

Modified risk factors for presence of microalbuminuria in Saudi adults with type 1 and type 2 diabetes mellitus

Abstract

Background: Diabetes is one of the most common chronic diseases. Diabetic nephropathy is one of the most serious chronic complications of type 1 and type 2 diabetes. We report on different risk factors between microalbuminuria presence in type 1 and type 2 diabetes patients attending a diabetes centre in Saudi Arabia.

Methods: The study was cross section conducted at the diabetes centre clinics at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. A total of 296 Saudi with type 1 and type 2 diabetes associated with presence of microalbuminuria were randomly selected.

Results: Total of 296 patients with diabetes associated microalbuminuria were included in this study; 99 (33.3%) with type 1 diabetes and 197 (66.6%) with type 2 diabetes. 119(40.2%) were male and 177 (59.8%) were female with mean age 35.0 ± 8.4 years. Significant female predominance (sex ratio male:female) 1:2.3 and 1:1.2 in type 1 diabetes with microalbuminuria and type 2 diabetes with microalbuminuria respectively ($p=0.01$). Hypertension was significantly more frequent in 131 (72.0%) of type 2 diabetes with microalbuminuria compared to 51 (28.0%) of type 1 diabetes with microalbuminuria ($p=0.004$) with significant difference between both gender. Type 2 diabetes with microalbuminuria have significant higher HbA1c than patients with type 1 diabetes with microalbuminuria and there was a nonsignificant difference between gender and when compared to HbA1c groups. Male and Female with type 2 diabetes with microalbuminuria have nonsignificant HbA1c (≥ 7.0) than patients with Male and Female with type 1 diabetes with microalbuminuria.

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Introduction

In both developed and developing countries, diabetes mellitus is common and result from both environmental etiological and genetic factors.¹⁻³ Over 90% of diabetes is type 2 diabetes (T2DM) The natural history of diabetic nephropathy (DN) from prospective data is less well described for T2DM.⁴ The earliest clinical sign of DN, defined as microalbuminuria (MA) which is an elevated urinary excretion of albumin. MA is defined as an albumin excretion rate (AER) of 20–199 g/min in a timed or a 24-hr urine collection which is an equivalent to 30–299 mg/g creatinine in a random spot sample).⁵ The increased risk for renal and cardiovascular disease in T2DM is associated with the development of MA.⁶⁻⁸ In many regions of the world, end-stage renal disease incidence in T2DM has risen.⁹⁻¹⁰ Diabetes is estimated to increase the risk of end-stage renal disease approximately 12-fold and is also one of the predictor for cardiovascular disease.^{11,12-16} MA was found in 17-40% of patients with T2DM.¹⁷⁻²²

Type 1 diabetes (T1DM) accounts for 7–12% of the total cases of diabetes and it is increasing globally by 3% each year.²³ DN is affecting approximately 20-30% of patients with T1DM and increasing the risk of cardiovascular disease and end-stage renal disease.^{5,24} The incidence of MA in T1DM individuals varies greatly among different populations. In T1DM, MA is found in 30–60% of patients. Parallel increase in the rate of complications, including DN will be in consistence with the global significant increase in incidence of T1DM

and T2DM. The American Diabetes Association recommends annual screening for MA by means of a semiquantitative dipstick test which is considered to be easy, accurate and immediate.^{5,25} Although T1DM and T2DM is more common in Saudi Arabia than in Europeans in the UK, very little is known about complications and their risk factors in Saudi Arabia. In this study we report on the difference in risk factors between MA presence in T1DM and T2DM patients attending a diabetes centre in Saudi Arabia.

Methods

A cross section study conducted at the diabetic centre Clinics at King Fahad Armed Forces Hospital. A total of 296 Saudi with diabetes were randomly selected. The medical history and demographic data were documented. Blood Pressure readings using a mercury sphygmomanometer by palpation and auscultation method in right arm in sitting position were measured within a gap of 15 minutes. Two readings, 15min apart, were taken and the average of both the readings was recorded. Hypertension (HTN) was also diagnosed based on anti HTN medications were classified as Hypertensive irrespective of their current blood pressure reading or if the blood pressure was greater than 140/90 mmHg i.e systolic BP more than 140 and diastolic BP more than 90mm of Hg according to the Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.²⁶ Fasting serum lipids were measured on a sample of blood after fasting for 14 hours.

