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Research Article

ARTERIAL STIFFNESS PROGRESSIVELY ASSOCIATED WITH DURATION OF TYPE 2 DIABETES MELLITUS IN OVERWEIGHT & OBESE MALE POPULATION OF WESTERN RAJASTHAN

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A B S T R A C T

Many studies show pathophysiological link between Type 2 Diabetes(T2DM), CardioVascular Diseases (CVD) and Arterial Stiffness. In this cross-section study 60 male Overweight, Obese adult patients of various durations of T2DM, 25to65 years age, of Western Rajasthan are examined for the arterial stiffness. Brachial-ankle Pulse Wave Velocities (BrAnkPWV) and carotid to femoral Pulse Wave Velocity (cfPWV) were taken as indices of central arterial stiffness. Brachial and ankle Arterial Stiffness Indexes (ASI) are taken as indices for corresponding local arterial stiffness. These parameters were measured by an automated oscillometric based device Periscope. Smokers and history of vascular diseases were excluded. Results stratified in groups of duration of T2DM, <5 years, 6to 10 years and >10years and compared. Regressions of PWVs and ASI on duration of T2DM were analysed unadjusted and adjusted for age, BMI and Blood Pressure. cfPWV, RBrAnkPWV & LBrAnkPWV are significantly higher in group of longer duration as compared to shorter duration($p<0.05$). All others are significantly higher in only >10 years of duration. cfPWV & LBrAnkPWV are moderately and remaining variables are mildly correlated with duration of T2DM. Study concluded that central arterial stiffness is moderately and Peripheral arterial stiffness mildly associated with duration of T2DM in studied population.

INTRODUCTION

Increased arterial stiffness is an important determinant of cardiovascular (CV) disease risk. (Meaume *et al*, 2001) Several epidemiological studies reported that increased arterial stiffness predicts mortality and morbidity, independently of other CV risk factor. (Mattace-Raso *et al*, 2006; Vlachopoulos *et al*, 2010) Arterial stiffness measured through carotid femoral Pulse wave velocity (PWV), a gold standard method has been associated with measures of subclinical CV disease (Zoungas *et al*, 2007). Furthermore clinical studies have shown that the arterial stiffness increases with aging or various pathological processes associated with hypertension, metabolic syndrome, chronic renal disease and diabetes. (Vaitkevicius *et al*, 1993; Stewart *et al*,2006; Whincup *et al*, 2005; Guerin *et al*, 2001; De Angelis *et al*, 2004)Diabetes is increasing rapidly in every part of world, to the extent that now it has been assumed epidemic proportions. (Shaw *et al*, 2010) In India, prevalence of type 2 Diabetes mellitus in urban and rural area is 18.67% and 9.21% respectively (Ramchandran *et al*, 2008) Over 30 million have now been diagnosed with diabetes in India. The estimate of actual number of diabetic in India is 40 million. This means that India actually has the highest number of diabetics of any one of country in the entire world. (Diabetes in India, 2017) There are an estimated 45 million patients of coronary artery disease in India. There are about 50.8 million patients of diabetes in India. India has been referred as "Diabetes Capital of the world". (Namrata *et al*, 2014) An abnormal metabolic state associated with DM promotes a number of alterations in arterial tree and subsequent vascular impairment may represent a patho-physiologic link between diabetes mellitus and cardiovascular disease. Arterial stiffness reflects changes in extracellular matrix in media layer. (Stehouwer *et al*, 2008) Increased arterial stiffness is associated with CV risk. (Laurent *et al*, 2006) Pulse wave velocity (PWV), Augmentation Index (AIx) and arterial stiffness index (ASI) are markers of arterial stiffness which are widely accepted and recommended from measure of arterial stiffness. (Laurent *et al*, 2006; Laurent *et al*, 2007) Various non invasive methods have developed to measure these parameters to detect arterial

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stiffness and quantify the risk of development of CVDs. PWV is a measure of regional arterial stiffness. CfPWV indicates the arterial stiffness in central arteries namely thoracic and abdominal aorta. An elevation in PWV indicates an increase in arterial stiffness or decrease in vascular compliance. ASI is a measure of local arterial stiffness. (Laurent *et al*, 2006) Ebtissam Zakaria *et al* suggest in their study in Egypt that PWV increased evidently earlier than clinical evident of atherosclerosis in diabetics. (Zakaria *et al*, 2013) Namrata BK *et al* in India have also suggested that longer duration of diabetics have increased PWV than recent diabetic individuals. (Namrata, 2014) In present study we compared PWV and ASI among diabetics of variable duration in adult male population of western Rajasthan, India.

