Prevalence of microalbuminuria and its correlates among diabetic patients attending diabetic clinic at National Guard Hospital in Alhasa

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Abstract:

INTRODUCTION: Diabetes mellitus is one of the most common diseases encountered in clinical practice. Diabetic nephropathy is a common consequence of long-standing diabetes mellitus; microalbuminuria (MA) is considered an early stage of diabetic nephropathy.

OBJECTIVES: To determine the prevalence of miciroalbuminuria in diabetic patients and factors associated with MA.

MATERIALS AND METHODS: This cross-sectional study was conducted in the diabetic clinic of the primary health center of the National Guard Hospital. Diabetes type 2 patients between the ages of 20–60 years who attended the clinic in 2012 were included in this study. Data were collected by reviewing medical records for demographic and disease-related variables. MA was detected by measuring the albumin to creatinine ratio, and MA was diagnosed if this ratio was between 30 and 300 mg/g on two occasions.

RESULTS: MA was found in 37.4% of the sample and the rate was significantly higher among females ($P < 0.027$). MA was positively related to body mass index (BMI) ($P < 0.002$), the presence of hypertension ($P < 0.000$), duration of diabetes ($P < 0.000$), glycated hemoglobin ($P < 0.000$), fasting plasma glucose ($P < 0.000$), and low-density lipoprotein (LDL) ($P < 0.043$). No statistically significant correlation was found between MA and age, creatinine level, high-density lipoprotein, and triglyceride.

CONCLUSION: The prevalence of MA in patients with diabetes in this study was high. The study suggests the need to screen for MA early, and the active management of modifiable risk factors, in particular, hyperglycemia, hypertension, LDL, and BMI, to reduce the burden of future end-stage renal disease.

Key words:
Diabetes, microalbuminuria, predictive factors, prevalence

Introduction

Diabetes mellitus is the most common metabolic syndrome disorder characterized by chronic hyperglycemia and disturbances of carbohydrate, fat, and protein metabolism on account of absolute or relative deficiency of insulin secretion or action. The prevalence of diabetes in Saudi Arabia is 34.1% in males and 27.6% in females.[1]

Morbidity from diabetes is a consequence of both macrovascular disease (atherosclerosis) and microvascular disease (retinopathy, nephropathy, and neuropathy). The progression of these complications can be slowed with interventions.

Diabetic nephropathy is a glomerulopathy defined by characteristic structural and functional changes.[2] The predominant structural changes include mesangial expansion, glomerular basement membrane thickening, and glomerular sclerosis.[2] The major clinical manifestations of diabetic nephropathy are albuminuria, less often hematuria, and in many patients, progressive chronic kidney disease, which can be slowed or prevented with optimal therapy. Increased urinary protein excretion is the earliest currently used clinical finding of diabetic nephropathy.[2] The normal rate of albumin excretion is <30 mg/day (20 mcg/min); persistent values between 30 and 300 mg/day (20–200 mcg/min) in a patient with diabetes is called microalbuminuria (MA).[2] A diagnosis of MA can be made by measuring its excretion rate in 24 h or in an overnight urine collection, or by measuring albumin/creatinine ratio or albumin concentration in the morning or a random urine sample.[2]

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Diabetic nephropathy is a common consequence of long-standing diabetes mellitus and is the leading cause of end-stage renal disease.[3] It constitutes the major workload of dialysis centers, and the cost per patient with diabetes is very high. Patients with diabetes on dialysis and transplant recipients also have higher morbidity and mortality rates.[4] Despite the knowledge gained in relation to early identification and intervention in high-risk patients with type II diabetes, diabetic nephropathy is still the leading cause of end-stage renal disease in most countries of the world.[5] MA is considered an early stage of diabetic nephropathy. The prevalence of MA in patients with type II diabetes has been reported from 20% to 61%.[6-8]

The majority of the studies show a significant correlation between MA and the duration of diabetes; the longer the duration of diabetes, the higher the risk of MA.[6,7] The relationship between MA and fasting blood sugar (FBS), age, and gender is debatable; the findings of various studies are contradictory.[6-8]

Usually, the patients are asymptomatic until complications become obvious. Generally, screening for MA is a relatively cheap and convenient procedure. It is used for detection in patients with diabetes to reduce cardiovascular risks and the rate of progression of diabetes-related nephropathy. Early intervention to control BP and hyperglycemia reverses MA and delays subsequent development.[2,9] The objective of the present study was to estimate the prevalence of microalbuminuria in patients with type II diabetes and determine factors related to it.

