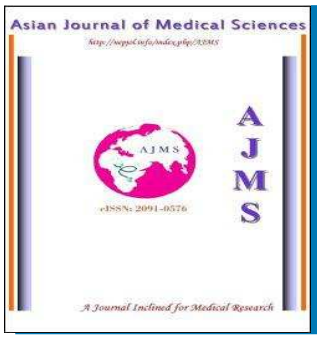

COMMON CAROTID ARTERY INTIMA-MEDIA THICKNESS REFLECTS THE CUMMULATIVE BURDEN OF ATHEROSCLEROSIS AND PREDICTED WELL BY TOTAL-C/HDL-C RATIO IN TYPE-II DIABETIC PATIENTS- A CASE CONTROLLED STUDY BASED FROM KOLKATA, INDIA

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"Common Carotid artery intima-media thickness reflects the cumulative burden of atherosclerosis which is significantly correlated with serum lipid variables in the patients attending at Medicine Department at NRS Medical College."

ABSTRACT

Background: Diabetes Mellitus (DM) is frequently associated with the development of premature atherosclerotic vascular disease and is the major cause of morbidity and mortality. Approximately 80% of all deaths and more than 75% of all hospitalizations are due to CAD. Individuals with DM are usually associated with accelerated atherosclerosis. Common Carotid artery intima-media thickness (CCAIMT) is now also considered as a surrogate marker of atherosclerosis.

Materials and Methods:
This case-control study was conducted from Jan, 2011 to June, 2012 among Type-II diabetes, aged between 30-80yrs. Patients with Type-I diabetes, aged <30yrs or >80yrs and other secondary causes of diabetes, hypertensive, smokers and patients under therapy with lipid lowering drugs were excluded from this study. The biochemical tests were done in the department of Biochemistry, Nilratan Sarkar Medical College and Hospital, using standardized reagent kits. CCAIMT was measured by high resolution imaging using 10MHz transducer in the department of Radiodiagnosis, Nilratan Sarkar Medical College and Hospital.

Results: The results of our study indicate that dyslipidemic diabetic patients had significantly higher blood glucose at any phase along with glycated haemoglobin compared to controls. The lipid variables were also significantly higher in the diabetes patients with dyslipidemia compared to controls except HDL levels were significantly higher in control. CCAIMT was higher in the dyslipidemic group (1.71 ± 0.57mm) compared to the non-dyslipidemic group (0.77 ± 0.10) which was statistically significant (p value <0.001).

Conclusion: CCAIMT reflects the cumulative burden of atherosclerosis and is highly correlated and predicted well by Total-C/HDL-C ratio in Type-II diabetic patients. So it is advised that a direct examination of the vessel wall is extremely essential for early detection of the affected individuals so that the cost burden in Intensive coronary care unit can be minimized and also the individual can be advised to control the extensive dyslipidemia through dietary restrictions and exercise.

Key Words: Diabetes Mellitus, Dyslipidemia, Glycated hemoglobin, Common Carotid Artery Intima-Media thickness, Kolkata.

INTRODUCTION

Diabetes Mellitus (DM) is frequently associated with the development of premature atherosclerotic vascular disease.[1] Patients with DM, cardiovascular disease is the major cause of morbidity and mortality.[2] Approximately 80% of all deaths and more than 75% of all hospitalizations in patients with diabetes are due to CAD.[3] In addition to coronary artery disease, cerebrovascular disease (CVD) is also increased in individuals with DM (threefold increase in stroke).[4] Individuals with DM are usually associated with accelerated atherosclerosis.[5] Unless in a severe form, atherosclerosis, is often asymptomatic and contributed by several risk factors for its progression including dyslipidemia. [6] The use of carotid ultrasound remains an attractive, non-invasive method to monitor atherosclerotic disease progression in patients with type 2 diabetes.[7] Carotid intima-media thickness is now also considered as a surrogate marker of atherosclerosis.[8]

Several studies have been conducted earlier in this direction which correlated well with different atherosclerotic risk factors including different lipid parameters like total cholesterol, triglyceride, low density lipoprotein (LDL), high density lipoprotein (HDL) levels and LDL: HDL ratio.

