intima medial thickness was significantly higher in dialysis patients than not on dialysis(p=0.001).

TABLE 5: CORRELATION OF GENDER WITH CAROTID INTIMA MEDIAL THICKNESS IN BOTH DIALYSIS / NON-DIALYSIS GROUP

Gender	Carotid intima Medial Thickness				Total	Chi-square value	p-value
	< 0.8	< 0.8	> 0.8	> 0.8			
Female	26	35%	6	40%	32	0.155	0.694
Male	49	65%	9	60%	58		

Table 5 shows that carotid intima medial thickness was more than 0.8mm in 60% of male population (9 patients) and 40% of female population (6 patients) but the correlation of gender with carotid intima medial thickness was not statistically significant (p=0.694).

TABLE 6: CORRELATION OF DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE WITH CAROTID INTIMA MEDIAL THICKNESS IN BOTH DIALYSIS / NON- DIALYSIS GROUP

Stage of chronic kidney disease	Carotid Intimal Medial Thickness				Total	Chi-square value	p-value
	< 0.8		> 0.8				
Stage 3a	1	1%	0	0%	1	3.319	0.345
Stage 3b	6	8%	1	7%	7		
Stage 4	20	27%	1	7%	21		
Stage 5	48	64%	13	86%	61		

Table 6 shows that number of patients having carotid intima media thickness more than 0.8mm were increasing from stage 3a to stage 5. In stage3a 0(1%) patients, stage3b 1(7%) patients, stage4 1(7%) patients and in stage5, 13 (86%) patients were having carotid intima medial thickness >0.8mm. No significant correlation was found between different stages of CKD and carotid intima medial thickness(p=0.345).

DISCUSSION

Lemos et al(18) and Satyanand Sathi (19) had similar observations in their studies as compared to the present study, that showed GFR was significantly low in patients on dialysis than those who were not on dialysis. This establishes that GFR significantly decreases as CKD progresses.

In our study 0.8 mm was taken as the cut off value for CIMT; below which CIMT was considered normal. It was less than 0.8 mm in 69% of patients on dialysis and in 98% cases of non- dialysis patients and more than 0.8 mm in 31% cases on dialysis and 2% cases not on dialysis; showing that carotid intima medial thickness was significantly higher (>0.8mm) in patients on dialysis than those who were not on dialysis. Tetsuo Shoji studied CIMT of CRF non dialysis group (0.889 ± 0.035 mm), dialysis group (0.868 ± 0.019 mm) and in healthy controls (0.685 ± 0.010 mm) which suggested that CIMT was higher in CRF non dialysis and dialysis patients than healthy controls but CIMT difference between CRF not on dialysis and dialysis group was not significant(20). Another study done by Tomasz Stompor et al found that CIMT before start of dialysis was 0.63±0.2mm and which after one year of dialysis increased to 0.83±0.21mm and difference was also statistically significant(21).

This present study showed that both mean right and left carotid intima medial thickness value was significantly high in patients on dialysis. Sashiraj Lahoti et al found out that right CIMT was 0.64mm ± 0.15 and left CIMT was 0.62mm ± 0.17 and 22% cases of non diabetic CKD had CIMT >0.8mm which was significantly higher than healthy controls (22).

In present study, correlation of gender with carotid intima medial

thickness in both dialysis and non- dialysis group was done and was observed that carotid intima medial thickness was more in male population in both groups. Dingwei Kuang et al found that there was no diiference between CIMT of male and female population(23).

In this study, we also correlated different stages of chronic kidney disease with carotid intima medial thickness in both dialysis and non-dialysis groups. There was no significant correlation between CIMT and different stages of CKD. Satyanand Sathi et al found that prevalence of increased CIMT was 47.5%, 50%, and 52.5% in CKD stage 3, 4 and 5 respectively but prevalence of increased CIMT was not statistically significant among the three CKD stages(19). A study done by Sashiraj et al also found that number of CKD patients with increased CIMT increased as stage progressed; from 20 patients in stage 3 to 30 in stage 4 to 48 in stage 5. But there was no significant difference in CIMT and number of patients in different stages of CKD(22).

CONCLUSION

The present study provided detailed comparison of various demographic, laboratory and radiological parameters in both dialysis and non-dialysis CKD patients. Chronic kidney disease is an independent risk factor for atherosclerosis. Thus, a direct causal relationship of CKD and atherosclerosis could be delineated from this study as other confounding causes of atherosclerosis such as diabetes mellitus, cigarette smoking have been eliminated. Carotid intima medial thickness is significantly increased in CKD patients on dialysis than in those not on dialysis. It is concluded that CKD patients who are on dialysis are more prone to develop atherosclerosis than those who are not on dialysis. Carotid ultrasonography is an optimal non-invasive modality for assessing atherosclerosis in patients with CKD.

Conflict of Interest: None

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Ethical Clearance: taken from Thesis Research Committee of the college

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