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Prevalence of Microalbuminuria and Risk Factor Analysis in Type 2 Diabetes Patients in Albania

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Abstract: ***Background: Microalbuminuria is often the first sign of renal dysfunction in diabetes. This study aimed to investigate the prevalence of microalbuminuria in Albanian type 2 diabetes patients and its association with other cardiovascular risk factors. Methods: Three hundred and twenty-one patients with type 2 diabetes attending diabetes centers in Albania were enrolled in this cross-sectional, multicenter study. The subjects, aged 40–70 years, had no known proteinuria or other kidney disease. Pregnant women and patients with acute infections were excluded. Data including waist circumference, duration of diabetes and history of hypertension were obtained by questionnaire. Blood samples were drawn after 12 h overnight fasting to measure glycosylated hemoglobin (HbA1c), serum cholesterol, triglyceride and creatinine. Microalbuminuria was assessed using dipstick kits in early morning urine samples. Results: The prevalence of normoalbuminuria was 56.3%, microalbuminuria 40.8% and macroalbuminuria 2.8%. Systolic and diastolic blood pressure ($p < 0.01$), HbA1c ($p < 0.01$) and fasting plasma glucose ($p < 0.001$) were significantly higher in microalbuminuricthan in normoalbuminuric subjects. Independent risk factors for microalbuminuria were duration of diabetes (OR=2.785, 95%CI=1.156–3.759), systolic blood pressure (OR=2.88, 95%CI=1.85–6.85) and waist circumference (OR=2.15, 95%CI=1.01–5.45) in males and poor glycemic control (OR=4.51, 95%CI=1.45–13.98), duration of diabetes (OR=2.568, 95%CI=1.702–3.778) and waist circumference (OR=4.87, 95%CI=1.80–13.11) in females. Conclusions: The high proportion of type 2 diabetes patients with microalbuminuria raises implications for health policy in Albania. Screening programs and optimized control of modifiable risk factors are needed to reduce the risk of diabetic nephropathy.***

Keywords: microalbuminuria, type 2 diabetes, epidemiology, Albania

1. Introduction

Over the past decades there has been a significant worldwide increase in the incidence of diabetes mellitus[1]. This current global epidemic is associated with an increase of cardiovascular diseases that primarily accounts for the increase in morbidity and mortality seen in patients with diabetes[2, 3]. The high prevalence of microvascular complications of diabetes such as diabetic nephropathy means that the number of patients with end-stagerenal disease (ESRD) due to diabetes will also increase dramatically[4]. Hence, diabetes, and especially type 2 diabetes, is becoming the main reason for patients to start renal replacement therapy[5, 6].

As in other developing countries, the prevalence of diabetes in Albania has increased rapidly in recent years[7] and is likely to continue to increase in the future, with important implications for health policy. According to the International Diabetes Federation[8], in 2012 there were about 65, 000 cases of diabetes in Albania (approximately 2.3% of the population). In local and limited studies, the prevalence was found to be significantly higher than this (6.3% in Tirana and 4.2% in southwest Albania)[9], and 7.5% of patients undergoing dialysis in Albania have diabetic nephropathy as the cause of renal failure.

On average, 20–40% of patients with diabetes will develop renal dysfunction[10]. Microalbuminuria is often the first sign of renal involvement predicting overt nephropathy[11]. For this reason, measurement of urine albumin is often used as a sensitive marker and predictor of ESRD in patients with diabetes[12]. Monitoring microalbuminuria and other risk factors associated with this condition is important to take measures to prevent or postpone overt nephropathy[13]. Measurement of microalbuminuria in a 24h urine collection is the gold standard[14], though an alternative is a spot urine sample adjusted to determine creatininuria. A spot urine collection is considered positive if the albumin/creatinine ratio (ACR) is 30–299 mg albumin/g creatinine[15, 16]. In many studies, ACR has been recognized as a valid method for screening populations[15, 17].

The primary aim of this study was to evaluate the prevalence of microalbuminuria and renal impairment in patients with type 2 diabetes without known proteinuria. In addition, we investigated the association of microalbuminuria with other potential cardiovascular risk factors in this population. The results could be important in increasing physicians' awareness of the importance of regular urinary albumin screening when caring for patients care with diabetes.

2. Methods

This cross-sectional study received ethical approval from the National Medical Ethics Committee. Data were obtained for 321 patients with type 2 diabetes attending diabetes centers in three districts of Albania. We recruited patients without known proteinuria or other kidney disease, aged between 40 and 70 years. We excluded pregnant women and patients with acute infections.

