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utjmed@utq.edu.iq bassim-a@utq.edu.iq
methaq-abd@utq.edu.iq

Relationship between carotid atheroma thickness and albuminuria in diabetic patients

Dr. Basim Audib Motar *, Dr. Methaq A. M. Hussein *,

Dr. Oras Majeed**

*Assistant professor, department of medicine, college of medicine / Thi-Qar University.

**Radiologist, Thi-Qar health Office

Abstract

Our aim in this study to assess the efficacy of albuminuria in type 2 diabetes mellitus to be as predictor and independent marker of atherosclerosis by measurement of carotid intimal-medial thickness (CIMT) by high frequency ultrasonography.

One hundred twenty participants in this study, 45 as a control healthy person and the others 75 patients with type 2 diabetes mellitus were included in this study.

We divided into three groups: group 1 which is the control group, and group 2 those patients who are the diabetic without albuminuria, and group 3 are the diabetic patients with albuminuria.

The intimal-medial thickness (IMT) was measured by high frequency ultrasonography. Other laboratory investigations were measured like HbA1c, fasting blood sugar, lipid profile.

The intimal-medial thickness (IMT) was found higher in group 3 than group 1 and group 2 (P value < 0.05).

In conclusion, there is a significant association between micro- albuminuria and IMT as a marker of atherosclerosis in type 2 diabetes mellitus.

INTRODUCTION

Diabetes is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from insufficient action of insulin. Type 2 diabetes mellitus is caused by a combination of genetic factors related to impaired insulin secretion and insulin resistance and environmental factors such as obesity, overeating, lack of exercise, and stress, as well as aging. It is typically a

multifactorial disease involving multiple genes and environmental factors to varying extents. Compared with people without diabetes, affected individuals are at increased risk for both cardiovascular events and kidney disease [1, 2]. In addition, diabetes mellitus is the most common cause of renal damage and end – stage renal disease, moreover, the earliest sign of diabetic nephropathy is microalbuminuria which can lead to macroalbuminuria and progressive kidney function impairment [3].

Increased urinary protein excretion may be an early clinical manifestation of diabetic nephropathy [4-8]. However, when assessing protein excretion, the urine dipstick is a relatively insensitive marker for initial increases in protein excretion, not becoming positive until protein excretion exceeds 300 to 500 mg/day (upper limit of normal less than 150 mg/day, with most individuals excreting less than 100 mg/day) [8].

Using a specific assay for albumin is a more sensitive technique. The normal rate of albumin excretion is less than 30 mg/day (20 µg / minute); persistent albumin excretion between 30 and 300 mg / day (20 to 200 µg/min) is called microalbuminuria [9].

Protein excretion above 300 mg/ day (200 µg/min) is considered to represent macroalbuminuria (also called overt proteinuria, clinical renal disease, or dipstick positive proteinuria) [9]. The reported prevalence of microalbuminuria among patients with type 2 diabetes mellitus approximately 10 years after the diagnosis ranges from 25 – 40 % (10-14). Increased urinary albumin excretion (albuminuria) and reduced glomerular filtration rate (GFR) are risk factors for progressive kidney failure and cardiovascular disease [15].

Several biochemical parameters including soluble vascular cell adhesion molecule 1, sialic acid, C-reactive protein, and fibrinogen have been proved to be significantly associated with microalbuminuria (15-18) and those paremeters were believed to indicate endothelial dysfunction and chronic inflammation, and these findings may support a hypothesis that microalbuminuria reflects generalized vascular damage which may promote atherosclerosis [19,20], moreover, microalbuminuria is the most reliable marker of diabetic nephropathy and an index of atherosclerosis and cardiovascular mortality in type 2 diabetic patients [21,23].

Atherosclerosis is the main cause of cardiovascular disease; measurement of intimal-medial thickness (IMT) enables the detection of atherosclerotic lesions of the arterial wall [24], on the other hand, the carotid intima-media thickness (CIMT) is a sensitive marker of early carotid atherosclerosis; thus, measurement of the CIMT by ultrasonography can be used to assess the cardiovascular risk and to determine indications for better management of diabetes and intensified treatment [23].

The CIMT can be measured by high frequency B mode ultrasonography, which provides a high degree of accuracy in estimating the arterial wall thickness [25]. The CIMT is significantly higher in diabetic patients than in non-diabetic patients [25], and the increased IMT can predict future events of silent brain infarction and coronary heart disease in the patients with type 2 diabetes mellitus [26,27]. Inaddition, the increases in the CIMT may be associated with an increased risk of myocardial infarction and stroke in aged patients without a history of cardiovascular disease [21].

