

# Prevalence and associated risk factors for the development of albuminuria in patients with type 2 diabetes at NCDEG Jordan

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## الملخص

تهدف هذه الدراسة إلى استقصاء مدى انتشار نسبة بيلة الألبومين المجهرية والصريحة وعوامل الخطورة عند مرضى السكري من النمط الثاني بين عينة عشوائية تتكون من ٨٦٩ مريض من مرضى الداء السكري المراجعين للمركز الوطني للسكري والغدد الصماء والوراثة، كما تهدف الدراسة إلى تحديد مدى وجود ارتباط بين بيلة الألبومين المجهرية والصريحة وعدد من المتغيرات المستقلة والتي تتضمن ارتفاع الخضاب الغليكوزي في الدم وارتفاع التوتر الشرياني ومدة الداء السكري وشحوم الدم ومشعر كتلة الجسم والتدخين والعمر والجنس ووجود اعتلال الشبكية السكري.

تم إجراء الدراسة في المركز الوطني للسكري والغدد الصم والوراثة (عمان-الأردن). تضمنت عينة الدراسة (٨٦٩) مريضاً والتي تتراوح أعمارهم من ٣٠ سنة فما فوق من الذين يعانون من الداء السكري النمط الثاني والذين يراجعون المركز الوطني للسكري والغدد الصم والوراثة.

لقد بدأت الدراسة بتاريخ ١ أيلول ٢٠٠٧ وامتدت إلى ١٠ كانون ثاني ٢٠٠٨. وقد تم تشخيص بيلة الألبومين المجهرية والصريحة عندما يكون هناك إيجابية في نسبة الألبومين على الكريتين في عينة الصباح العشوائية، على الأقل في عينتين من ثلاث عينات متوالية خلال فترة الجمع التي امتدت من شهر إلى ثلاثة شهور على حسب تعريف جمعية السكري الأمريكية. وقد تم الحصول على النتائج المخبرية والفحوص السريرية من ملفات المرضى الطبية.

- بلغت نسبة الذكور (56.0%) ونسبة الإناث (44.0%) من بين جميع المرضى المفحوصين.
  - بلغ كل من متوسط العمر ومدة السكري ٥٧,٨ و ٩,٥ سنة على التوالي.
  - تبين أن ٦٢,٤% من المرضى كانوا يعالجون بخافضات السكر الفموية، و ٤,٣% كانوا يعالجون بالإنسولين، و ٣١,٧% كانوا يعالجون بخافضات السكر الفموية و الإنسولين معاً، بينما ١,٦% كانوا يعتمدون على الحمية وحدها.
  - بلغ متوسط قيمة الخضاب الغليكوزي 7.71%.
  - بلغت نسبة بيلة الألبومين الكلية بين المشاركين ٣٤,٦%، وذلك على النحو التالي:
    1. بيلة الألبومين المجهرية وجدت في ٢٩,٣% من المشاركين.
    2. بيلة الألبومين الصريحة وجدت في ٥,٣% من المشاركين.
- باستخدام تحليل الانحدار الخطي المتعدد تبين أن بيلة الألبومين المجهرية تتأثر بمعدل الخضاب الغليكوزي وبمعدل ضغط الدم الانقباضي و الانبساطي واعتلال الشبكية السكري، بينما تتأثر بيلة الألبومين الصريحة بمعدل ضغط الدم الانقباضي وعامل الجنس واعتلال الشبكية السكري.

تبين من نتائج الدراسة أن بيلة الألبومين الكلية هو مرض شائع بشكل كبير بين المرضى الأردنيين. وكذلك يتضح أن المسح المبكر لبيلة الألبومين والجهود الحثيثة لتحسين السيطرة على السكري، وتخفيض الضغط الشرياني، مع أهمية التداخل العلاجي بمثبطات الخميرة القابلة للأنجيوتنسين الذي ينبغي أن تؤخذ بعين الاعتبار لمقاومة هذا الداء وإمراضيته بشكل جدي حيث أنها تساهم في الحد من انتشاره.

## ABSTRACT

**Objective:** To investigate the prevalence of albuminuria (microalbuminuria and macroalbuminuria) in patients with type 2 diabetes mellitus (DM) attending the National Center of Diabetes, Endocrinology, and Genetics (NCDEG) in Jordan. The second objective of the study was to determine if there is any association between albuminuria (microalbuminuria and macroalbuminuria) and a number of independent variables, including glycemic control, hypertension, duration of diabetes mellitus, serum lipids, body mass index, smoking, age, gender and the presence of retinopathy.

