

A Study of Correlation between Carotid Intima – Media Thickness and Diastolic Dysfunction in Asymptomatic Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Subclinical diastolic dysfunction and ongoing atherosclerosis is a common occurrence in diabetics. Carotid Intimal-Medial Thickness (CIMT) is being used as a marker to assess subclinical atherosclerosis. Study was aimed to find out prevalence of subclinical atherosclerosis and diastolic dysfunction in asymptomatic diabetics and correlate CIMT with left ventricular diastolic dysfunction (LVDD).

Material and methods: A prospective, cross sectional study was conducted over 12 months in asymptomatic diabetics attending OPD/IPD of a tertiary care teaching hospital in north India. Patients were screened to rule out cardiovascular involvement and any other complication related to diabetes. After noting Weight and Height, BMI was calculated. CIMT was measured by B mode high resolution ultra sound. Echocardiography was done and E/A ratio calculated. Patients were divided into those with and without diastolic dysfunction; Also they were divided in two groups taking CIMT into consideration and patient parameters were studied in both the settings and statistical significance tested in between these subgroups using SPSS.

Results: The present study population included 100 asymptomatic diabetics (age range 30-75). Sixty percent were females, twenty two percent smokers and eighteen were alcoholics. The CIMT was less than 1 in 28 subjects, were considered to have less CV risk. CIMT and E/A ratio were significantly different between high risk and low risk groups ($P < 0.0001$). LV Diastolic dysfunction was found in 30% patients. The mean E/A ratio in this group was 0.76 ± 0.04 msec. Female preponderance was observed in the group with diastolic dysfunction and two third of these ladies were post menopausal.

Conclusion: A positive correlation exists between CIMT and low E/A ratio. CIMT increases with age and value more than 1 in young adults is associated with high CV risk. Females have higher CIMT value and post menopausal ladies are more prone to diastolic dysfunction.

Keywords: Carotid Intima, Media Thickness, Diastolic Dysfunction

INTRODUCTION

Atherosclerosis is a chronic disease of vascular endothelium which develop gradually with varying velocity, depending on the presence of risk factors like age, male gender, post menopausal ladies, smoking, abdominal obesity, dyslipidemia, hypertension, insulin resistance and Type2 diabetes mellitus.¹ The process is 2-4 times more in diabetics leading to complications like stroke, heart attack and peripheral vascular disease.¹ These macro vascular complications account for 75–80% of mortality in patients with diabetes.²

Carotid Intimal Medial Thickness (CIMT) is the area of tissue starting at the luminal edge of the artery and ending

at the boundary between the media and the adventitia. Its measurement by high resolution ultrasound B scan is an effective, noninvasive tool which can assist in identifying people with who are at higher risk of developing sub clinical atherosclerosis and subsequent macro vascular complications. It may also help to evaluate the effectiveness of various treatment strategies used to treat people with diabetes.³ CIMT is age dependant. In healthy middle-aged adults it measures 0.6 to 0.7 mm and greater than 1.20 mm is considered abnormal. CIMT is age-dependent and increases at a rate of 0.005 to 0.010 mm/year.⁴ Increase in CIMT can predict future events of silent brain infarction and coronary heart disease.⁴⁻⁷

Diabetes is an important risk factor for atherosclerosis also it can affect cardiac structure and function even in the absence of changes in blood pressure or coronary artery disease, a condition called diabetic cardiomyopathy.^{5,8,9} Left ventricular diastolic dysfunction (LVDD) is considered the earliest manifestation of diabetic cardiomyopathy, preceding the development of systolic dysfunction. The pathogenesis of diabetic cardiomyopathy is multifactorial.⁵ Here not only atherosclerosis accelerated by insulin resistance but also sustained hyperglycemia increases deposition of advanced non enzymatic glycation end products (AGE) in the extracellular matrix, resulting in a further increase in myocardial stiffness. Hence LVDD may be useful markers of progressive arteriosclerosis in type 2 diabetic patients.¹⁰ The present study was conducted on asymptomatic diabetics without any complications with an aim to assess subclinical atherosclerosis and diastolic dysfunction in this group. CIMT was used as early marker of atherosclerosis. An attempt is made to correlate CIMT with LVDD.

