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Association Between Diabetic Retinopathy and Carotid Intima-Media Thickness in type 2 Diabetic Egyptian patients

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Abstract

Patients with diabetes generally have a greater extent of atherosclerosis with increase in CVD risk however, the increase in CVD risk is not homogeneous. To predict cardiovascular outcomes carotid intima-media thickness (CIMT) is utilized in diabetic patients. The aim of our study was the evaluation of the relationship between diabetic retinopathy and carotid intima-media thickness (CIMT) in type 2 diabetic patients as valuable non-invasive methods for early detection of macrovascular complication of diabetes. This cross-section study was conducted in Internal Medicine department and outpatient clinic, Kasr El Aini University Hospital in Eygpt from August 2019 to April 2022. One hundred ninety-eight patients with type 2 diabetes mellitus were enrolled in the study after taking informed consent. CIMT was evaluated by a Doppler ultrasound for both carotid arteries. Ophthalmological examination was done to screen patients for DR. Then patients are divided in to 3 groups according to presence or absence of DR into no retinopathy, non prolifrative DR and prolifrative DR. Carotid artery intimal thickness was more in patients with retinopathy compared to patients without retinopathy but it was not statistically significant (p value 0.209, 0.095) on the right and left sides respectively. In our study, there was no correlation between DR and CIMT. Screening for DR cannot be used as early marker for macrovascular complications.

Keywords: diabetes type 2, carotid intima-media thickness, association, diabetic retinopathy, macrovascular complication.

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1. Introduction

Diabetic retinopathy (DR) is a common complication of diabetes and remains the leading cause of blindness among working-age individuals in most developed countries [1]. Complications in common in diabetes and are responsible for significant morbidity and mortality [2]. The long-term complications of diabetes are commonly divided into micro- and macrovascular complications [3]. Atherosclerosis is another complication of diabetes and is the primary cause of cardio cerebral diseases and is associated with cardio-cerebrovascular risk in patients with type 2 diabetes mellitus. Atherosclerosis comprises two different processes, namely structural changes presenting as carotid plaque, increased carotid intima-media thickness and ankle-brachial index and functional changes presenting as increased arterial stiffness [4].

Measurement of the common or internal carotid intima-media thickness (CIMT) can be used for the recognition of diabetic atherosclerosis and constitutes an established marker for the diagnosis of subclinical atherosclerosis and a predictor for future cardiovascular events [5]. The purpose of our study was to evaluate the relationship between retinopathy and CIMT in type 2 diabetic patients as valuable non-invasive method for early detection of macrovascular complication of diabetes.

2. Materials and Methods

This cross-section study was conducted in Internal Medicine department and outpatient clinic Kasr El Aini University Hospital in Eygpt from August 2019 to April 2022. One hundred ninety-eight patients with type 2 diabetes mellitus were enrolled in the study after getting informed consent. CIMT was evaluated by a Doppler ultrasound for both carotid arteries. Ophthalmological examination was done to screen patients for DR. Then patients are divided in to 3 groups according to presence or absence of DR. Patients with history of lower limb amputation, serious lower limb oedema and patients with cataract or history of previous

ocular surgery were excluded from the study. After inclusion, patients' detailed history was taken to gather data related to their age, gender and hypertension. Blood was drawn via phlebotomy and sent to the laboratory to test for glycated hemoglobin (HbA1C) and lipid profile (HDL, LDL, triglycerides and total cholesterol). Ophthalmological examination was done to screen the patients for DR via fundoscopy. CIMT was evaluated by a Doppler ultrasound for both carotid arteries.

Statistical analysis was done using Statistical Packages for Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test or analysis of variance (ANOVA) with multiple comparisons post hoc test in normally distributed quantitative variables while non-parametric Kruskal-Wallis test and Mann-Whitney test were used for non-normally distributed quantitative variables (Chan, 2003a). For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). Correlations between quantitative variables were done using Pearson correlation coefficient (Chan, 2003c). P-values less than 0.05 meant that there is a difference between the two groups that are considered statistically significant.

3. Results and discussion

Prevalence of diabetic retinopathy in the study population is 50.5%. Among198 patients, Fundus examination was normal in 98 patients (49.5%) 27 males and 71 females. Proliferative diabetic retinopathy was found in 36 patients (18.2%), 15 males and 21 females while non proliferative diabetic retinopathy was found in 64 patients (32.3%) 22 males and 42 females. Among patients in the group on normal fundus, 35 patients were hypertensive (35.7%) while in the NPDR group 33 patients were hypertensive (51.6%). 18 patients were hypertensive in the proliferative group (50.0%). Patients with diabetic retinopathy were older 58.27 ± 8.08, 60.89 ± 7.09 years vs. 56.48± 7.50 years and has higher systolic blood pressure 134.31± 11.90 129.30 ±11.33 vs. 126.48 ± 10.18 mmhg and higher diastolic blood pressure 86.67 ± 8.45, 83.67 ±9.10 vs. 82.09 ±8.49 mmhg; p-value: 0.001, .027 respectively. However there no difference between male and female. Patients with retinopathy had longer duration of diabetes (15.59 ± 5.26 years, 16.81± 6.02 vs. 13.82 ± 4.43 years; p-value: 0.004. There was no significant difference in carotid artery intimal thickness between patients with diabetic retinopathy and patients with normal fundus.

