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Sonographic Intima-Media Thickness Evaluation of Common Carotid and Internal Carotid Arteries in Type-2 Diabetes Mellitus

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Intima-media thickness (IMT) is a useful marker in early detection of atherosclerotic lesions in carotid arteries in Type-2 Diabetes Mellitus (T2DM) patients. The study was conducted to determine the association of IMT with various physical and biochemical parameters in the Indian population. To compare IMT of common and internal carotid arteries in T2DM patients and healthy individuals and study the correlation of IMT with physical and biochemical parameters. Case group with T2DM (n=27) were matched with Control group consisting of healthy individuals (n=27) of similar age and sex were included. Physical parameters and routine biochemical data were collected and compared. Ultrasonographical imaging of the common and internal carotid arteries of both sides were performed presence of plaque was observed. Data was analyzed by software IBM® SPSS Statistics V20.0. For all analyses, P<0.05 was considered as statistically significant. Mean IMT value obtained in case and control group are 0.711±0.14 mm and 0.601±0.16 mm respectively (P=0.005). Presence of plaque was noticed in 37.03% subjects in case group and in 14.81% subjects in control group. Mean IMT was significantly higher for smoker than non-smokers (P=0.004). Fasting blood sugar, postprandial blood sugar, Postprandial triglycerides and total cholesterol were significantly higher in case group (P<0.05). There was a strong family history of T2DM in case group (51.85%) compared to control group (14.81%) with a statistical significance between them (P=0.009). IMT of common and internal carotid arteries have a significant association in T2DM patients compared to healthy subjects and IMT is significantly associated with physical and biochemical parameters.

Keywords: Atherosclerosis; Body mass index; : Carotid intima-media thickness; Smokers; Type 2 Diabetes Mellitus.

Type-2 Diabetes Mellitus (T2DM) is known to be associated with increased prevalence of cardiovascular diseases (CVD) and atherosclerosis.[1] T2DM acts as an independent risk factor for development of stroke in 37 to 42% of the patients, particular among those under 65 years of age.[2] Risk factors such as older age, increased body mass index (BMI), diabetes and hypertension have been associated with development of future atherosclerotic events.[3] These risk factors vary with different population and ethnicity. Furthermore, it has been shown that different patients with comparable symptoms of hyperglycemia have different microvascular problems and these findings suggest that genetic differences have a significant impact.[4]

Atherosclerosis in carotid and coronary arteries in particular are the most common

complications of patients with T2DM. In diabetic patients, one of the methods to detect the intima-media carotid changes and histological differences is by ultrasonography. Ultrasonography is a non-invasive and accurate imaging technique to evaluate IMT in carotid arteries.[5] Visualisation of Intima-media thickness using ultrasonography is useful in studying the development of atherosclerotic lesions and CVD in carotid and peripheral arteries.[6] IMT of carotid arteries has been used as a surrogate marker of early atherosclerotic activity and according to a recent review, IMT has also been shown to be a strong predictor of CVD like stroke and myocardial infarction.[7]

There is scarcity of literature regarding the IMT of carotid arteries in T2DM in Indian population. Since, the IMT value can vary with different ethnicities, this study was undertaken to add more information to the existing literature about IMT in Indian T2DM patients. The aim of this study is to evaluate and compare the IMT of common and internal carotid arteries in T2DM patients and in age and sex matched healthy individuals and study the correlation of IMT with physical and biochemical parameters.

METHODOLOGY

Study design

This observational case control study was conducted over a duration of one year from Jun 2017 to Aug 2018. The ethical approval was obtained from the Institutional Ethical Committee. The patients fulfilling the selection criteria were recruited after obtaining the informed consent. A sample size of 50 patients were required to detect the difference between the groups, with significance level of 95% and desired precision of 18%. However, the final sample size was made up to '54' subjects (T2DM: 27 and Controls :27) considering the availability of cases.

Selection criteria

The patients with T2DM (both newly diagnosed and old cases) aged more than 25 years belonging to both sexes and healthy individuals of similar age and sex matched with the patients were included in this study. These patients were divided into two groups i.e. cases with T2DM (n=27) and controls consisting of healthy individuals (n=27). Those patients with Type-1 Diabetes Mellitus, uncontrolled T2DM and on treatment with lipid lowering agents were excluded.

Data collection

A predesigned structured proforma was used to collect the demographic data and a brief history of the patients regarding medical history, family history of T2DM, duration of diabetes in the case group, history of smoking and/or alcoholism (>10 years). Physical parameters like BMI, blood pressure and routine biochemical data like fasting blood sugar (FBS), postprandial blood sugar (PPBS), fasting triglycerides (FTG), PPTG, total cholesterol (TC), HDL, very low density lipoprotein (VLDL) and LDL were collected and compared in both groups. The presence of plaque was obtained from the sonographic evaluation of the carotid artery.

