Microalbuminuria in Saudi Adults with Type 1 Diabetes Mellitus

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Abstract

Background: Diabetes mellitus is among the most common chronic non-communicable diseases. The development of microalbuminuria in type 1 diabetes increases the risk for renal and cardiovascular disease.

Methods: A cross sectional study was conducted at the Primary Health Care Clinics at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. A total of 334 Saudi with type 1 diabetes were randomly selected.

Results: Total of 334 patients with T2DM included in this study; 102 (30.5%) male and 232 (69.5%) female with mean age 25.8±3.4. MA was present in 99 (29.6%). MA was not significantly more prevalent in female (69.4%) with female predominance (sex ratio male: female) 1:2.3. HTN with MA was significantly more prevalent in 51(51.5%) of MA group with odd ratio 1.7 (1.2-2.4), p=0.001 with no siginificant difference between both gender. Patients with MA have significant higher HbA1c than patients with normal buminuria and there was a significant difference between gender (p<0.0001) and when compared to HbA1c groups (p=0.002).

Conclusion: The frequency of microalbuminuria in patients with type 1 diabetes in this study is high. It is mandatory to have adequate diagnostic, therapeutic and educational resources in addition to competent physicians who can manage microalbuminuria in diabetic patients by using a continuing, comprehensive and coordinated approach.

Keywords : Type 1 diabetes; Microalbuminuria

Introduction

Diabetes is one of the largest health emergencies of the 21st century. The International Diabetes Federation Diabetes Atlas estimated that in 2015, there were 415 million patients with diabetes worldwide and by 2040 this figure will rise to 642 million people. Type1 diabetes (T1DM) is less common, accounting for 7-12% of the total cases and it is still increasing by approximately 3% each year globally, particularly among children [1]. T1DM leads to an increased risk of morbidity and early mortality due to chronic complications affecting both the micro-and microvasculature [2]. Diabetic nephropathy (DN) is one of the most serious chronic complications of T1DM, affecting approximately 20-30% of patients and increasing the risk of cardiovascular disease and end-stage renal disease [3,4]. The incidence of microalbuminuria (MA) in T1DM individuals varies greatly among different populations. There is a racial difference in prevalence of DN and end stage renal failure. MA is a common finding in T1DM and is found in 30-60% of patients with a diabetes duration of 10-20 years [5-8]. MA is defined as an albumin excretion rate of 20-199g/min in a timed or a 24-h urine collection (equivalent to 30–299mg/g creatinine in a random spot sample) [4].

In adults with T1DM MA is an early marker of structural renal disease and a risk factor for the development of macroalbuminuria [9,10]. The presence of macroalbuminuria is associated with subsequent development of end stage renal disease and increased coronary mortality [11-13]. After about 18 years of diabetes the cumulative prevalence of MA is 34%5. 6,13MA occurs in association with poor glycaemic control, elevated blood pressure and longer diabetes duration. It is important to assess factors related to the development of MA in young people with T1DM in order to identify whether such changes are due to underlying renal pathology or may be related to functional changes. Renal haemodynamic changes may occur during pubertal growth and development or may reflect uncontrolled diabetes and glycaemic variability, both of which are common during puberty [14-16].

In consistence with the global significant increase in incidence of T1DM of almost 3% per year Therefore we anticipate a parallel

increase in the rate of complications, including DN. DN is more prevalent among African Americans, Asians, and Native Americans than in Caucasians [17-21]. The frequency and risk factors of MA are not fully described among adults with T1DM in our region. The identification of such individuals is an important challenge to care providers. This single center study reports the prevalence of DN in adults with T1DM in Saudi Arabia and explore the risk factors associated with it. In this study, we report on the frequency of MA in T1DM patients attending a diabetes centre in Saudi Arabia.

Methods

A cross sectional study was conducted at the Primary Health Care Clinics at King Fahad Armed Forces Hospital. A total of 334 Saudi with T2DM were randomly selected. The demographic data and medical history were documented. Blood pressure readings were performed within a gap of 15 minutes using a mercury sphygmomanometer by palpation and auscultation method in right arm in sitting position. Two readings were taken 15 minutes apart and the average of both the readings was taken for analysis. Hypertension (HTN) was also diagnosed based on antihypertensive 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 140/90mmHg based on American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [22]. The HbA1c was divided into three groups; <7.0, 7.0-8.9 and ≥9.0. MA was assessed by measurement of mean albumin excretion rate (AER) on timed, overnight urine collections. Fasting serum lipids were done on a sample of blood after fasting for 14 hours. The method used for determining the cholesterol and triglyceride levels in the laboratory was the Enzmatic method. Albumin was measured using a polyclonal radioimmunoassay. MA was defined as AER 30g/ min in overnight urine collections (equivalent to 30–299mg/g creatinine in a random spot sample).