MATERIAL AND METHODS

This was a prospective study conducted in a tertiary care teaching hospital in north India. All the patient attending diabetic clinic/IPD during June 2014 - May 2015 who were diagnosed as diabetes mellitus using WHO criteria (1999); were first subjected to a detailed history and examination including calculation of body mass index (BMI). And those

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patients who had no cardiovascular complaints, ECG, TMT, X-ray chest PA view were included in the study after informed consent. The clearance was taken from Institutional ethical committee (vide -IEC/03/2013).

Inclusion criteria- 1) Asymptomatic Patients who had normal BP, ECG, TMT. 2) patients without any complications related to diabetes.

M mode and 2D echo was performed to assess subclinical LVDD. The ratio of early-diastolic peak flow velocity (E) and late-diastolic peak flow velocity (A), was noted and LVDD E/A <0.78 for men and <0.79 for women was taken as normal.

High resolution ultrasound B mode was done in supine patient with head turned 45° opposite to the side being tested. Measurements were taken from both far wall and near wall in both the carotid

Assessment for glycaemic control was done by FBS (10 hr fasting) / PPBS estimation which was estimated by glucose oxidase- peroxidase method (GOD-POD).¹¹

HbA1C was determined directly (without measurement of

total hemoglobin) by immunoturbidimetric method.¹² Serum total cholesterol was measured by cholesterol oxidase-phenol aminoantipyrine (CHOD-PAP) method.¹³ Serum triglycerides were measured by GPO-PAP method.¹⁴

High density lipoprotein (HDL) and LDL cholesterol estimations were done by assay based on Poly vinyl sulphonic acid and polyethylene glycol methyl ether coupled classic precipitation method with improvement in using optimized quantities of PVS-PEGME and selected detergent.¹⁵

The patients were sub divided in two group –one with low CV risk and High CV risk based on CIMT values (Table-2) and mean of the entire patient variables were compared in these subgroup using t test. The patients were also divided into two more groups depending on presence /absences of LVDD (Table-3) and patient characteristics were studied using SPSS software. Comparison of mean values of patient variables was done in these groups using unpaired students t test.

RESULTS

The present study population included 100 diabetics age (range 30-75) attending diabetic clinic at a teaching hospital in north India; who had no cardiovascular symptoms and signs, normal BP and ECG/TMT. Sixty percent were females; twenty two percent smokers and eighteen were alcoholics. Table-1 shows patient characteristics. The CIMT was less than 1 in 28 subjects, were considered to have less CV risk.⁶ Table-2 shows comparison of mean of various risk factors amongst the group with low probability and those with high probability of CV risk. CIMT and E/A ratio were significantly different between these groups ($P<0.0001$) LV Diastolic dysfunction was found in 30% patients. The mean E/A ratio in this group was 0.85 ± 0.19 ms prevalsalva and 0.77 ± 0.16 msec post valsalva. For convenience the group was sub divided into those with E/A >1(no diastolic

Patient variables (n=100; without complications of DM)	Mean value
Age (years)	53.05±10.72; F: M=3:2
BMI (kg/m ²)	25.46±4.29
Duration of DM (years)	4.26±4.04
AverageHbA1c(%)	7.1±0.21
Average Triglyceride(mg%)	190±73.96
Average LDL(mg%)	102.9±21.8
Average HDL(mg%)	35. 7±.23
Average total cholesterol(mg%)	195 ±38.43
Mean CIMT (mm)	1.41±0.65
Mean E/A	1.10±0.28.

Table-1: Patient characteristics of the study group.

	CIMT (<1) n=28	CIMT (>1) n=72	F value	Overall n=100
CIMT(mm)	0.82 ^a ± 0.02	1.62 ^b ± 0.07	54.90**	1.41 ± 0.06
EA ratio	2.61 ^a ± 1.38	1.05 ^b ± 0.03	9.66**	1.49 ± 0.39
Age(years)	51.64 ± 1.84	53.59 ± 1.30	1.18	53.05 ± 1.07
Sex	1.53 ± 0.09	1.62 ± 0.05	1.49	1.60 ± 0.04
Duration DM(years)	3.89 ± 0.43	4.15 ± 0.52	1.63	4.08 ± 0.39
BMI(kg/m ²)	26.49 ± 0.78	25.33 ± 0.60	0.01	25.65 ± 0.48
LDL(mg%)	113.60 ± 8.92	101.54 ± 2.48	1.96	104.92± 3.09
TG(mg%)	148.22 ± 14.09	199.36 ± 8.35	0.17	185.04 ± 7.52
HBA1C(%)	6.99 ± 0.17	7.07 ± 0.11	0.22	7.05 ± 0.09