Ultrasonographic assessment of IMT of the carotid artery

The ultrasonographical imaging of the common and internal carotid arteries of both sides were performed with a high frequency pulse-wave Doppler ultrasonography fitted with a linear array transducer (11 MHz). The patients were examined in supine position with the examiner seated near the patient's head. Patient's head was tilted away from the side being examined to facilitate neck exposure. Two parallel echogenic lines separated by an anechoic space at levels of the artery wall, generated by the lumen-intima and media adventitial interfaces were visualized with this method. The distance measured between these two lines gives the index of the thickness of the intimal-media complex.[8] The examination of IMT of common and internal carotid artery was done ~1 cm of the carotid bulb from the plaque-free segment.

The IMT values are classified and measured as below:

1. IMT near wall of Right Common Carotid Artery (RCN)
2. IMT far wall of Right Common Carotid Artery (RCF)
3. IMT near wall of Right Internal carotid artery. (RIN)
4. IMT far wall of Right Internal carotid artery. (RIF)
5. IMT near wall of Left Common carotid artery. (LCN)
6. IMT far wall of Left Common carotid artery. (LCF)
7. IMT near wall of Left Internal carotid artery. (LIN)
8. IMT far wall of Left Internal carotid artery. (LIF)

The mean of the above eight classification was calculated and defined as the mean IMT value.

Statistical analysis

Data were tabulated in Microsoft Excel Spreadsheet and analyzed by software IBM

SPSS Statistics V20.0. Pearson's correlation coefficient (r), Proportion test, Unpaired t-test and Kolmogorov Smirnov test were used to determine the significance. For all the analysis, P<0.05 was considered as statistically significant.

RESULTS

Ultrasonographic evaluation of carotid arteries was conducted on all the 54 subjects. Mean age of case group was 56.62±10.78 years and control group was 45.51±12.39 years (*P*<0.05 Unpaired t-test). There was equal distribution of males and females in both groups. There were more subjects with mixed diet in the control group (81.48%) than the case group. Most subjects in case and control groups do not smoke (81.48% and 81.48%) or consume alcohol (81.48% and 92.59%). There was a strong familial history of diabetes mellitus in the case group (51.85%) compared to control group (14.81%) with a significance difference between them (*P*=0.009; Proportion test). Most cases had a duration of Type 2 diabetes mellitus less than 10 years (62.96%) (Table 1).

The mean BMI in both groups were similar. Mean value of sBP was significantly higher in the case group (*P*<0.05). Similarly, FBS and PPBS were significantly higher in the case group (*P*<0.05). PPTG and TC were also significantly higher in the case group (*P*<0.05) (Table 2).

The mean IMT value obtained in case and control groups are 0.711±0.14 mm and 0.601±0.16 mm, respectively. There was a significant difference between the mean IMT in case and control groups (*P*=0.005 Unpaired t-test). The presence of plaque was noticed in 10 subjects (37.03%) in case group and in 4 subjects (14.81%) in control group. This difference is not statistically significant (*P*=0.12; Proportion test).

The mean IMT (0.84±0.18 mm) for smoker was significantly higher than in non-smoker (0.68±0.12 mm) in the case group. There was statistical significance between the mean IMT in smokers and non-smokers (*P*<0.05). With respect to consumption of alcohol, there was no statistical difference between the mean IMT and alcoholic and non-alcoholics in both groups (*P*=0.112). The mean IMT value was found to be less in patients with diabetes less than 10 years (0.69±0.14 mm) than in patients with diabetes of more than 10 years (0.7362±0.1453 mm). There was no significant association found between the mean IMT value and the duration of diabetes (*P*=0.239)

A positive correlation was found between the mean IMT and sBP and dBP in both case and control groups with statistical significance (*P* <0.05) (Table 3).

DISCUSSION

The purpose of the study was to assess and compare the carotid IMT in Type 2 Diabetes Mellitus in Indian population and to correlate IMT with physical and biochemical parameters. The mean IMT value found in diabetic patients is higher than healthy individuals in this study which is in agreement with previous studies who also found that IMT was higher in the diabetic group.[9] This could be due to hyperglycemia which is associated with thickening of the intima-media and can accelerate the progression of atherosclerosis and other CVD through several mechanisms.[10] There was a greater number of plaque present in the case group compared to control group. Similarly, Kwon et al. observed that presence of plaque was mostly seen in the diabetic group.[11] The IMT was significantly higher in smokers compared to non-smokers. There is evidence that smoking is associated with impaired endothelial dysfunction, stiffening of arteries and thickening of intima-media.[12,13]

The patients with longer duration of diabetes (>10 years) were found to have higher IMT. This is simply due to longer effect of hyperglycemia on the intima-media.[14] Taniwaki et al. have indicated that age, increased TC, low HDL and longer duration of diabetes were independent risk factors for increase in the IMT in diabetes mellitus.[14] The BMI was higher in cases with diabetes than healthy subjects, as obesity is associated with diabetes mellitus. Oren et al. has indicated that higher BMI is associated with greater mean IMT value.[15] There was a strong positive family history of diabetes mellitus in most patients in case group. A study has demonstrated that genetic disposition of diabetes mellitus along with long standing hyperglycemia may accelerate the progression of atherosclerosis.[14]