Subjects, Materials and methods

Barticipants: The study included 120 persons, 45 healthy persons (control group, group 1), age range 40 – 62 years, 23 were males and 22 were females. The other 75 persons were type 2 diabetic patients and divided into 2 groups:

Group 2 involved 46 patients with normoalbuminuria, 26 males and 20 patients were females.

Group 3 involved 29 patients with microalbuminuria (urinary albumin excretion rate {UAER} is 30 – 300 mg / 24 hours' urine collection) and include 14 males and 15 females.

The age in both groups 2 and 3 was range from 42 – 74 years and the duration of type 2 diabetes mellitus was 4 – 11 years and all patients on diet and oral hypoglycemic drugs.

Medical history was obtained and physical examination was performed in all patients. Blood samples were withdrawn from all subjects following 12 hour of fasting. We measured body mass index (BMI), Blood pressure both systolic and diastolic blood pressure, fasting blood sugar (FBS) and glycated hemoglobin (HbA1c), lipid profile, UAER, IMT by carotid artery ultrasonography.

Serum concentrations of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), and FBS were measured by enzymatic method. HbA1c was measured by high performance liquid chromatography. UAER was obtained by a 24-hour urine collection. Body mass index (BMI) was calculated as weight in kilograms divided by height in meter squared.

Exclusive criteria:

Renal impairment, type 1 diabetes mellitus, hypertension, ischemic heart disease, valvular heart disease was excluded from the study.

The conditions that could cause transient elevations in urinary albumin excretion, such as exercise, urinary tract infection, febrile illness, were also excluded from the study.

Carotid artery ultrasonography:

An experienced specialist performed carotid artery ultrasonography. A real-time ultrasound scan was used: Hitachi EUB 7500 with an electrical linear transducer (mid frequency of 7.5 MHz probe, Hitachi Medical System, Japan). All subjects were examined in the supine position with the head turned 45º contralateral to the side of scanning. The scanning session lasted for an average of 30 minutes. B-mode images were obtained in longitudinal section. IMT was defined as the distance between the lumen-intima and the media-adventitia ultrasound interfaces. The IMT on the far wall of the bilateral common carotid artery about 10 mm proximal to the bifurcation of the carotid artery was measured Three measurements on both sides .manually [28, 29] were performed for each subjects and the mean value was obtained for analysis. Carotid IMT values below 0.8 mm were considered as normal [29].

The presence of plaques and degree of stenosis was noted and analyzed. Plaque was defined as a localized lesion of thickness ≥ 1 mm; 50% occlusion with >stenosis was defined as systolic frequency peak ≥ 4 KHz and spectral broadening [30].

Statistical analysis: The software of SPSS version 13 for Windows (SPSS Inc., IL USA) was used for statistical analysis. Statistical significance between two groups was determined by Wilcoxon rank-sum test. Continuous variables were expressed as median and range. Pearson's chi-square test was used to compare groups regarding categorical variables. Correlation analysis including Pearson's for continuous and Spearman's for discrete variables

and multiple linear stepwise regression analysis was used to show the influences of variables on IMT. Multivariate regression analysis was computed with <the SPSS statistical software package and P values 0.05 were considered significant.

RESULT

A total of one hundred and twenty (120) participants were included in the study; 45 healthy persons as control group (group 1) which are non diabetic, and 75 patients with type 2 diabetes mellitus with or with out albuminuria (group 2 and group 3).

Table 1 shows the characteristics of this study which revealed that Group 3 showed elevated UAER and also more BMI with poor HbA1c, and this group showed more IMT than those with group 2 as evident in figure 1.

Table 1: characteristics of the study

Characteristics	Group 1 No. = 45	Group 2 No.= 46	Group 3 No.= 29	*P* value
Sex (M / F)	23 / 20	26 / 20	14 / 15	NS
Age (years)	50.1	47.7	53.6	NS
Smokers (%)	37 %	29 %	33 %	NS
Duration of DM	NO	5.9	7.3	0.05 <
BMI (Kg/M^2)	24.1	25.1	26.2	NS
Systolic BP	118.2	120.1	119.1	NS
Diastolic BP	75.1	76.1	75.2	NS
FBG (mmol)	5.5	8.9	119	< 0.05

HbA1c (%)	5.8	7.1	8.2	< 0.05
IMT (mm)	0.49	0.72	0.94	< 0.05
UAER(mg / 24 hr)	10.9	11.1	70.2	< 0.05
TG (mmol/L)	1.4	1.56	2.4	< 0.05
LDL (mmol/L)	3.2	3.33	4.1	< 0.05
HDL (mmol/L)	0.89	0.91	0.92	NS

(intimal – medial the three groups:

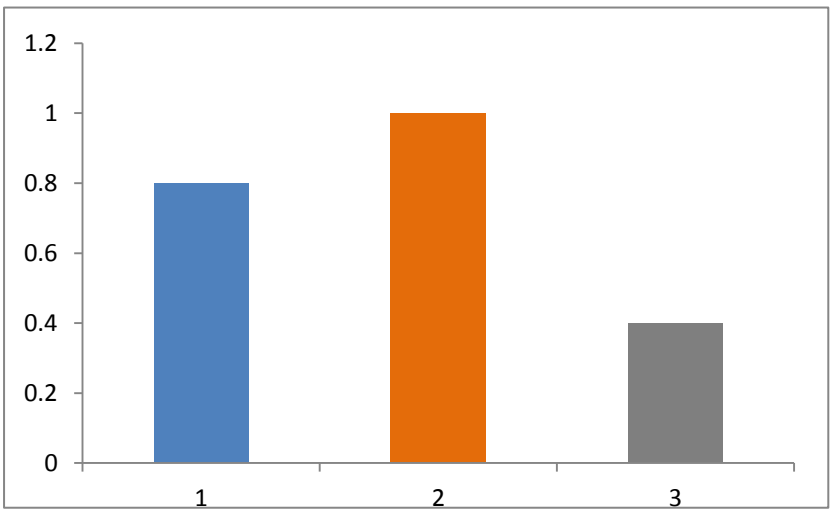
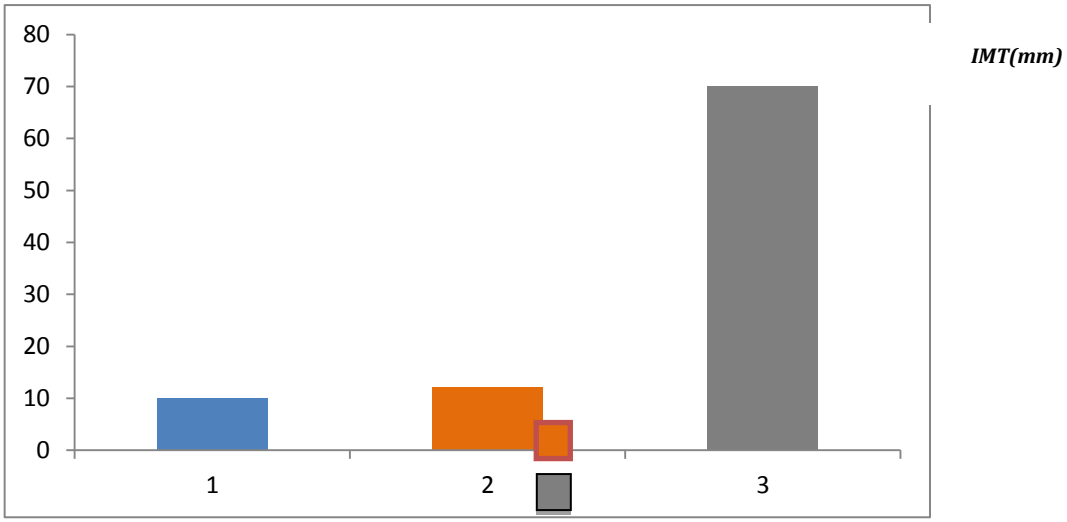


Figure 1: Shows IMT thickness) between

1- DM type 2 with no albuminuria (group

2- DM type 2 with albuminuria (group
3- Control group (group 1

Figure 2: shows the differences regarding UAER between the three groups.



(group 1)
(group 2)
(group 3)

Figure : 4 shows percent of patient with pooly control DM in groub 2 (with out albuminuria

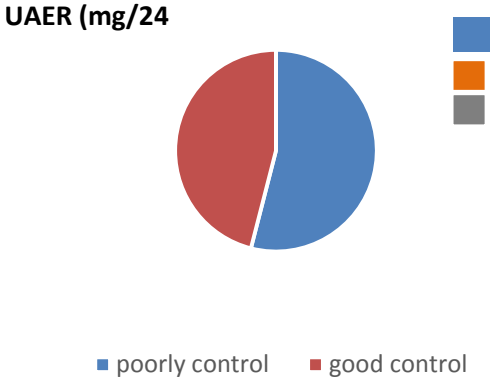
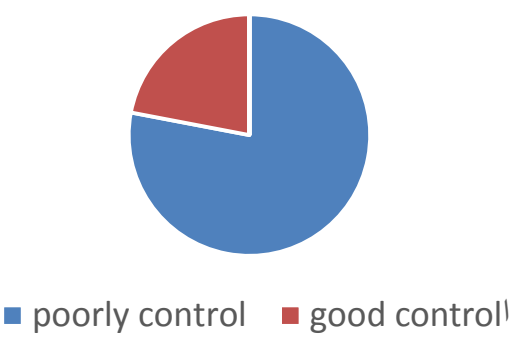


figure 3 : shows the percent of patient in group 3 whose poorly control DM



DISCUSSION

In our study, we found that IMT (as a marker of atherosclerosis) was higher in type 2 diabetic patients with albuminuria than those with normal urinary albumin excretion, so the presence of albuminuria in type 2 diabetic patients considered as independent risk factor and predictor of IMT and atherosclerosis.

