

# **Microalbuminuria predictor of cardiovascular disease in Iraqi type 2 diabetes mellitus**

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## **Abstract**

Microalbuminuria is strongly associated with risk for cardiovascular disease , it's a widely recognized , strong and independent risk marker of cardiovascular disease among individuals with diabetes.

This study was done in the period from October to December 2014 in the national diabetes center , university of al – Mustansiriya , Baghdad , Iraq. The study groups , one is 50 patients with type 2 diabetes mellitus and cardiovascular disease and the second group is 30 patients with only diabetes mellitus as control , their aged ranged between (45-65 )years.

The results were shown an increasing in FBG, HbA1c, hs-CRP, LDL, TG, AIP, Urea, creatinine, and Microalbuminuria in patients compared with control group at (  $P < 0.001$ ). While the concentration of HDL was significantly lower in patients compared with control group at ( $P < 0.001$ ). There is a positive correlation between AIP and HbA1c, hs-CRP, TG, Urea, creatinine, and Microalbuminuria. So microalbuminuria has become a prognostic marker for cardiovascular disease.

**Key words:** microalbuminuria , HDL, LDL , creatinine , diabetes mellitus, AIP, hs-CRP

## **Introduction**

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia and disturbances of carbohydrate , fat and protein metabolism associated with absolute or relative insulin deficiency. Diabetes mellitus is two types : type 1 and type 2 (1). Type 2 diabetes mellitus is an important public health problem worldwide because of its high prevalence and complications (2) , T2DM is characterized by insulin resistance coupled with an inability of the pancreas to sufficiently compensate by increasing insulin secretion , with onset generally in middle or old age (3,4). Cardiovascular disease (CVD) a group of medical problems that affect the heart and surrounding blood vessel (5). CVD can take many forms such as high blood pressure , coronary artery disease , Valvular heart disease or rheumatic heart disease. There are many factors affected as CVD such as cholesterol , triglyceride , and lipoprotein ( HDL-c , VLDL , TG ,

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LDL-c )(6,7). Over the last few decades several risk factors have been found to be associated with CVD like smoking , age , sex , diabetes , hypertension etc. Despite lower prevalence of such risk factors in Asian , incidence of CVD has been reported to high and is constantly rising (8).

Microalbuminuria , slightly elevated urinary albumin excretion , was initially demonstrated in the patient with diabetes mellitus , where was shown to be associated with atherogenic changes in the cardiovascular risk profile (9,10) and to predict increasing mortality and cardiovascular disease (11,12). Microalbuminuria is an independent predictor of CVD and all case mortality both diabetic and non-diabetic men and women (13,14). Detecting microalbuminuria is an important screening tool to identify people who are at high risk for CVD and who need more intensive therapy compared with the subjects with the normal albumin excretion rates ( 15,16 ). C-reactive protein ( CRP) is a liver protein composed of five identical non glycosylated subunits with a total molecular weight of 105 kDa. CRP has a variety of powerful effects related to immunology , inflammation , and coagulating ( 17,18). As a marker of low – level inflammation , CRP appears to predict future cardiovascular disease events among apparently health individuals , high plasma concentration of CRP was associated with increased risk of stroke , infraction , and peripheral vascular disease (19). Dobiasova and Frohlich (20) proposed the term Atherogenic Index of plasma (AIP) defined as  $\log (TG/ HDL-c)$  , on the basis that people with high AIP have a higher risk for CVD(21,22).

### **Material and Methods**

The present study included (50) patients with type 2 diabetes mellitus and cardiovascular disease , there age ranged between ( 45-65 ) years and (30) aged matched DM2 as a control subjects, were conducted in the National Diabetes Center , University of Al-Mustansiriya , Baghdad – Iraq during the period from October to December 2014. Blood sample (10 ml) was taken from each subject after overnight fasting (>12 hours ). The samples were put in plain tubes without any additive. Disposable syringes and needles were used for blood collection. After allowing the blood to clot at  $37^{\circ}C$  for about 15 minute , blood samples were centrifuged at 3000 rpm for 15 minute. Sera were separated in disposable tubes.

