



# Effect of Weight on the Frequency of Albuminuria in Saudi Population with Type 2 Diabetes Mellitus

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## Abstract

**Background:** Diabetes is one of the most common chronic diseases. The development of albuminuria in Type 2 Diabetes (T2DM) increases the risk for renal disease.

**Methods:** The study was retrospective conducted at the Primary Health Care Clinics at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. A total of 1583 Saudi with T2DM were randomly selected.

**Results:** Total of 1583 patients with T2DM included in this study; 636 (40.2%) male and 8947 (59.8%) female with mean age  $56.0 \pm 11.7$  years. Hypertension was present in 896 (56.6%). Mean Body Mass Index (BMI)  $31.8 \pm 6.7$ , HbA1c was  $8.2 \pm 2.2$  and mean albumin excretion rate was  $72.3 \pm 225.3$ . Albuminuria was present in 521 (32.9%) and was significantly more prevalent in female (52.2%) with female predominance (sex ratio male:female) 1:1.1. Cases with albuminuria have significantly higher HbA1c compared to normalalbuminuria,  $8.6 \pm 2.2$  vs.  $8.0 \pm 2.2$  respectively,  $p < 0.0001$ . HTN with MA was more frequent in 349 (67.0%) of albuminuria group with odd ratio 1.9 (1.5 to 2.4),  $p < 0.0001$ . The frequency of albuminuria categorized by BMI groups is consistently statistically non significant increasing with BMI groups ( $p < 0.0001$ ) with significant difference for male cases above BMI of  $\geq 25$  years,  $p = 0.003$ . Moreover, the frequency of albuminuria is consistently statistically significant increasing with age groups ( $p = 0.02$ ) with significant difference for male cases above the age of  $\geq 60$  years,  $p = 0.003$ .

**Conclusion:** The frequency of albuminuria in patients with T2DM in this study is high. The study has also shown that comorbidities such as age, hypertension, obesity, and poor glycaemic control are likely to be additional risk factors for diabetic nephropathy. It is mandatory to have adequate diagnostic, therapeutic and educational resources in addition to competent physicians who can manage MA in diabetic patients by using a continuing, comprehensive and coordinated approach.

**Keywords:** Type 2 diabetes; Albuminuria

## Introduction

Diabetes mellitus is one of the most common disease and result from both genetic and environmental etiological factors [1-3]. Type 2 Diabetes (T2DM) accounts for over 90% of diabetes, and yet the natural history of nephropathy from prospective data is less well described for T2DM [4]. The earliest clinical sign of diabetic nephropathy is an elevated urinary albumin excretion, referred to as Microalbuminuria (MA). MA is defined as an Albumin Excretion Rate (AER) of 20 g/min to 199 g/min in a timed or a 24 hour urine collection (equivalent to 30 mg/g to 299 mg/g creatinine in a random spot sample) [5-13]. MA was found in 17% to 40% of patients with T2DM [14-20].

The association between obesity and diabetes is well established. The US National Health and Nutrition Examination Survey showed that the incidence of diabetes in men aged 25 years to 54 years with a Body Mass Index (BMI) between 30 kg/m<sup>2</sup> and 34.9 kg/m<sup>2</sup> is 10.1-fold higher [21]. The effects of obesity on kidney function and disease have been identified and become a subject of increased study and concern [22,23]. Actually, an effect of obesity on albuminuria in kidney disease was reported as early as 1923, when actuarial data first began to identify overweight as a risk factor for mortality, but were forgotten or neglected when cardiovascular mortality emerged as the principal cause of obesity-related mortality [24,25]. Based on a Meta analysis, it has been estimated that the presence of kidney disease is related to overweight (BMI=25 to 29.9) and obesity (BMI >30) [26]. An association between obesity and kidney disease could be made in 24.2% of males and 33.9%

