Association between Intima-Media Thickness of the Carotid Artery and Risk Factors for Cardiovascular Disease in Patients on Maintenance Hemodialysis

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Abstract- Cardiovascular risk factors were recorded and then carotid intima-media thickness was measured by using B-Mode high-resolution ultrasonography, 1 cm proximal to the carotid bulb in the posterior wall. Finally, correlation between other risk factors and CIMT was made. Total 106 patients were participated in the study but 6 patients were lost to follow up. 100 patients with chronic and advanced renal disease were evaluated, including 55% females and 45% males. The mean age of these patients was 60.2 ± 13.1 years, with a range of 25-81 years. Correlations between CIMT and age ($P = 0.023$), dialysis duration ($P = 0.017$), number of cigarettes smoked ($P = 0.026$), diastolic blood pressure ($P = 0.013$) and fasting blood sugar ($P = 0.045$) were significant. Risk factors for cardiovascular disease in patients on hemodialysis are of significant interest because of the high prevalence and frequency of the disease in this group of patients. However, in the present study, we were not able to find a very consistent and definite role for some risk factors in our patients. More studies are required to make clear the role of these factors in patients on hemodialysis.

Index Terms- CIMT, ESRD, maintenance hemodialysis, cardiovascular risk factor

I. INTRODUCTION

Patients with end stage renal failure commonly have different cardiovascular problem and cardiovascular disease is the most common cause of death in patients with end-stage renal disease and accounts for most of the morbidity in this group. Renal data show that CV diseases are the cause of death in 51-55% of dialysis and 37% of kidney transplant recipient patients in the western countries[1,2,3]. Burden of chronic kidney disease is very much alarming in our country. It United States one of nine people suffers from cardiovascular disease is the most common cause of morbidity and mortality in patients with end-stage renal disease. Atherosclerosis is a systemic disease, carotid and coronary vessels are at comparable risk for developing pathologic changes. For this reason, increase in the thickness of the intima-media layers of carotid arteries can be a harbinger of coronary atherosclerosis and also a prognostic factor for cardiovascular accidents.

Atherosclerosis, which is the most important cause of mortality and morbidity in patients with ESRD, begins many years before the development of clinical manifestations.[4,5] Studies have shown that hemodialysis patients have advanced changes in the walls of their arteries, which can present as increased intima-media thickness (IMT) in the carotid and femoral arteries[6,7] Considering the fact that atherosclerosis is a systemic disease, carotid and coronary vessels have equivalent risks for developing atherosclerosis, increased carotid IMT (CIMT) can be used as a sign of atherosclerosis in the coronary arteries and as a prognostic factor after CV accidents.[8] In multiple studies, a significant association has been shown between pathologic changes in coronary vessels and increased IMT in the carotid arteries[3]. The aim of this study was to assess vascular changes in hemodialysis patients in the course of the disease and the CIMT is highly correlated with other CV risk factors in our population. In this study we present our findings on the use of high-resolution carotid ultrasonography as a non-invasive technique for diagnosing, and thus slowing or halting the progress of atherosclerosis in patients on dialysis.

In this study, we evaluated the status of carotid intima-media thickness (CIMT) in patients with ESRD on dialysis and analyzed its association with other risk factors for cardiovascular diseases.

II. MATERIALS AND METHODS

This cross-sectional study was carried out in Department of Medicine, CSM Medical University, Lucknow, UP, India during January 2009 to December 2011 in patients with renal failure, who were referred for hemodialysis to the nephrology unit, and fulfilled the inclusion criteria of the study, were evaluated. Patients with ESRD on regular hemodialysis and who gave written consent for participation were included in the study. Patients in whom carotid Doppler ultrasonography could not be performed were excluded from the study. Data required for the study were extracted from the record files of patients (regarding CV risk factors). ESRD was defined as chronic advanced kidney disease in which the glomerular filtration rate (GFR) was less than 15 mL/min. Diabetes was defined as the presence of hyperglycemic symptoms (polyuria, polydipsia) plus random blood glucose concentration ≥ 200 mg/dL or fasting blood sugar ≥ 126 mg/dL as per ADA guidelines.[9] Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg.[10] Obesity was defined as body mass index

(BMI) >30 kg/m^2,[11] and hyperlipidemia was defined as plasma cholesterol levels ≥240 mg/dL or plasma low-density lipoprotein (LDL) levels ≥160 mg/dL [12] or plasma triglyceride levels ≥150 mg/dL.[13] Carotid Doppler ultrasonography was performed by a single operator expert ultrasonologist and intima media thickness (IMT) was measured; the operator was blinded about the history and laboratory findings of the patients.