Our study had enrolled 198 diabetic participants, out of which 50.5% showed a prevalence of retinopathy. In our study, there were more female (67.7%) participants compared to male (32.2%); however, the ratio was similar between both groups. Our results showed that Fundus examination had a statistically significance with age of the patients, systolic, diastolic blood pressure and duration of diabetes. This emphasizes the hypothesis of the importance of diabetes duration as a risk factor for fundus changes and atherosclerosis in spite of other traditional risk factors. This was consistent with previous studies where there was no significant difference noted among male and female genders [6,7]. Previous studies showed same results, one in Chinese patients showed that DR was positively related to age, diabetic duration, hypertension, SBP and DBP [4]. Furthermore, our study did not find a significant link between BMI and CIMT, which is in accordance with a study conducted by Momeni et al. [8]. Whereas another study proved to show a significant correlation between maximum BMI and retinopathy [9]. The most posssible explanation of the differences in these results could be the difference in the sample sizes.

In our study, we cannot correlate CIMT with the presence or absence of diabetic retinopathy. The results were consistent with several studies, Cardoso et al., 2012 concluded that none of the diabetic chronic microvascular complications had any significant association with CIMT measured at any site [10]. As well as Cardoso et al., 2019 when evaluating the relationships between ultrasonographic parameters of carotid atherosclerosis, CIMT and plaques and the future occurrence of microvascular complications in type 2 diabetic patients and they found that carotid atherosclerosis parameters can predict cardiovascular and renal outcomes, but not diabetic retinopathy. There was no significant relation between CIMT and DR at the start of study and even during follow up with p value 0.36, 0.18 [11]. Also, Alonso et al., 2015 found that the mean CIMT at different territories (common, bulb and internal carotid) did not differ between the patients with DR and those without DR [12]. Previous study by Yun et al., 2011, support our results and reported that no significant association between CCA-IMT, carotid plaque and diabetic retinopathy among type 2 diabetic patients. They explain their results suggesting that the association between macroangiopathy and microangiopathy may be due to a functional rather than structural process within the vascular system as assessed by CIMT and carotid plaque. [13]. Whereas, another study proved to show an association of CIMT with diabetic retinopathy which was statistically significant P value (P =<0.001). This difference may be attributed to different study population, exclusion criteria, sample size and cut off value of CIMT 0.7mm instead of 0.9mm in our study [14]. As well as cross-sectional study on diabetic patients divided into two equal groups of 77 patients that were case group (with retinopathy) and control group (without retinopathy), CIMT of the patients of group 1 was significantly greater than group 2 (P < 0.001) [8]. Our limitations were being an observational study looks at patients' data at single point of time without manipulating variables and being hospital based the study targets type 2 diabetic patients at a single institution in a certain area and does not represent the general population across the nation.

Table 1: Characteristics of the participants. NPDR: non proliferative diabetic retinopathy, PDR: proliferative diabetic retinopathy, BMI: body mass index; DR: diabetic retinopathy; HbA1C: glycated hemoglobin; SD: standard deviation

	Normal (98 patients)		**NPDR** (64 patients)		**PDR** (36 patients)		**P value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Age (years)	56.48	7.50	58.27	8.08	60.89	7.09	0.012
Duration of DM (yrs.)	13.82	4.43	15.59	5.26	16.81	6.02	0.004
BMI	31.23	4.35	30.39	4.27	31.46	4.45	0.379
systolic BP	126.48	10.18	129.30	11.33	134.31	11.90	0.001
Diastolic Bp	82.09	8.49	83.67	9.10	86.67	8.45	0.027
Total Cholesterol	197.47	50.58	196.72	53.33	203.75	71.93	0.813
LDL	119.05	35.33	114.47	30.54	113.11	39.48	0.579
HDL	43.21	10.09	41.77	8.46	41.14	8.00	0.422
HbA1c	8.84	1.59	9.06	1.49	9.23	1.74	0.397
TG	177.08	78.43	170.14	87.90	198.81	116.33	0.348

Table 2: fundus Differences between Males & Females

		Fundus						
		Normal		**NPDR**		**PDR**		**P value**
		Count	**%**	**Count**	**%**	**Count**	**%**	
Gender	**Male**	27	27.6%	22	34.4%	15	41.7%	0.275
	Female	71	72.4%	42	65.6%	21	58.3%	

Table 3: Comparison of intimal thickness in patients with and without retinopathy.

	Normal (98 patients)		**NPDR** (64 patients)		**PDR** (36 patients)		**P value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
CIMT – Right	0.102	0.016	0.105	0.017	0.107	0.015	0.209
CIMT – Left	0.100	0.017	0.105	0.015	0.106	0.015	0.095

4. Conclusions

Diabetic retinopathy has no significant relation with central or peripheral vascular affection and the fundus cannot be used as a predictive test for atherosclerosis in type 2 diabetic patients. Duration of diabetes and higher Systolic and diastolic blood pressure are risk factors for development of micro vascular diabetic complications.

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