Materials and Methods

A cross-sectional study was conducted at the diabetic clinic in the primary health center of the National Guard Hospital. Patients with type II diabetes between 20 and 60 years old who visited the clinic in 2012 were included in this study. Patients with overt albuminuria (>300 mg/day), congestive cardiac failure, urinary tract infection, or pregnant patients were excluded from the study. The study population comprised 2974 patients with type II diabetes attending the diabetic clinic in the primary health center of the National Guard Hospital, Al-Ahsa, during the year 2012. Using a simple random sampling technique, 494 patients were selected from the study population. A questionnaire of demographic data and disease-related variables was designed. Data were collected by reviewing medical records for demographic and disease-related variables. Body mass index (BMI) of <25 was considered normal. BMI of 25.0–29.9 fell within the overweight range, BMI of 30–39.9 was within the obese range, and more than 40 was considered morbidly obese. Patients were categorized as hypertensive if the systolic blood pressure was >140 mmHg and/or the diastolic blood pressure was >90 mmHg. MA was defined as an albumin-to-creatinine ratio of ≥30 μg/mg on 2 of 3 urine samples collected over a 3-month period. Glycated hemoglobin (HbA1c) <7% was considered normal, and fasting glucose between 3.9 and 5.8 mmol\L was normal.

Definitions
Cardiovascular disease
As documented in the medical record is the presence or absence of stable and unstable angina, myocardial infarction.

Nephropathy disease
As documented in the medical record is the presence or absence of weakness or diminished sensation, loss of ankle jerks and vibratory sensation, wasting of the small muscles of hands and feet.

Retinopathy disease
As documented in the medical record as the presence or absence of a sign of nonproliferative or proliferative retinopathy. Signs of nonproliferative retinopathy include microaneurysm, venous loops, retinal hemorrhages, and hard and soft exudates. Proliferative retinopathy includes new vessels in the eyes or vitreous hemorrhage.

Statistical analysis
All statistical analysis were performed using SPSS (Statistical Package for Social Sciences version 20.0, SPSS Inc. Chicago, IL; 2010). Descriptive analysis results were presented as mean ± standard deviation for all quantitative variables, whereas, categorical variables were presented as frequencies and percentages. Chi-square test or Fisher's Exact test, as appropriate, were used to compare all the demographics and clinical characteristics of the patients with microalbuminuric versus those not having MA; $P<0.05$ was considered statistically significant."

Results

Male patients constituted 50.2% while females were 49.8%. The mean age of the patients was 52.01 years with standard deviation of 11.43; majority were between 35-54 (59.5%) followed by 55 years or older (34.4). Other complications such as cardiovascular, neuropathy, and retinopathy were absent in 94.9%, 90.7%, and 97%, respectively. The majority of the patients (70.4%) had hypertension. The analysis of collected data showed that 25% had had diabetes for 1–4.9 years, 28.5% had had it for 5–9.9 years, 18% for 10–14.9 years, and 27.5% for more than 15 years. The mean duration of diabetes was 9.83 ± 6.59 years. Nearly 31.8% of the patients were obese and 27.9% were morbidly obese. The mean BMI was 31.89 ± 6.88 kg/m² [Table 1].