The IMT was defined as a hypo-echogenic space between two echogenic lines containing intima-media interface and media-adventitia interface on the posterior wall of the carotid artery[6,14,15]. For performing carotid Doppler ultrasonography, the patient was asked to lie down on the examination table in the supine position. His/her neck was rotated in a superior and leftward direction so that the right carotid artery was exposed. Following this, using a B-mode high-resolution ultrasonography system (HDI 5000 Sono CT Philips), the length of the artery was determined, and at the site of bifurcation of the common carotid artery (carotid bulb), the posterior wall was exposed and IMT was measured. If atherosclerotic plaques were found on the carotid artery, their presence and number were recorded on the data collection forms. An atherosclerotic plaque was defined as a local thickness of intima greater than 1 mm or two times more than its adjacent normal layer[11].

For statistical analysis of data, ratio and rate were used for qualitative variables and mean and standard deviation for quantitative data. Also, χ^2 test was used for comparison of rates and t-test was used for comparison of means. Correlation test was used for evaluating the association of quantitative variables. In this study, statistical significant level was considered as P value <0.05.

III.   RESULTS

In this study, 100 patients with advanced and chronic renal disease were evaluated; 45% were males and 55% were females. Their mean age was 60.2±13.1 years (range 25-81 years). Past medical history revealed that 45 patients were diabetic (45%), 72 patients (72%) hypertensive, 18 had history of myocardial infarction (MI), 8 had history of cardiovascular accident (CVA) and 18 were smokers. The mean number of cigarettes smoked in this group was 144.75 ± 23.5 cigarettes/ year, with a range of 50-200 cigarettes/year. The mean duration on dialysis was 3.75 ± 4.14 years (range 2-6 years). The mean BMI was 29.88 ± 3.75 Kg/m^2 (range 18.6 to 35.9); the mean systolic blood pressure was 144.4 ± 23.5 mmHg (range 110-190 mmHg) and mean diastolic blood pressure was 77.8 ± 7.45 mmHg (range 60-90 mmHg).

On high-resolution carotid ultrasonography, carotid plaques were detected in 58 patients (58%). Among them, 68% had a single plaque and 32% had two or more plaques. The mean right CIMT was 0.938 ± 0.304 mL (range 0.40- 1.80 mL). The results of serum bio-chemical tests have been summarized in (Table-1). Correlation coefficients between right CIMT and quantitative variables in the study for detecting their associations are shown in (Table-2). The means of studied variables in patients with and without plaques in the carotid artery are shown in (Table-3). Data in this study show that 61% of female patients and 63% of male patients had plaques in their carotids. The difference was not statistically significant (P > 0.05). In patients with history of diabetes, the prevalence of carotid plaques was 46.5% compared with 19% in non-diabetic patients; this difference was statistically significant (P = 0.011). In patients with a history of hypertension, 65.7% had carotid plaques compared with 33.0% in the normotensive patients. Comparison of these rates by χ^2 test showed a statistically significant difference (P = 0.035). In patients with a history of MI, 76% had carotid plaques compared with 60% in patients with no history of MI. This difference was not statistically significant (P >0.05). About 33.1% of the patients with a history of CVA had carotid plaques compared with 63.8% without history of CVA, a difference which was not significant (P> 0.05). Among patients with history of smoking, 75% had carotid plaques compared with 39.5% among non-smokers; this difference was statistically significant (P = 0.011). Patients with longer duration on dialysis and elderly patients had high IMT (P=0.017 and 0.023, respectively).