With the above background the aim of the current study was to pinpoint out if at all there is any correlation among the common carotid artery intima-media thickness and some common risk factors including total cholesterol and HDL-cholesterol ratio (Total-C/HDL-C ratio) in patients of Type-II diabetes mellitus among patients attending at NRS Medical College and Hospital.

MATERIALS AND METHODS

This case-control study was conducted from Jan, 2011 to June, 2012 among the patients suffering from Type-II diabetes in the Department of Medicine, Nilratan Sarkar Medical College and Hospital. Patients with Type-II diabetes, aged between 30-80yrs were included following American Diabetes Association (ADA) 2010 criteria for diabetes. Patients with Type-I diabetes, aged <30yrs or >80yrs and other secondary causes of diabetes, hypertensive, smokers and patients under therapy with lipid lowering drugs were excluded from this study. Blood samples were collected from the patients with informed consents after obtaining clearance by the institutional ethics committee. The biochemical parameters including lipid profile, blood glucose levels, HbA_1C were estimated in the department of Biochemistry, Nilratan Sarkar Medical College and Hospital, using standardized reagent kits. CCAIMT was measured by high resolution imaging using 10MHz transducer in the department of Radiodiagnosis, Nilratan Sarkar Medical College and Hospital.

The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS AND DISCUSSION

The results of different clinical and biochemical parameters of the study subjects is shown in Table 1.

The results of our study indicates that the diabetes patients with dyslipidemia had significantly higher fasting blood glucose (158.22 ± 22.15 mg/dl) and post prandial blood glucose levels (226.52 ± 38.89 mg/dl) compared to the patients without diabetes associated with dyslipidemia (FBS 129.23 ± 20.34mg/dl and PPBS 198.29 ± 30.2 mg/dl respectively). Similar to the current findings, reports have been published earlier.[9] The HbA_1C levels were also found significantly higher in the dyslipidemic patients (8.01 ± 0.88 %) compared to non-dyslipidemic subjects (6.53±0.38). HbA1c levels has also been correlated previously with dyslipidemia.[10] In our study TC, TG, LDL, VLDL were significantly higher in the diabetes patients suffering from dyslipidemia (230.49 ± 51.82 mg/dl, 177.07 ± 50.84 mg/dl, 158.60 ± 45.56 mg/dl and 35.36 ± 10.20 mg/dl respectively) compared to controls (167.62 ± 7.30 mg/dl, 137.81 ± 6.24 mg/dl, 91.86 ± 3.89 mg/dl and 27.69 ± 1.47mg/dl respectively) and HDL levels were significantly higher(49.07± 4.47) in later group than the former group (33.18 ± 4.55).

On further analysis both LDL/HDL and TC/HDL were significantly higher in the dyslipidemic group (4.35 ± 1.38 and 6.78 ± 1.79 respectively) compared to the non-dyslipidemic group (1.91 ± 0.18 and 3.33± 0.24 respectively).

CCAIMT was higher in the dyslipidemic group (1.71 ± 0.57mm) compared to the non-dyslipidemic group (0.77± 0.10) which was statistically significant (p value<0.001) as shown in figure 1.

In a study conducted by Mohan.V et al. on intima-medial thickness of carotid artery in the South Indian diabetic versus non-diabetic subjects, it was reported that the mean intima-medial thickness in diabetic subjects were significantly higher compared to healthy controls. [11]

In the current study there was a significant correlation between CCAIMT and TC, TG, LDL, VLDL ($p< 0.001$ for all). It was also seen that CCAIMT increased with increase in the TC, TG, LDL, VLDL levels [12] with correlation coefficient r= 0.759, 0.652, 0.754 & 0.644 respectively. It was observed that CCAIMT was more significantly correlated with TC & LDL than with TG & VLDL(r= 0.759, 0.754 versus 0.652, 0.644 respectively). This finding has been reported for the first time in Nilratan Sarkar Medical College and Hospital.