The overall prevalence of MA was 37.4%. Most patients had high glycated hemoglobin (80.4%) and high fasting sugar (83%). The percentage of abnormal laboratory value in patients with diabetes was as follows: creatinine 23.7%, low-density lipoprotein (LDL) 53%, high-density lipoprotein (HDL) 91.1%, and triglyceride 40.9%. The mean FBS, HbA1c, and creatinine levels were 8.82 ± 2.93 mg/dL, 8.28 ± 1.94, and 1.33 ± 1.14, respectively. The mean serum triglyceride, LDL, and HDL levels were 1.56 ± 0.85, 3.1 ± 1.104, and 1.06 ± 0.95 mg/dL, respectively [Table 2].

The analysis showed that MA was more prevalent in females (56.2%) than in males (43.8%) ($P < 0.027$). The prevalence of MA was not statistically different between the various age groups ($P < 0.100$). MA was statistically significantly associated with the presence of diabetic retinopathy (66.7%) ($P < 0.018$) and diabetic neuropathy (56.5%) ($P < 0.005$). The prevalence of MA showed no statistically significant associations with cardiovascular disease. The albumin to creatinine ratio between 30 and 300 mg/g was more in patients with hypertension (43.7) than in those with normal blood

Table 1: Diabetics' sociodemographic features and disease-related variable characteristics in Primary Health Care in the National Guard Hospital, Al-Ahsa (*n*=494)

Variable	N (%)
Gender	
Male	248 (50.2)
Female	246 (49.8)
Age (years)	
20-34	30 (6.1)
35-54	294 (59.5)
55 or above	170 (34.4)
Mean±SD	52.01±11.4
Cardiovascular disease	
Present	25 (5.1)
Absent	469 (94.9)
Neuropathy	
Present	46 (9.3)
Absent	448 (90.7)
Retinopathy	
Present	15 (3.0)
Absent	479 (97.0)
Hypertension	
Yes	348 (70.4)
No	146 (29.6)
Duration of diabetes (years)	
1-4.9	128 (25.9)
5-9.9	141 (28.5)
10-14.9	89 (18.0)
15 or above	136 (27.5)
Mean±SD	9.83±6.6
BMI	
Normal (<25.0)	51 (10.3)
Overweight (25.0-29.9)	148 (30.0)
Obese (30.0-39.9)	157 (31.8)
Morbidly obese (40 or above)	138 (27.9)
Mean±SD	31.89±6.9

BMI = Body mass index, SD = Standard deviation

Table 2: Frequency of biochemical variables at Diabetic Clinic in Primary Health Care in National Guard Hospital, Al-Ahsa (*n*=494)

Variable	N (%)
Albumin to creatinine ratio	
<30	309 (62.6)
30-300	185 (37.4)
Mean±SD	35.06±46.9
HbA1c	
≤7	97 (19.6)
>7	397 (80.4)
Mean±SD	8.28±1.9
Fasting sugar (mg/dL)	
Normal (what is normal value) (<130)	84 (17.0)
Abnormal (what is abnormal value) (>130)	410 (83.0)
Mean±SD	8.82±2.9
Creatinine level	
Normal (<1.3)	377 (76.3)
Abnormal (>1.3)	117 (23.7)
Mean±SD	1.33±1.1
LDL	
Normal (<100)	232 (47.0)
Abnormal (>100)	262 (53.0)
Mean±SD	3.1±1.1
HDL	
Normal (>40)	44 (8.9)
Abnormal (<40)	450 (91.1)
Mean±SD	1.06±0.9
Triglyceride	
Normal (<150)	292 (59.1)
Abnormal (>150)	202 (40.9)
Mean±SD	1.56±0.9

HbA1c = Glycated hemoglobin, SD = Standard deviation, LDL = Low-density lipoprotein, HDL = High-density lipoprotein

pressure ($P < 0.000$). The prevalence of MA was significantly higher in the overweight, obese, and morbidly obese compared to individuals of normal weight (94.5% vs. 5.4%) ($P < 0.002$). A significant correlation was found between the prevalence of MA and duration of diabetes of 15 years or more (66.2%) ($P < 0.000$) [Table 3].

