IJKD KIDNEY DISEASES

Albuminuria and Its Correlates in Type 2 Diabetic Patients

Mehrnoosh Zakerkish, Hajieh Bibi Shahbazian, Heshmatollah Shahbazian, Seyed Mahmoud Latifi, Armaghan Moravej Aleali

Diabetes Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Keywords. type 2 diabetes mellitus, microalbuminuria, diabetic nephropathy, glycosylated hemoglobin A

Introduction. The aim of this study was to determine the prevalence of albuminuria and its correlates and investigate disease management for patients with type 2 diabetes mellitus in Ahvaz.

Materials and Methods. This was a cross-sectional study on the 350 patients with type 2 diabetes mellitus attending the Diabetes Clinic at Golestan Hospital, from October 2010 to September 2011. Demographic characteristics were recorded and height, weight, and blood pressure were measured. Blood urea nitrogen and serum levels of creatinine, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, and glycosylated hemoglobin A were measured in fasting blood samples. Spot urine and 24-hour urine collection were tested for albumin and kidney ultrasonography was done.

Results. A total of 72 of 350 patients (20.6%) had microalbuminuria and 18 (5.1%) had macroalbuminuria. Elevated serum creatinine was seen in 6.9% and azotemia in 6.0%. In multivariable analysis, blood urea nitrogen level, glycosylated hemoglobin A, and duration of diabetes mellitus were associated with urinary albumin excretion (P = .04). A small proportion of the participants achieved optimal treatment goals for modifiable risk factors.

Conclusions. Abnormal urinary albumin excretion is seen in one-quarter of type 2 diabetic patients and a small but important number of them have azotemia. Albuminuria was found to be associated with long-term duration of diabetes mellitus, poor glucose control (revealed by high glycosylated hemoglobin A levels), and high blood urea nitrogen. Poor glycemic control may have a significant role in the progression of diabetic nephropathy in these patients.

IJKD 2013;7:268-76
www.ijkd.org

Original Paper

INTRODUCTION

Global prevalence of diabetes mellitus (DM) has increased dramatically over the past 2 decades (from about 30 million cases in 1985 to 177 million in 2000 and 285 million in 2010) and if this situation continues, by 2030 more than 360 million people will have DM.[1] The increasing rate of type 2 DM is much larger that type 1. Increasing prevalence of obesity and reduced physical activity are the main reasons.[2] In the United States, DM is the main cause of end-stage renal disease, nontraumatic limb amputation, and blindness in adults. With the increasing prevalence of DM worldwide, it is expected that DM remains among the main causes of human mortality.[3]

One of the first clinical symptoms of diabetic nephropathy is microalbuminuria that may progress to macroalbuminuria and the progressive loss of glomerular filtration rate (GFR) and finally the end-stage renal disease. This process was identified in

type 1 DM and there is also a similar sequence in a significant percentage of type 2 DM patients. In one study, 38% of type 2 diabetic patients followed over a period of 7 years showed progressive increase in urinary albumin without reduced GFR, 33% showed an increase in urinary albumin excretion associated with decreased GFR, and 30% showed a reduction in GFR without increase in urinary albumin excretion. However, kidney disease in type 2 DM is more complex for several reasons, mainly because the onset of DM is almost unknown and may be many years before diagnosis.[4]

Most patients with type 2 DM are elderly and age per se can affect kidney function; after 40 years of age, GFR reduce by 8 mL/min to 10 mL/min every 10 years.[5] In addition, old patients often suffer from other diseases, including hypertension and atherosclerosis, which can also damage the renal parenchyma. If no therapeutic intervention is in place, about 20% to 40% of type 2 diabetic patients with microalbuminuria, progress to overt nephropathy and finally approximately 20% develop end-stage renal failure.[6,7]

Microalbuminuria is not only the predictive factor of macroalbuminria and renal injury, but also associated with an increased risk of cardiovascular event and mortality.[8-13] Early recognition and treatment of microalbuminuria can prevent irreversible complications such as kidney problems, which ultimately leads to kidney failure and cardiovascular events.