The current study also observed a significant negative correlation between CCAIMT and HDL levels ($p <0.001$). It was also observed that CCAIMT was inversely proportional to HDL levels with correlation coefficient r= - 0.730. It was noticed that CCAIMT was more significantly correlated with HDL than with TG and VLDL(r= -0.759 versus 0.652, 0.644 respectively).

Also very significant positive correlation between CCAIMT and HbA_1C ($p <0.001$) in the present study was observed. The glycated hemoglobin also correlated positively with the CCAIMT with correlation coefficient r = 0.811 as shown in figure2.

In the current study, a very significant correlation between CCAIMT and LDL/HDL & TC/HDL levels ($p <0.001$ for both) was also observed. CCAIMT also well correlated with increasingly higher values of LDL/HDL and TC/HDL with correlation coefficient r= 0.835 and 0.867 respectively. Therefore it was noticed that CCAIMT was more significantly correlated with LDL/HDL and TC/HDL than with individual values of TC, TG, LDL, VLDL&HDL (r= 0.835, 0.867 versus 0.759, 0.652, 0.754, 0.644, -0.730 respectively) as shown in figures 3 and 4.

In a study conducted and reported by Mika Enomoto, et al [13] after adjusting for age, sex, BMI, and smoking habits, multiple linear regression analysis showed significant relationships between IMT and total cholesterol ($p< 0.05$), HDL-C ($p < 0.001$; inversely), LDL-C ($p < 0.001$) and LDL-C/HDL-C ratio($p < 0.0001$). This was the first epidemiological report in a community cohort to show that LDL-C/HDL-C ratio is a better predictor of carotid IMT progression than HDL-C or LDL-C alone. The finding is similar to the current study.

In another study conducted by Kumar, et al [14,15,16,17] also observed that TC, TC/HDL-C ratio, TG, LDL-C, LDL-C/HDL-C ratio were higher in MI patients ($p<0.001$). HDL-C concentration was significantly lower in MI patients than controls ($p<0.001$). Higher ratio of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C was observed in acute myocardial infarct patients as compared with controls.

In a study done by Haraki T.et al it was observed that by univariate analysis, CCA-IMT was positively correlated with age ($r=0.51$, $p < 0.01$), LDL-c/HDL-c ratio ($r=0.37$, $p<0.01$), triglycerides ($r=0.23$, $p < 0.05$), and negatively correlated with HDL-cholesterol ($r=-0.31$,$p< 0.01$).[18] Our findings are very similar to the findings of Haraki et al, [15] excepting for the age. In a study done by Nagasaki T, et al. [19] it was observed that CCAIMT change was closely associated with basal levels of total cholesterol ($r = 0.472$, $p= 0.0031$), low-density lipoprotein (LDL) cholesterol ($r = 0.441$, $p= 0.0076$) and the total/HDL cholesterol ratio ($r = 0.435$, $p= 0.0057$)[55] which is similar to the current study.

In a nutshell, the current study based on the population of Kolkata, we ascertain that the total cholesterol/HDL-c ration is also increased in our population, which is the new finding in this region, as no such reports have been documented previously. It is always better to check the carotid intima thickness as it is due to cumulative effects of disarranged lipid profile in subjects, so that proper prognostic measurements can be taken before hand to avoid the risk of cardiovascular diseases.

CONCLUSION

Even though the sample size is small, but our study revealed that CCAIMT reflects the cumulative burden of atherosclerosis and is highly correlated and predicted well by Total-C/HDL-C Ratio in type-2 diabetic patients. So it is advised that a direct examination of the vessel wall is extremely essential for early detection of the affected individuals so that the cost burden in Intensive coronary care unit can be minimised and also the

