Carotid artery intimal media thickness and ankle brachial index as predictors for atherosclerosis in pre-diabetic patients

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INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the healthcare system.[¹]

People with IFG (Impaired Fasting Glucose) have been shown to have endothelial dysfunction and are at increased risk of cardiovascular disease (CVD).[²] Carotid intimal media thickness (CIMT) has been observed to be increase in people who would subsequently develop diabetes vascular complication due to atherosclerosis are a major cause of morbidity and mortality in Type 2 diabetes.

Insulin resistance is a central pathogenetic feature of prediabetes, the incidence of which is rising substantially. The principal cause of end organ damage in prediabetes is

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ABSTRACT

Background: Atherosclerosis still remains as the major cause of death and premature disability in developed societies. Insulin resistance is a central pathogenesis feature of prediabetes, the incidence of which is rising substantially. The principal cause of end organ damage in prediabetes is premature cardiovascular atherosclerosis. Objectives: To assess the atherosclerosis in prediabetes. Materials and Methods: Patients who were nondiabetic of age group between 18 and 50 years were screened for fasting blood sugar, post-prandial blood sugar, hemoglobin A1c, after obtaining informed consent and were divided to study group and control group according to inclusion criteria. Results: In this study, abnormal carotid intimal thickness (CIMT) was observed in 7 (17.1%), out of 41 pre-diabetic patients. This difference in CIMT findings between two groups was statistically significant. Prediabetics are at 8 times higher risk of developing abnormal CIMT than nondiabetics. Abnormal CIMT was associated with greater body mass index, waist-hip ratio, low high-density lipoprotein, high triglycerides, and abnormal ABI. Conclusion: Prediabetes was associated with higher risk of developing subclinical atherosclerosis when compared to non-diabetic patients. Lifestyle modification should be adopted to prevent the conversion of prediabetes into Type 2 diabetes mellitus and thus prevention of its complication.
premature cardiovascular atherosclerosis and patient with prediabetes have a similar risk of fatal cardiovascular events as non-diabetic patient who have sustained a myocardial infarction.

Prediabetes is characterized by a long period of insulin resistance during which a compensatory increase in pancreatic cell function maintains normal glycemic at the expense of fasting and postprandial hyperinsulinemia which later advances in to increase fasting plasma glucose state.[1] Insulin resistance is well established as a independent risk factor for the development of cardiovascular atherosclerosis and prediabetes.[4]

Endothelial dysfunction precedes the development of atherosclerosis and is believed to play a central role in the pathophysiology.[5] CIMT is a surrogate marker of atherosclerosis and provides a non-invasive method for the risk assessment of CVD. It is a strong predictor of future cardiovascular events and is associated with conventional markers of cardiovascular risk such as diabetes.[6]

Prediabetes, though not a disease entity by itself is associated with a significant degree of risk for both macrovascular and increasingly microvascular pathology. It is important to identify these conditions to prevent the incidence of diabetes and to take measures to prevent the vascular complications. We need programs to prevent the development of the pre-diabetic state, as well as diabetes from prediabetes and its associated complication.[11]

This study was undertaken to assess cardiovascular risk using CIMT and ankle brachial index (ABI) as a marker to identify subclinical atherosclerosis in pre-diabetic patients.

Objectives

The objective of the study is to assess the atherosclerosis in prediabetes.

MATERIALS AND METHODS

Source of Data

This study was conducted on 41 prediabetic and 41 within normal glycemic control between age group of 18 and 50 years attending the General Medicine outpatient section and inpatients of RL. Jalappa Hospital and Research Centre Tamaka, Kolar. Patient who was nondiabetic, of age group between 18 and 50 years was screened for fasting blood sugar, post-prandial blood sugar, hemoglobin A1c (HbA1c), after obtaining informed consent was divided to study group and control group according to inclusion criteria. Carotid intimal medial thickness was measured using B mode ultrasound “Siemens ACUSON® X300 Premium” and ABI done using hand held Doppler in both group.

Inclusion Criteria

- Age between 18 and 50 years.
- Study group: Prediabetes defined as fasting plasma glucose 101-125 mg/dl, post-prandial glucose.
- 141-199 mg/dl, HbA1c 5.7%-6.4%.
- Control group: Normal people with fasting plasma glucose <100 mg/dl and post-prandial glucose <140 mg/dl, HbA1c <5.7%.

Exclusion Criteria

- Chronic kidney disease.
- Congestive cardiac failure.
- Established coronary artery disease and stroke.
- Hypothyroidism.
- Patients on statin therapy for more than 6 months.
- Pregnancy.

Data were entered into Microsoft excel data sheet and was analyzed using SPSS 22 Version software.

RESULTS

Mean age of individuals in controls was 38.5 ± 7.4 years and in prediabetes was 38.8 ± 7.1 years. In control group, 31.7% and pre-diabetes group 46.3% had family history of diabetes. Mean body mass index (BMI) in control group was 25.5 ± 3.4 and in pre-diabetes group was 27.1 ± 5.3. In the Control group, 4.9% were underweight, 43.9% were overweight, and 9.8% had Class I obesity. Similarly in pre-diabetics group 2.4% were underweight, 46.3% were overweight, 19.5% were Class I obese, and 4.9% were Class III obese (Figures 1-4).