The prevalence rates of microalbuminuria and macroalbuminuria in diabetic patients in Iranian studies vary from 16.7% to 35.2% and 1.1% to 10.6%, respectively.[14,15] Considering the significant prevalence of DM in Iran,[16] the aim of this study was to determine the prevalence of microalbuminuria and macroalbuminuria and its correlates in patients with type 2 DM attending to Golestan Hospital in Ahvaz.

MATERIALS AND METHODS

Patients

This cross-sectional study was conducted from October 2010 to September 2011 in the outpatient diabetes clinic of Golestan Hospital, a teaching hospital of Ahvaz Jundishapur University of Medical Sciences (Ahvaz, Iran). Type 2 diabetic patients who attended to the diabetes clinic were included in the study. The exclusion criteria included severe hyperglycemia (blood glucose > 400 mg/dL), severe hypertension (blood pressure > 190/110 mm Hg), heart failure grade III and IV, heavy exercise, urinary infection, acute fever, pregnancy, menstruation, and urinary calculus. All of the participants provided informed consent.

The World Health Organization's criteria were used for the diagnosis of DM.[17] Out of 380 visited eligible type 2 diabetic patients, 350 individuals participated in the biochemical examination and completed the study with valid measurements.

Data Collection and Procedures

After registration, patients' demographic and clinical characteristics including age, sex, duration of DM, history of heart disease, hyperlipidemia, smoking, and medications were recorded and weight, height, and blood pressure were measured. Weight was measured with the possible lightest clothing and without shoes by a special DM nurse. Body mass index was considered normal if it was between 18.5 kg/m^2 to 24.9 kg/m^2, overweight if it was 25 kg/m^2 to 29.9 kg/m^2, and obesity if it was equal or greater than 30 kg/m^2.

Blood pressure was measured in the sitting position, of the right arm after 5 minutes of rest with a standard mercury sphygmomanometer and the average of 2 measurements was recorded. According to the 7th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[18] hypertension was defined as a systolic blood pressure equal to or greater than 140 mm Hg or diastolic blood pressure equal to or greater than 90 mm Hg, or both, or the use of antihypertensive medications.

Blood samples were taken from all patients after at least 10 hours of fasting. Blood glucose, total serum cholesterol, triglyceride, and high-density lipoprotein cholesterol (HDLC) were measured using Pars Azmoon kit (Tehran, Iran) by photometric method with Biotecnika instrument BT3000 (Rome, Italy). Low-density lipoprotein cholesterol (LDLC) level was calculated by Friedewald equation if triglyceride level was less than 400 mg/dL and measured directly if triglyceride level was higher[19]:

LDLC = total cholesterol – HDLC – triglyceride/5

According to American Diabetes Association,[20] the European Society of Hypertension, and European Society of Cardiology,[21] the following recommended targets were considered as normal

range: Hb A1C, < 7%; blood pressure, < 13/80 mm Hg; LDLC, < 100 mg/Dl; serum cholesterol, < 200 mg/dL; serum triglyceride, < 150 mg/dL; body mass index, < 25 kg/m^2; and HDLC, > 40 mg/dL for men and 50 mg/dL for women. Patients who were already being treated by lipid-lowering agents and those whose triglyceride, cholesterol, or LDLC were higher than normal values listed above were considered as hyperlipidemic. Hemoglobin A1c was measured by ultraviolet absorption method using the Nico Card equipment (Oslo, Norway).

Glumerular filtration rate (GFR) was calculated based on the Cockroft-Gault formula estimated creatinine clearance. Serum and urine creatinine were measured with Pars Azmoon kit (Tehran, Iran) with photometric method. Diabetic nephropathy was defined as persistent albuminuria (greater than 300 mg in 24-hour urine) and the absence of other clinical and laboratory evidence of kidney or urinary disease in a person with type 2 DM.[22]