METARIAL AND METHOD

60 T2DM suffering Male Participants of age 25 to 65 Years (50.38±9.08), natives and residents of Western Rajasthan, India were examined for Arterial Stiffness. Type 2 Diabetes mellitus was diagnosed as WHO recommendations. (Definition and diagnosis, 2006) Smokers and individual with history of any Vascular diseases such as peripheral arterial disease, Cardiovascular disorders, cerebro-vascular disorders, Renal Disease were excluded from study. History of duration of T2DM was recorded. Anthropometric data such as weight and height was were measured by calibrated electrical weighing Scale and Calibrated non stretchable measuring tape respectively.

BMI were calculated from Weight and Height of participants. Blood Glucose level is measured by Robonik automatic biochemical analyser in a biochemical laboratory. Participants with Fasting Blood Glucose level more than 126mg/dl with history of atleast 1 year of detection of type 2 DM were included in study. Only history of T2DM but spot fasting glucose level was less than 126mg/dl were not included in study. Indices of Arterial Stiffness is measured by Periscope (developed by Genesis Medical Systems, Hyderabad, India) based on Oscillometeric Technique in morning in fasting condition with 8 to 10 hours over night sound sleep. Periscope records arterial Blood pressure (BP) and arterial pressure Waveform, non invasively through Cuffs Wrapped on all four limbs. Simultaneously it records Electrocardiogram (ECG) by 4 limb leads. Time taken by pressure wave to reach limbs is calculated by time point recording of peak R Wave of ECG and of foot of arterial pressure Waveform. The system software of this device supports sophisticated digital signal-processing algorithm to calculate all the results. It calculates right and left brachial ankle PWV (RBrAnkPWV & LBrAnkPWV), carotid to femoral PWV (cfPWV), Arterial Stiffness Index (ASI), Ankle Brachial Index (ABI) & Augmentation Index (AIx). Participants were asked to refrain from drinking caffeine containing beverages 12 hrs before the test. They were also informed not to speak or sleep during the procedure. All subjects were explained about the procedure to be undertaken and written consent was obtained from all the subjects prior to the study.

Results obtained from the Participants were then statistically analyzed using Data Analysis ToolPak in Microsoft Excel. Data are stratified in 3 groups of durations of T2DM. Mean and standard deviation (SD) were calculated for all the parametric variables. Associations between durations of T2DM and indices of arterial stiffness were assessed with Pearson correlation coefficient. Partial correlation coefficient derived by an online programme StatTools: Multiple Regression Program (Home O&G, 2017) Comparison of data among groups was done using student-'t' test. The p value of less than 0.05 was considered as statistically significant.

RESULT AND DISCUSSION

Table 1 gives the Mean±SD of variables in 3 groups according to duration of T2DM and significance level of mean differences between groups. Age and BMI of the all 3 groups are not significantly different. It was observed that mean difference of systolic blood pressure (SBP), diastolic blood pressure (DBP), RBrAnkPWV, right brachial ASI (R Br ASI), left brachial ASI (L Br ASI), right ankle ASI (R Ank ASI) and left ankle ASI (L Ank ASI) when compared between 1-5 and 6-10 years group were not significant statistically (p value >0.05), but differences were significant when compared in group of 6-10 years and 11-15 years as well as in group of 1-5 and 11-15 years. (p value <0.05) whereas RBrAnkPWV and cfPWV were different significant statistically when compared between group of 1-5 and 6-10 years, 6-10 to 11-15 years, and 1-5 and 11-15 years (p value <0.05). Br Ank PWV and cfPWV were measures of generalized and central arterial stiffness. Brachial and ankle ASI were measure of peripheral local arterial stiffness. (Laurent *et al*, 2006) Present study suggested generalized and central arterial stiffness were increased earlier with duration of T2DM and later peripheral local arterial stiffness also elevated gradually with T2DM. Hypertension, a independent factor for increased arterial stiffness, also elevated with T2DM with longer duration. Same results were suggested in study performed by Namarat *et al* (2014) on 144 adults. But De Oliveira R *et al* suggested no significant rise in cfPWV in Diabetics as compare to normal control subjects in a 5 year follow-up study. (De Oliveira *et al*, 2013)

