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ORIGINAL ARTICLE

Study of Atherosclerotic Risk Factors in Patients with Prediabetes and Type II Diabetes Mellitus with Special Reference to Carotid Intima–media Thickness

[1]Anita Bhosale, [2]MV Krishna, [3]Das Suraj, [4]M Gautam

ABSTRACT

Background: The present study was carried out to study various atherosclerotic risk factors in prediabetes and type II diabetes mellitus (DM) patients, with special reference to carotid artery intima–media thickness (CIMT). The mean value of CIMT as an indicator of early atherosclerosis was determined and the various atherosclerotic risk factors in patients with prediabetes and type II DM were studied.

Materials and methods: A Comparative two group study was conducted involving 50 patients each with prediabetes and type 2 diabetes mellitus in the age group of 30 to 65 years, Confirmed by FPG/2hour PG/HbA1C/Random plasma glucose values according to ADA criteria, over a period of one year. The study consisted of interview regarding demographic profiles, vascular risk factors, fundoscopy and investigation like FPG, 2hour PG with OGTT, HbA1C, lipid profile, Renal function tests, urine for microalbuminuria, ECG, 2DECHO and CIMT Measurement using B mode ultrasonography.

Results: The association between age of the patients and occurrence of type II DM and prediabetes was found to be statistically significant. Mean duration of type II DM in our study was 6.64 ± 6.71 years. 66% Diabetics and 62% Pre-Diabetics had a BMI over 23. Mean TGs levels in diabetics and Pre-diabetics where 268 mg/dl and 193mg/dl respectively. Mean CIMT in Diabetics and Pre-diabetics were 0.81mm and 0.67mm respectively. Incidence of hypertension in diabetics and Pre-diabetics were 30% and 26% respectively. CIMT had a positive association with hypertension, smoking, and a moderate significance with alcohol use.

Conclusion: The present study emphasizes on the role of CIMT measurement as a routine investigation among diabetics and pre-diabetics for early recognition of atherosclerosis and cardiovascular risk reduction.

Keywords: Body mass index, Carotid intima–media thickness, Diabetes mellitus, Fasting blood sugar, High-density lipoprotein, Impaired fasting glucose, Impaired glucose test, Low-density lipoprotein, Postprandial blood sugar, Triglycerides, Very low-density lipoproteins.

[1]Postgraduate Student, [2]Professor and Head, [3]Senior Resident [4]Associate Professor

[1-4]Department of General Medicine, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India

Corresponding Author: MV Krishna, Professor and Head Department of General Medicine, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India, e-mail: krishnamsr@rediffmail.com

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INTRODUCTION

The metabolic dysregulation associated with diabetes mellitus (DM) causes secondary pathophysiological changes in multiple organ systems that impose a tremendous burden on the individual and on the health care system. Aging and rampant obesity underlie a current epidemic of type II DM.[1] People with impaired glucose tolerance (IGT) have been shown to have endothelial dysfunction and are at increased risk of cardiovascular disease (CVD).[2]

Carotid intima–media thickness (CIMT) has been observed to be increased in people who would subsequently develop diabetic vascular complications due to atherosclerosis and is a major cause of morbidity and mortality in type II diabetes, atherosclerosis being a major risk factor which is accelerated in diabetes.[3] Endothelial dysfunction precedes development of atherosclerosis and plays a major role in its pathophysiology.[4] The CIMT is a surrogate marker of atherosclerosis and provides a noninvasive method for risk assessment of CVD.[5] The progression of CIMT is influenced by cardiovascular risk factors and is directly related to the risk factors of future cardiovascular events.[6] It has, therefore, become a valuable research tool in clinical trials in the assessment of therapeutic agents directed against atherosclerosis.[7] Studies have also demonstrated association of cardiovascular risk and increase in CIMT in people with prediabetes and type II diabetes.[8]

MATERIALS AND METHODS

A total of 100 patients comprising 50 prediabetics and 50 type II DM patients were studied who presented to RajaRajeswari Medical College and Hospital, Bengaluru, Karnataka, India, over a period of 1 year. It was a comparative study.