**Methods:** A cross-sectional study was carried out at the National Center for Diabetes, Endocrinology, and Genetics (NCDEG), Jordan. A total of 869 diabetic patients aged 30 years and above with type 2 diabetes mellitus who attended the clinic from 1<sup>st</sup> September 2007 through 10<sup>th</sup> January 2008 were included. At least two out of three random morning spot urine samples were collected in a three-month period to determine the urinary albumin-creatinine ratio (ACR). Microalbuminuria is defined as an ACR of 30-299 mg/g and macroalbuminuria is defined as an ACR  $\geq$ 300 mg/g according to the definition proposed by the American Diabetes Association (ADA). Socio-demographic, clinical, and laboratory data

were obtained from the medical records of patients. Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS, version 11.5).

**Results:** Out of the 880 patients recruited, 5 (0.6%) were excluded due to the presence of urinary tract infections and 6 (0.7%) for the presence of congestive heart failure, leaving 869 patients for evaluation. There were 56.0% male and 44% female. The mean age and duration of diabetes were 57.8 years and 9.5 years, respectively. Approximately 62% were being managed by oral hypoglycemic agents alone, 4.3% by insulin alone, 31.7% were on a combination of oral hypoglycemic agents and insulin and slightly less than 2% were on dietary measures alone. The mean value for HbA1c was 7.71%. The overall prevalence of albuminuria among participants was found to be 34.6%; microalbuminuria (29.3%) and macroalbuminuria (5.3%). Multivariate logistic regression analysis identified HbA1c, SBP, DBP and the presence of retinopathy as independent risk factors for microalbuminuria and SBP. Male gender and presence of retinopathy were identified as independent risk factors for macroalbuminuria.

**Conclusion:** Albuminuria is highly prevalent among Jordanians with type 2 diabetes. This calls for early and universal screening of urinary albumin. There is also an urgent need for measures that target tight glycemic and optimal blood pressure control and the use of renin-angiotensin system blockade.

**Keywords:** diabetes mellitus; microalbuminuria; macroalbuminuria; Jordan

## INTRODUCTION

Diabetes mellitus (DM) is considered to be a major health problem that is predicted to turn into a global epidemic, affecting around 171 million people worldwide. The World Health Organization predicts that this number will rise to 366 million by 2030. In Jordan, the reported prevalence of diabetes among adults was 13.4% in 1998, while in a recent study the age standardized prevalence of DM was 17.1%; confirming that the prevalence of DM in Jordan is also increasing<sup>2</sup>.

Among all the complications of diabetes mellitus, nephropathy is the diabetes-specific complication with the greatest mortality<sup>3</sup>. Although in the past the risk of renal complications were thought to be considerably lower among patients with type 2 diabetes than among those with type 1 diabetes<sup>3</sup>, there is an increasing body of evidence that the risk of nephropathy with progression to end-stage renal disease (ESRD) is not dissimilar in the two groups<sup>4</sup>.

It is not surprising to see the emergence of more patients with ESRD among type 2 diabetics because of the increasing prevalence of type 2 diabetes and the improved survival rates of diabetic patients with renal failure<sup>4</sup>. Nephropathy associated with type 2 diabetes is the most frequent cause of ESRD in the United States, Europe, and Japan<sup>3</sup>. In Jordan, DM was the cause of ESRD in 10.5% of patients on haemodialysis in 1992<sup>5</sup>, increasing to 29.2% in 2003<sup>6</sup>. Although the magnitude of the disease has been better defined in developed countries, the situation is particularly serious in the developing countries where healthcare resources may often be limited<sup>7</sup>. One of the initial markers of this condition is microalbuminuria, which generally indicates an increased risk of deteriorating renal function and mortality<sup>8</sup>. Microalbuminuria is also a well-established marker of increased cardiovascular disease risk<sup>8</sup>. It is defined as 30 to 299 mg/dl in a 24-hr collection or 30 to 299 µg/mg in a spot collection, whereas macroalbuminuria is defined as ≥300 mg/dl in a 24-hr collection or ≥300 µg/mg in a spot collection<sup>9</sup>. Without specific interventions, 20-40% of type 2 diabetic patients with microalbuminuria

progress to macroalbuminuria (overt nephropathy), but by 20 years after the onset of overt nephropathy, only ~20% will have progressed to end-stage renal disease<sup>9</sup>. Macroalbuminuria is a strong and independent predictor of increased cardiovascular morbidity and mortality and its presence predicts loss of kidney function<sup>10</sup>. Diabetic retinopathy can be found in more than 90% of type 1 diabetic patients with nephropathy<sup>11</sup>. However, the relationship between albuminuria and diabetic retinopathy (DR) was less predictable in type 2 diabetes<sup>11</sup>.

Several studies have shown that there is a significant association between diabetic nephropathy and variables such as glycemic control, hypertension, hyperlipidemia, smoking, obesity, and duration of DM<sup>8, 9, 11, 12, 13, 14</sup>.