The 24-hour urinary albumin measurement was done with immonoturbidometric method using Pars Azmoon kit (Tehran, Iran) with Autonalayzer Biotecnica model BT 3000 (Rome, Italy). Assessment of 24-hour urinary albumin measurement was done if there was no evidence of infection in urine and the person had no severe hyperglycemia, severe hypertension, heart failure and febrile illness, and heavy exercise. Normoalbumin urine was defined as 24-urine albumin less than 30 mg, microalbuminuria as urine albumin level of 30 mg to 300 mg, and macroalbuminuria as greater than 300 mg. For all patients with albuminuria, urine analysis and culture was done to rule out urinary tract infection and kidney ultrasonography was done to rule out urinary calculi. If there was more than 30 mg of albumin in 24-hour urine, another 24-hour urine albumin was taken at least 1 month later and if albumin level was greater than the abovementioned level, the diagnosis of microalbuminuria was established. Subjects with only one urinary albumin excretion greater than 30 mg/24 h were not included.

A serum creatinine level greater than 1.2 mg/dL in women and greater than 1.4 mg/dL in men was considered azotemia.

Statistical Analysis

Results for continuous variables were demonstrated as mean ± standard deviation. Statistical significant difference between the groups was determined by the chi-square test for categorical variables and unpaired Student *t* test for continuous variables. Comparison of clinical variables among the groups was performed by 1-way analysis of variance. Multiple logistic regression, linear regression, 1-way analysis of variance, and independent *t* tests were used to describe the association of variables with microalbuminuria. A *P* value less than .05 was considered significant. All analyses were performed with the the SPSS software (Statistical Package for the Social Sciences, version 17.0, SPSS Inc, Chicago, Ill, USA).

RESULTS

Of 350 participants, 238 (68%) were women and 112 (32%) were men. The mean age of the patients, duration of DM, and body mass index were 54.0 ± 10.5 years, 54.81 ± 65.80 months, and 28.06 ± 4.30 kg/m^2, respectively. Demographic and laboratory data of the patients are listed in Table 1. The mean levels of serum total cholesterol, LDLC, and HDLC and the mean body mass index were greater in the women than the men. There were no significant differences between the women and the men in age, DM duration, blood pressure, Hb A1c, and blood triglyceride level.

Out of 350 patients, 87 (24.9%) were treated with insulin (23% of the men and 25.6% of the women). Hypertension, history of cardiovascular disease, and smoking were seen in 34.6%, 27.7%, and 16.9% of the patients, respectively. Hypertension and a history of cardiovascular disease were not significantly different between the men and the women ($P = .62$ and $P = .44$, respectively). Antihypertensive drugs received by patients were angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, and diuretics. Smoking was significantly more frequent among the men (42.9% versus 4.6% in the women, $P < .001$). Hyperlipidemia was seen in 52.9% of patients (52.9% had a serum triglyceride level above 150 mg/dL, 32.6% had a serum cholesterol level over 200 mg/dL, and 21.7% of patients had both).

A total of 72 patients (20.6%) had microalbuminuria and 18 (5.1%) had macroalbuminuria. A serum creatinine higher than 1.2 mg/dL was seen in 19 women (8%), 9 of whom (47.4%) were in the normal urine albumin excretion group, 4 (21.1%) were in the microalbuminuria group, and 6 (31.6%)