Statistical analysis

Univariate analysis of baseline and follow up demography and clinical laboratory endpoints were accomplished using unpaired t-test. Chi square(X^2) test were used for categorical data comparison. Pearson's correlations between continuous variables were used as a measure of association. All statistical analyses. Were performed using SPSS Version 22.0. All P values were based on two-sided tests where $P<0.05$ was considered statistically significant.

Results

A total of 334 patients with T2DM included in this study; 102 (30.5%) males and 232 (69.5%) females with mean age 25.8±3.4, (Table 1). MA was present in 99 (29.6%). MA was not significantly more prevalent in female (69.4%) with female predominance (sex ratio male: female) 1:2:3. HTN with MA was significantly more prevalent in 51(51.5%) of MA group with odd ratio 1.7(1.2-2.4), p=0.001 with no siginificant difference between both gender, (Figure 1). Patients with MA have significant higher HbA1c than patients with normoalbuminuria and there was a significant difference between gender (p<0.0001) and when compared to HbA1c groups (p=0.002)-see (Figure 2 & 3).

**Table 1:** Demographic patients parameters and Comparison of features between microalbumin groups.

| Parameters		Normoalbuminuria 235 (70.4)	Microalbuminuria 99 (29.6)	P value
Gender	Male	71(30.3)	30(30.6)	0.9
	Female	163(69.7)	69(69.4)	
Age(years)		32.3±6.6	26.3±3.0	0.09
Body mass index(kg/m²)		75(59.5)	31.2±6.0	0.2
Hypertension		7.5±2.2	51(40.5)	0.001
HbA1c		63.6±14.9	8.6±2.5	<0.0001
Serum creatinine (umol/l)		10.1±7.0	64.1±16.3	0.8
Urine microalbumin(g/min)		5.0±1.0	185.1±385.0	<0.0001
Total cholesterol (mmol/l)		2.9±0.9	4.9±1.1	0.9
Low density lipoprotein (mmol/l)		1.9±1.9	2.9±0.9	0.9
Triglyceride (mmol/l)		1.2±0.3	2.0±1.3	0.6
		1.2±0.3	1.2±0.3	0.9