A better understanding of the prevalence of albuminuria and the associated risk factors is required to enable the further development of strategies for diabetic nephropathy in Jordanian patients diagnosed with type 2 diabetes, in view of the increased prevalence of diabetes and IFG in Jordan<sup>2</sup>. To date, there is no data available documenting the prevalence of albuminuria among type 2 diabetics in Jordan.

## METHODS

A cross-sectional study was conducted at the National Center for Diabetes, Endocrinology and Genetics (NCDEG) in Amman, Jordan. It comprised a systematic sample of 869 type 2 diabetic patients attending the NCDEG from 1<sup>st</sup> September 2007 through 10<sup>th</sup> January 2008. The study was approved by the NCDEG Ethics Committee. Relevant sociodemographic, clinical and laboratory data were obtained from the medical records of the patients. Anthropometric measurements were taken, including weight and height to estimate body mass index (BMI) [Kg/m<sup>2</sup>]. 'Overweight' is classified as having a BMI of 25.0 to 29.9, and obesity as having a BMI of ≥30 as defined by the WHO<sup>15</sup>. Blood pressure was measured using standardized sphygmomanometers on the right upper arm while the

subject was in a sitting position after 5 minutes' rest. Fasting blood sugar, serum cholesterol, serum triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were assayed by enzymatic methods. Glycosylated hemoglobin (HbA1c) was analyzed by using a high-performance liquid chromatography (HPLC) method (Bio-Rad); HbA1c was considered normal if <7%<sup>16</sup>.

Fresh random morning spot urine was examined by the strip test (Combur 9 Test) for leucocytes, nitrites and blood. Patients with positive nitrites, indicative of significant bacteriuria, and patients with erythrocytes and/or leucocytes equal to or above 5 cell counts per microliter, indicative of hematuria or/and pyuria, were excluded from the analyses. Microalbuminuria can be diagnosed when the urinary albumin to creatinine ratio is 30-299 mg/g in at least two of three urine collections in a three-month period. Whereas to designate a patient as having macroalbuminuria the same ratio is  $\geq 300$  mg/g<sup>9</sup>.

Diabetic retinopathy was detected by direct ophthalmoscopy. The International Clinical DR severity scale, adopted by the American Academy of Ophthalmology (AAO)<sup>17</sup> and the International Council of Ophthalmology (ICO)<sup>18</sup>, was used to classify patients into non-proliferative DR (NPDR), and proliferative diabetic retinopathy (PDR).

### Statistical Analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS, version 11.5). Chi-square tests and multivariate logistic regression was used to assess the correlation between microalbuminuria and macroalbuminuria and their risk factors. Separate regression models were used for microalbuminuria and macroalbuminuria.

## RESULTS

### Characteristics of the Study Population

Of the 880 patients recruited, 5 (0.6%) were excluded due to the presence of urinary tract infections and 6 (0.7%) for the presence of congestive heart failure, leaving 869 patients for evaluation. There were 487 (56%) men and 382 (44%) women. The mean age of the total study population was  $57.8 \pm 9.1$  years and the mean duration of diabetes was  $9.5 \pm 7.5$  years. Of the total sample, 15.9% were smokers while 20.7% were past smokers and 90.4% were obese or overweight. The majority of the patients had systolic and diastolic blood pressure below the 130/80 mm Hg target (see Table 1).

### Clinical and Biochemical Characteristics of the Study Population

As shown in Table 2, the majority of the sample population (67.9%) had hypertension. Dyslipidemia was present in 94.6% of the study patients. Hypertriglyceridemia, hypercholesterolemia, high LDL cholesterol, low HDL cholesterol levels among males and low HDL cholesterol levels among females were reported among 40.4%, 13.5%,

46.1%, 46.4%, 58.9% of these patients, respectively. Only 35.3% had HbA1c <7%. About one-third of patients had retinopathy.

Variable	n	(%)
Gender		
Males	487	(55.0)
Females	382	(44.0)
Age (year)	Mean(SD)=57.8 (9.1)	
<45	79	(9.1)
45-55	266	(30.6)
56-65	362	(41.7)
>65	162	(18.6)
Duration of DM(years)	Mean(SD)=9.5 (7.5)	
$\leq 5$	331	(38.1)
6-10	234	(26.9)
$\geq 11$	304	(35.0)
Smoking		
Non	551	(63.4)
Current	138	(15.9)
Past	180	(20.7)
Body Mass Index(Kg/m <sup>2</sup> )	Mean(SD)=31.5 (5.5)	
<25	83	(9.6)
25-29.9	275	(31.6)
$\geq 30$	511	(58.8)
Systolic Blood Pressure (mm Hg)	Mean(SD)=128 (14.5)	
<130	541	(62.3)
$\geq 130$	328	(37.7)
Diastolic Blood Pressure(mm Hg)	Mean(SD)=76.8 (7.5)	
<80	654	(75.3)
$\geq 80$	215	(24.7)

