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CORRELATION BETWEEN MICROALBUMINURIA AND SEVERITY OF CORONARY ARTERY STENOSIS IN PATIENTS WITH TYPE II DIABETES MELLITUS

By

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ABSTRACT

Background: Cardiovascular disease is the major cause of death in patients with diabetes mellitus. Microalbuminuria (MAU) is defined as persistent subclinical elevation of urinary albumin excretion rate (UAER), which is insufficient to be demonstrated by reagent strips.

Objective: to determine the correlation between microalbuminuria and the severity of coronary artery stenosis assessed by Gensini score in patients with type II diabetes mellitus

Patients and methods: This study included sixty-one patients with type II diabetes mellitus and suspected coronary artery disease that underwent elective coronary angiography in Al-Azhar University Hospital, New Damietta, during the period between October 2013 and October 2014. Patients were classified into two groups based on the level of urinary albumin: creatinine ratio (UACR): ***Group I*** included 32 patients (52.5 %) with microalbuminuria (UACR level ranging from 30 to less than 300 mg/g), and ***Group II*** included 29 patients (47.5 %) with normoalbuminuria (UACR level less than 30 mg/g). All patients were subjected to full history taking, clinical assessment, standard 12-lead surface electrocardiogram (ECG), echocardiography, laboratory investigations, and coronary angiography**.**

Results: This study showed that UACR and Gensini score increased with age. There was a significant positive correlation between UACR and total cholesterol, triglycerides, LDL-C and glycosylated hemoglobin (HgbA1c), while there was a significant negative correlation with HDL-C and smoking. There was a significant positive correlation between Gensini score and urinary albumin level. The Gensini score was correlated with LDL- C and no correlation with total cholesterol, triglycerides, HDL-C and glycosylated hemoglobin (HgbA1c) or smoking. In the present study, the number of coronary vessels affected was higher in patients with microalbuminuria than those without microalbuminuria. The severity of coronary artery disease assessed by Gensini score was significantly higher in patients with microalbuminuria than those without microalbuminuria, and there was a correlation between UACR and Gensini score as a measurement of severity of coronary artery stenosis.

Conclusion: In patients with type II DM, microalbuminuria can be used as a predictor for coronary artery disease severity.

Keywords: Gensini Score, Diabetes Mellitus, microalbuminuria; coronary artery stenosis.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease, wide spread through the world with huge social, health and economic consequences. It estimates approximately 360 million people had DM in 2011and more than 95% of them had type II DM. This number will be increased to 552 million by 2030 and it is thought that about half of those will be unaware of their diagnosis **(Lars et al., 2013)**.

Cardiovascular disease is the major cause of death in those patients. Many of diabetic patients with coronary artery disease (CAD) do not have any other classic risk factor for coronary artery disease and half of them have normal lipid profile **(Pahor et al., 1999)**.

Microalbuminuria (MAU) is defined as persistent subclinical elevation of urinary albumin excretion rate (UAER). It is considered a marker of endothelial dysfunction and vascular damage which could be a predictor of coronary artery atherosclerosis **(Stehouwer et al., 2004).**

The urinary albumin: creatinine ratio (UACR) has been shown to be convenient, and efficient in screening patients for microalbuminuria when compared with 24-hour collections and has been suggested for diabetic and hypertensive patients (**Afkhami et al., 2007).**

Description of a coronary artery disease by Gensini scoring system was intended to take into account the geometrically increasing severity of lesions by diameter reduction, cumulative effect of multiple lesions, lesion location and influence of collaterals **(Gensini, 1975).**

The aim of this study was to determine the correlation between micro-albuminuria and the severity of coronary artery stenosis assessed by Gensini score in patients with type II diabetes mellitus.

PATIENTS AND METHODS

This study was a cross-sectional study included sixty-one patients with type II diabetes mellitus and suspected coronary artery disease that underwent elective coronary angiography in Al-Azhar University Hospital, New Damietta, during the period between October 2013 and October 2014. Twenty-seven patients of the study population were males (44.3%) and thirty-four were females (55.7%).

Inclusion criteria: This study included patients with type II DM with suspected CAD candidate for elective coronary angiography

Exclusion criteria: Patients with macroalbuminuria, renal impairment, acute myocardial infarction (MI), or congestive heart failure (CHF) were excluded from the study. Also, patients already receiving angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) were excluded.

Patients were classified into two groups based on the level of UACR: ***Group I*** included 32 patients (52.5 %) with microalbuminuria (UACR level ranging from 30 to less than 300 mg/g); and ***Group II*** included 29 patients (47.5 %) with normoalbuminuria (UACR level less than 30 mg/g).