The patients completed a questionnaire to obtain information regarding their gender, age, height and weight to calculate body mass index, waist circumference, duration of diabetes, history of hypertension and drugs used, and history of

smoking. Patients were defined as hypertensive if they were undergoing treatment with antihypertensive drugs or if their untreated systolic blood pressure was >130 mmHg and/or diastolic blood pressure >85 mmHg. Normal waist circumference was defined as <102 cm for males or <88 cm for females. A sample of blood was drawn after overnight fasting for 12 h to measure glycosylated hemoglobin (HbA1c), serum cholesterol, triglyceride and creatinine levels. Microalbuminuria was assessed using Bayer DCA 2000 Microalbumin test kits in urine samples collected in the early morning. Patients were classified as normoalbuminuric if their ACR was <30 mg albumin/g creatinine ormicroalbuminuricif their ACR was 30–300 mg albumin/g creatinine. When the ACR was >300 mg albumin/g creatinineon two consecutive tests, patients were considered to have macroalbuminuria or overt nephropathy.

Data analysis was conducted using the Statistical Package for Social Sciences (SPSS) for Windows version 11. The chi-square test and logistic regression analysis were used to determine correlations between microalbuminuria and other risk factors.

3. Results

Three hundred and twenty one type 2 diabetes patients (163 females and 158 males) were included in this study. Their mean age was 58.2±11.8 years. Of the 321subjects, 27 (8.4%) were found to have diabetes at their first visit to their health care provider and nine of these had microalbuminuria at the time of diagnosis. The mean duration of diabetes was 8.2±6.9 years. The prevalence of normoalbuminuria, microalbuminuria and macroalbuminuria were 56.3%, 40.8% and 2.8%, respectively. Macroalbuminuric patients (2.8% of the study population) had creatinine serum levels >1.5mg/dl. The prevalence of microalbuminuria was 40.5% in males and 41.1% in females. There was no significant difference between males and females in the prevalence of macroproteinuria or microproteinuria. The prevalence of microalbuminuria increased with the duration of diabetes (Figure 1). Taking ≤5 years as the reference value, odds ratios (ORs) for durations of 6–10, 11–15, 16–20 and >20 years were calculated. The OR for microalbuminuria became statistically significantly increased 16 years after the diagnosis of type 2 diabetes, by which time 48.2% of patients had microalbuminuria.

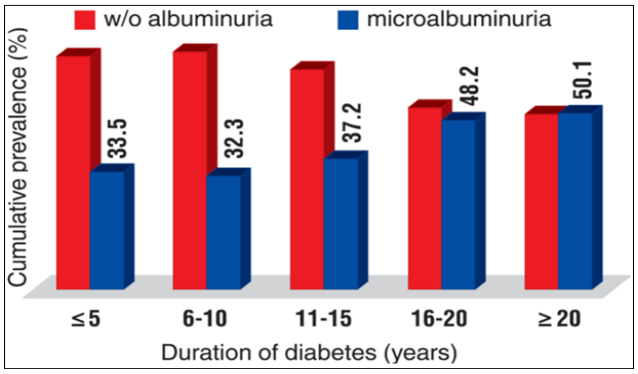

Figure 1: Cumulative prevalence of microalbuminuria in relation to duration of diabetes.

Microalbuminuric patients had significantly increased systolic and diastolic blood pressure compared with normoalbuminuric subjects (p<0.01). HbA1c concentrations and fasting plasma glucose levels were significantly higher with microalbuminuria than with normoalbuminuria (p<0.001).Taking an HbA1c concentration of <7% as the reference value, there was a significant increase in the OR for microalbuminuria (OR: 2.0, 95% confidence interval (CI): 1.04–3.87) in microalbuminuric patients with HbA1c levels of 8–10% (Figure 2).