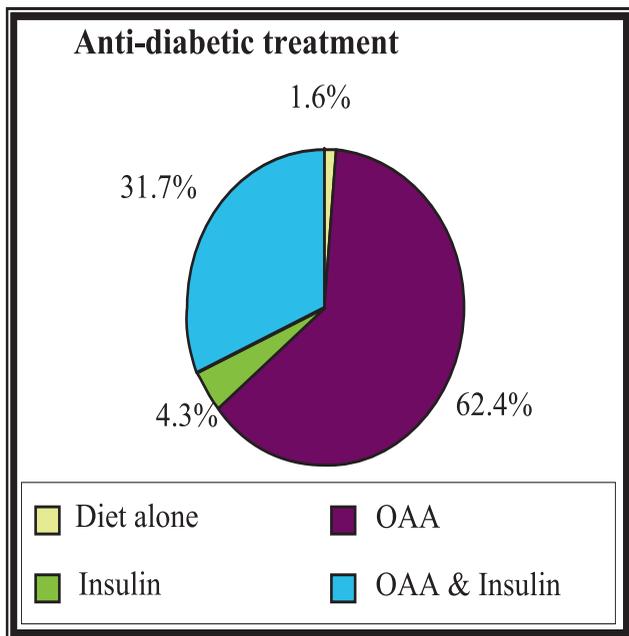
**Table 1. Sociodemographic and anthropometric characteristics**

Variable	n	%
Hypertension		
Yes	590	(67.9)
No	279	(32.1)
Dyslipidemia		
Yes	822	(94.6)
No	47	(5.4)
Diabetes retinopathy(DR)		
Yes	268	(30.8)
No	601	(69.2)
Glycated hemoglobin	Mean(SD)=7.716 (1.5)	
<7.0%	307	(35.3)
$\geq 7.0\%$	562	(64.7)
Cholesterol(mg/dl)	Mean(SD)=162.4 (35.3)	
<200	752	(86.5)
$\geq 200$	117	(13.5)
Low density lipoprotein	Mean(SD)=101.5 (32.4)	
<100	468	(53.9)
$\geq 100$	401	(46.1)
High density lipoprotein male	Mean(SD)= 42.0 (10.3)	
<40	266	(46.4)
$\geq 40$	261	(53.6)
High density lipoprotein female	Mean(SD)=48.2 (13.4)	
<50	225	(58.9)
$\geq 50$	157	(41.1)
Triglyceride(mg/dl)	Mean(SD)=153.6 (82.8)	
<150	518	(59.6)
$\geq 150$	351	(40.4)

**Table 2. Clinical and biochemical characteristics of the participants**

## Treatment Modalities

A high proportion of the diabetic patients (62.4%) were managed by oral medication alone, 4.3% by insulin alone, 31.7% of the patients were on a combination of oral medication and insulin, while 1.6% of the patients were following only a dietary regimen as part of their diabetes management.



OAA: Oral Anti-diabetic Agents

Figure 1. Anti-diabetic treatment

Most of the study participants (74.8%) were also on antihypertensive treatment. Drugs used were angiotensin-converting enzyme inhibitors (ACE) (38.1%), angiotensin receptor blockers (ARBs) (27.5%), combined ACEI and ARBs (1%), beta-blockers (32.1%), alpha-blockers (1.4%), dihydropyridine calcium channel blockers (18.9%),

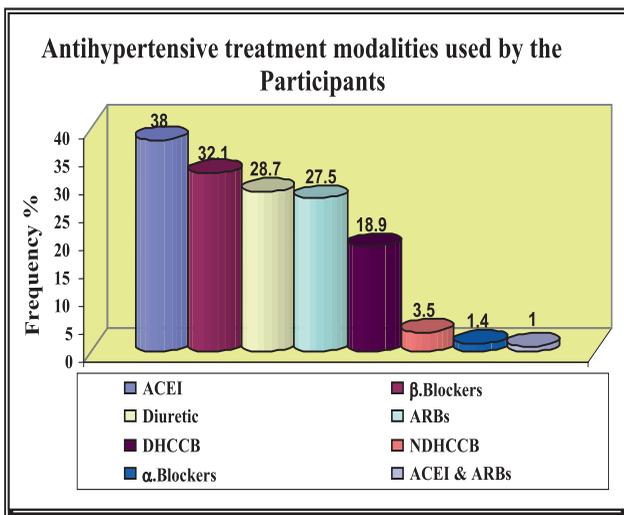


Figure 2. Antihypertensive treatment

nondihydropyridine calcium channel blockers (3.5%) and diuretic (28.7%) (see Figure 2). The majority of patients (74.5%) were receiving a lipid-lowering agent.

