EVALUATION OF VASCULAR HEALTH BY CAROTID INTIMA-MEDIA THICKNESS IN EGYPTIAN PRE-DIABETIC PATIENTS

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Abstract

Endothelial dysfunction (ED) is one of the major pathophysiological links between exposure to cardiovascular risk factors and the early development of atherosclerotic disease. It represents an initial reversible step in the development of atherogenesis. The identification of early stages of atherosclerotic diseases in diabetic and pre-diabetic persons is a fundamental step in the risk stratification protocols adopted by physicians in order to have a complete overview of the clinical status of such individuals. Carotid intima-media thickness is instrumental tool for the detection of early impairment in cardiovascular system and to stratify the cardiovascular risk of individuals.

The aim of our work is to estimate the arterial wall thickness by carotid intima-media thickness CIMT.

In our study CIMT is statistically higher in the pre- diabetic group (0.63±0.08 mm) than the control group (0.59±0.09 mm; p value 0.006).

The current study shows that arterial thickness start early in patients suffering pre-diabetes and emphasizes the importance of early detection and treatment to prevent cardiovascular affection in such individuals.

Keywords: Carotid intimal medial thickness; endothelial dysfunction; pre-diabetes

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1. INTRODUCTION

Pre-diabetes is the general term that refers to an intermediate stage between normal glucose tolerances (NGT) and overt Type 2 Diabetes Mellitus (T2DM). Individuals with pre-diabetes are at high risk to develop T2DM [1]. Evidence indicates that pre-diabetes may be associated with increased cardiovascular risk profile of individuals and that obese young patients suffering from pre-diabetes are more prone to show increased CIMT (a well- known early marker of atherosclerosis) than obese youth with normal glycemic control. Apart from the morphological alterations in systemic vascular beds, pre-diabetes is able to worsen the performance of coronary vessels which increases the overall cardiovascular risk of individuals [2]

The increased risk for CVD in pre-diabetes appears to be due to a combination of related factors common in the metabolic syndrome (insulin resistance, hyperglycemia, dyslipidemia, hypertension, and systemic inflammation).In particular, insulin resistance appears to promote CVD via effects on BP, endothelial cell function, lipids, platelet function and blood coagulation. Even in the absence of frank diabetes or the metabolic syndrome, insulin resistance is associated with coronary artery endothelial dysfunction, suggesting that vascular injury is already present [3].

Endothelial dysfunction plays a crucial role in the development of any vascular process and occurs early in the process of atherosclerosis [4]. It is one of the major pathophysiological links between exposure to cardiovascular risk factors and the development of atherosclerotic disease [5] and represents an initial reversible step in the development of atherogenesis. Therefore, early clinical identification of ED may become an important tool in the prevention or reversal of progression to atherosclerosis and IHD [6].

Endothelial dysfunction precedes the development of T2DM and is seen in both IFG and IGT [7]. Pre-diabetic status is a further expression of incipient atherosclerosis development. The synergism between

a systemic inflammatory condition and the presence of high blood glucose concentrations and insulin resistance are the mix able to impair vascular endothelium in its function, thus predisposing to atherosclerotic lesions. Thus, all these patients should be carefully evaluated in order to detect early sign of alterations by means of all the available non-invasive techniques [8].

Carotid intima-media thickness (CIMT) is a simple and inexpensive tool to assess the cumulative effect of atherosclerotic risk factors and is an independent predictor of future cardiovascular (CV) risk.

The current study evaluates endothelial function by arterial wall thickness in adults with pre-diabetes by carotid intima-media thickness (CIMT) and correlates that parameters with levels of serum blood glucose and HbA1c.

2. PATIENTS AND METHODS

Our study is a cross sectional study that analyzed data from 200 Egyptian adults with any laboratory evidence of pre-diabetes, as diagnosed by ADA guidelines, and 50 healthy control subjects with age ranging from 18-50 years.

All subjects were recruited from the internal medicine department, endocrinology and diabetes outpatient clinic, Kasr El Aini teaching Hospital Cairo University from April 2020 to April 2021.

- **Inclusion criteria:**

Egyptian patients aged from 18 to 50 years with documented laboratory evidence of pre-diabetes. Patients with pre-diabetes were defined by the presence of IFG and/or IGT and/or A1C 5.7–6.4% (39–47 mmol/mol), IFG is defined as FPG levels between 100 and 125 mg/dL (between 5.6 and 6.9 mmol/L) and IGT as 2-h PG during 75-g OGTT levels between 140 and 199mg/dL (between7.8 and11.0mmol/L) [9].