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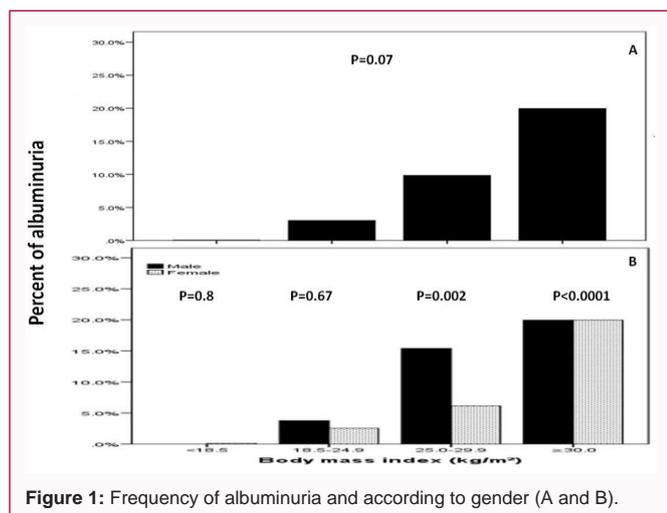


Figure 1: Frequency of albuminuria and according to gender (A and B).

of females in the U.S., and in industrialized countries in 13.8% of men and 24.9% of women [27]. Weight gain complicates intensive insulin therapy and metabolic abnormalities and has emerged as a potential new threat [28]. These characteristics are associated with kidney disease in the general population, but causes of kidney disease may differ for individuals with diabetes [29]. The pathogenesis is unclear and could be mediated primarily by adipogenic inflammation and endothelial dysfunction giving microalbuminuria or secondarily by hypertension and hyperglycemia, which accompany central obesity.

Although T2DM is more common in Saudi Arabia than in Europe, very little is known about complications and their risk factors in Saudi Arabia. There have been few studies on the influence of weight on albuminuria in Saudi populations. In this study we report on the frequency of albuminuria in patients with T2DM attending a primary care clinics in Saudi Arabia.

### Materials and Methods

The study is a retrospective conducted at the Primary Health Care Clinics at King Fahad Armed Forces Hospital. A total of 1583 Saudi with T2DM were randomly selected. The demographic data and medical history were documented. Blood Pressure readings were within a gap of 15 minutes using a mercury sphygmomanometer by palpation and auscultation method in right arm in sitting position. Two readings, 15 min apart, were taken and the average of both the readings was taken for analysis. Hypertension (HTN) was also diagnosed based on anti HTN medications or having a prescription of antihypertensive drugs and were classified as Hypertensive irrespective of their current blood pressure reading or if the blood pressure was greater than 140 mmHg/90 mmHg *i.e.*, systolic BP more than 140 and diastolic BP more than 90 mm of Hg. Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [30]. BMI values classified into groups as lean ( $BMI < 18.5$ ), normal weight ( $BMI = 18.5 \text{ kg/m}^2$  to  $24.9 \text{ kg/m}^2$ ), overweight ( $BMI = 25.0 \text{ kg/m}^2$  to  $29.9 \text{ kg/m}^2$ ), obesity ( $BM \geq 30 \text{ kg/m}^2$ ) [31]. HbA1c was expressed as percentage. High performance liquid chromatography was used. Albuminuria was assessed by measurement of mean Albumin Excretion Rate (AER) on timed, overnight urine collections. We use a polyclonal radioimmunoassay for albumin measurement. Albuminuria was defined as  $AER \geq 30 \text{ g/min}$  in overnight urine collections (equivalent to  $\geq 30 \text{ mg/g}$  creatinine in a random spot sample) [32].

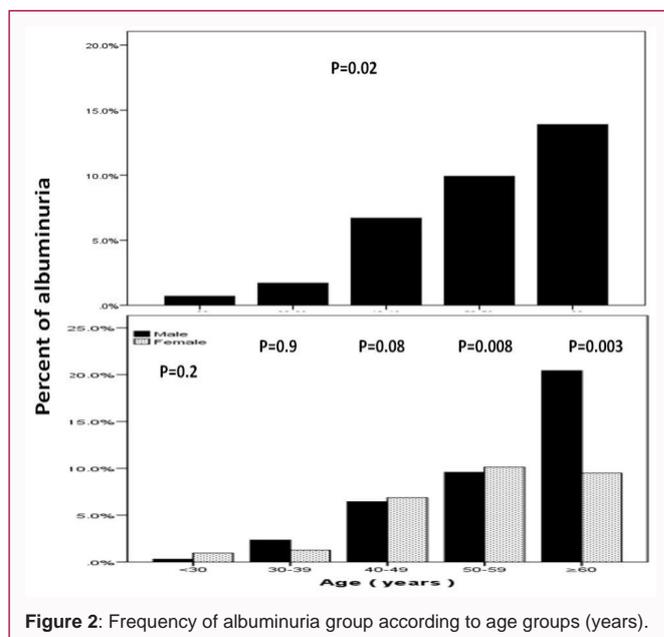


Figure 2: Frequency of albuminuria group according to age groups (years).