## The Prevalence of Diabetic Microalbuminuria and Macroalbuminuria According to Sociodemographic and Anthropometric Characteristics

Overall, 34.6% of the patients with diabetes had albuminuria (29.3% had microalbuminuria and 5.3% had macroalbuminuria). No significant differences in gender and smoking were noted among patients with microalbuminuria and macroalbuminuria. The microalbuminuric patients were older compared with the normoalbuminuric group ( $p=0.001$ ). There was an increase in frequency of microalbuminuria and macroalbuminuria in patients who had diabetes of more than 11 years duration. Mean SBP were significantly higher with microalbuminuria and macroalbuminuria compared with normoalbuminuria ( $p<0.0005$ ). However, diastolic blood pressure was higher only in the normoalbuminuric patients ( $p<0.0005$ ). Patients with microalbuminuria were predominantly obese and overweight ( $p=0.02$ ). See Table 3.

## The Prevalence of Diabetic Microalbuminuria and Macroalbuminuria According to Clinical and Biochemical Characteristics

The presence of hypertension, hypertriglyceridemia and hypercholesterolemia were significantly higher with both microalbuminuric and macroalbuminuric groups. HbA1c levels were significantly higher in all groups with abnormal albumin. The prevalence of diabetic retinopathy was significantly higher in microalbuminuric and macroalbuminuric patients, compared with those with normoalbuminuria ( $p<0.0005$ ). See Table 4.

## Multivariate Analysis of Factors Associated with Diabetic Microalbuminuria after Adjusting for Other Factors

In the bivariate analysis, microalbuminuria was significantly associated with age, BMI, duration of diabetes, diabetic retinopathy, HbA1c, hypercholesterolemia, hypertriglyceridemia, SBP, and DBP. After using stepwise logistic regression analysis, the only variables remaining significantly associated with microalbuminuria were mean HbA1c, mean SBP and the presence of retinopathy. For each 1% increase in HbA1c, the odds of having microalbuminuria increased by 86%. Patients with mean SBP  $\geq 130$  mm Hg were found to be 1.85 times more likely to have microalbuminuria than those with SBP  $< 130$  mm Hg. Patients with mean DBP  $\geq 80$  mm Hg were found to be 1.47 times more likely to have microalbuminuria than those with DBP  $< 80$  mm Hg. The odds of having microalbuminuria for those who had diabetic retinopathy are 1.45 times more than those who did not have diabetic retinopathy. See Table 5.

Variable		Normoalbuminuria n (%) 568(65.4)	Microalbuminuria 255(29.3)	Macroalbuminuria 46(5.3)
<b>Gender</b>	Men	316 (64.9)	139 (28.5)	32 (6.6)
	Women	252 (66.0)	116 (30.4)	14 (3.7)
	P-value	–	<b>0.764</b>	0.067
<b>Age(years)</b>	<45	59 (74.7)	17 (21.5)	3 (3.8)
	45-55	187(70.3)	65 (24.4)	14 (5.3)
	56-65	236(65.2)	108 (29.8)	18 (5.0)
	>65	86 (53.1)	65 (40.1)	11 (6.8)
	P-value	–	<b>0.001</b>	0.416
<b>Body mass index</b>	<25	65 (78.3)	15 (18.1)	3 (3.6)
	25-29.9	188 (68.4)	75 (27.3)	12 (4.4)
	≥30	315 (61.6)	165 (32.3)	31 (6.1)
	P-value	–	<b>0.020</b>	0.461
<b>Duration of DM (years)</b>	≤5	241 (72.8)	77 (23.3)	13 (3.9)
	6-10	156 (66.7)	70 (29.9)	8 (3.4)
	≥11	171 (56.3)	108 (35.5)	25 (8.2)
	P-value	–	<b>0.001</b>	<b>0.003</b>
<b>Smoking</b>	Non	370 (67.2)	153 (27.8)	28 (5.1)
	Current	89 (64.5)	42 (30.4)	7 (5.1)
	Past	109 (60.6)	60 (33.3)	11 (6.1)
	P-value	–	<b>0.229</b>	0.737
<b>SBP (mmHg)</b>	<130	406 (75.0)	116 (21.4)	19 (3.5)
	≥130	162 (49.4)	139 (42.4)	27 (8.2)
	P-value	–	<b>&lt;0.0005</b>	<b>&lt;0.0005</b>
<b>DBP (mmHg)</b>	<80	453 (69.3)	168 (25.7)	33 (5.0)
	≥80	115 (53.5)	87 (40.5)	13 (6.0)
	P-value	–	<b>&lt;0.0005</b>	0.192

**Table 3. Prevalence of diabetic microalbuminuria and macroalbuminuria according to sociodemographic and anthropometric characteristics**