The prevalence of MA in patients with abnormal HbA1C was 95.1% with a statistically significant correlation ($P < 0.001$). Abnormal fasting glucose was in 94.6% of patients with statistically significant correlation ($P < 0.001$). A significant correlation was noted with abnormal LDL (41.6%) and MA ($P < 0.043$). The prevalence of MA showed no statistically significant associations with other variables including creatinine levels, HDL, and triglycerides [Table 4].

Discussion

In the present study, 494 patients with type II diabetes were studied and the overall prevalence of MA found was 37.4%.

A statistically significant correlation was found between the prevalence of MA and females, BMI, presence of hypertension, duration of diabetes, HbA1c, fasting plasma glucose, and LDL. Several epidemiological studies have reported the prevalence rates of MA as ranging between 20% and 61% in patients with type II diabetes.[7-12] This variation in the prevalence of MA can be attributed to several factors such as differences in populations, the definition of MA, the methods of measurement and urine collection.

No statistical correlation was found between the prevalence of MA and the age of patients in the present study, a result which is similar to what was reported in another study.[13] However, some studies found a statistical correlation between age and MA.[8] These variations are probably related to the varied distribution of patients' ages in the different studies.

This study shows gender-wise correlation of MA, in which the prevalence of MA shows a female dominance. A study in Northern Tanzania showed no difference of prevalence of MA across genders,[8] but another study reported increased prevalence of MA in men compared to women.[14] The differences in results may be because of the selection of samples or certain differences in population.

Table 3: Relation of microalbuminuria with sociodemographic features and disease-related variables A diabetic Clinic in Primary Health Care at the National Guard Hospital, Al-Ahsa (n=494)

Variable	Microalbuminuria		p-value
	Absent, N (%)	Present, N (%)	
Gender			
Male	167 (67.3)	81 (32.7)	0.027
Female	142 (57.7)	104 (42.3)	
Age (years)			
20-34	24 (80.0)	6 (20.0)	0.100
35-54	184 (62.6)	110 (37.4)	
55 or above	101 (59.4)	69 (40.6)	
Cardiovascular disease			
Present	12 (48.0)	13 (52.0)	0.123
Absent	297 (63.3)	172 (36.7)	
Neuropathy			
Present	20 (43.5)	26 (56.5)	0.005
Absent	289 (64.5)	159 (35.5)	
Retinopathy			
Present	5 (33.3)	10 (66.7)	0.018
Absent	304 (63.5)	175 (36.5)	
Hypertension			
Yes	196 (56.3)	152 (43.7)	<0.001
No	113 (77.4)	33 (22.6)	
Duration of diabetes (years)			
1-4.9	105 (82.0)	23 (18.0)	<0.001
5-9.9	104 (73.8)	37 (26.2)	
10-14.9	54 (60.7)	35 (39.3)	
15 or above	46 (33.8)	90 (66.2)	
BMI			
Normal (<25.0)	41 (80.4)	10 (19.6)	0.002
Overweight (25.0-29.9)	95 (64.2)	53 (35.8)	
Obese (30.0-39.9)	102 (65.0)	55 (35.0)	
Morbidly obese (40 or above)	71 (51.4)	67 (48.6)	

BMI = Body mass index, SD = Standard deviation

Table 4: Relation of microalbuminuria with disease-related variable at Diabetic Clinic in Primary Health Care at the National Guard Hospital, Al-Ahsa (n=494)

Variable	Microalbuminuria		p-value
	Absent N (%)	Present N (%)	
HbA1c			
≤7	88 (90.7)	9 (9.3)	<0.001
>7	221 (55.7)	176 (44.3)	
Fasting sugar			
Normal	74 (88.1)	10 (11.9)	<0.001
Abnormal	235 (57.3)	175 (42.7)	
Creatinine level			
Normal	249 (66.0)	128 (34.0)	0.004
Abnormal	60 (51.3)	57 (48.7)	
LDL			
Normal	156 (67.2)	76 (32.8)	0.043
Abnormal	153 (58.4)	109 (41.6)	
HDL			
Normal	33 (75.0)	11 (25.0)	0.074
Abnormal	276 (61.3)	174 (38.7)	
Triglyceride			
Normal	191 (65.4)	101 (34.6)	0.114
Abnormal	118 (58.4)	84 (41.6)	