We used the Enzymatic method for determining the cholesterol and triglycerides levels. The HbA1c was divided into three groups; <7.0, 7.0-9.0 and >9.0. MA was assessed by measurement of mean albumin excretion rate (AER) on timed, overnight urine collections. We use a polyclonal radioimmunoassay for albumin measurement. MA was defined as AER 30 g/min in overnight urine collections (equivalent to 30–299mg/g creatinine in a random spot sample).

Statistical analysis

Unpaired t-test was used to analyze univariate analysis of baseline and follow up demography and clinical laboratory endpoints. Categorical data comparison was accomplished using Chi square(X^2). 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

1416 patients with T2DM and 334 patients with T1DM were screened for MA. Total of 296 patients with diabetes associated MA were included in this study; 99 (33.3%) with T1DM and 197 (66.6%) with T2DM. 119 (40.2%) were male and 177 (59.8%) were female with mean age 35.0 ± 8.4 , table. Significant female predominance (sex ratio male: female) 1:2.3 and 1:1.2 in T1DM+MA and T2DM+MA respectively ($p=0.01$). HTN was more frequent in 131 (72.0%) of T2DM+MA compared to 51 (28.0%) of T1DM+MA ($p=0.004$) with significant difference between both gender, Figure 1. T2DM+MA have significant higher HbA1c than patients with T1DM+MA and there was a nonsignificant difference between gender and when compared to HbA1c groups, Figure 2. Male and Female with T2DM+MA have nonsignificant higher HbA1c (≥ 7.0) than patients with Male and Female with T1DM+MA, Figure 3.

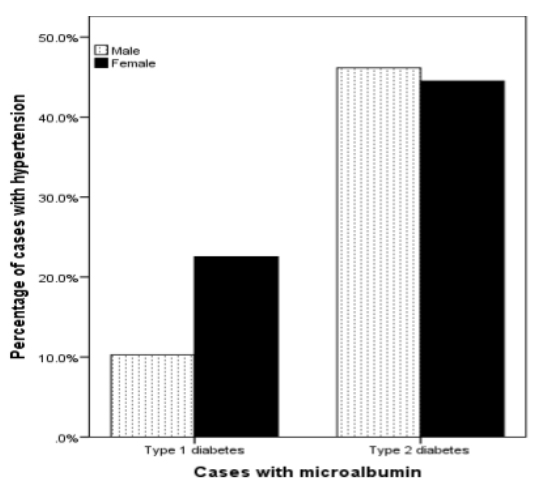


Figure 1 Frequency of hypertension in cases with type 1 and type 2 diabetes associated microalbuminuria according to gender

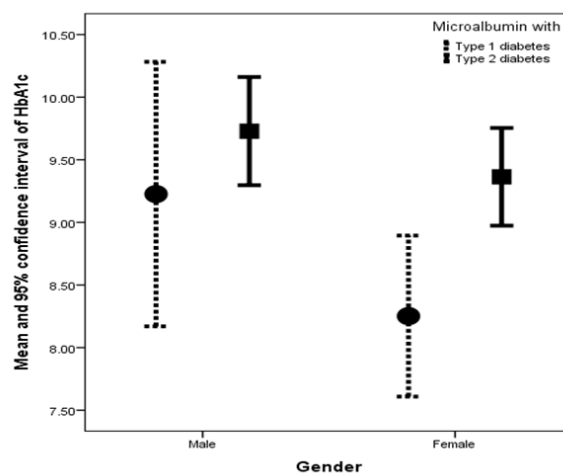


Figure 2 Mean HbA1c in Type 1 diabetes and type 2 diabetes associated microalbuminuria according to gender