### Statistical analysis

Univariate analysis of baseline demography and clinical laboratory were accomplished using unpaired t-test. Chi square ( $X^2$ ) test were used for categorical data comparison. All statistical analyses were performed using SPSS Version 22.0. All P values were based on two-sided tests.  $P < 0.05$  was considered to be significant.

### Results

Total of 1583 patients with T2DM included in this study; 636 (40.2%) male and 947 (59.8%) female with mean age  $56.0 \pm 11.7$  years, (Table 1). Hypertension was present in 896 (56.6%). Mean BMI  $31.8 \pm 6.7$ , HbA1c was  $8.2 \pm 2.2$  and mean albumin excretion rate was  $72.3 \pm 225.3$ . Albuminuria was present in 521 (32.9%) and was significantly more prevalent in female (52.2%) with female predominance (sex ratio male:female) 1:1.1, (Table 2). Cases with albuminuria have significantly higher HbA1c compared to normal albuminuria,  $8.6 \pm 2.2$  vs.  $8.0 \pm 2.2$  respectively,  $p < 0.0001$ . HTN with albuminuria was more frequent in 349 (67.0%) of albuminuria group with odd ratio 1.9 (1.5 to 2.4),  $p < 0.0001$ . Figure 1 shows the frequency of albuminuria categorized by BMI groups, and shows the frequency of albuminuria is consistently statistically non significant increasing with BMI groups ( $p < 0.0001$ ) with significant difference for male cases above BMI of  $\geq 25$  years,  $p = 0.003$ , (Figure 1A,B). Moreover, the frequency of albuminuria is consistently statistically significant increasing with

Table 1: Demographic patient's parameters.

Parameters	Total	
N (%)	1583	
Age (years)	$56.0 \pm 11.7$	
Gender	Male	636 (40.2)
	Female	947 (59.8)
Body mass index (kg/m <sup>2</sup> )	$31.8 \pm 6.7$	
Hypertension	896 (56.6)	
HbA1c	$8.2 \pm 2.2$	
Serum creatinine ( $\mu\text{mol/L}$ )	$73.0 \pm 24.7$	
Urine albumin (g/min)	$72.3 \pm 225.3$	

**Table 2:** Comparison of features between albuminuria groups.

Parameters		Albuminuria 521 (32.9)	Normoalbuminuria 1062 (67.1)	P value
Gender	Male	249(47.8)	387(36.4)	<0.0001
	Female	272(52.2)	675(63.6)	
Age (years)		56.7 ± 12.4	55.7 ± 11.4	0.1
Body Mass Index (kg/m <sup>2</sup> )		32.3 ± 6.6	31.6 ± 6.7	P=0.07
Hypertension		349(67.0)	547(51.5)	<0.0001
HbA1c		8.6 ± 2.2	8.0 ± 2.2	<0.0001
Serum creatinine(μmol/L)		80.4 ± 34.2	69.3 ± 22.6	<0.0001
Urine microalbumin (g/min)		198.7 ± 361.2	10.2 ± 7.3	<0.0001

age groups ( $p=0.02$ ) with significant difference for male cases above the age of  $\geq 60$  years,  $p=0.003$ , (Figure 2A,B).

## Discussion

Diabetic nephropathy is a serious complication that occurs in 20% to 40% of all diabetics. Diabetic nephropathy is the primary single cause of End-Stage Kidney Disease (ESKD) [28]. Both Type 1 and T2DM can lead to nephropathy, but in T2DM, a smaller proportion of patient's progress to ESKD. Because of the higher prevalence of T2DM, these patients represent more than half of diabetics on dialysis. The incidence of diabetic nephropathy as a cause of ESKD is increasing each year [28]. For clinical care and epidemiological studies, diabetic kidney disease is defined by elevated urine albumin excretion or reduced glomerular filtration rate or both.

