



CAROTID PLAQUE AND TYPE 2 DIABETES MELLITUS.

1. MCPS, FCPS
Professor
Department of Medicine
United Medical and Dental College,
Karachi.
2. FCPS
Assistant Professor
Department of Medicine
United Medical and Dental College,
Karachi.
3. MCPS, FCPS
Associate Professor
Department of Medicine
United Medical and Dental College,
Karachi.
4. FCPS, M.Phil
Professor & Head
Department of Medicine
United Medical and Dental College,
Karachi.

Correspondence Address:

Dr. Farhat Bashir
40-B, 1st East Street, Phase 1,
DHA, Karachi.
drfarharbashir@gmail.com

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INTRODUCTION

As the epidemic of diabetes mellitus extends throughout the world and is being projected to affect around 370 million people by the year 2030¹, the related complications are also expected to increase. Along with the control of hyperglycemia, early diagnosis and treatment of its manifold complications is seen as a major challenge to the management of this disease. In areas of the world where the life style modifications and early management of cardio-metabolic risk factors is in place they have been able to reduce the mortality caused by cardiovascular disease.² Diabetes mellitus, due to atherosclerosis, is a major risk factor for cardiovascular disease like coronary artery disease, cerebrovascular disease and peripheral vascular disease.

Carotid Doppler ultrasound is a reliable and non-invasive method to measure CIMT, presence

Farhat Bashir¹, Ayesha Nageen², Saera Sohail Kidwai³, Jamal Ara⁴

ABSTRACT: Atherosclerosis is the basic cause of macrovascular complications of diabetes mellitus. It affects all parts of the circulatory tree. An easy and reliable method of diagnosing atherosclerosis is Carotid Doppler ultrasonography. Increased Carotid Intima-Medial thickness (CIMT) and presence of carotid plaque is an important predictor of ischemic heart disease and cerebrovascular accidents. The purpose of this study was to find the association of carotid plaque with cardio-metabolic risk factors in type 2 diabetes mellitus. **Study Design:** Cross-sectional study. **Setting:** Medical Out-patient Department of Creek General Hospital, Karachi. **Period:** One year from June 2015 to May 2016. **Materials and Methods:** The study population included 119 cases of type 2 diabetes mellitus. All subjects underwent Carotid Doppler ultrasonography. The demographic, anthropometric, clinical and laboratory data was collected and analyzed through SPSS ver.20.0. The relationship of carotid plaque with different atherosclerotic variables was assessed by Student's t-test and Chi-square test. P-value of <0.5 was considered significant. **Results:** Out of 119 patients with type 2 diabetes mellitus, 18.5% had a carotid plaque. The presence of plaque was associated with duration of diabetes, presence of hypertension, BMI, diastolic blood pressure, total cholesterol, triglyceride levels and CIMT. **Conclusion:** We need to focus on management of the multiple metabolic abnormalities associated with diabetes mellitus in order to prevent atherosclerosis and its associated cardiovascular disease.

Key words: Carotid Plaque, Cardio-Metabolic, CVA, Ischemic heart disease, Type 2 Diabetes Mellitus.

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of carotid plaque and degree of stenosis in the carotid arteries. This procedure provides a safe assessment of atherosclerosis not only in the carotid circulation but also gives an estimation of atherosclerosis in the coronary and peripheral circulation.^{3,4} Atherosclerosis in the carotid artery leads to increased carotid intima-media thickness, carotid plaque formation and carotid stenosis. The degree of carotid stenosis and plaque vulnerability are related to the greater risk of stroke.⁵ Indeed they can independently predict cerebrovascular accidents.⁶ Presence of carotid plaque shows a stronger association with cardiovascular risk compared with diffuse CIMT increase.⁷ The echogenicity of the plaque also determines the vulnerability of the plaque and thus the risk of cerebrovascular accidents.^{8,9}

Many factors are associated with an increased CIMT and presence of plaque. These include age,

male gender, diabetes mellitus, hypertension, dyslipidemia, obesity and smoking. Carotid plaque is frequently found in diabetic patients.¹⁰ In this study we assess the association of carotid plaque with various cardio-metabolic risk factors in type 2 diabetes mellitus.