AIMS AND OBJECTIVES

- To study the various atherosclerotic risk factors in patients with prediabetes and type II diabetes.
- To study the CIMT as an indicator of early atherosclerosis in patients with prediabetes and type II diabetes.

Inclusion Criteria

All patients with prediabetes defined as fasting plasma glucose (FPG) 100 to 125 mg/dL or 140 to 199 mg/dL following oral glucose challenge or hemoglobin (Hb) A1c of 5.7 to 6.4% in the age group of 30 to 65 years were included. All patients with type II DM in the age group of 30 to 65 years with no past history of atherosclerotic events with FPG > 126 mg/dL or random blood sugar >200 mg/dL or HbA1c > 6.5% were also included.

Exclusion Criteria

- Type I diabetes mellitus
- Diabetes with chronic kidney disease
- Diabetes with congestive cardiac failure
- Diabetes with established coronary artery disease
- Patients on statin therapy for more than 6 months

Detailed history was taken followed by anthropometric measurements, weight, height, body mass index (BMI), and systemic examination. Biochemical tests in the form of fasting blood serum (FBS), oral glucose tolerance test, HbA1c, lipid profile, renal function test and urine micro albuminuria, echocardiography (ECG), two-dimensional ECG were observed.

The CIMT thickness measurement was done by trained professionals using high-resolution B-mode ultrasonography system having an electrical linear transducer mid-frequency of 7.5 MHz on both left and right extracranial carotid arteries. The IMT is measured as the distance from the leading edge of the first echogenic line to the second echogenic line. First echogenic line – luminal intimal interface. Second echogenic line – collagen containing upper layer of intimal adventitia. At each longitudinal projection, determination of IMT was conducted at the side of greatest thickness and at two points: 1 cm upstream and 1 cm downstream. Mean of six IMT measurements was taken from both sides and cutoff was taken as 0.8 mm.

Descriptive and interferential statistical analysis was carried out. Results on continuous measurements are presented as mean ± standard deviation (SD). Significance was assessed at 5% using Student's t-test (between two groups) and Chi-square/Fisher's exact test (between two or more groups). Significance: Mild 0.05 to 0.10, moderate 0.01 to 0.05, strong ≤0.01. Statistical software: SAS 9.2, Statistical Package for the Social Sciences 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0, R environment 2.11.1, Microsoft Word and Excel.

RESULTS

Mean age of distribution in diabetics was 52.20 ± 9.91 years, while in prediabetics was 45.70 ± 9.81 years.

Mean CIMT in diabetic group and prediabetics was statistically significant ($p < 0.001$)

The CIMT has a moderate significance with the mean duration of DM being 6.64 ± 6.71 years with $p = 0.015$* and the mean duration of DM with CIMT > 0.8 mm is around 8.74 ± 7.40 years. It has a strong significance with total cholesterol levels, with mean levels being 185.36 ± 52.44 mg/dL (p-value = 0.001)**; CIMT has a suggestive significance with high-density lipoprotein (HDL) levels, with mean HDL being 41.54 ± 18.65 mg/dL with p-value of 0.082^{+}. The CIMT has a strong significance with triglyceride level (TGL) with mean TGL being 267.70 ± 124.6 mg/dL ($p = 0.001$)** and with postprandial blood serum (PPBS) with mean being 263.40 ± 109.18 mg/dL ($p = 0.002$)**.

The CIMT in prediabetic group had a positive association with low-density lipoprotein (LDL), whereas other variables could not reach statistical significance. In type II diabetes patients, BMI had a positive association with CIMT, 33% patients were overweight with a BMI > 23 kg/m^2. Out of 33 overweight patients, 19 patients had a CIMT of > 0.8 mm. Out of 50 diabetic patients, 27 had a CIMT > 0.8 mm. Out of those 27 patients, 10 patients (37%) had a duration of 11 to 20 years of type II DM; CIMT had a positive association with hypertension, smoking, and a moderate significance with alcohol use.