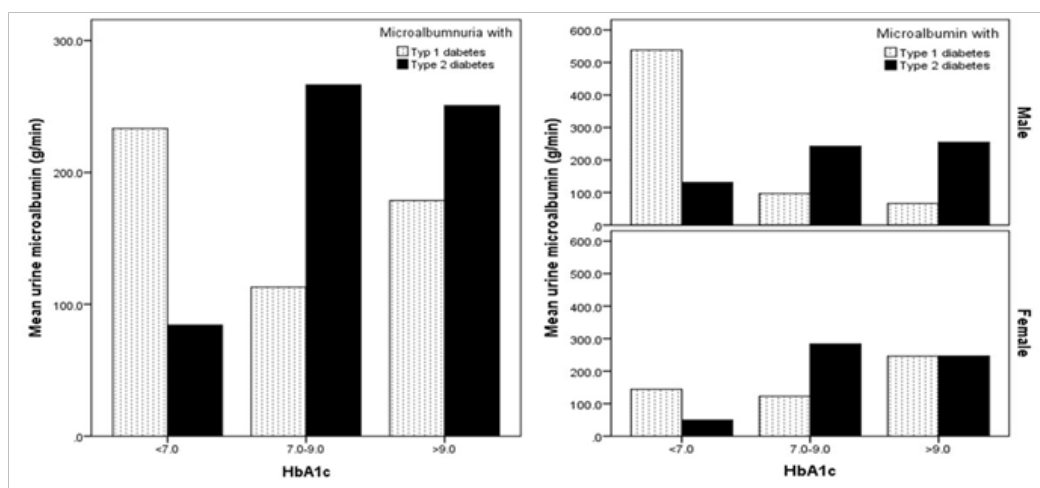


Figure 3 Mean microalbumin in Type 1 diabetes and type 2 diabetes associated microalbuminuria according to HbA1c groups and gender.

Discussion

For all health care systems in both developed and developing countries, the chronic diseases represent one of the most difficult challenges, due to their continuous and relentless growth. The care

of patients with diabetes contributes significantly to health care costs. DN is the leading cause of end-stage renal disease and of patients with T1DM, 20%-30% will develop DN, whereas about 10%-20% of those with T2DM will do so.^{27,28} There have been in the past couple

of decades advances in our knowledge regarding the DN, including pharmacological interventions that can significantly slow or even reverse the course of progressive disease.

We have shown in unpublished data that MA frequency in T2DM to be 33.2%. Marked variation in MA prevalence was reported from cross sectional and various epidemiological studies.²⁹⁻³⁴ In Asia, Micro Albuminuria Prevalence Study is a large epidemiological multicentre study to determine the MA prevalence in T2DM patients with hypertension.³⁵ They found that 39.8% have MA in a population of 5,549 patients. This is higher than the prevalence rates reported by us (33.2%) and 17% to 21% prevalence for Western diabetic patients in

population-based studies.²¹ In another Asian study, in southern India, MA was detected in 36.3% of T2DM.²² The different range in the prevalence of MA in T2DM is likely due to populations differences, in the definitions of MA, urine collection method, genetic and cardiovascular risk factors. Where as we have shown in unpublished data that high frequency of MA in T1DM to be 29.6%. Compared to international rates, this result was far more than reported in many countries worldwide including 5% in UK, 3.3% in Germany and 3.3% in USA.³⁷⁻³⁸ These were comparable to 13.4% reported in Indian children and 13% reported in west Australian children with T1DM.^{39,40} DN patients are a problem at the interface between general medicine, primary care physician, diabetology and nephrology. Thus, possible vascular disease could be indicated by the finding of MA and it is an indication to reduce all cardiovascular risk factors by aggressive intervention. The need for nationwide larger scale studies is important to assess the cost-effectiveness of such frequent and early screening.

The present study showed significant female predominance (sex ratio male:female) 1:2.3 and 1:1.2 in T1DM+MA and T2DM+MA respectively ($p=0.01$). In discordance with our study, an increased prevalence of MA+T2DM in male compared with female was reported in earlier studies. Some studies in T2DM have revealed male sex as major risk factors for MA.³¹ In our study, T2DM+MA and T1DM+MA were more frequent in females and nonsignificantly correlated with younger age ($r=-0.1$, $p=0.3$) and ($r=-0.01$, $p=0.08$) respectively in discordance with other studies.³³⁻³⁴ Where as female predominance (sex ratio male:female) 1:2.3 was shown in T1DM. Female gender was a risk factor in adolescent patients with T1DM while male gender was found to be a risk factor for DN in adult diabetic patients in studies on German and Swiss children with T1DM.^{36,40-43}

Few studies have investigated the association between MA and body mass index. We have also found nonsignificant association of T2DM+MA and T1DM+MA with obesity ($r = 0.02$, $p=0.8$) and ($r=0.07$, $p=0.5$) respectively in discordance with other studies. In our study, there was significant difference in body mass index between T2DM+MA and T1DM+MA patients. This result is in agreement with the result of the study done in Sweden Finland, and Finland while this result was in contrast to studies in Denmark. Insulin resistance is associated with both central obesity and MA.^{42,44-46}