Serum glucose was measured by enzymatic method using kits supplied by Biocon company , (Germany). Determination of triglycerides ( TG ) were determined by totally enzymatic methods, using kits supplied by bio Merieux company , (France). Estimation of serum HDL-c was done by precipitation with phosphotungstate  $MgCl_2$  solution, using kits supplied by

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bio Merieux company , (France). Serum LDL-c level was calculated by the method of Bairaktari *et al*, 2004 (23) .

Microalbuminuria was determining by timed ( overnight ) collection of urine used to measure albumin /creatinine ratio (micral test )(24). And urine creatinine by using Jaffe method (25). Glycated hemoglobin ( Hb1c) was measured by Jeppson *et al*. (26). Urea was determined by enzymatic method (Urease–modified Berthelot reaction)(27).

Hs-c-reactive protein was assayed according to the procedure of the manufactures of its kits (Ridker 1998)(28). Athergenic index was calculated by using formula =log ( TG/ HDL-c )(29).

**Data Analysis:** To compare the significance of the difference in the mean values of any two groups, student's t-test was applied and  $P \leq 0.001$  was considered statistically significant. The correlation coefficient (r) test is used to describe the association between the different studied parameters.

### Result and Discussion

Table (1) shows that serum triglyceride and LDL-c were significantly increased in patients group ( $2.16 \pm 0.291$ )(  $4.694 \pm 0.685$ ) respectively compared to the control group ( $1.31 \pm 0.150$ )(  $3.099 \pm 0.27$ ) respectively, while HDL-c was significantly decreased in patients ( $0.912 \pm 0.134$ ) as compared to the control group ( $1.099 \pm 0.064$ ), the results were in agreement with the finding of many similar study (30,31). However , khan *et al* (32) reported no significant differences were observed in the levels of serum LDL and HDL. There is also an inverse relationship between serum levels of HDL and triglyceride in diabetic patients with low serum HDL levels possible representing an independent risk factor for cardiovascular disease (33). Although in another study low triglyceride concentration was found in type 2 diabetic patients in African Americans (30). Plasma HbA1c and FBG values were also significantly higher in patients ( $10.87 \pm 1.072$ )(  $10.74 \pm 0.949$ ) respectively as compared to the control group ( $4.729 \pm 0.192$ )(  $4.863 \pm 0.530$ ) respectively. The findings of present study are concordant to the finding of Saricka *et al* (34). The levels of creatinine was significantly increased in patients ( $1.34 \pm 0.530$ ) compared with the control ( $0.943 \pm 0.12$ ) and that similar to the finding of Philp *et al*(35).

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Table (1): serum levels of different parameters in patients and control

Parameters	Mean $\pm$ SD of patients	Mean $\pm$ SD of control	P-value
TG(mmol/L)	2.16 $\pm$ 0.291	1.31 $\pm$ 0.150	<0.001
LDL-c(mmol/L)	4.694 $\pm$ 0.685	3.099 $\pm$ 0.27	<0.001
HDL-c(mmol/L)	0.912 $\pm$ 0.134	1.099 $\pm$ 0.064	<0.001
HbA1c(mg/dl)	10.87 $\pm$ 1.072	4.729 $\pm$ 0.192	<0.001
FBG(mmol/L)	10.74 $\pm$ 0.949	4.863 $\pm$ 0.530	<0.001
Creatinine(mg/dl)	1.34 $\pm$ 0.530	0.943 $\pm$ 0.12	<0.001
Microalbuminuria(mg/L)	54.544 $\pm$ 10.744	15.048 $\pm$ 1.092	<0.001
Urea(mg/dl)	51 $\pm$ 5.051	30.152 $\pm$ 1.518	<0.001
hs-CRP(mg/L)	4.91 $\pm$ 0.177	1.12 $\pm$ 0.539	<0.001
AIP	0.38 $\pm$ 0.12	0.07 $\pm$ 0.26	<0.001