All patients were subjected to full history taking, clinical assessment including general and local examinations, and laboratory investigations including complete blood count (CBC), glycosylated hemoglobin (HgbA1c), serum creatinine (Cr.), liver function tests (liver enzymes, serum albumin, and bilirubin), lipid profile, and urinary albumin to creatinine ratio, standard 12-lead surface electrocardiogram (ECG), echocardiography, and coronary angiography.

Statistical analysis of data: The collected data were coded, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 16, running on IBM-compatible computer. Quantitative data were expressed in arithmetic mean ± standard deviation (SD), while qualitative data were expressed in relative frequency and percentage. Comparison between groups was done by unpaired (t) test for normally distributed and Mann Whitney (U) test for non-normally distributed quantitative data of two independent samples; and Chi-square test (χ^2) for comparison of qualitative data. Receiver operating characteristics (ROC) curve was used to determine the sensitivity and specificity of different cut-off points and Pearson's correlation coefficient (r) was used to detect association between different variables. The level of significance was taken at $p \leq 0.05$, for interpretation of results.

RESULTS

There was a significant increase of age in group I when compared to group II (58.78±6.36 vs 54.38 ± 5.97 respectively). In addition, there were significant increases of hypertension, dyslipidemia, and hyperuricemia in group I when compared to group II (78.1%, 46.9% and 15.6% vs 37.9%, 10.3% and 0.0% respectively), while smoking significantly higher in group II when compared to group I (31.0% vs 3.1% respectively). Furthermore, there were significant increases of HbA1c, triglycerides (TG), cholesterol and LDL in group I when compared to group II (8.47±1.20, 237.01±69.42, 247.58±40.62 and 140.68±27.50 vs 7.14±1.13, 123.87± 71.63, 147.20±53.80 and 58.36±37.95 respectively), while there was significant decrease of HDL in group II when compared to group I (34.12±5.29 vs 53.20±10.01 respectively). Finally, there were significant increases of urinary albumin, UACR, Gensini score and number of affected vessels in group II when compared to group I (52.77±29.38, 64.76±17.94, 59.89±42.24 and 2.16±1.14 vs 19.18±10.99, 16.12± 7.11, 27.78±32.52 and 1.17±1.23 respectively - Table 1).

As regard correlation between UACR and other variables, there were significant positive (proportional) correlations between UACR from one side and each of age, number of affected vessels, TG, cholesterol, LDL and HbA1c from the other side, while there were significant negative (inverse) correlations between UACR from one side and each of HDL and smoking. In addition, there were positive significant correlations between Genisini score from one side and each of age, LDL and urinary albumin from the other side (table 2). Finally, based on ROC curve, 31.7 mg/dl was the best cut off point for urinary albumin level that differentiates Gensini score above and below 70. Area under the curve was 0.89;

sensitivity and specificity were 89.5 % and 78.6%, respectively (Figure 1). In addition, 41.3 mg/g was the best cut-off point for microalbuminuria by UACR that differentiates Gensini score above and below 70. Area under the curve was 0.69; sensitivity and specificity were 73.7% and 64.3%, respectively (figure 2).

Table (1): Comparison between group I and II as regard to different variables of the study population.

Variables \ Groups		Group I (n=32) (microalbuminuria)	Group II(n=29) (normoalbuminuria)	P value
Age (years)		58.78±6.36	54.38±5.97	***0.007****
Male gender		12(37.5%)	15(51.7%)	0.19
Risk factors	Hypertension	25(78.1%)	11(37.9%)	***0.002****
	Dyslipidemia	15(46.9%)	3(10.3%)	***0.002****
	Smoking	1 (3.1%)	9(31.0%)	***0.004****
	Hyperuricemia	5(15.6%)	0(0.0%)	***0.034****
	Rheumatoid arthritis	1(3.1%)	0(0.0%)	0.52
Systolic blood pressure (mmHg)		138.75±8.23	134.83±8.61	0.07
Diastolic blood pressure (mmHg)		83.75±7.41	83.79±7.15	0.9
Investigations	HbA1c (%)	8.47±1.20	7.14±1.13	***<0.001****
	TG (mg/dl)	237.01±69.42	123.87±71.63	***<0.001****
	Cholesterol (mg/dl)	247.58±40.62	147.20±53.80	***<0.001****
	LDL (mg/dl)	140.68±27.50	58.36±37.95	***<0.001****
	HDL (mg/dl)	34.12±5.29	53.20±10.01	***<0.001****
	Serum creatinine (mg/dl)	0.98±0.19	0.96±0.22	0.51
	Urinary albumin (mg/dl)	52.77±29.38	19.18±10.99	***<0.001****
	UACR (mg/g)	64.76±17.94	16.12±7.11	***<0.001****
Gensini score		59.89±42.24	27.78±32.52	***0.002****
Number of affected vessels		2.16±1.14	1.17±1.23	***0.002****

* Significant.