Table 1: Clinical and Biochemical Parameters of Study Subjects

Parameters	With dyslipidemia *(n=30)*	Without dyslipidemia *(n=35)*	P Value
Sex (Male/Female)	16/14	20/15	
BMI (kg/m^2)	25.51± 1.35	26.04 ± 1.98	NS
Age (years)	49.13 ± 7.18	51.55 ±4.84	NS
FBS(mg/dl)	129.23± 20.34	158.22 ± 22.15	<0.001
PPBS (mg/dl)	198.29 ± 30.2	226.52 ± 38.89	<0.001
HbA1C (%)	6.53 ± 0.38	8.01 ± 0.88	<0.001
Total Cholesterol (mg/dl)	167.62 ± 7.30	226.71 ± 54.78	<0.001
Triglycerides (mg/dl)	137.81 ± 6.24	177.07 ± 50.84	<0.001
HDL-c (mg/dl)	49.07 ± 4.47	33.18 ± 4.55	<0.001
LDL-c (mg/dl)	91.86 ±3.89	158.60 ± 45.56	<0.001
VLDL (mg/dl)	27.69 ± 1.47	35.36 ± 10.26	<0.001
LDL/HDL ratio	1.91 ± 0.18	4.35 ± 1.51	<0.001
TC/HDL	3.33 ± 0.24	6.30 ± 1.95	<0.001
CCAIMT (mm)	0.77 ± 0.10	1.71 ± 0.57	<0.001

Figure 1: Association of CCAIMT(mm) with Group

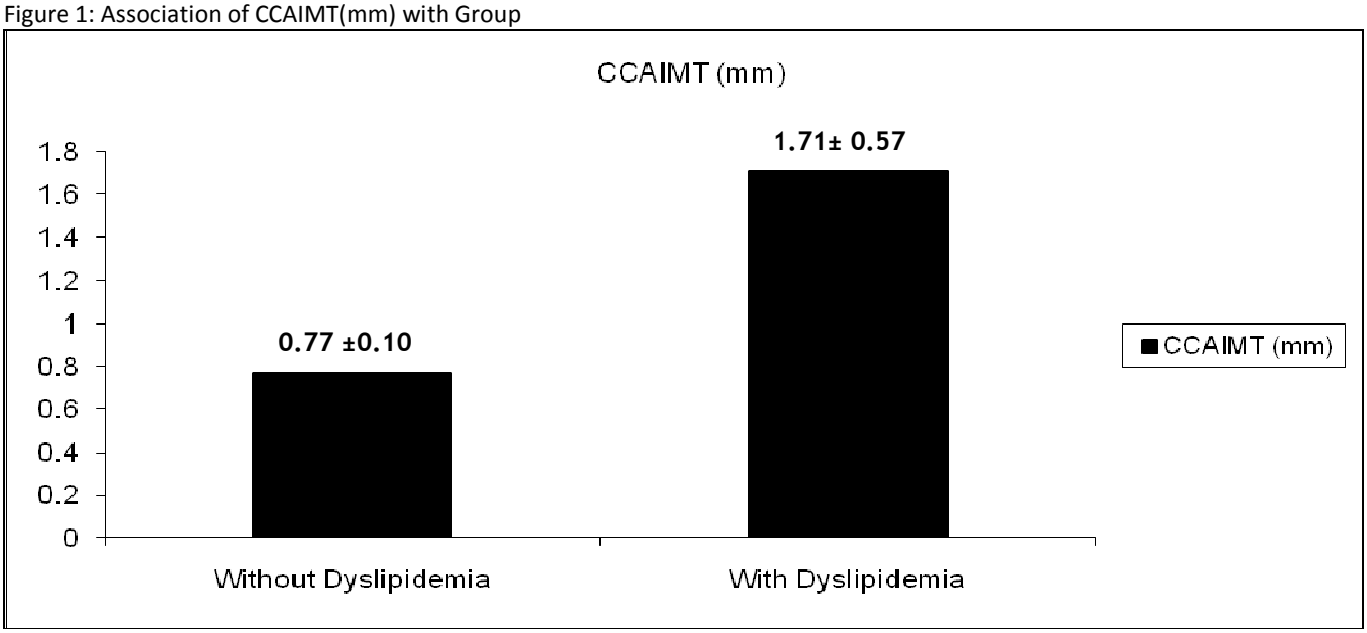
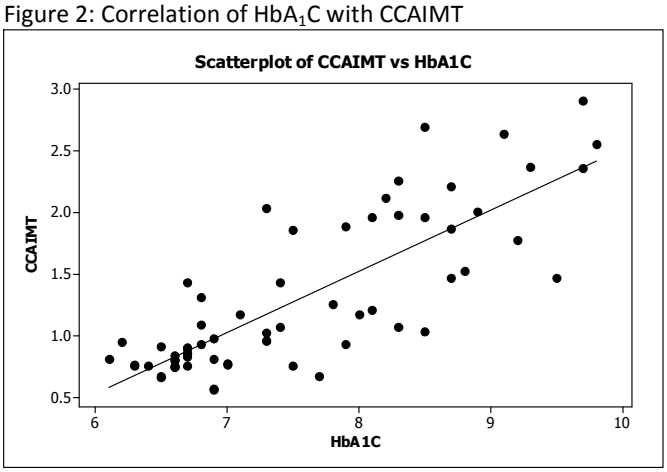
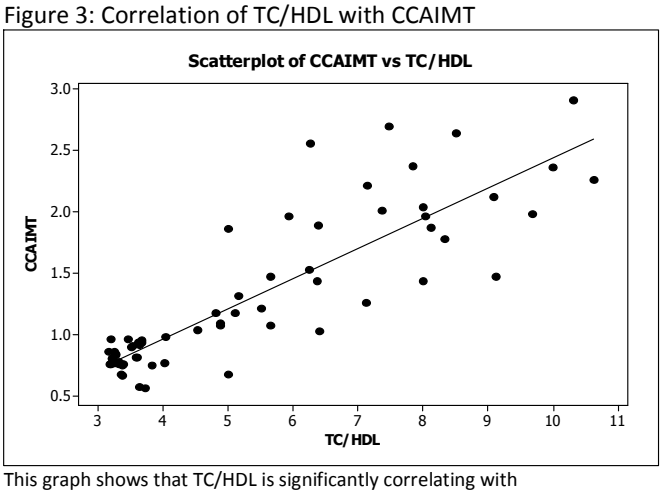