The present study revealed a prevalence rate of 32.9% for albuminuria (representing incipient diabetic nephropathy). This finding may suggest the heavy burden of diabetic nephropathy in the study environment. Nevertheless, this observation may not be surprising because previous studies had shown similarly high prevalence rates in Saudi Arabia. In Saudi Arabia, the rate of MA among T2DM patients during the period of September 2004 to April 2005 was 45.6% [33]. About 54.3% of patients with T2DM attending a primary care center in southern Saudi Arabia, had proteinuria [34]. Micro Albuminuria Prevalence Study is a large multicentre epidemiological study in Asia to determine the prevalence of MA in T2DM patients with hypertension [35]. In a population of 5,549 patients, 39.8% have microalbuminuria. This is higher than the prevalence rates, reported by us (33.2%) and in population-based studies for Western diabetic patients (17% to 21%) [20]. In another Asian study, in southern India, microalbuminuria was detected in 36.3% of T2DM [19]. These variations in the prevalence rate of proteinuria can be attributed to differences in several factors such as; study design, source of study population, sample selection, race, age, sex structure of the study population, diagnostic criteria, as well as the methods of measurement of proteinuria and urine collection, diabetic duration, diabetic treatment, and presence of hypertension [36].

Obesity increases the risk of developing T2DM, and most T2DM patients are overweight or obese [37,38]. This was confirmed in our study, as 57.8% were obese, and 88.1% had overweight or obesity. The corresponding prevalence's in diabetic patients in (National Health and Nutrition Examination) NHANES III 1988 to 1994 were 42% and 79%, and in NHANES 1999 to 2000 was 55% and 84% [38].

Causative mechanisms of renal damage due to obesity may be related to low-grade inflammation or to hormonal changes in the renin angiotensin and sympathetic nervous systems and may account for the hemodynamic disorders of obesity-related hyper filtration,

glomerulomegaly, and albuminuria that are also the characteristics of early diabetic nephropathy [39]. Insulin resistances, often present in obese subjects, might also predate the onset of albuminuria [40]. Although an association between albuminuria and BMI is a feature of non-diabetic obese subjects, in clinical studies of diabetics it is rather difficult to separate the effects of increased BMI alone from its concomitant effects on glycemic control [41]. Regression of albuminuria has been associated with use of renin-angiotensin system blocking drugs and tight glycemic control [42]. However, moderate weight loss reduces the metabolic demands on the kidney and may lead to substantial regression of urine albumin excretion [43].

In the present study, statistically significant differences were demonstrated in the mean values of HbA1c in the albuminuria group compared to the normalalbuminuria group. These observations suggested poor glycaemic control in the study population. This is another factor responsible for the frequent occurrence of diabetic nephropathy. The observation of poor glycaemic control was not peculiar to this study as similar findings had been reported earlier [44-46]. In addition, the role of poor glycaemic control as an additional risk factor for diabetic nephropathy had been suggested in a previous study [47].

We have found the frequency of HTN in patients with albuminuria is 67.0%. In adults, HTN frequently coexists with T2DM. The prevalence of HTN is  $>50\%$  in patients with T2DM [48]. HTN which is often accompanied is itself a risk factor for albuminuria. Parving et al. [20], in 1974 was the first to report albuminuria in hypertensive patients without diabetes. Since then, several studies have shown that albuminuria occurs in about 30% of patients with mild or moderate hypertension, ranging from 7% to 40% depending on age and ethnic group [49].

A clinic based study introduces referral bias, is one of the limitations of this study. This could have introduced some degree of referral bias. However the prevalence of albuminuria is similar to that reported in other studies. A single urine spot collection with semi quantitative dipstick determinations was used to detect albuminuria. The American Diabetes Association guidelines stated that this technique has acceptable sensitivity and specificity, but recommend that several collections should be done in a 3 month to 6 month period before diagnosing a patient as having albuminuria [5].

We conclude that the frequency of albuminuria in patients with T2DM in this study is high. The study has also shown that comorbidities such as age, hypertension, obesity, and poor glycaemic control are likely to be additional risk factors for diabetic nephropathy. It is mandatory to have adequate diagnostic, therapeutic and educational resources in addition to competent physicians who

can manage albuminuria in diabetic patients by using a continuing, comprehensive and coordinated approach.

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