DISCUSSION

The mean age of distribution among diabetic group was 52.20 ± 9.91 years. A similar association was found by Agarwal et al,[9,10] in which the mean age distribution among study group was 59.78 ± 8.81 years, while in a study by ArunKumar and Lokesh[11] mean age of distribution was 56.10 ± 9.03 years. The mean age of distribution in prediabetics was 45.70 ± 9.81 years. The mean duration of type II DM in our study was 6.64 ± 6.71 years. The mean duration of diabetes among the study group was 11.23 ± 6.89 years as per Agarwal et al.[9,10]

In our study, TGL levels in diabetics and prediabetics were 267.70 ± 124.6 and 193.30 ± 89.87 respectively (Table 1). The LDL levels in diabetics and prediabetics were 125.86 ± 30.90 and 129.68 ± 31.99 respectively. Agarwal et al[9] found in their study, mean total cholesterol of 182.08 ± 41.61 mg%, TGL of 155 ± 82.557, LDL of 110.16 ± 34.69 among diabetics. Kumar et al[12] in their study found a mean total cholesterol of 186.3 ± 42.2 mg%, TGL of 145 ± 85.3, and LDL of 123.2 ± 40.8 among diabetics.

In our study, CIMT among diabetics was 0.81 ± 0.13 and 0.67 ± 0.07 mm among prediabetics (Table 2). In Rema et al[13] study, CIMT among diabetics was 0.95 ± 0.31 mm,

whereas Agarwal et al[9] study showed a CIMT among diabetics of 0.840 ± 0.20 mm and Ahmad et al[14] study showed CIMT among diabetics was 0.93 ± 0.34 mm. Department of Endocrinology and Metabolism, Turkey, showed CIMT among prediabetics was significantly higher than the control group.[15] Our study showed CIMT had moderate significance with duration of diabetes, with mean duration being 6.64 ± 6.71 years (Table 3). In patients with CIMT > 0.8 mm, the mean duration of diabetes was 8.74 ± 7.40 years. ArunKumar and Lokesh[11] showed statistically significant increase in CIMT with duration of diabetes.

Similar findings were noted in a study done by Wagenknecht et al.[16] The CIMT was strongly significant with PPBS in diabetics with mean values being 263.40 ± 109.18, and in patients with CIMT > 0.8, the value was 306.15 ± 112.43, with p-value of 0.002. Niskanen et al[17] concluded that there is a small but significant relationship between PPBS and CIMT. Similar findings were found in the study done by Cercillo.[18] Significant relationship exists between postprandial glucose levels and CIMT. These events, in turn, have been associated with adverse cardiovascular events, such as stroke and myocardial infarction. Since the measurement of CIMT is noninvasive, it may prove to be a useful tool, both in diagnosing potential problems and also in monitoring treatments and their outcomes.

Table 1: Comparison of lipid parameters in two groups studied

mg/dL	*Type II DM*	*Prediabetic*	*p-value*
Total cholesterol	185.36 ± 52.44	180.82 ± 48.05	0.653
High-density lipoprotein	41.54 ± 18.65	40.30 ± 11.50	0.690
Low-density lipoprotein	125.86 ± 30.90	129.68 ± 31.99	0.545
Very low-density lipoprotei	30.38 ± 16.69	23.76 ± 8.49	0.014
Triglyceride levels	267.70 ± 124.6	193.30 ± 89.87	0.001

Table 2: Carotid artery intima–media thickness levels in two groups studied

Carotid artery intima–media thickness (in mm)	*Type II DM*		*Prediabetic*	
	No.	*%*	*No.*	*%*
< 0.7	11	22	36	72
0.71–0.8	12	24	11	22
0.81–0.9	12	24	3	6
0.91–1	13	26	0	0
>1	2	4	0	0
Total	50	100	50	100
Mean ± SD	0.81 ± 0.13		0.67 ± 0.07	

Mean CIMT in diabetic group and prediabetics was statistically significant (p < 0.001)

In the prediabetes group, CIMT had a suggestive significance with LDL, with mean value being 129.68 ± 31.99 mg/dL (Table 4). In patients having CIMT > 0.8, the mean value was 159.67 ± 55.19 mg/dL with p-value ±0.094, but could not attain statistical significance with other parameters.