Variable		Normoalbuminuria n (%) 568(65.4)	Microalbuminuria 255(29.3)	Macroalbuminuria 46(5.3)
<b>Hypertension</b>	Yes	349 (59.2)	204 (34.6)	37 (6.3)
	No	219 (78.5)	51 (18.3)	9 (3.2)
	P-value	–	<b>&lt;0.0005</b>	<b>0.010</b>
<b>Dyslipidemia</b>	Yes	537 (65.3)	240 (29.2)	45 (5.5)
	No	31 (66.0)	15 (31.9)	1 (2.1)
	P-value	–	<b>0.806</b>	0.335
<b>Diabetes retinopathy (DR)</b>	Yes	136 (50.7)	103(38.4)	29 (10.8)
	No	432 (71.9)	152(25.3)	17 (2.8)
	P-value	–	<b>&lt;0.0005</b>	<b>&lt;0.0005</b>
<b>Glycated hemoglobin (HbA1c %)</b>	<7%	235 (76.5)	63 (20.5)	9 (2.9)
	≥7%	333 (59.3)	192 (34.2)	37 (6.6)
	P-value	–	<b>&lt;0.0005</b>	<b>0.004</b>
<b>Cholesterol (mg/dl)</b>	<200	505 (67.2)	211(28.1)	36 (4.8)
	≥200	63 (53.8)	44 (37.6)	10 (8.5)
	P-value	–	<b>0.015</b>	<b>0.032</b>
<b>Low density lipoprotein (LDL)</b>	<100	311 (66.9)	129 (27.7)	25 (5.4)
	≥100	257 (63.6)	126 (31.2)	21 (5.2)
	P-value	–	<b>0.268</b>	<b>0.958</b>
<b>High density lipoprotein (HDL) male</b>	<40	135 (59.7)	74 (32.7)	17 (7.5)
	≥40	181 (69.3)	65 (24.9)	15 (5.7)
	P-value	–	0.060	0.258
<b>High density lipoprotein (HDL) female</b>	<50	145 (64.4)	68 (30.2)	12 (5.3)
	≥50	107 (68.2)	48 (30.6)	2 (1.3)
	P-value	–	<b>0.845</b>	<b>0.073</b>
<b>Triglyceride (mg/dl)</b>	<150	358 (69.1)	141 (27.2)	19 (3.7)
	≥150	210 (59.8)	114 (32.5)	27 (7.7)
	P-value	–	<b>0.036</b>	<b>0.004</b>

**Table 4. Prevalence of diabetic microalbuminuria and macroalbuminuria according to clinical and biochemical characteristics**

Variables	OR (95% CI)	P-value
Mean HbA1c (Uncontrolled vs. control)	1.86(1.30, 2.64)	<b>0.001</b>
Mean SBP (Uncontrolled vs. control)	1.85(1.57, 3.01)	<b>0.001</b>
Mean DBP (Uncontrolled vs. control)	1.47(1.02, 2.15)	<b>0.043</b>
Diabetes retinopathy (Yes vs. no)	1.61(1.02, 2.28)	<b>0.007</b>

OR: Odds ratio; HbA1c: Glycated hemoglobin;  
SBP: Systolic blood pressure;  
DBP: Diastolic blood pressure

**Table 5. Logistic regression analysis of factors associated with microalbuminuria**

#### Multivariate Analysis of Factors Associated with Diabetic Macroalbuminuria After Adjusting for Other Factors

In the bivariate analysis, macroalbuminuria significantly associated with duration of diabetes, diabetes retinopathy, HbA1c, hypercholesterolemia, hypertriglyceridemia, SBP and DBP. After using stepwise logistic regression analysis, the only variables which remained significantly associated with macroalbuminuria were mean SBP, male gender and the presence of diabetic retinopathy. Patients with mean SBP  $\geq$ 130 mm Hg were found to be 2.33 times more likely to have macroalbuminuria than those with SBP <130 mm Hg. Males were found to be 2.13 times more likely to have macroalbuminuria than females. Patients with diabetic retinopathy were found to be 4.77 times more likely to have macroalbuminuria than those without diabetic retinopathy.