Table (2): Correlation between UACR and Gensini score with other variables.

Correlation	UACR		Gensini score	
Variables	*r*	*P*	*R*	*p*
Age (Years)	***0.32***	***0.01****	***0.41***	***0.001****
Number of affected vessels	***0.3***	***0.02****	0.85	<0.001*
TG (mg/dl)	***0.62***	***<0.001****	0.22	0.88
Cholesterol (mg/dl)	***0.7***	***<0.001****	0.18	0.17
LDL (mg/dl)	***0.81***	***<0.001****	***0.30***	***0.03****
HDL (mg/dl)	***-0.76***	***<0.001****	-0.19	0.13
HbA1c (%)	***0.62***	***<0.001****	0.04	0.7
Smoking	***-0.37***	***0.004****	-0.08	0.5
Systolic blood pressure (mmHg)	0.25	0.051	0.25	0.057
Diastolic blood pressure (mmHg)	0.017	0.90	-0.11	0.41
Urinary albumin (mg/dl)	0.66	<0.001	***0.7***	***<0.001****
Serum creatinine (mg/dl)	0.17	0.19	0.16	0.2

* Significant.

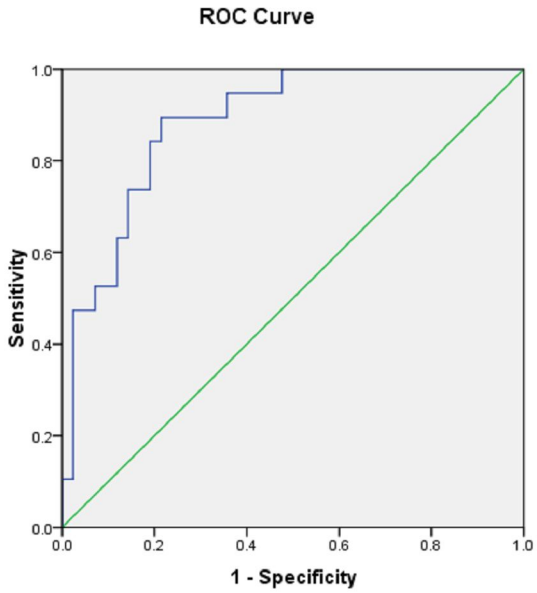

Figure (1): ROC curve of urinary albumin level that differentiates patients with Gensini score above and below seventy.

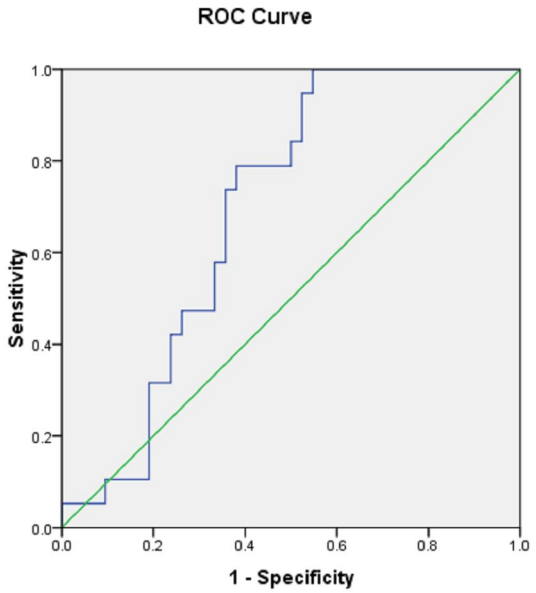

Figure (2): ROC curve of microalbuminuria level that differentiates patients with Gensini score above and below seventy

DISCUSSION

Microalbuminuria is a significant risk factor for cardiovascular mortality in type I and type II diabetes mellitus, as well as in non-diabetic population. It reflects systemic vascular damage, closely associated with microangiopathy and increased risk of coronary heart disease (**Klasen et al., 2004).**

Cardiovascular diseases are the leading cause of death in patients with type II diabetes mellitus. Similarly, in patients with established cardiovascular diseases diabetes caries a greater risk of worse outcomes and increases the risk of morbidity and mortality especially when associated complications such as nephropathy, retinopathy and possibly neuropathy are present **(Barkoudah et al., 2012).**