IV.   DISCUSSION

Atherosclerosis is a systemic disease and both carotid and coronary vessels are at equal risk for developing it. For this reason, increased CIMT is a harbinger of coronary atherosclerosis and a prognostic factor for CV outcome. In addition, the risk factors for involvement of both arteries are more or less similar. Findings of this study suggest that presence of diabetes is significantly associated with increased CIMT. Our findings are in corroboration with findings reported by Modi et al from India[14] and Ishimura et al from Japan.[16] It seems that diabetes acts as a risk factor for developing atherosclerotic plaques in patients on hemodialysis.

In the present study, there was no association between history of MI and CVA, and CIMT, which is different from the findings of Modi et al [14] The difference may be related to the existence of multiple risk factors in this group of patients; thus, the other risk factors might have a role to play in patients with increased CIMT and without previous history of MI. In this regard, smoking has shown a significant association.

Our study showed a direct association between diastolic blood pressure and CIMT. Such association was not seen for systolic blood pressure. Study conducted by Abdolghaffar et al,[17] showed significant association between systolic and diastolic blood pressure and CIMT in non-HD CRF patients. Ishimura et al from Japan[16] and Poyrazoglu HM et al from Turkey[15] failed to show significant association between these two variables.
In our findings, diabetes is a risk factor for developing plaques in the carotids. However, there was no significant correlation between CIMT and other estimated variables. Definite conclusions about correlation between other evaluated variables and CIMT can be drawn only after further studies with more participants.

This study shows a direct and significant correlation between CIMT and duration on dialysis; the CIMT increased with a direct association with duration on dialysis. In our study, age of the patients had a positive and somewhat significant association with CIMT such that in the older patients, average level of CIMT was more than in the younger group. Similar results have been reported by Modi et al.[14] These results are predictable when one understands the pathophysiology of atherosclerosis and its known association with aging process.

V. CONCLUSION

We summarize that there is a significantly increased frequency and prevalence of cardiovascular risk factors in patients on hemodialysis. These factors, based on previous investigations, play a key role in the development of atherosclerosis. In this study, age, dialysis duration, number of cigarettes smoked, diastolic blood pressure and diabetes were shown to be atherogenic.

Table 1: Results of laboratory test in the studied patients (N=100)

Biochemical parameter	Minimum	Maximum	Mean	Standard deviation
Hemoglobin (g/dl)	6.4	14.5	10.4	1.73
Blood urea nitrogen (mg/dl)	22	110	66	17.45
Creatinine (mg/dl)	3.1	9.80	6.45	2.29
Phosphorus (mg/dl)	2.95	9.75	6.35	1.64
Calcium (mg/dl)	7.35	13.0	10.17	1.28
Albumin (gm/dl)	3.1	9.4	6.25	1.36
Triglyceride (mg/dl)	33	334	1183.5	64.86
Cholesterol (mg/dl)	60	235	147.5	40.30
Low density lipo-protein (mg/dl)	42	192	117	30.32
High-density lipoprotein (mg/dl)	17	100	58.5	16.54
Fasting plasma glucose (mg/dl)	85	248	166.5	41.20

Table 2: Correlation coefficient between right carotid intima media thickness and quantified variables in the studied patients

Variables	Pearson correlation coefficient with right CIMT	P-value
Age	+0.475	0.025
Number of plaque	+0.245	0.167
Duration of dialysis	+0.436	0.18*
Number of cigarette studied	+0.430	0.027*
Systolic blood pressure	+0.215	0.136
Diastolic blood pressure	+0.454	0.014*
Hemoglobin	+0.130	0.366
Blood urea nitrogen	-0.103	0.483
Creatinine	-0.01	0.493
Phosphorus	-0.216	0.142
Calcium	-0.216	0.142
Albumin	-0.158	0.276
Triglyceride	+0.165	0.256
Cholesterol	+0.075	0.608
Low density lipoprotein	+0.064	0.665
High density lipoprotein	0	0.998
Fasting plasma glucose	+0.345	0.046*

* Significance

Table 3: Mean of the evaluated variables in patients with and without plaques in the carotids.