Table 1. Characteristics of Studied Patients With Type 2 Diabetes Mellitus*

Variable	Total	Male (n = 112)	Female (n = 236)	*P*
Age, y	54.0 ± 10.5	55.1 ± 12.0	53.5 ± 9.7	> .05
Diabetes duration, mo	54.8 ± 65.8	51.5 ± 62.2	56.3 ± 67.5	> .05
Body mass index, kg/m^2	28.1 ± 4.3	26.3 ± 3.8	28.8 ± 4.3	< .001
Systolic BP, mm Hg	120.7 ± 18.5	120.8 ± 20.1	120.6 ± 17.8	> .05
Diastolic BP, mm Hg	76.4 ± 11.4	75.2 ± 11.5	76.9 ± 11.3	> .05
Hemoglobin A1c, %	8.66 ± 2.02	8.60 ± 2.25	8.69 ± 1.90	> .05
Serum cholesterol, mg/dL	182.2 ± 43.8	169.1 ± 40.2	188.4 ± 44.1	< .001
LDLC, mg/dL	100.5 ± 36.4	94.4 ± 34.2	103.3 ± 37.1	.03
HDLC, mg/dL	47.2 ± 11.4	42.5 ± 9.6	49.9 ± 11.5	< .001
Triglyceride, mg/dL	178.6 ± 90.4	169.8 ± 87.1	182.7 ± 91.9	> .05
GFR, mL/min	85.88 ± 28.69	87.86 ± 29.40	84.30 ± 28.27	> .05
Blood urea nitrogen, mg/dL	17.1 ± 9.0	19.5 ± 12.6	15.9 ± 6.5	.006
Serum creatinine, mg/dL	0.98 ± 0.31	1.09 ± 0.30	0.92 ± 0.29	< .001
Smoking (%)	59 (16.9)	48 (42.8)	11 (4.0)	< .001
IHD (%)	97 (27.7)	34 (30.3)	63 (26.4)	> .05

*BP indicates blood pressure; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; GFR, glomerular filtration rate; and IHD, ischemic heart disease.

were in the macroalbuminuria group. A serum creatinine higher than 1.4 mg/dL was seen in 5 men (4.5%), 3 of whom (6%) were in the normal urine albumin excretion group, 1 (20%) was in the microalbuminuria group, and 1 (20%) was in the macroalbuminuria group. Six percent of the patients had azotemia, 50% of them had normal urine albumin excretion, 20% had microalbuminuria, and 30% had macroalbuminuria.

Age, sex, smoking, history of heart disease and GFR were not different between subjects with normal and abnormal albumin excretion (Table 2). Those who had microalbuminuria or macroalbuminuria had greater amounts of blood

Table 2. Clinical and Demographic Characteristics of Type 2 Diabetic Patients by Nephropathy Stage*

Variable	Normoalbuminuria	Microalbuminuria	Macroalbuminuria	*P*
Number of patients	260	72	18	
Age, y	54.1 ± 10.4	54 ± 10.6	54.2 ± 11.5	.99
Sex, %				
Male	81 (31.2)	26 (36.1)	5 (27.8)	
Female	179 (68.8)	46 (63.9)	13 (72.2)	.67
Body mass index, kg/m^2	28.1 ± 4.5	27.5 ± 4.1	28.3 ± 3.1	.71
Systolic BP, mm Hg	120.2 ± 16.9	119.3 ± 20	133.3 ± 28.0	.01
Diastolic BP, mm Hg	76.4 ± 11.0	74.8 ± 12.0	82.7 ± 12.7	.03
Hemoglobin A1c, %	8.3 ± 1.8	9.4 ± 2.2	9.8 ± 2.0	< .001
Serum cholesterol, mg/dL	179.8 ± 42.5	183.7 ± 42.4	211.4 ± 56.6	.01
LDLC, mg/dL	98.1 ± 34.5	103.5 ± 38.7	123.2 ± 45.7	.01
HDLC, mg/dL	47.4 ± 11.5	46.8 ± 10.7	46.6 ± 12.9	.90
Triglyceride, mg/dL	177.0 ± 97.3	199.1 ± 137.5	218.7 ± 167.9	.13
GFR, mL/min				
Men	87.92 ± 30.15	88.10 ± 28.18	86.07 ± 32.67	.99
Women	100.94 ± 29.50	97.04 ± 27.70	73.13 ± 39.20	.01
Blood urea nitrogen, mg/dL	16.1 ± 7.5	18.7 ± 10.8	25.5 ± 14.7	< .001
Serum creatinine, mg/dL				
Men	1.07 ± 0.23	1.08 ± 0.34	1.39 ± 0.79	.08
Women	0.89 ± 0.19	0.92 ± 0.20	1.43 ± 0.85	< .001
Diabetes duration, mo	48.5 ± 62.0	72.8 ± 71.2	73.7 ± 83.0	.01
IHD (%)	72 (27.7)	20 (27.8)	5 (27.8)	.90
Smoking (%)	47 (18.1)	10 (13.9)	2 (11.1)	.56

*BP indicates blood pressure; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; GFR, glomerular filtration rate; and IHD, ischemic heart disease.

urea nitrogen, serum creatinine, total cholesterol, LDLC, Hb A1c, and systolic and diastolic blood pressure, and longer duration of DM than those with normal urinary albumin excretion levels (Table 2).