The age of the patients with micro-albuminuria was significantly higher than those with normoalbuminuria which was in agreement with those results reported by **Hashim et al. (2006), Hoseini & Rasouli (2009), El Sherif et al. (2011), and Parsa et al. (2013)** who found that microalbuminuria increasing with age. While in studies by **Parvizi et al. (2005) and Sukhija et al. (2006)** there was no correlation between MAU and age due to small sample size. In the present study, there was no difference between the 2 groups as regards gender distribution, and this was in agreement with results by **Parvizi et al. (2005) and Sukhija et al. (2006)** who reported that there was no difference between males and females as regards microalbuminuria. However, **Hashim et al. (2006), Hoseini & Rasouli (2009), Parsa et al. (2013) and Sadaka et al. (2013)** found that microalbuminuria was higher in males with no statistically significant difference.

The present study showed that there was a significant correlation between UACR and number of vessels affected.

This result was in agreement with those reported by **Parvizi et al. (2005), Hoseini & Rasouli (2009) and Sadaka et al. (2013)** who found that MAU was correlated with number of vessels affected.

In the present study serum cholesterol, triglycerides and LDL-C levels were higher in patient with MAU than those without MAU while HDL-C was lower, and there was a significant correlation between MAU and lipid profile, and these results were in agreement with those reported by **Johnsen et al. (1999), Sigdel et al. (2008) and Aziz et al. (2014)** who concluded that TC, TG, and LDL-C levels were higher in MAU group. While**, Sukhija et al. (2006), Hoseini & Rasouli (2009) and Parsa et al. (2013)** showed that there was no correlation between MAU and lipid profile, it could be due to race, medications and geographic or nutritional factors.

In the present study, the serum glycosylated hemoglobin (HgbA1c) was higher in patients with MAU than those without MAU and there was a significant correlation between MAU and HgbA1c. This result was in agreement with those reported by **Sukhija et al. (2006) and El Sherif et al. (2011)** who concluded that MAU was correlated with HgbA1c, while **Jun et al. (2010)** showed that MAU was not correlated with HgbA1c.

In the present study, there was a negative correlation between microalbuminuria and smoking. This result was not in agreement with those reported by **Parvizi et al. (2005), Hoseini et al. (2009), Parsa et al. (2013) and He et al. (2014)** who concluded that there was no correlation between microalbuminuria and smoking, it could be due to sample size with female predominance.

This study showed that there was a significant positive correlation between Gensini score and age, and this was in agreement with those reported by **El Sherif et al. (2011), Kim et al. (2013), Parsa et al. (2013), He et al. (2014) and Hong et al. (2014)** who found a significant positive correlation between Gensini score and age.

In the present study, there was a significant correlation between Gensini score and urinary albumin level, and there is no data available to compare with them. Also, Gensini score was significantly correlated with LDL-C level, while there was no correlation between Gensini score and triglycerides, cholesterol, HDL-C, HgbA1c or smoking. These results were not in agreement with those reported by **El Sherif et al. (2011) and Hong et al. (2014)** who concluded that there was a correlation between Gensini score and HgbA1c. **Kim et al. (2013)** found that there were correlations between Gensini score and triglycerides, HDL-C and LDL-C. **Sukhija et al. (2006) and Parsa et al. (2013)** found that there was no correlation between Gensini score and triglycerides, cholesterol, HDL-C, LDL-C or smoking. These differences could be due to survey period, sample size and medications.

In the present study, Gensini score, as a measurement of severity of coronary artery disease, was significantly higher in patients with microalbuminuria than those without microalbuminuria. This result was in agreement with those reported by **El Sherif et al. (2011) and Parsa et al. (2013)** who concluded that the Gensini score of patients with MAU is signifi-

cantly higher than patients without MAU. Also, our study showed that there was a significant positive correlation between microalbuminuria and Gensini score. This result was in agreement with those reported by **El Sherif et al. (2011) and Parsa et al. (2013)** who concluded that the Gensini score and MAU were correlated significantly. Other studies showed that there was a correlation between microalbuminuria and severity of coronary artery disease as those reported by **Sadaka et al. (2013)** who found that patients with MAU had more extensive and complex angiographic CAD compared to those without MAU with a direct relationship between MAU and extension of atherosclerotic coronary lesions. Also, **Hoseini and Rasouli (2009)** concluded that MAU was more prevalent in CAD-positive patients than in CAD-negative patients, and MAU exhibited a significant correlation with the severity of CAD. In addition, the patients with MAU had a much greater atherosclerotic burden in the form of multi-vessel disease than those without MAU. Similar results were presented by **Sukhija et al. (2006)** who studied 4 groups patients with DM and MAU, patients with DM and without MAU, patients with MAU and without DM and patients without DM and MAU and concluded that there was a graded increase in extent of angiographic CAD from group of patients with DM and MAU to group of patients without DM and MAU. Thus, patients with MAU had more severe angiographic CAD than those without MAU. In another study performed by **Parvizi et al. (2005),** the results showed that the UACR in patients with CAD was higher than that of the control group patients with normal coronary arteries with a significant correlation between the extend of atherosclerotic lesions and UACR.