Figure 2: Correlation of HbA_1C with CCAIMT



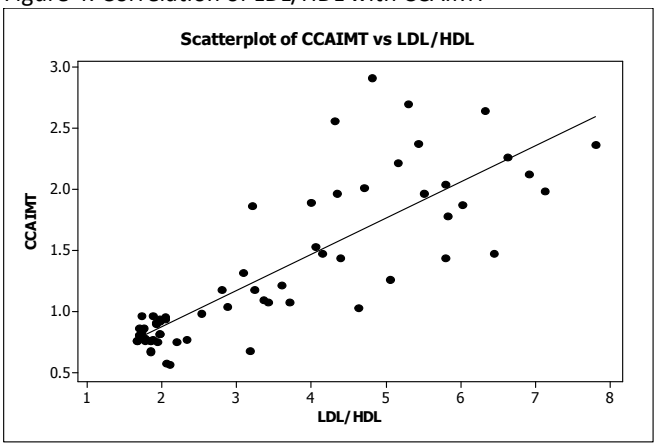
This graph shows that HbA_1C is significantly correlating with CCAIMT(r=0.811).

Figure 3: Correlation of TC/HDL with CCAIMT



This graph shows that TC/HDL is significantly correlating with CCAIMT (r=0.867, p<0.001).

Figure 4: Correlation of LDL/HDL with CCAIMT



This graph shows that LDL/HDL is significantly correlating with CCAIMT (r =0.835).

individual can be advised to control the extensive dyslipidemia through dietary restrictions and exercise.

Limitations of the study:

Small sample size of the patients and its future direction is to substantiate the findings with large number of sample size.

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Authors Contributions:
TJS: Designed the concept of the study and did physical and clinical examination of the patients.
SKD: Collected sample and manuscript preparation.
AC: Collected sample and manuscript preparation.
AK: Conceptual design and proof read of the manuscript.
UKB: Manuscript preparation along with statistical analysis

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