Table 3 demonstrates health characteristic of participants with respect to sex and urinary albumin excretion. Women who had abnormal albumin excretion had greater amounts of blood urea nitrogen ($P = .009$), serum creatinine ($P = .03$), LDLC ($P = .019$), and Hb A1c ($P = .002$), and longer duration of DM ($P = .001$) than those with normal urinary albumin excretion. Men who had abnormal urinary albumin excretion only had greater Hb A1c levels ($P < .001$). In Table 4, GFR distribution of the patients is shown by sex and levels of urinary albumin excretion.

Logistic regression analysis was used to assess the association of various factors to the occurrence of microalbuminuria. Results of regression analyses are shown in Table 5. In univariable analysis, urinary albumin excretion was correlated with blood urea nitrogen ($r = 0.19$, $P < .001$), duration of DM ($r = 0.16$, $P = .002$), and Hb A1c ($r = 0.25$; $P < .001$). Urinary albumin excretion had no significant correlation with age, body mass index, systolic blood pressure and diastolic blood pressure, creatinine, total cholesterol, LDLC, triglyceride, GFR, smoking, ischemic heart disease, or sex. Two models including blood urea nitrogen, Hb A1c and duration of DM with and without creatinine and LDLC were designed for multivariable analysis of correlates of abnormal urinary albumin excretion. In both models, blood urea nitrogen, Hb A1c, and duration of DM were associated with urinary albumin excretion ($P = .04$). In model 1, all significant variables, and in model 2, only variables that were significant in model 1 were evaluated.

A small proportion of the participants achieved optimal treatment goals for modifiable risk factors (Table 6).

DISSCUSION

In this study, the prevalence of microalbuminuria was 20.6%, macroalbuminuria was 5.1%, and azotemia was 6% in a population of Iranian type

Table 3. Characteristics of Participants by Sex and Urinary Albumin Excretion*

Variable	Men (n = 112)		Women (n = 238)		All (n = 350)	
	Normal UAE (n = 81)	Abnormal UAE (n = 31)	Normal UAE (n = 179)	Abnormal UAE (n = 59)	Normal UAE (n = 260)	Abnormal UAE (n = 90)
Age, y	55.7 ± 12.2	53.6 ± 11.5	53.3 ± 9.5	54.2 ± 10.4	54.0 ± 10.4	54.0 ± 10.7
Diabetes duration, mo	49.2 ± 58.3	57.7 ± 72.1	48.2 ± 63.7	81.0 ± 73.1	48.5 ± 62.0	72.9 ± 73.2
Body mass index, kg/m^2	26.1 ± 3.6	26.6 ± 4.5	29.0 ± 4.6	28.2 ± 3.4	28.1 ± 4.5	27.6 ± 3.9
Systolic BP, mm Hg	118.8 ± 18.2	126.1 ± 23.7	120.8 ± 16.3	120.0 ± 21.7	120.2 ± 16.9	122.1 ± 22.4
Diastolic BP, mm Hg	74.2 ± 11.5	77.9 ± 11.3	77.4 ± 10.7	75.6 ± 13.0	76.4 ± 11.1	76.4 ± 12.4
Hemoglobin A1c, %	8.1 ± 1.9	9.9 ± 2.5	8.4 ± 1.8	9. 3 ± 1.9	8.3 ± 1.8	9.5 ± 2.1
Serum cholesterol, mg/dL	167.8 ± 38.5	172.2 ± 44.8	185.2 ± 43.3	198.2 ± 45.4	179.8 ± 42.5	189.2 ± 46.6
LDLC, mg/dL	41.6 ± 9.1	44.9 ± 10.7	50.0 ± 11.6	47.7 ± 11.3	47.4 ± 11.5	46.8 ± 11.1
HDLC, mg/dL	94.3 ± 33.3	94.8 ± 37.2	99.8 ± 35.1	114.1 ± 41.1	98.1 ± 34.5	107.4 ± 40.7
Triglyceride, mg/dL	168.3 ± 84.7	173.6 ± 94.0	177.6 ± 88.2	198.2 ± 101.4	174.7 ± 87.1	189.7 ± 99.1
GFR, mL/min	87.9 ± 30.1	87.7 ± 28.3	100.9 ± 29.5	91.7 ± 39.0	96.8 ± 30.2	90.3 ± 35.5
Blood urea nitrogen, mg/dL	18.0 ± 10.9	23.1 ± 15.7	15.1 ± 5.0	18.5 ± 9.1	16.0 ± 7.5	20.1 ± 11.9
Serum creatinine, mg/dL	1.0 ± 0.2	1.1 ± 0.4	0.8 ± 0.1	1.0 ± 0.4	0.9 ± 0.2	1.0 ± 0.4
Smoking (%)	39 (48.1)	9 (29)	8 (4.5)	3 (5.1)	48 (42.9)	11 (4.6)
IHD (%)	23 (28.4)	11 (35.5)	49 (27.4)	14 (23.7)	72 (27.7)	25 (27.8)