Table 3: Comparison of study variables according to CIMT in type II DM group of patients

	Carotid artery intima–media thickness			
Variables	*≤0.8*	*≥0.8*	*Total*	*p-value*
Age in years	51.52 ± 10.8	52.78 ± 9.26	52.20 ± 9.91	0.660
Duration of DM (years)	4.17 ± 4.86	8.74 ± 7.40	6.64 ± 6.71	0.015
Body mass index (kg/m^2)	24.14 ± 4.10	24.93 ± 3.75	24.57 ± 3.90	0.480
Total cholesterol	158.91 ± 38.12	207.89 ± 52.98	185.36 ± 52.44	0.001
High-density lipoprotein	36.57 ± 10.50	45.78 ± 22.83	41.54 ± 18.65	0.082
Low-density lipoprotein	120.48 ± 27.26	130.44 ± 33.52	125.86 ± 30.90	0.260
Very low-density lipoprotei	24.35 ± 12.36	35.52 ± 18.33	30.38 ± 16.69	0.017
Triglyceride levels	199.91 ± 85.73	325.44 ± 124.55	267.70 ± 124.6	0.001
Fasting blood serum	158.65 ± 72.53	191.85 ± 76.41	176.58 ± 75.76	0.124
Postprandial blood serum	213.22 ± 82.07	306.15 ± 112.43	263.40 ± 109.18	0.002

Table 4: Comparison of study variables according to CIMT in prediabetic group of patients

	Carotid artery intima–media thickness			
Variables	*≤0.8*	*≥0.8*	*Total*	*p-value*
Age in years	45.55 ± 9.74	48 ± 13	45.70 ± 9.81	0.680
Body mass index	24.71 ± 4.89	23.23 ± 2.80	24.62 ± 4.78	0.610
Total cholesterol	179.11 ± 46.71	207.67 ± 72.42	180.82 ± 48.05	0.323
High-density lipoprotein	40.04 ± 11.67	44.33 ± 9.07	40.30 ± 11.50	0.537
Low-density lipoprotein	127.77 ± 29.92	159.67 ± 55.19	129.68 ± 31.99	0.094$^{\pm}$
Very low-density lipoprotei	23.55 ± 8.32	27.00 ± 12.49	23.76 ± 8.49	0.501
Triglyceride levels	188.19 ± 82.82	273.33 ± 172.93	193.30 ± 89.87	0.112
Impaired fasting glucose	107.21 ± 14.58	118 ± 7	107.86 ± 14.43	0.213
Impaired glucose tolerance	154.72 ± 24.45	166.33 ± 17.04	155.42 ± 24.10	0.424

In our study, CIMT has a positive association with BMI in the diabetic group, but no association was found among BMI in prediabetic group; p = 0.193; not significant (but positive association), Fisher's exact test. Out of 33 overweight patients, 19 patients had a CIMT > 0.8 mm. The BMI was associated with common carotid artery (CCA)-IMT in patients with type II DM.[19] Ciccone et al,[20] Naya et al,[21] and Poredos et al[22] found that CCA-IMT was correlated with smoking and BMI.

CONCLUSION

The study is a two-group comparative study comprising 100 patients, of which 59 are males and 41 are female patients. The CIMT which is a noninvasive marker of atherosclerosis is raised more in diabetics compared with prediabetics. Dyslipidemia was a feature in diabetic patients with increased TGL. Duration of diabetes, BMI, TGL, total cholesterol, and postprandial blood glucose levels were recognized as risk factors in diabetics, which correlated with increased CIMT, while in prediabetics BMI and LDL levels had a positive correlation. Through our study we can summarize that CIMT being a noninvasive marker of atherosclerosis should be routinely used to diagnose potential problems and treatment outcomes in type II diabetes and prediabetes, and lifestyle modifications should be adopted to prevent the conversion of prediabetics into type II diabetes. The CIMT should be included as a routine investigation due to its noninvasive status and its utility for early recognition of atherosclerosis, which will help in cardiovascular risk reduction in diabetes and prediabetes.

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