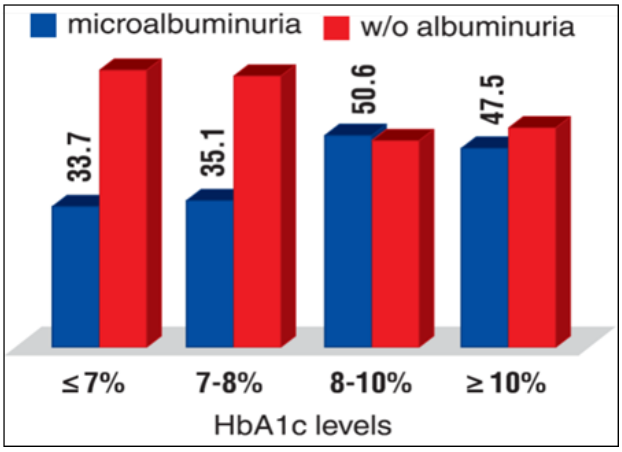

Figure 2: Prevalence of microalbuminuria and normoalbuminuriain relation to glycosylated hemoglobin (HbA1c).

Univariate analysis, summarized in Table 1, revealed that the risk factors associated with microalbuminuria were duration of diabetes, systolic blood pressure (OR: 1.99, 95% CI: 1.22–3.25), waist circumference in females (OR: 4.35, 95% CI: 1.68–12.58) and HbA1c concentration. Microalbuminuric patients had a more deranged lipid profile, with higher serum total cholesterol and triglyceride levels than normoalbuminuric patients.

Table 1: Univariate analysis of risk factors associated with microalbuminuria

	Odds ratio	95% confidence interval	p-value
Gender	1.334	0.958–3.243	0.152
HbA1c*	2.011	1.596–4.253	< 0.005
Waist circumference (male)	1.854	0.833–4.120	0.332
Waist circumference (female)	4.358	1.687–12.584	< 0.005
Cholesterol	1.450	0.858–2.246	0.323
Triglyceride	1.086	0.665–1.786	0.210
Smoking	0.856	0.568–1.956	0.041
Duration of diabetes	2.596	1.236–3.569	< 0.005
Systolic blood pressure	1.998	1.223–3.254	< 0.005
Diastolic blood pressure	1.235	0.847–2.547	0.210

*HbA1c, glycosylated hemoglobin.

Table 2 shows the results of multiple logistic regression analysis using microalbuminuria as the dependent variable in males and females with microalbuminuria. Independent risk factors for male diabetes patients with microalbuminuria were duration of diabetes, systolic blood pressure (OR: 2.88, 95% CI: 1.85–6.85) and waist circumference (OR: 2.15, 95% CI: 1.01–5.45). In females, there were significant associations with poor glycemic control (OR: 4.51, 95% CI: 1.45–13.98), duration of diabetes and waist circumference (OR: 4.87, 95% CI: 1.80–13.11).

Table 2: Multiple regression analysis using microalbuminuria as the dependent variable

	Males		Females	
	Odds ratio	95% CI*	Odds ratio	95% CI
HbA1c† (8–10%)	1.254	0.951–2.567	4.512	1.452–13.985
Waist circumference	2.156	1.012–5.125	4.875	1.802–13.115
Duration of diabetes	2.785	1.156–3.759	2.568	1.702–3.778
Systolic blood pressure	2.889	1.852–6.854	1.023	0.858–2.568

*CI, confidence interval.
†HbA1c, glycosylated hemoglobin

The following factors were used as independent variables: duration of diabetes in5 year intervals; systolic blood pressure >140 mm Hg and/or diastolic blood pressure >90 mm Hg; waist circumference >102 cm in males or>88 cm in females; and HbA1c. Independent risk factors for microalbuminuria in males were duration of diabetes, systolic blood pressure and waist circumference; poor glycemic control was significantly associated in females only.

4. Discussion

Recent figures released by the International Diabetes Federation confirm the enormity of the diabetes epidemic and indicate that the number of patients with renal failure due to diabetes will continue to increase dramatically. Several small and large scale trials in the United States, Canada and Europe have tried to evaluate the incidence and prevalence of diabetic nephropathy[18]. In general, microalbuminuria is a sensitive marker for damage induced by diabetes[19]. Epidemiologic studies have shown that identifying and monitoring patients with microalbuminuria is important because its treatment can prevent or postpone overt nephropathy[19, 20].

As in other developing countries, the prevalence of diabetes in Albania has increased rapidly[7]. The prevalence of type 2 diabetes in southwestern rural areas of Albania was found to be 4.17%[9]. The difference in prevalence observed between rural and urban areas may reflect differences in lifestyle and nutrition. In the present cross-sectional study, we investigated the prevalence of microalbuminuria and its association with potential risk factors in 321 type 2 diabetes patients from three cities in Albania. To our knowledge, this is the first study to determine the prevalence of diabetic nephropathy in Albania. Standard assays for urinary microalbuminuria are not widely available in Albanian laboratories, which made the study of diabetic nephropathy difficult in this country. We measured microalbuminuria using Bayer dipsticks, which is an easy and accurate method.