Patients who are younger than 18 years or older than 50 years and patients with diabetes mellitus, hypertension, known atherosclerotic cardiovascular disease (or ankle/brachial index < 0.9), hepatic or renal disease, primary dislipidemia and pregnant ladies were excluded from the study. The study was approved by Cairo University Ethical Committee and Review Board. All the patients and control subjects who participated in the study provided written informed consents.

The study population was subjected to detailed history taking, thorough clinical examination including assessment of weight, height, body mass index, systolic and diastolic blood pressure, laboratory investigations in the form of: CBC, kidney functions, fasting blood glucose, 2h pp blood glucose, HbA1C, lipid profile (serum cholesterol, LDL-C, HDL-C and serum triglycerides) and serum TSH.

- **Measurement of CIMT**

All subjects were examined in the supine position with the neck in extension position and the head tilted slightly opposite to the side being examined. B-mode ultrasonographic images of the carotid artery were obtained in longitudinal view with a High resolution color coded ultrasound system Siemens ACUSON P500 with a linear transducer 5 to 12 MHz is used. CIMT a measurement of the thickness of intima and media the innermost two layers of the arterial wall The mean of 3 measurements of intima-media thickness 2cm before the carotid bulb from the posterior wall were taken and calculated for both the right and left common carotid artery.

STATISTICAL METHODS:

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs. 26. Numerical data were summarized using means and standard deviations. Categorical data were summarized as numbers and percentages. Estimates of the frequency were done using the numbers and percentages. Numerical data were explored for normality using Kolmogrov- Smirnov test and Shapiro-Wilk test. Chi square test was used to compare between the independent groups with respect to categorical data. Comparisons between two groups for normally distributed numeric variables were done using the Student ‘s t-test. To measure the strength of association between the normally distributed measurements, Pearson ‘s correlation coefficients was computed (r is the correlation coefficient & it ranges from -1 to +1 where +1 indicates positive correlation -1 indicates negative correlation 0 indicates no correlation). Precisely, r values: from 0 to 0.25 (-0.25) = little or no correlation; from 0.25 to 0.50 (-0.25 to 0.50) = fair degree of correlation; from 0.50 to 0.75 (-0.50 to -0.75) = moderate to good correlation; greater than 0.75 (or -0.75) = very good to excellent correlation.

3. RESULTS

Table (1): Shows age and sex distribution in both groups

	Prediabetic	**Control**	**P value**
	n=200 (%) *	**n=50 (%) ***	
Age			
Mean ± SD	38.5±8	36.5±9	0.060
Sex			

Female	114 (57)	24 (48)	0.269
Male	86 (43)	26 (52)	

SD: standard deviation, P value <0.05 is considered significant,
* Percentages were calculated within column.

Table (1) summarizes the sociodemographic characteristics of the patients whereas the clinical and laboratory data in both groups.

Table (2): Shows clinical and laboratory data in both groups

	Pre-diabetic	**Control**	**P value**
	Mean ± SD	**Mean ± SD**	
SBP	118±14	116±12	0.467
DBP	74±9	73±8	0.54
Weight	101±18	88±15	<0.001
Height	163±7	171±7	<0.001
BMI	38±6.5	30.2±5.6	<0.001
FBG	105±10	87±7	<0.001
PPBG	128±22	110±10	<0.001
HbA1c	5.9±0.3	5.3±0.2	<0.001
LDL	125.2±40.5	92.9±22.6	<0.001
HDL	45.5±10	43.3±9.4	0.167
TGs	135±53	126±31	0.115
Total cholesterol	198±44	155±29	<0.001
TSH	2.5±1.3	1.9±0.6	<0.001
CIMT	0.63±0.08	0.59±0.09	0.006

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, FBG: Fasting blood glucose, PPBG: Post prandial blood glucose, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: Triglyceride, TSH: Thyroid stimulating hormone, CIMT: Carotid intima-media thickness

Mean total cholesterol and LDL were statistically significantly higher in prediabetics 198±44 than control 155±29 (p value < 0.001). In our study CIMT was statistically higher in pre- diabetic group (0.63±0.08 mm) than control group (0.59±0.09 mm) (p value 0.006).