It is known that there is a relationship between diabetic nephropathy and atherosclerosis in many studies, N. Nand, et al. [31] results showed that albuminuria was associated with carotid atherosclerosis in middle age individuals. But this study not limited to diabetic patients.

D. A. Stehouwer, et al. [32] showed that albuminuria was associated with impaired endothelium – dependent, flow-mediated vasodilatation in old age group with and without diabetes.

Yu-Hong Zhang, et al. [33] showed that there was significant association between microalbuminuria and IMT in diabetic patients only.

Dick de Zeeuw study showed that albuminuria is a clear marker of cardiovascular morbidity and mortality [34].

In the same time, this study showed that the value of HbA1c in type 2 diabetic patients with microalbuminuria was significantly higher than that in patients with normoalbuminuria. IMT was significantly associated with HbA1c. The result indicated that HbA1c may be played an important role in the relationship between carotid atherosclerosis and microalbuminuria. HbA1c can accurately reflect long term glycemic control. HbA1c is now used to assess glycemic control in diabetic patients, and also consider an important test for screening and diagnosis of the diabetes.

HbA1c is considering a very beneficial marker for diabetic microvascular complications [35].

Also, HbA1c is associated with advanced glycation end products (AGEs) [36].

Our study has its limitations; including the study population is small, and some patients with type 2 diabetes mellitus have been already treated with antihyperlipidemic agents which may lead to inaccuracy of the results.

CONCLUSIO

Our study shows that there is significant association between microalbuminuria and IMT which consider as the early sign of carotid atherosclerosis in patients with type 2 diabetes mellitus. Detection of carotid artery IMT and plaque in type 2 diabetic patients with microalbuminuria is very important for detecting early atherosclerosis and prevent toward the development of diabetic nephropathy and cardiovascular insults. Larger and further studies are needed to confirm our results.

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العلاقة بين تصلب الشريان السباتي والبول الزلالي عند مرضى داء السكري

ا.م.د. باسم عذيب مطر*، ا.م.د. ميثاق عبد المهدي حسين*، د. اوراس مجيد **

الهدف من الدراسة هو لتقييم فعالية إيجاد البول الزلالي لدى مرضى السكري النوع الثاني ليكون عامل تنبؤ ومستقل لتصلب الشرايين من خلال قياس سماكة الباطنة الوسطية للشريان السباتي بواسطة السونار ذات التردد العالي.

تمت الدراسة على (١٢٠) شخصا ، ٤٥ منهم كانوا أشخاصا اصحاء ليس لديهم داء السكري واعتبروا مجموعة السيطرة. الباقي كان ٧٥ مريضا يعاني من داء السكري النوع الثاني.

قسموا ال (١٢٠) شخصا الى ثلاثة مجاميع: المجموعة الأولى كانت مجموعة السيطرة وهم الأشخاص الاصحاء الذين كان عددهم ٤٥ شخصا، المجموعة الثانية كانت مجموعة المرضى الذين يعانون من داء السكري من النوع الثاني وليس لديهم البول الزلالي، اما المجموعة الثالثة كانت مجموعة المرضى المصابين بداء السكري وتميزوا بان لديهم البول الزلالي.

تم اخذ عينات الدم من كل المجاميع لقياس مستويات السكر الصيامى والدهون الكلية ومستويات السكر التراكمي. كما تم قياس سماكة الباطنة الوسطية للشريان السباتي بواسطة السونار ذات التردد العالي لكل مجاميع الدراسة.

أظهرت النتائج بان سماكة الباطنة الوسطية للشريان السباتي كانت الأعلى لدى المجموعة الثالثة وهي مجموعة مرضى السكري الذين لديهم البول الزلالي أكثر من المجموعة الأولى والثانية وكانت النتائج ذات قيمه إحصائية مهمة.

تم الاستنتاج بان هناك علاقة قيمه بين البول الزلالي وسماكة الباطنة الوسطية للشريان السباتي واعتبارها عامل تنبؤ مهم لتصلب الشرايين عند مرضى السكري من النوع الثاني.

*أستاذ مساعد – فرع الطب الباطني – كلية الطب / جامعة ذي قار

**طبيبة اختصاصية اشعه وسونار – دائرة صحة ذي قار