Table-2: Comparison of means of patient variables in group with low(CIMT <1) and high(CIMT>1) probability of CV risk

	E:A ratio (<1) n=27	E:A ratio (>1) n=73	F value
EA ratio	0.76 ± 0.04	1.76 ± 0.53	1.03*
CIMT	1.69 ± 0.13	1.30 ± 0.07	5.20*
Age(years)	54.33 ± 2.06	52.57 ± 1.25	0.12
Sex	1.74 ± 0.08	1.54 ± 0.05	17.49**
Duration DM (years)	3.27 ± 0.50	4.38 ± 0.50	0.50
BMI(kg/m ²)	25.35 ± 0.76	25.77 ± 0.60	0.58
LDL(mg%)	102.44 ± 3.56	105.83 ± 4.03	1.53
TG(mg%)	168.55 ± 11.99	191.14 ± 9.24	2.45
HBA1C(%)	7.24 ± 0.16	6.97 ± 0.11	0.14

Table-3: comparison of mean value of the patient variables amongst the group with and without LVDD.

dysfunction) and E/A <1(diastolic dysfunction). Table-3 shows comparison of mean of various variables in between these subgroups. (Table-3) It is evident that the two groups were significantly different with respect to gender ($P<0.001$). Female preponderance was observed in the group with diastolic dysfunction and two third of these ladies were postmenopausal. A significant difference in CIMT was also noted in these groups ($p<0.05$).

DISCUSSION

The study was conducted with the aim to verify role of CIMT in assessment of subclinical atherosclerosis and study the association with LVDD –earliest marker of cardiovascular involvement. So the study group constituted of randomly selected diabetic patients without cardiovascular symptoms, who had no evidence of any complication related to diabetes. Amongst 100 patients ranging 35-75 years; 23% were above 60 years and 60% were females. 22% patients were smokers and 18% were alcoholic. Increasing age, male gender, smoking, alcohol consumption, obesity, dyslipidemia, diabetes are responsible for augmenting CV risk factors in atherosclerosis.^{16,17} CIMT is a surrogate marker of cardiovascular risk. It is considered in clinical trials evaluating the efficacy of cardiovascular risk factor modification.^{1,3,4,16,17}

It is value increase with age, in young adults (age <45 year) value <1 should be considered abnormal.^{3,6,16} In present 28% had CIMT <1 where mean age was 51.64 years.

Subclinical LVDD was found in 30% asymptomatic diabetic patients in our study as noted by E/A ratio. The prevalence of subclinical/preclinical diastolic dysfunction was noted to be 54.33% in a similar case control study conducted over 5 years in 127 asymptomatic diabetics.¹⁷ The of 11% control had LVDD in the same study. LVDD was found to increase with duration of diabetes, Hb A1C and obesity indices. Boyer et al. observed LVDD in 75% asymptomatic, normotensive patients with type 2 diabetes. They also found that, TDI detected diastolic dysfunction more often than any other echocardiography parameter.¹⁸

Table-2 demonstrates highly significant difference amongst the values of CIMT and EA ratio in low probability and high probability of CV Risk group ($p<0.001$). There exist and inverse correlation between E/A ratio and CIMT values. Our finding were comparable with those of a large Chinese population based study on healthy subjects; where a positive correlation of CIMT significantly associated with lower E/A ratio; more so in women.¹⁹ Female preponderance was also noted in the diastolic dysfunction group of the present study (Table-3, gender $p<0.001$). Two third of these women were post menopausal; which is another risk factor of atherosclerosis.

Study limitations: It is a cross sectional study on 100 diabetics and there is no control group to compare the age related atherosclerosis occurring in healthy Individual. As atherosclerosis and diabetes are chronic continuous processes the longitudinal study (long term follow up study) is needed to study about risk factors and development of macro vascular complications.

CONCLUSION

A positive correlation exists between CIMT and low E/A

ratio. Hence CIMT can be used as simple non invasive tool for screening of subclinical atherosclerosis and diastolic dysfunction. CIMT increases with age and value more than 1 in young adults is associated with high CV risk. Females have higher CIMT value and post menopausal ladies are more prone to diastolic dysfunction. As atherosclerosis is a chronic continuous process, monitoring of CIMT is recommended to assess its progress over time. Further study of longer duration with age and sex matched controls is needed to exactly assess the diabetic control/obesity indices /CIMT as risk factor for cardiovascular and cerebrovascular events.

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