Table (3): Correlation between CIMT and other factors

Factors	**Carotid intima-media thickness (CIMT)**		
	r	**P value**	**Degree of correlation**
Age	0.55	<0.001	Significant moderate positive correlation
SBP	0.28	<0.001	Significant fair positive correlation
DPB	0.25	<0.001	Significant fair positive correlation
Weight	0.05	0.377	Non significant correlation
Height	-0.25	<0.001	Significant fair negative correlation
BMI	0.18	0.005	Significant little positive correlation
FBG	0.15	0.021	Significant little positive correlation
PPBG	0.29	<0.001	Significant fair positive correlation
Hb A1C	0.30	<0.001	Significant fair positive correlation
LDL	0.40	<0.001	Significant fair positive correlation
HDL	-0.01	0.876	Non-significant correlation
TGS	0.18	0.005	Significant little positive correlation
Total cholesterol	0.39	<0.001	Significant fair positive correlation
TSH	0.04	0.486	Non-significant correlation

There was significant positive correlation between CIMT and BMI (p value 0.005), FBG (p value 0.021), TGs (p value 0.005), SBP and DBP (p value <0.001), PPBG (p value <0.001), HbA1c (p value <0.001), LDL (p value <0.001), total cholesterol (p value <0.001). No significant correlation was detected between CIMT and weight, HDL or TSH.

4. DISCUSSION

Our study is a cross sectional study that was conducted on 200 Egyptian adults from endocrinology outpatient Cairo university hospital with any laboratory evidence of Pre-diabetes diagnosed by ADA guidelines and 50 age- and sex-matched subjects as controls ranging from 18-50 years.

Dyslipidemia plays a major role in the pathophysiology of atherosclerosis and is associated with increased risk for the development of CVD in diabetic patients.

Our study revealed positive significant correlation of CIMT with FBG, 2hPPBG and HbA1c. As an easy noninvasive marker, CIMT measurement has been widely used for the detection of subclinical atherosclerosis.We assessed CIMT, using high-resolution color-coded Doppler ultrasonography in patients with diabetes. Our patients had no risk for atherosclerosis other than dyslipidemia. In our study CIMT was significantly higher in patients with prediabetes were increased significantly as compared to the values obtained in control subjects (p value 0.006).

Our results were similar to Liu et al. who showed CIMT was significantly higher in pre-diabetics than control and this was also similar to our study, although mean CIMT in their IGT group was higher than our group but this may be related to the higher mean age of their IGT group and different population race/ethnicity [10].

In a study that included 100 patients and 45 control subjects, Salam et al., showed that CIMT was statistically higher in pre-diabetics than control as our study [11]. Shah et al. studied 102 pre-diabetics and 139 NGT and found higher CIMT in pre-diabetics than control [12]. In a study conducted by Parildar et al. on 110 pre-diabetics and 76 controls, the results showed significantly higher CIMT in pre-diabetics than control and significant positive correlation for CIMT with FBG, HbA1c and BMI which is consistent with the current study [13]. Similar to our study, Behinder et al. study on 100 pre-diabetics and 100 control showed higher CIMT in pre-diabetics (p value < 0.05) [14].

Our study confirmed that the increases in CIMT in patients with diabetes mellitus start in the prediabetic stage.

The results in our study are similar to a study conducted by Mahat et al on 200 pre-diabetics and 200 controls. In their study CIMT was significantly increased in pre-diabetic (p value < 0.001), and there was positive significant correlation between CIMT with athrogenic indices SBP, DBP, age, BMI, FBG, 2hPPBG, TC, LDL and TGs demonstrating that atherogenic indices could be used for the assessment of the risk of subclinical atherosclerosis in prediabetic subjects. [15].

This study clearly shows that endothelial dysfunction, and arterial thickness start early in patients suffering pre-diabetes and emphasize the importance of early detection and treatment to prevent cardiovascular affection in such individuals.

Larger patient population-based studies in the future may provide a more robust assessment of ED and arterial wall thickness and give more accurate results, also using of more than one method to assess endothelial function could increase the credibility of the results. Other studies can be done to study the effect of different modalities of treatment on CIMT in patients with prediabetes

ETHICAL COMMITTEE APPROVAL:

The study was approved by the IRB of the Faculty of medicine, Cairo University.

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