In control group, among female gender, majority of them were overweight (52.9%) and among males majority of them had normal BMI (54.2%). In the control group, among females 58.8% and among males 45.8% were at risk with respect to Waist–hip ratio and among pre-diabetics individuals 76.5% of females and 33.3% of males were at risk. Total cholesterol in control and prediabetes was 182.1 ± 48 mg/dl and 190.5 ± 58.4 mg/dl, triglycerides in control 161.7 ± 43.7 mg/dl and prediabetes 169.8 ± 64.5 mg/dl, low-density lipoprotein levels in control 118.9 ± 33.8 mg/dl and prediabetes 102.7 ± 40.8 mg/dl.

High-density lipoprotein (HDL) in control and prediabetes was 38.4 ± 7.6, 38.9 ± 13.8, respectively. Whereas in control group 36.6% had reduced HDL and in prediabetics 46.3% had reduced HDL. In control group, 51.2% had acceptable ABI, 36.6% had normal and 12.2% had some ABI grading. In prediabetic group, 26.8% had acceptable, 9.8% had moderate, 41.5% had normal, and 22% had some ABI grading. In the control group, 2.4% had abnormal CIMT and in pre-diabetic group 17.1% had abnormal CIMT. This difference in CIMT findings between two groups was statistically significant. Odds
ratio for prediabetics for CIMT was 8.235, i.e., prediabetics are at 8 times higher risk of developing abnormal CIMT than controls. In Control individuals who had abnormal CIMT, all of them had normal ABI. In individuals with normal CIMT, 52.5% had acceptable, 35% had normal and 12.5% had some ABI grade, respectively. In pre-diabetic individuals who had abnormal CIMT, 14.3% had acceptable, 28.6% had moderate and 57.1% had some ABI grade. In individuals with normal CIMT, 29.4% had acceptable, 5.9% had moderate, 50% had normal and 14.7% had some ABI grade, respectively. There was significant association between ABI grade and CIMT grade in pre-diabetic group (Figures 5 and 6).

**DISCUSSION**

Prediabetes is a state where blood sugar level is higher than normal but not yet high enough to be classified as Type 2 DM, without intervention prediabetes is likely to become Type 2 diabetes in 10 years or less. Testing should be considered in all adults of any age who are overweight or obese (BMI >25 kg/m²), and who have one or more diabetes risk factor. The major detrimental outcomes in persons with prediabetes are macrovascular diseases and Type 2 diabetes, leading contributors to microvascular disease.

In India, incidences of CAD have doubled over the past three decades. By 2015, CVDs alone would amount to 1.5 million deaths, including 34% of male and 32% of female global deaths.\(^{[7]}\)

CIMT is defined as the area of tissue starting at the luminal intimal interface and the media adventitia interface of
common carotid artery. Close histological relationship between coronary, cerebral, and carotid atherosclerotic diseases. Since then, the ultrasonographic assessment of easily accessible arteries has become a surrogate marker for evaluation of less accessible vessels such as coronary and cerebral arterial system. Ultrasound imaging provided information on IMT, the presence and type of plaque, calcification, and wall diameter. This information enabled assessment of presymptomatic lesion, atherosclerotic burden, and reduced death and disabilities from CVD. The ankle-brachial index (ABI) is the ratio of the systolic blood pressure (SBP) measured at the ankle to that measured at the brachial artery. Originally described by Winsor in 1950, this index was initially proposed for the noninvasive diagnosis of lower-extremity peripheral artery disease (PAD). Later, it was shown that the ABI is an indicator of atherosclerosis at other vascular sites and can serve as a prognostic marker for cardiovascular events and functional impairment, even in the absence of symptoms of PAD.[10-12]

In control group, 51.2% had acceptable ABI, 36.6% had Normal and 12.2% had some ABI grading. In pre-diabetic group 26.8% had acceptable, 9.8% had moderate, 41.5% had normal, and 22% had some ABI grading. In the control group, 2.4% had abnormal CIMT and in pre-diabetic group 17.1% had abnormal CIMT. This difference in CIMT findings between two groups was statistically significant. Odds ratio for prediabetics for CIMT was 8.235, i.e., prediabetics are at 8 times higher risk of developing abnormal CIMT than controls. In control individuals who had abnormal CIMT, all of them had normal ABI.

In a study done by Gomez-Marcos et al., the CIMT showed a positive correlation with fasting plasma glucose, post-prandial glucose, and HbA1c and concluded that the patients who present with a metabolic glucose alteration have more risk of developing carotid target organ damage (TOD).[13] Another study done by Ghosh et al concluded that CIMT on right side was higher in DM and Pre diabetics compared to Non diabetics, but CIMT on left side did not differ. The IR was significantly high only in DM. Age and BMI correlations were predominantly positive and lipids variable except in PDM. Age and IR had better impacts on CIMTs in DM while BMI was poor.[14] Anitha et al. concluded that mean CIMT in diabetic and nondiabetics were 0.81mm and 0.67mm, respectively. With incidence of hypertension was 30% in diabetic patients.[15]

Since measurement of CIMT and ABI is non-invasive, it may prove to be a useful tool both in diagnosing potential problems but also in monitoring treatment and their outcomes, especially in prediabetes. In a word use of the concept of prediabetes can be useful tool for intervention to prevent both macrovascular and microvascular disease in clinical and public health spheres.

Considering the conflicting outcomes of different studies it is suggested that further research is required in larger number of patients to find out the interrelationship and contribution of various risk factors for atherosclerosis in pre-diabetes patients.

**CONCLUSION**

CIMT and ABI in prediabetes should be included as a routine investigation due to its non-invasive nature and its utility in detecting atherosclerosis at subclinical stage which will finally help in cardiovascular risk reduction in prediabetes. Lifestyle modification should be adopted to prevent the conversion of prediabetes into Type 2 DM.

**REFERENCES**


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