Higher level of TC was observed in case group in this study. Yamasaki et al. have

established that TC was strongly associated with the progression of thickening of intima-media.[16] A study by Agarwal et al. showed that triglycerides strongly predict the increase in IMT of carotid arteries.[17] PPTG was significantly higher in diabetic patients. PPTG is known to be an independent risk factor for thickening of carotid intima-media.[18] The HDL level was comparably similar in both groups. An inverse relationship between the HDL and IMT was observed by Davidson et al., who found a negative correlation between the HDL and IMT.[19] However, we found a nonsignificant but positive correlation in the current study, whereas HDL prevents atherosclerosis by inhibiting cytokine-induced endothelial cell adhesion in the blood vessels.[20]

The study showed that there is a good correlation between sBP and IMT in case group, which is in accordance with Wang et al. who also reported a correlation between the sBP nd IMT.[21] A study reported that higher sBP is associated with severe thickening of carotid IMT.[22] The mean age in this study is comparable to Agarwal et al., where mean age was reported to be 59.78±8.81 years.[17]

Hence, the present study showed that increased IMT levels is significantly associated with T2DM and traditional risk factors such as BMI, hypertension, smoking, increased lipid profile and longer duration of diabetes have been shown to have statistical association with IMT of CICA. Meanwhile, the higher levels can be of a predictive marker. But,the study beholds certain limitation like having limited sample size. In the future, performing the study on higher sample size as a multi-centred study will be highly beneficial and may be useful in providing new insights regarding the disease.

Table 1. Demographic data and Medical history

Variable	Case group (%)	Control group (%)
Gender		
Male	11 (40.74)	11 (40.74)
Female	16 (59.26)	16 (59.26)
Diet		
Mixed	15 (40.74)	22 (81.48)
Veg	12 (59.26)	5 (18.52)
Smoking		
Yes	5 (18.52)	5 (18.52)
No	22 (81.48)	22 (81.48)
Alcohol		
Yes	5 (18.52)	2 (7.41)
No	22 (81.48)	25 (92.59)
Family history of DM		
Yes	14 (51.85)	4 (14.81)
No	13 (41.15)	23 (85.18)
Duration of Diabetes (years)		
<10	17 (62.96)	NA
11-20	8 (29.63)	
>21	2 (7.41)	

NA: Not applicable

Table 2. Physical and biochemical parameters

Parameters	Case group Mean±SD	Control group Mean±SD	*P* value
BMI (Kg/m^2)	26.37± 4.63	24.82±2.78	0.141*
sBP (mmHg)	140.7± 11.20	126±7.01	<0.05#
dBP (mmHg)	86.52±4.76	84.74±5.58	0.212*
FBS (mg/dl)	155.93±47.90	95.04±15.66	<0.05*
PPBS (mg/dl)	211.78±61.52	103.11±24.45	<0.05*
FTG (mg/dl)	160.78±46.40	143.70±50.30	0.2*
PPTG (mg/dl)	203.89±50.21	165.22±3.95	<0.05*
HDL (mg/dl)	41.40±6.24	40.52±3.95	0.538#
LDL (mg/dl)	121.41±37.68	132.85±20.80	0.173*
VLDL (mg/dl)	35.55±9.54	30.67±9.74	0.068*
TC (mg/dl)	178.67±26.74	206.11±26.62	<0.05*

FBS: Fasting blood sugar; PPBS: Postprandial blood sugar; FTG: Fasting triglyceride; PPTG: Postprandial triglyceride, HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; TC: Total cholesterol; *: Unpaired t test; #: Kolmogorov Smirnov test

Table 3. Correlation of physical and biochemical parameters with IMT

Parameters	Case Group		Control Group	
	Correlation (r)	P value	Correlation (r)	P value
Age	0.3585	0.066	0.3664	0.06
BMI	0.0567	0.778	0.1923	0.336
sBP	0.5052	0.007	0.544	0.003
dBP	0.5781	0.001	0.65	<0.05
FBS	0.1539	0.443	-0.1105	0.582
FTG	-0.0839	0.677	0.158	0.431
PPBS	0.1995	0.318	0.1094	0.586
PPTG	0.1212	0.546	0.0435	0.829
HDL	0.0456	0.82	0.1627	0.417
VLDL	0.0961	0.633	-0.0215	0.915
LDL	-0.0357	0.859	0.0734	0.715
Duration of diabetes	0.0706	0.726	NA	NA

BMI: Body mass index; sBP: Systolic blood pressure; dBP: Diabtolic blood pressure; FBS: Fasting blood sugar; FTG: Fasting triglyceride; PPBS: Postprandial blood sugar; PPTG: Postprandial triglyceride, TC: Total cholesterol; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; NA: Not applicable; r: Pearson's correlation coefficient

CONCLUSION

The study has shown that IMT of common and internal carotid arteries have a significant association in patients with Type 2 Diabetes Mellitus compared to healthy subjects and IMT is significantly associated with physical and biochemical parameters.

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