CONCLUSION

In patients with type II DM, microalbuminuria can be used as a predictor for coronary artery disease severity.

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خلفية البحث: تعتبر أمراض القلب والشرايين التاجية من الأسباب الرئيسية للوفاة في مرضى السكري، ويعرف الزلال الدقيق فى البول علي أنه الإرتفاع المستمر في معدل إفراز زلال الألبيومين الدقيق فى البول والذي لا يمكن تحديده والكشف عنه بأشرطة الكواشف التقليدية.

الهدف من البحث: تقييم العلاقة بين الزلال الدقيق بالبول وشدة ضيق الشرايين التاجية محددة بمقياس جنسيني في مرضى النوع الثاني من مرض السكري.

مواد وطرق البحث: إشتملت هذه الدراسة على واحد وستين مريضا من النوع الثاني لمرض السكري الذين تم عمل لهم قسطرة تشخيصية نتيجة اشتباه في وجود قصور بالشرايين التاجية و تم إختيار المرضى من المستشفيات والعيادات الخارجية لجامعة الأزهر، في الفترة من أكتوبر ٢٠١٣، وحتى أكتوبر ٢٠١٤ . وتم تقسيم المرضي إلى مجموعتين بناء علي نسبة الزلال الدقيق بالبول حيث اشتملت المجموعة الأولى على اثنين و ثلاثين مريضا (52.5 %) يعانون من وجود الزلال الدقيق بالبول (حيث معدل الألبيومين إلى الكرياتينين في البول يتراوح من ٣٠ إلى٣٠٠مليجرام/جرام)، و اشتملت المجموعة الثانية على تسعة وعشرون مريضا (47.5%) لا يعانون من وجود الزلال الدقيق بالبول (حيث معدل الألبيومين إلى الكرياتينين في البول أقل من ٣٠ مليجرام/جرام). وقد خضع جميع الأشخاص لأخذ تاريخ مرضى كامل مع فحص إكلينيكى ، كما تم عمل رسم قلب كهربائي، وموجات فوق صوتية علي القلب، وفحوصات معملية وقسطرة تشخيصية لشرايين القلب.

النتائج: أظهرت هذه الدراسة وجود زيادة لمعدل الألبيومين إلى الكرياتينين بالبول ومقياس جينسيني مع تقدم العمر، كما كان هناك ارتباطاً موجباً معتبراً بين معدل الألبيومين إلى الكرياتينين بالبول، ونسبة الكوليستيرول الكلي، والدهون الثلاثية، والبروتينات الدهنية منخفضة الكثافة و نسبة الهيموجلوبين السكرى بالدم، بينما كان هناك ارتباطاً سالباً معتبراً مع نسبة البروتينات الدهنية عالية الكثافة والتدخين .

كما كان هناك ارتباطاً موجباً معتبراً بين مقياس جنسيني ونسبة الألبيومين بالبول وبين مقياس جينسيني ونسبة البروتينات الدهنية منخفضة الكثافة، بينما لم يكن هناك أي ارتباط بين مقياس

جينسيني من جهة وبين نسبة الكوليستيرول الكلي، والدهون الثلاثية، والبروتينات الدهنية عالية الكثافة، ونسبة الهيموجلوبين السكري والتدخين .

كما أظهرت هذه الدراسة أن عدد الشرايين التاجية التي بها قصور كان أعلي في المرضي الذين يعانون من وجود الزلال الدقيق بالبول. وقد كانت شدة قصور الشرايين التاجية التي تم قياسها بمقياس جينسيني أعلى في المرضي الذين لديهم نسبة زلال دقيق بالبول عن المرضي الذين لا يعانون من وجود الزلال الدقيق بالبول. كما كان هناك ارتباطاً بين معدل الألبيومين إلى الكرياتينين بالبول وشدة ضيق الشرايين التاجية محددة بمقياس جينسيني.

الإستنتاج: فى المرضى الذين يعانون من النوع الثاني من مرض السكري يمكن استخدام الزلال الدقيق بالبول كمؤشر علي شدة إصابة الشرايين التاجية.