Variables	OR (95% CI)	P-value
Mean SBP (Uncontrolled vs. control)	2.33(1.19, 4.53)	<b>0.013</b>
Gender (Male vs. female)	2.13(1.06, 4.29)	<b>0.034</b>
Diabetes retinopathy (Yes vs. no)	4.77(2.47, 9.22)	<b>0.000</b>

OR: Odds Ratio. SBP: Systolic blood pressure

**Table 6. Logistic regression analysis of factors associated with macroalbuminuria**

#### DISCUSSION

This study measures the prevalence of the different stages of albuminuria in type 2 diabetic patients attending the NCDEG. As a national center receiving patients from all the country, either directly or referred from other clinics in Jordan, we believe that patients included in this study are representative of all diabetics in Jordan. Numerous studies have been carried out to determine the prevalence of

albuminuria in patients with type 2 diabetes. These studies yielded rates between 17 and 58.6% for albuminuria<sup>19, 20, 21</sup>. Our study showed the prevalence rate at 34.6% which is in the median range. The marked variation in rate might be due to study design, sample selection, the method used for collecting urine, race and the age and gender structure of the population<sup>21</sup>. The prevalence of microalbuminuria and macroalbuminuria in our study was 29.3% and 5.3% respectively. The prevalence of microalbuminuria in this study is comparable to that found in the Hungarian study conducted by Molnár et al.<sup>22</sup>, which showed close prevalence (27.5%), but considerably higher prevalence of macroalbuminuria, 38.5% vs. 5.3% in our study. In Finland, a study conducted by Wirta et al. in recent-onset diabetic patients, showed almost the same prevalence as in our study: microalbuminuria and macroalbuminuria prevalence values of 29%, 4% vs. 29.3%, 5.3% among our patients<sup>23</sup>. However, a study carried out in the United Kingdom on NIDDM patients showed a lower prevalence of albuminuria (19%)<sup>24</sup>. Concerning Arab countries, studies in the Kingdom of Saudi Arabia<sup>25</sup> and the United Arab Emirates<sup>26</sup> showed a relatively higher rate of microalbuminuria, 41.3%, 61%, respectively, than that observed in our results. On the other hand, a study in Sultanate of Oman<sup>21</sup>, showed a nearly similar rate (27%).

Hyperglycemia is considered to be one of the important risk factors for the development and progression of diabetic retinopathy<sup>27</sup>. Several studies clearly demonstrated the benefits of improving glycemic control and decreasing HbA1c concentration in decreasing this complication rate<sup>12, 28</sup>. In our study, HbA1c showed a high correlation with microalbuminuria. On the other hand, macroalbuminuria showed no significant association with HbA1c. This finding is consistent with the results obtained by De Pablos et al.<sup>29</sup>, but results must be considered with caution because of the cross-sectional design of the study.

Our study showed a significant association between systolic blood pressure and both microalbuminuria and macroalbuminuria. Systolic blood pressure is identified as a risk factor for microalbuminuria and macroalbuminuria in many studies<sup>11, 19, 30</sup>. On the other hand, our data showed that diastolic blood pressure is significant with microalbuminuric groups only, which is consistent with the results of (CURES-45) study<sup>30</sup>.

The association observed between albuminuria and the number of years since diagnosis was not significant in our study. However, this effect is difficult to determine in type 2 diabetes. A plausible explanation for this is the fact that non-insulin dependent diabetes may be silent for many years before clinical recognition, as well as the fact that these patients are subject to recall bias. This may explain why previous studies have reported both significant<sup>14, 29</sup> and non-significant<sup>14, 22</sup> associations between albumin excretion and duration of the disease.

The study data failed to show a positive association with smoking. The hazardous effect of smoking may be blurred by the substantially lower proportion of current smokers 15.9% in our patients sample than that in the United Kingdom study (31%)<sup>31</sup>. A plausible explanation for this association is that on diagnosis of nephropathy patients tend to quit smoking as part of a nephropathy interventional program, which is not the case in patients with normal albumin who see no reasons to quit smoking. In addition, no information was recorded regarding when they quit and therefore this finding justifies further research for this phenomenon. Contrary to our results, smoking was significantly associated with albuminuria<sup>22</sup>. However, Gall et al.<sup>14</sup> and Varghese et al.<sup>27</sup> did not observe any significant differences.

Surprisingly, gender was not statistically different when tested alone against the occurrence of microalbuminuria and macroalbuminuria. In the final regression model it shows significant correlation with male gender and with macroalbuminuria. Earlier studies have reported an increased association of microalbuminuria<sup>32</sup> and macroalbuminuria<sup>20</sup> with men compared with women. On the other hand, another study revealed that female gender was positively associated with microalbuminuria<sup>25</sup>. However, principally because women have a lower creatinine excretion due to less muscle mass than men, it can be problematic when using the albumin-creatinine ratio to compare prevalence across genders. Thus some investigators often use a lower threshold for men than women<sup>25</sup>. It remains to be seen whether the difference in albumin excretion between men and women has significance for long-term risk of chronic disease or merely reflects the increased size of men compared to women.