Data are number (%) and mean standard±deviation
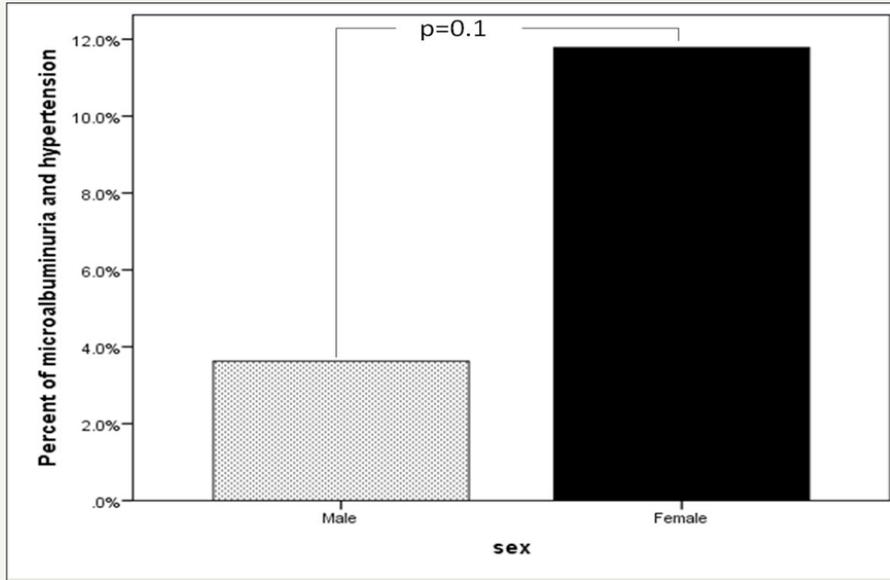
Figures 1: Frequency of microalbuminuria and hypertension according to gender.
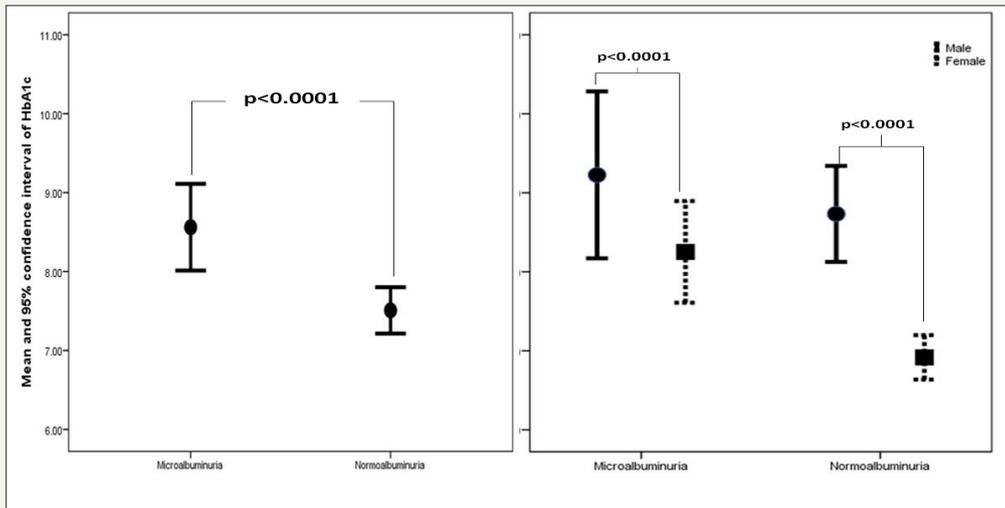
Figures 2: Mean HbA1c of microalbuminuria group and gender.
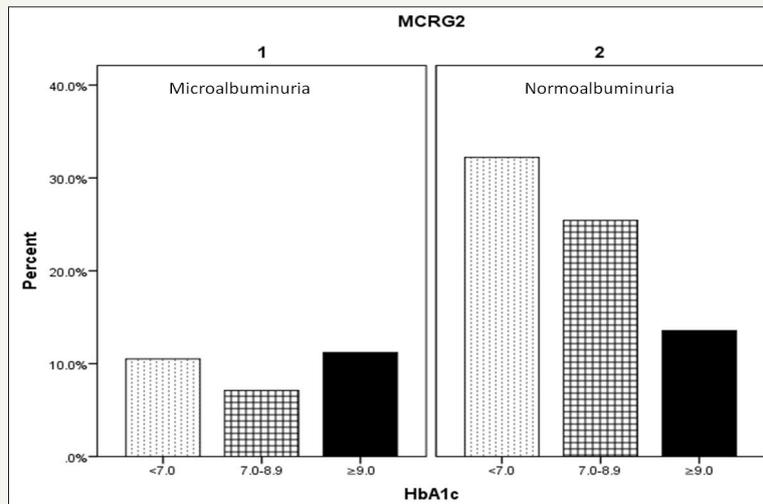
Figures 3: Frequency of Microalbuminuria group according to HbA1c groups.

Discussion

Diabetes mellitus is one of the most frequent chronic diseases in adult, the seriousness of which is still often not recognized, although the complications that the condition implies can be very damaging as well as costly and are often brought on by a lack of knowledge about the condition and lack of care [22]. T1DM leads to an increased risk of morbidity and early mortality due to chronic complications affecting both the micro- and macro vasculature. 2 DN is one of the most serious chronic complications of T1DM, affecting approximately 20-30% of patients and increasing the risk of cardiovascular disease and end-stage renal disease [3,4]. DN consists of several stages. Early MA is considered to be one of its most important predictors and is also associated with the development of cardiovascular disease [23,24]. Furthermore, the progressive decline of renal function in patients with T1DM is an early event that occurs in a large proportion of patients with MA [25]. Metabolic and hemodynamic factors contribute to the development of DN, probably by interacting with a genetic susceptibility [26,27].

We have shown high frequency of MA in T1DM to be 29.6%. Various epidemiological and cross-sectional studies have reported marked variation in the prevalence of MA. Compared to international rates, this result was far more than reported in many countries worldwide including 3.3% in USA in 2015, 5% in UK and 3.3% in German diabetic children [17-19]. These were comparable to 13% reported in west Australian children with T1DM and 13.4% reported in Indian children [28,29]. The need for nationwide and larger scale studies are essential to assess the cost-effectiveness of such early and frequent screening.