SUBJECTS AND METHODS

A cross-sectional study was designed and all adult cases of type 2 diabetes mellitus presenting to the Medical Out-patient Department of Creek General Hospital, Karachi, were enrolled in the study. Patients with type 1 diabetes mellitus and those with secondary diabetes were excluded from the study. The duration of the study was one year from June 2015 to May 2016. The study was approved by the Ethical Review Committee of the institution. At the time of recruitment, consent was taken and a proforma including history, examination findings, anthropometric measurements and the laboratory results were recorded. The investigations included fasting and random blood glucose levels, HbA1c and fasting lipid profile. Carotid Doppler studies were performed for all the study participants. A single radiologist performed the procedure using a linear transducer of 7.5 Hz in B mode (Toshiba Nemio 35). CIMT was measured at the far wall of the Common Carotid Artery and was taken as

distance between the leading edge of the lumen intima interface and the leading edge of the media adventitia interface. Plaque was defined as more than 50% focal thickening of the vessel wall compared to the adjacent segment.

The data was entered on SPSS version 20.0. The variables were described as mean with standard deviation or as percentages with numbers. The variables were analyzed for association using Chi-square and t-test. P-value of <0.05 was considered significant.

RESULTS

The study population of 119 demonstrated a mean age of 55 ± 14 years. There were 49.6% males. Around 18.5% of the population showed presence of a Carotid plaque. The baseline characteristics of the population are seen in Table-I.

The presence of a carotid plaque showed significant association with duration of diabetes, high BMI, presence of hypertension and diastolic blood pressure. Among the lipid fractions only total cholesterol and triglyceride levels showed association with presence of carotid plaque. Increased Carotid intima media thickness also was associated with carotid plaque. (Table-I)

Variables		Total Population n=119	Patients with Plaques n=22(18.5%)	Patients without Plaques n=97(81.5%)	P-Value
Age(Years)		55.1±14.0	52.59±10.9	55.7±14.6	0.34*
Gender	Male	59(49.6%)	7(31.8%)	52(53.6%)	0.097#
	Female	60(50.4%)	15(46.4%)	45(68.2%)	
Hypertension	Yes	63(52.9%)	16(72.7%)	47(48.5%)	0.05#
	No	56(47.1%)	6(27.3%)	50(51.5%)	
Duration of Diabetes (years)		6.9±5.2	9.4±4.4	6.3±5.2	0.01*
BMI (kg/m ²)		26.4±6.6	30.34±7.0	25.6±6.2	0.002*
Systolic BP (mmHg)		129.2±15.2	132±14.9	128.6±15.3	0.34*
Diastolic BP (mmHg)		82.6±8.3	87.9±7.8	81.3±7.9	0.001*
Fasting Blood Glucose (mg/dl)		151.2±54.7	147.8±47.1	151.9±56.5	0.75*
Random Blood Glucose (mg/dl)		261.9±92.5	238.4±75.5	267.2±95.5	0.18*
HbA1c %		8.8±2.3	8.5±2.1	8.9±2.3	0.46*
Total Cholesterol (mg/dl)		191.0±32.4	205.7±28	187.7±32.5	0.017*
LDL (mg/dl)		122.0±26.0	127.4±36.3	120.8±23.1	0.289*
HDL (mg/dl)		39.6±10.6	42.3±11	39±10.4	0.19*
Triglyceride (mg/dl)		215.8±99.1	267.7±81.7	204±99.3	0.006*
Intimal Thickness (cm)		1.0±0.18	1.11±0.14	0.97±0.17	0.001*

Table-I. Comparison of the study population
*Student t-test # Chi-square test

DISCUSSION

A person with diabetes has a three times greater probability of death because of a cardiovascular cause compared to a person without diabetes mellitus.¹¹ Atherosclerosis can be assessed by both coronary and carotid angiography or non-invasively by Carotid Doppler scanning. Carotid atherosclerosis is detected by this procedure through measuring CIMT and carotid plaques. Carotid intima media thickness increases in diabetic patients due to the atherosclerotic process. Diabetes mellitus leads to atherosclerosis because of the multiple metabolic changes that are part of the diabetic complex. Atherosclerosis itself is an inflammatory process while the hyperglycemia in diabetes mellitus also contributes to the inflammation and results in a higher cardiovascular mortality.¹²

In patients with type 2 diabetes aging, hypertension, duration of diabetes, hyperglycemia, dyslipidemia, and smoking have been identified as significant risk factors for stroke.^{13,14,15} As diabetes mellitus is a metabolic syndrome, the multiple entities associated with it all lead to thickening of the carotid wall as evidenced by increased CIMT in these patients. Duration of diabetes, systolic blood pressure and total cholesterol was found to have a stronger relationship with CIMT in persons with type 2 diabetes mellitus in a study.¹⁴ There is also evidence that presence of multiple risk factors will lead to greater increase in CIMT.³ As mentioned earlier this is the case in subjects with diabetes mellitus as they have multiple cardio-metabolic risk factors present concurrently.