Variables	Mean		P values
	Patients without plaques	Patients with plaques	
Age (years)	52.83±14.65	63.5±10.9	0.022*
Duration on dialysis (years)	2.16±3.15	4.15±4.66	0.025*
Body mass index	25.1±3.74	25.2±3.65	0.785
Number of cigarette smoked (pack/year)	100±70.65	158±82.1	0.018*
Systolic blood pressure (mmHg)	145.15±23.32	142.1±23.85	0.870
Diastolic blood pressure (mmHg)	72.2±5.6	88.04±8.22	0.058
Hemoglobin (gm/dl)	10.36±1.58	10.90±1.75	0.285
Blood urea nitrogen (mg/dl)	58+80±16.80	63.82±17.75	0.317
Creatinine (mg/dl)	8.85±1.96	7.85±2.5	0.145
Phosphorus (mg/dl)	5.94±1.42	6.10±1.75	0.732
Calcium (mg/dl)	8.94±0.95	9.45±1.46	0.165
Albumin (gm/dl)	4.86±1.58	4.46±1.24	0.275
Triglyceride (mg/dl)	134.21±62.45	150.51±65.65	0.392
Cholesterol (mg/dl)	137.75±44.75	154.75±36.12	0.577
Low density lipoprotein (mg/dl)	107.06±32.3	110.36±29.12	0.970
High density lipoprotein (mg/dl)	37.25±14.86	39.10±17.5	0.58
Fasting plasma glucose (mg/dl)	118.8±36.56	134.48±44.48	0.033*
Right carotid intima-media thickness (mm)	0.76±0.26	0.97±0.33	0.030*

*significance

REFERENCES

[1] Ehrich JH, Loirat C, Brunner FP, et al. Report on management of renal failure in children in Europe, 1991. Nephrol Dial Transplant 1991; 7(suppl 2):36-48.

[2] Disney AP. ANZDATA report 1996. Australia newzealand dialysis and transplant Registry, Adalide. 1996.

[3] Sarnak MJ, Levrely AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular diseases: a statement from the American heart association councils on kidney in vascular disease, high pressure research, clinical cardiology, and Epidemiology and prevention. Circulation 2003;108:2154-69.

[4] Lindner A, Charra B, Sherraol DJ, Serbner BH. Accelerated atherosclerosis in prolonged maintenance hemodialysis. N Engl J Med 1975;290:697-701.

[5] Ross R. The pathogenesis of atherosclerosis. N Engl J Med 1993;392:801-9.

[6] Kawaghishi T, Nishizawa Y, Konishi T, et al. High resolution B-Mode ultra sonography in evaluation of atherosclorosis. N Engl J Med 1974;200:697-701.

[7] Shoji T, kawaghishi T, Emoto M, et al. Additive impact of diabetes and renal failure on carotid atherosclerosis. Atheroclerosis 2000; 153:257-8.

[8] Jadhv UM, Kadam NN. Carotid intima-media thickness as an independent predictor of coronary artery disease. Indian Hearts J 2001;53: 458-62.

[9] Genuth S, Alberti KG, Bennett P, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26:3160.

[10] Chobanian AV, Bakris GL, Black HR, Cushman, WC. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. JAMA 2003;289:2560.

[11] World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO convention, Geneva, 1999. WHO technical report series 894, Geneva 2000.

[12] Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). JAMA 2001;285:2486.

[13] Third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Circulation 2002;106:3143.

[14] Modi N, Kappor A, Kumar S, Tewari S, Garey N, Shinha N. Utility of carotid intima- media thickness as a screening tool for evaluation of coronary artery disease in pretransplant end Stage renal disease. J Postgard Med 2006;52 (4):266-70.

[15] Poyrazolu HM, Dunsel R, Yikilmaz A, et al. Carotic artery thickness in children and young adult with ESRD. Pediatr Nephrol 2007;27:109-16.

[16] Ishimura E, Taniwaki H, et al. Cross sectional association of serum phosphate with carotid intima-media thickness in hemodialysis patients. Am J Kidney Dis 2005:45(5):859-69.

[17] Abdeloghaffar S, et al. Carotid intima-media thickness: An index for subclinical atherosderosis in type I diabetes. J Trop Pediatr 2006;52(1):39-45.

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