Age was not identified as a risk factor in our study, which is in agreement with the findings of several other investigators who reported no significant correlation between age and microalbuminuria<sup>11, 20, 28</sup> and macroalbuminuria<sup>27</sup>. In contrast, some other studies showed that age is highly predictive of microalbuminuria<sup>14, 32</sup> and macroalbuminuria<sup>40</sup>. This could be attributed to the fact that our study was cross-sectional and as such its results cannot be used to correctly trace or establish the role of age in the development of microalbuminuria and macroalbuminuria in the sample patients.

It is of interest that body mass index did not correlate significantly with either microalbuminuria or macroalbuminuria in the logistic regression analysis. These results are in agreement with previously published data<sup>21, 27, 28, 37</sup>. On the other hand, a cross-sectional study by Cederholm et al. reported that the prevalence of microalbuminuria was positively associated with BMI<sup>32</sup>. Furthermore, one study reported that patients with BMI <18kg/m<sup>2</sup> were more likely to have proteinuria<sup>33</sup>. This issue is still unresolved and as such needs further investigation.

According to serum lipid, our study showed no association between serum lipids and either microalbuminuria or macroalbuminuria and is consistent with a number of other studies<sup>26, 27</sup>. This study showed that a high percentage of patients are on antilipidemic drugs. This might have afforded a degree of protection against diabetic kidney disease, as evidenced by several studies that lipid reduction by antilipidemic agents might decrease proteinuria in diabetic patients<sup>21, 26</sup>. While there are a number of studies showing a significant association between serum lipid and either microalbuminuria or macroalbuminuria<sup>14, 22</sup>, this result remains a debatable issue concerning albuminuria and needs to be addressed by future longitudinal studies.

In this study we found that the number of patients with microalbuminuria, macroalbuminuria and retinopathy was statistically significant which was a finding supported by other studies<sup>17, 30</sup>. Moreover, our results revealed that the prevalence of DR in microalbuminuria patients was higher than that in macroalbuminuria patients (38.4% vs.10.8%), which confirmed that even patients who have microalbuminuria were at high risk of developing retinopathy<sup>11</sup>. It was surprising to note that in our 46 patients with macroalbuminuria, 29 (63%) of them had DR, whereas diabetic retinopathy was absent in 17 (37%) of the 46 patients with macroalbuminuria. In a different study, analysis of type 2 diabetics with proteinuria found that approximately 30% did not have diabetic nephropathy on renal biopsy among those without retinopathy<sup>34</sup>. Type 2 diabetics with marked proteinuria and retinopathy are most likely to have DNP, whereas in those without retinopathy it may be caused by disease other than diabetic glomerulopathy (hypertension, atherosclerosis, chronic glomerulonephritis, chronic pyelonephritis)<sup>22</sup>.

## CONCLUSIONS

This is a center-based study which explored the prevalence of albuminuria in patients attending the NCDEG in Amman, Jordan, a tertiary center with referrals from all over Jordan. Our study showed:

- The prevalence of albuminuria (microalbuminuria and macroalbuminuria) observed in Jordanian patients diagnosed with type 2 diabetes aged  $\geq 30$  years in NCDEG reached up to 34.6% (29.3% with microalbuminuria and 5.3% with macroalbuminuria).
- The main risk factors for the development of albuminuria and its related stages in our study are HbA1c, SBP, presence of DR and male gender.
- Microalbuminuria is significantly associated with HbA1c, SBP, and the presence of retinopathy.
- Macroalbuminuria is significantly associated with SBP, presence of diabetic retinopathy, and male gender.

In conclusion, given the large numbers of persons with diabetes in Jordan<sup>2</sup>, the number of diabetic patients with microalbuminuria and macroalbuminuria is significant. The large pool of those with microalbuminuria suggests that there could be large increases in those with macroalbuminuria over time<sup>9</sup>. Most patients with macroalbuminuria eventually reach end-stage renal disease (ESRD)<sup>9</sup>. Although the cost of hemodialysis in Jordan is relatively low (US\$ 17,385/patient/year), the burden is huge in a country with limited resources<sup>10</sup>. There is thus a degree of urgency for implementing early and universal screening programs for microalbuminuria in type 2 diabetic patients. Through cardiovascular risk reduction, lowering blood pressure, renin-angiotensin system blockade and glycemic control, such early and targeted intervention could significantly reduce the occurrence of renal complications. In addition, early referral to nephrologists should be mandatory, especially for those with macroalbuminuria in the absence of retinopathy, for further evaluation of “non-diabetic” glomerulopathies. Since DR is a frequent occurrence in the presence of diabetic nephropathy, it is particularly important to investigate all patients with albuminuria for DR by an experienced ophthalmologist. This should be according to ADA guidelines which recommended annual measurement of serum creatinine for the estimation of GFR in addition to measurement of urine albumin excretion<sup>15</sup>. Further research is recommended to evaluate these guidelines, especially in those patients who manifest with decreased GFR in the absence of increased urine albumin excretion.

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