While microalbuminuria was significantly increased in patients (54.544 $\pm$ 10.744) compared with control group (15.048 $\pm$ 1.092). Considering microalbuminuria as risk factor for cardiovascular disease. A substudy of the heart outcomes prevention evaluation study found that microalbuminuria was strong predictor of cardiovascular disease (36). Level of hs-CRP was increased significantly in patients (4.91 $\pm$ 0.177) compared with control group (1.12 $\pm$ 0.539), these results are comparable to other previous results reported by Gani *et al* (37) and Fitzsimmons *et al* (38). Therefore concentration of hs-CRP were considered as predictor to incident by cardiovascular disease, several studies have earlier shown that hs-CRP predicates cardiovascular disease in western populations as a biomarker of inflammation (39,40). The Atherogenic Index of plasma was significantly higher in patients (0.38 $\pm$ 0.12) compared to controls group (0.07 $\pm$ 0.26). That agreement to results obtained by some researchers on (5,41).

Table (2): the correlation between AIP and HbA1c, hs-CRP, Urea, creatinine, and microalbuminuria in patients and their P value

Parameters	Correlation coefficient (r)	P- value
<b>HbA1c</b>	<b>0.8</b>	<b>&lt;0.001</b>
<b>hs-CRP</b>	<b>0.8</b>	<b>&lt;0.001</b>
<b>Urea</b>	<b>0.7</b>	<b>&lt;0.001</b>
<b>creatinine</b>	<b>0.5</b>	<b>&lt;0.001</b>
<b>microalbuminuria</b>	<b>0.6</b>	<b>&lt;0.001</b>

Table (2) shows that there was a correlation between AIP and HbA1c, hs-CRP, creatinine, and microalbuminuria. The AIP been successfully used as an additional index when assessing cardiovascular risk

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factor (42,43). Indeed , it has been suggested that AIP values of -0.3 to 0.1 are associated with low , 0.1 to 0.24 with medium and above 0.24 with high cardiovascular risk (44) , and thus according to the finding of this study , patients were are at high risk of developing CVD. While microalbuminuria has become a prognostic marker for cardiovascular disease (CVD) and finding of microalbuminuria is an indication for screening for possible vascular disease and aggressive intervention to reduce all cardiovascular risk factors (45).

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## البول الزلالي كأداة للتنبؤ وأمراض القلب عند مرضى السكري النوع

الثاني في العراق

ايناس جبار حسن

قسم العلوم / كلية التربية الأساسية / الجامعة المستنصرية

### الخلاصة

لقد تمت دراسة البول الزلالي كأحد العلامات الدالة على امراض القلب في مرضى السكري النوع الثاني . اجريت هذه الدراسة للمدة من تشرين الاول الى كانون الاول ٢٠١٤ في مركز السكري / الجامعة المستنصرية , حيث تضمنت الدراسة مجموعتين : المجموعة الاولى شملت ٥٠ مريض من مرضى السكري النوع الثاني والقلب . المجموعة الثانية شملت ٣٠ مريضا من مرضى السكري النوع الثاني كمجموعة ضابطة , وبمعدل اعمار تراوحت بين ٤٥-٦٥ سنة .

اظهرت النتائج وجود زياده معنويه في تراكيز كلوكوز مصل الدم الصيامي , الكليسيريدات الثلاثية , البول الزلالي , البروتين واطى الكثافة , معامل التصلب الشرياني ( AIP ) , و ج - البروتين الفعال عالي الحساسية مقارنة مع المجموعة الضابطة مع وجود نقصان معنوي في تراكيز البروتين عالي الكثافة مقارنة مع المجموعة الضابطة عند (  $P<0.001$  ) . فضلا عن وجود علاقة ارتباط موجبة بين AIP والكرياتينين , البول الزلالي , ج- البروتين عالي الحساسية , الكليسيريدات الثلاثية و اليوريا عند (  $P<0.001$  ) . من نتائج هذه الدراسة يمكن اعتماد مستويات البول الزلالي كمتنبئ وأمراض القلب عند مرضى السكري النوع الثاني.

الكلمات المفتاحية : البول الزلالي , البروتين عالي الكثافة , البروتين واطى الكثافة , الكرياتينين , السكري , ج - البروتين الفعال عالي الحساسية