Male gender was found to be a risk factor for DN in adult diabetic patients while female gender was a risk factor in adolescent patients with T1DM [29]. Studies on German and Swiss children with T1DM concluded that male gender is a risk factor of DN [17,30]. Other studies had concluded that female sex is a risk factor for development of MA [17,31,32]. Our finding was inconsistent with previous studies as MA was found to be nonsigificanly more common in females. Females constitute 69%of our studied population; therefore, this result can be attributed to gender bias in recruited patient.

The mean age for MA patients was 26.3±3.0 and for normoalbuminuric patients was 25.6±3.6. This difference in mean age of both groups was not statistically significant. In addition to that, the frequency of MA increases nonsignificantly with increasing age of diabetic patients (r=0.03, p=0.6), this result is in disagreement with other studies in other countries like Italy, Finland, UK and France which had revealed that the age is a risk factor for development of MA and onset of diabetic nephropathy. In a longitudinal study done in UK, it was found that the cumulative probability for developing MA was 40% after 11 years of age [33-36].

The influence of blood pressure on MA in children with T1DM was evaluated and there was no significant difference between microalbuminuric and normoalbuminuric patients in relation to the mean systolic and diastolic blood pressure in disscordance

with us. Various studies have revealed conflicting results, some of these studies did not show any significant role of blood pressure on MA, while others have revealed that high blood pressure especially diastolic pressure is one of important predictors of developing MA [17,33,37].

Few studies have investigated the association between MA and body mass index. In our study, there was no significant difference in body mass index between microalbuminuric and normoalbuminuric patients. This results is in agreement with the result of the study done in Denmark while this result was in contrast to studies in Finland, and Sweden, who had demonstrated that patients with MA have a higher BMI than normoalbuminuric patients and controls. Insulin resistance is associated with both central obesity and MA and may play a prominent mediating role [31,37-39].

Glycemic control is one of the important predictors of the development of MA in T1DM and poor glycemic control is a well-known risk factor of DN. While MA can be substantially delayed by tight glycemic control, achieving the degree of control encouraged by the results of the Diabetes Control and Complications Trial remains impractical for many centers. Additionally, there are claims that there is a glycemic threshold below which the risk of progression to MA remains static, and although not confirmed by other reports. [40-43]. In this study, the mean HbA1C of MA patients is 8.6±2.5 which is significantly higher than that of the normalbuminuric patients, 7.5±2.2 (P<0.0001). Although, the study has shown that the frequency of MA increases nonsignificantly with the increase in the level of HbA1C (r=0.1, p=0.6). Other studies also have concluded that HbA1C is a determinant risk factor for MA, and that poor glycemic control predisposes to MA [17,44-48]. The finding of a higher mean HbA1c in our albuminuric patients which supports the fact that MA is, most likely, due to poor glycemic control. Nevertheless, it is believed that the accelerated early onset DN cannot solely be explained on the basis of poor glycemic control and other factors, such as genetic and environmental, might play a major role in its pathogenesis.

Apart from well-known risk factors such as HbA1c, there were no associations were also observed with fasting lipid parameters. Data from previous cross-sectional studies show that lipids are abnormal in patients with MA and LDL cholesterol are elevated in those at risk of subsequent MA [49,50]. Interestingly, in discordance with other reports, while many of the lipid parameters measured here are negatively correlated, it is striking that only total cholesterol correlates significantly (r=-0.1, p=0.02).

One of the limitations of this study is that it is a clinic based study. This could have introduced some degree of referral bias. However the prevalence of MA is similar to that reported in other studies. MA detection was based on a single urine spot collection with semi quantitative dipstick determinations. The ADA guidelines acknowledge that this technique has acceptable sensitivity and specificity, but recommend that positive tests be reconfirmed with more specific methods and, due to the marked day-to-day variability, that several collections should be done in a 3 to 6 month period before designating a patient as having MA [5].

We conclude that the frequency of MA in patients with T1DM in this study is high. 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.

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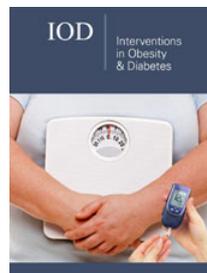
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