Our study showed 18.5% of the diabetic patients had a carotid plaque. A study showed 28 % of diabetic patients were having carotid plaques. The prevalence of carotid plaques increased with time in these patients.¹⁶ Another study revealed carotid plaques in 77% of diabetic patients. But this study was in patients older than 65 years which may be a factor for such a high percentage of plaque presence.¹⁰

A study revealed that association between atherosclerosis as assessed by ankle brachial index and carotid artery stenosis was similarly

associated with diabetes in both genders.¹⁷ There was no gender based difference seen in our study either. This may be due to the fact that most of the population was elderly. At older age females lose the protective effect of gender on atherosclerosis. But other studies have shown that CIMT was closely associated with age, gender and smoking.¹⁸

LDL cholesterol is seen to be associated with CIMT.¹⁹ In our preceding study CIMT showed a relationship with both total cholesterol and LDL.¹⁴ But the current study shows that carotid plaque was only associated with total cholesterol and triglyceride levels. All fractions of the blood lipids are associated with cardiovascular disease. Different fractions have been observed to be deranged in type 2 diabetes mellitus in different studies.

Patients with diabetes are at greater risk of suffering from a stroke associated with more morbidity and mortality as compared to non-diabetic individuals.²⁰ Studies in prediabetes have shown significant association of HbA1c with CIMT indicating that it may successfully predict vascular disease.²¹ This was also confirmed in patients with metabolic syndrome.²² HbA1c is also associated with presence of microvascular complications in diabetic patients.²³ Multiple studies have shown the association of CIMT with different glycemic parameters in patients with diabetes and impaired glucose tolerance.^{24,25,26}

Patients in our study did not demonstrate any association of blood glucose levels or glycated hemoglobin percentages with presence of carotid plaque as it is the duration of exposure to the atherogenic effect of diabetes rather than specific glucose levels.

We demonstrated an association of BMI to presence of carotid plaque. There have been varying results associated with obesity and its relationship with obesity. Some studies have not demonstrated an association^{4,27} while others show a relationship of obesity with carotid atherosclerosis.²⁸

The process of atherosclerosis is observed initially as increased CIMT the progression of which leads to plaque formation and vascular narrowing. Therefore it was observed in our study that a higher CIMT was significantly associated with carotid plaque. Carotid plaques are also sources of thromboemboli leading to both higher coronary and cerebral vascular diseases.

This study was a continuation of previous studies showing the relationship of CIMT with different cardio-metabolic risk factors in diabetic patients.¹⁴ This study was focused on presence of plaque as this would be related to a more severe disease indicating greater atherosclerosis. The patients with carotid plaques are more prone to develop cardiovascular complications. We need to know which cardio-metabolic risk factors are associated with the presence of plaques. Our study showed a significant relationship of hypertension especially diastolic blood pressure, increased BMI and increased total cholesterol and triglyceride levels with presence of plaque.

Our management of the diabetic patient will thus be focused on weight optimization, control of blood pressure and management of dyslipidemia in addition to glycemic control. So the management of these multiple factors may play a role to prevent progression of atherosclerosis and even its' regression. Interestingly CIMT has been used to assess the response to therapeutic intervention in patients with atherosclerosis.^{29,30,31}

CONCLUSION

Atherosclerosis occurs early and is extensive in diabetes mellitus due to clustering of multiple risk factors in this condition. Management of these co-existing abnormalities is required to prevent or delay cardiovascular disease in these patients.




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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Farhat Bashir	Concept, Data collection, Statistical analysis, Write up.	<i>Farhat Bashir</i> 
2	Ayesha Nageen	Data collection, Statistical analysis, Literature review.	<i>Ayesha Nageen</i> 
3	Saera Sohail Kidwai	Literature review, Statistical analysis.	<i>Saera Kidwai</i> 
4	Jamal Ara	Concept, Final write up.	<i>Jamal Ara</i> 