Table 2 shows the association between indices of arterial stiffness and duration of T2DM. PWVs are moderately associated with duration of T2DM (r>4, p<0.001) whereas ASI mild to moderately associated with duration of T2DM (r =2 to 6, p<0.001) unadjusted. In a multivariate model, when adjusted with age, BMI, SBP and DBP, partial correlation coefficients (pCor) were 0.64, 0.43 and 0.57 of LBrAnkPWV, cfPWV and R Br ASI respectively with duration of T2DM (p<0.001). It is suggested, in present study, Central arterial stiffness is more associated with duration of T2DM than peripheral arterial stiffness. Ebtissan Zakaria *et al* and Toshiaki Kakibe *et al* also suggested the same result as duration of T2DM is associated with cfPWV. (Zakaria *et al*, 2013; Ha BK *et al*, 2012) In a study Hideaki Sato *et al*. suggested that ASI is associated with Hypertension and longer duration of T2DM. (Sato H *et al*, 2005). The growth promoting activity of insulin is enhanced due to supra-physiological level of insulin in insulin resistance in T2DM. It causes the smooth muscle cell proliferation of vasculature. (Cusi K *et al*, 2000) As well as the persistent hyperglycemic condition in T2DM causes non enzymatic glycation of proteins with covalent cross-linking of collagen of tunica media of vasculature. (Brownlee *et al*, 1988) Thus It is progressively increasing in smooth muscle cell tone and rigidity due to collagen cross-linking gradually may raise the arterial stiffness more with longer duration of T2DM.

Table 1 Mean±SD and significance level of differences of various parameters in 3 groups of Duration of T2DM

Parameters	1-5 yrs(n=28) Mean±SD	6-10 yrs (n=16) Mean±SD	11-15 yrs (n=16) Mean±SD	Significance* *a*	*b*	*c*
Age (yrs)	48.57±10.09	50.75±9.28	53.19±6.38	NS	NS	NS
BMI(kg/m^2)	28.47±4.80	27.31±4.98	28.30±5.67	NS	NS	NS
SBP (mm Hg)	137.21±18.08	138.31±17.91	163.31±22.29	NS	S	S
DBP (mm Hg)	85.43±11.07	84.88±9.67	95.25±10.34	NS	S	S
RBrAnkPWV (Cm/Sec)	1590.18±244.42	1698.65±317.55	2348.20±1011.11	NS	S	S
LBrAnkPWV (Cm/Sec)	1323.7±232.42	1489.26±185.32	1743.21±227.68	S	S	S
cfPWV (Cm/Sec)	968.50±171.86	1094.18±181.27	1471.31±466.50	S	S	S
R Br ASI (mmHg)	29.13±6.59	31.71±10.05	45.28±10.09	NS	S	S
L Br ASI (mmHg)	30.48±9.17	30.47±11.68	41.82±10.60	NS	S	S
R Ank ASI (mmHg)	42.26±8.07	42.28±11.33	55.91±10.10	NS	S	S
L Ank ASI (mmHg)	39.99±13.30	38.48±12.65	51.07±19.73	NS	S	S

SD = Standard Deviation, BMI = Body Mas Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, R = Right, L= Left, Br = Brachial, Ank = Ankle, PWV = Pulse Wave Velocity, ASI = Arterial Atiffness Index, S = Significant, NS = Not Significant.
a = significance level between 1-5 yrs duration group and 6-10 yrs duration group
b = significance level between 6-10 yrs duration group and 11-15 yrs duration group
c = significance level between 1-5 yrs duration group and 11-15 yrs duration group
* = by student 't' test, considering p <0.05 as significant

Table 2 Unadjusted pearson's correlation coefficient (r) and partial correlation coefficient (pCor) adjusted with age, BMI, SBP and DBP between various arterial stiffness indices and duration of T2DM

Parameters	Pearson's correlation coefficient (unadjusted)		partial correlation coefficient (Adjusted)	
	Pearson's r	p Value	pCor	p Value
RBrAnkPWV (Cm/Sec)	0.47	<0.001	0.2	0.104
LBrAnkPWV (Cm/Sec)	0.69	<0.001	0.64	<0.001
cfPWV (Cm/Sec)	0.61	<0.001	0.43	<0.001
R Br ASI (mmHg)	0.6	<0.001	0.57	<0.001
L Br ASI (mmHg)	0.39	0.001	0.16	0.23
R Ank ASI (mmHg)	0.49	<0.001	0.29	0.03
L Ank ASI (mmHg)	0.27	0.02	0.2	0.13

BMI = Body Mas Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, R = Right, L= Left, Br = Brachial, Ank = Ankle, PWV = Pulse Wave Velocity, ASI = Arterial Atiffness Index, pCor = Partial Correlation

CONCLUSION

It is concluded in this study that arteries were stiffer in obese patients who have longer duration history of T2DM as compare to same age, BMI patients of shorter duration of T2DM in Western Rajasthan. Arterial Stiffness and Blood Pressure increased rapidly after 10 years duration of T2DM. Elastic properties of Central arteries were affected more than peripheral arteries.

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