HbA1c = Glycated hemoglobin, SD = Standard deviation, LDL = Low-density lipoprotein, HDL = High-density lipoprotein

The American Diabetes Association recommends screening adults ≥45 years of age and especially those with BMI ≥25 kg/m^2 since weight gain was significantly associated with diabetes. The present study also found a significant correlation between MA and BMI, similar to the study reported in a study.[8] However, a study from Africa showed no relation of MA to BMI.[20]

Most patients with MA in the present study had hypertension, which was also observed in another study,[6] which suggests that increased blood pressure, particularly systolic blood pressure, induces systemic artiole dysfunction in the kidney and damage to glomerular filtration membrane. This is the most important reason for microalbuminuria.[21]

In the present study, a statistically significant correlation was found between the prevalence of MA and HbA1c, which was similar to findings reported by other studies.[7,8,10,18,22,23] However, in another study, there was no significant association of MA with HbA1c,[6] but there was a strong association with fasting glucose, which is similar to an earlier study.[6,24] Hyperglycemia is a crucial factor in the development of diabetic nephropathy because of its effects on glomerular and mesangial cells though not causative on its own. Mesangial cells are crucial for the maintenance of glomerular capillary structure and for the modulation of glomerular filtration through smooth muscle activity. Hyperglycemia is associated with an increase in mesangial cell proliferation and hypertrophy, as well as increased matrix production and basement membrane thickening.[25] Thus, tight glycemic control and monitoring on a regular basis should be the primary goal for any patient with diabetes.

The present study found a statistical correlation between the prevalence of MA and presence of diabetic retinopathy and neuropathy, similar to other reported studies.[7,11,15] No statistical correlation was found between the prevalence of MA and presence of coronary artery disease. However, some studies have found a statistical correlation between cardiovascular disease and MA.[7,16,17] This difference may be due to poor documentation in our medical files and the possible distortion of percentages by the smallness of the population.

In the present study, a good statistically significant correlation was found between the prevalence of MA and the duration of diabetes. Earlier studies reported a significant correlation between MA and the duration of diabetes[6,7,11,18,19] though another study reported no significant correlation between MA and the duration of diabetes.[8] This conflicting observation may be the result of the difficulty in dating the onset of diabetes. In many countries, diabetes goes undetected for a long period, and newly diagnosed patients with diabetes sometimes present with well-established complications.

The present study failed to show any correlation between MA and creatinine, a result which is similar to an earlier study.[6] Other studies, however, showed higher serum creatinine levels,[8] which can be an important warning sign of possible irreversible renal damage if ignored.[8]

The result of the present study showed an association of MA with LDL but not with HDL triglyceride. Prospective studies suggest that an adverse lipid profile might cause nephropathy in patients with type II diabetes through certain mechanisms including mesangial cell proliferation, recruitment of macrophages, altered cytokine responses, and increased matrix deposition.[25]

One strength of this study was a good sample size of high-risk individuals though there were some limitations. First, the study is not population based and only patients who presented at diabetes centers were included in the study. This may have introduced ferral bias, so it would be inappropriate to extend our findings to cover the general population of diabetes patients. Second, the cross-sectional nature of the study design limits the reliability of the observed associations between risk factors and diabetic nephropathy.

Conclusion

There is evidence that early therapeutic intervention in diabetic patients can delay onset of complications and improve outcomes. To act fast we need to prevent type 2 diabetes mellitus, and screen for early diabetic kidney disease. The control of modifiable risk factors, especially hyperglycemia, obesity and hypertension, as well as timely detection can decrease the prevalence of albuminuria in diabetic patients.

Conflicts of interest
There are no conflicts of interest.

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