Poor glycaemic control is a risk factors for MA. In patients with T2DM, observational studies have reported that poorer glycaemic control is associated with the development of MA.^{31,47-49} Glycaemic control has been shown to prevent development of nephropathy and to reverse established pathology. Several prospective, interventional studies showed that a decrease in the development and progression of albuminuria in most cases by improved glycaemic control, statistical significance finding was precluded by the small sizes of the cohorts.^{50,51}

A meta-analysis study showed intensive therapy significantly reduced the progression of nephropathy risk.⁵² In patients with T1DM, glycaemic control is one of the important predictors of the development of MA and poor glycaemic control is a well-known risk factor of DN. While tight glycaemic control could delay MA, achieving the degree of control by the results of the Diabetes Control and Complications Trial remains impractical. Additionally, there are claims that there is a glycaemic threshold below which the risk of progression to MA remains static, and although not confirmed by other reports.⁵³⁻⁵⁶ In this study, the mean HbA1C of T2DM+MA patients is 9.5 ± 2.0 which is significantly higher than that of the T1DM+MA patients, 8.6 ± 2.5 ($P < 0.0001$). Other studies also have concluded that HbA1C is a determinant risk factor for MA, and that poor glycaemic control predisposes to MA.^{31,57-61} The finding of a higher mean HbA1c in our T2DM+MA and T1DM+MA patients which supports the fact that MA is, most likely, due to poor glycaemic control. Nevertheless, other factors such as genetic and environmental might play a major role in its pathogenesis.

However, as evidenced by available mean HbA_{1c} values above 7.0%, 57.1% of T2DM+MA patients as compared to 42.9% of T1DM+MA patients could not achieve adequate glycaemic control, $p = 0.003$.⁵⁴

We have shown that HTN is significantly more frequent in T2DM+MA compared to T1DM+MA. HTN frequently associated with T2DM in adults. The prevalence of HTN is more than 50% in patients with T2DM.⁶² HTN which is often accompanied is itself a risk factor for MA. 1972 was the first to report MA in hypertensive patients without diabetes.²² Several studies have shown that MA occurs in about 30% of patients with hypertension, ranging from 7% to 40% depending on age and ethnic group.^{63,64} In T1DM, Various studies have revealed conflicting results, some of these studies showed that HTN especially diastolic pressure is one of important predictors of developing MA while others did not show any significant role of HTN on MA.^{36,44}

Many patients with T2DM will require lipid-lowering therapy. However, it is interesting to note that animal studies have shown that high-cholesterol diets worsen renal injury, whereas lowering blood lipids by medications ameliorates the renal injury. Epidemiological studies showed a relationship between hyperlipidemia and DN. A meta-analysis studies in humans concluded that compared with no treatment, treatment was associated with a lower rate of decline in glomerular filtration rate. This effect did not correlate with either the percent change in cholesterol or with the type of lipid-lowering agent. Seven of the trials included only patients with DN.⁶⁵ There were significant associations were also observed with fasting lipid parameters namely total cholesterol and triglyceride. Data from previous cross-sectional studies show that lipids are abnormal in patients with MA and low density lipoprotein are elevated in those at risk of subsequent MA.^{66,67-70} Interestingly, in patients with T2DM+MA, in concordance with other reports, it is striking that only low density lipoprotein correlates significantly ($r=0.2$, $p=0.02$).

One of the limitations of this study is that it is a clinic based study. This could have introduced some degree of referral bias. 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. Several collections should be done in a 3-6 month period before diagnosing a patient as having MA.⁵

We conclude that the frequency of MA in patients with T2DM in this study is high. It is mandatory to have adequate therapeutic and educational resources in addition to competent physicians who can manage MA in diabetic patients by using a continuing, comprehensive and coordinated approach.

Conclusion

The high frequency of hypertension and poor glycemic control were present in patients with type 2 diabetes complicated with presence of microalbuminuria in this study. It is mandatory to have adequate therapeutic and educational resources in addition to competent physicians who can manage microalbuminuria in diabetic patients by using a continuing, comprehensive and coordinated approach.

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None.

Conflict of interest

The author declares that there is no conflict of interest.

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