Of our study population, 40.8% had microalbuminuria, which is similar to the prevalence in other European countries[21, 22]. Data from the DEMAND study, a large cohort of type 2 diabetes patients, found the prevalence of normoalbuminuria and microalbuminuria to be 51% and 39%, respectively[23]. An earlier study conducted on the framework of the ALBDIAB study of 2004[24] showed that 9.4% of diabetes patients had diabetic nephropathy. However, that study did not include microalbuminuria in the prevalence of nephropathy and dealt only with overt nephropathy, which could be the reason for the low reported prevalence of kidney damage. In the present study, we did not find any difference between males and females regarding the presence of microalbuminuria, which is similar to the findings reported by Mather et al. for European diabetes patients[25]. Other studies have reported a greater prevalence of microalbuminuria in men compared with women[25], probably due to the use of ACR as a method of urinary albumin estimation.

The microalbuminuric patients in our study had a longer duration of diabetes than the normoalbuminuric group, consistent with findings from other studies[26]. We found that the OR for microalbuminuria became statistically significantly increased only at 16 years after the diagnosis of type 2 diabetes. At this time, 43.7 % of patients had microalbuminuria; this figure remained constant thereafter. However, it is well known that the duration of disease is difficult to establish in type 2 diabetes. Microalbuminuric patients in the present study had higher systolic and diastolic blood pressure, suggesting that systolic blood pressure is a significant risk factor for diabetic nephropathy, but multivariate analysis did not confirm this finding. The reason may be the definition used for hypertension, because the patients we classified as non-hypertensive were not reevaluated. Microalbuminuric patients tend to have higher levels of cholesterol and triglyceride, but no independent significant association was observed in the present study. A possible explanation for this result may be the use of statins in this group. In most studies, a good correlation has been observed between the prevalence of microalbuminuria and cholesterol and triglyceride levels[27]. In a prospective observational study, Gall et al. found that baseline cholesterol was an independent risk factor for the development of microalbuminuria[28].

In the present study, multiple logistic regression analysis revealed that duration of diabetes, systolic blood pressure, HbA1c and waist circumference were risk factors for microalbuminuria in males, whereas poor glycemic control, duration of diabetes and waist circumference were associated with microalbuminuria in females. The Diabetes Control and Complications Trial Research Group showed that intensive therapy for blood glucose control reduced the occurrence of microalbuminuria by 39%[29]. This emphasizes the need for good control of blood glucose in type 2 diabetes patients to prevent diabetic nephropathy.

Several limitations were encountered in this study. First, the study was not population-based and only patients who presented at diabetes centers were included. This may have introduced referral bias and it would therefore be difficult to extend our findings to the general population of diabetes patients. Second, we had difficulties determining the duration of diabetes. Third, the cross-sectional nature of the study design limits the reliability of the observed associations between risk factors and diabetic nephropathy. Despite these limitations, the high number of patients with microalbuminuria raises implications for future health policies. Because microalbuminuria is widely used as a sensitive risk marker to identify those at risk for renal dysfunction[30], screening programs should be implemented at an early stage to prevent or postpone ESRD. However, a recent study by Thomas et al. showed that renal impairment in type 2 diabetes it is not always preceded by albuminuria[31] and other markers are therefore needed to monitor renal function[32]. Prospective studies should be undertaken to confirm the relationship between risk factors and the progression of diabetic nephropathy, and to monitor renal dysfunction in these patients.

5. Conclusions

This cross-sectional multicenter study found the prevalence of microalbuminuria in type 2 diabetes patients in Albania to be 40.8%. In males, high systolic blood pressure, duration of diabetes and central obesitywere associated with development of microalbuminuria; in females, poor glycemic control, duration of diabetes and waist circumference were associated factors. Control of modifiable risk factors, especially blood glucose and blood pressure, should be optimized to reduce the risk of diabetic nephropathy.According to the American Diabetes Association, type 2 diabetes patients should be screened annually for microalbuminuria. Unfortunately, we are far from routine screening and other recommended goals for these patients in Albania. In the present study, we investigated the prevalence of microalbuminuria in Albanian diabetes patients to emphasize the need for routine screening and better control of risk factors.

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