*UAE indicates urinary albumin excretion; BP, blood pressure; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; GFR, glomerular filtration rate; and IHD, ischemic heart disease.

Table 4. Urine Albumin Excretion and Sex of Diabetic Patients by Glomerular Filtration Rate (GFR) Estimates

GFR, mL/min	All patients (%)	Male (%)	Female (%)	Normoalbuminuria (%)	Micoalbuminuria (%)	Macroalbuminuria (%)
< 30	4 (1.1)	1 (0.9)	3 (1.3)	0	1 (1.5)	3 (16.7)
30 to 59	39 (10.9)	18 (16.1)	21 (8.8)	25 (9.6)	10 (13.9)	4 (22.2)
60 to 89	127 (35.7)	48 (42.9)	79 (33.2)	97 (37.3)	28 (38.9)	2 (11.1)
> 89	180 (52.3)	45 (40.2)	135 (56.7)	138 (53.1)	33 (45.9)	9 (50.0)

Table 5. Correlates of Increased Urinary Albumin Excretion

Variable	Logistic Regression			Linear Regression	
	Odds Ratio	95% Confidence Interval	*P*	Beta	*P*
Univariable Analysis					
Age	0.99	0.96 to 1.03	.77	-0.002	.97
Body mass index	0.95	0.87 to 1.03	.28	-0.04	.35
Systolic blood pressure	1.02	0.99 to 1.05	.13	0.04	.41
Diastolic blood pressure	0.96	0.92 to 1.01	.18	0.002	.97
Duration of diabetes	1.00	1.00 to 1.00	.03	0.16	.002
Blood urea nitrogen	1.04	1.01 to 1.08	.01	0.19	< .001
Creatinine	3.25	0.77 to 13.71	.10	0.16	.002
Triglyceride	1.00	0.99 to 1.00	.15	0.07	.17
Cholesterol	0.99	0.97 to 1.00	.32	0.09	.07
High-density lipoprotein cholesterol	1.00	0.97 to 1.03	.57	-0.02	.65
Low-density lipoprotein cholesterol	1.01	0.99 to 1.03	.13	0.11	.03
Hemoglobin A1c	1.28	1.12 to 1.45	< .001	0.25	< .001
Glomerular filtration rate	1.01	0.99 to 1.02	.29	-0.09	.09
Smoking	0.68	0.26 to 1.58	.34	-0.05	.30
Sex (referent: female)	0.99	0.50 to 1.94	.97	0.03	.56
Ischemic heart disease	0.96	0.52 to 1.79	.92	0.001	.98
Multivariate Analysis Model 1					
Blood urea nitrogen	1.04	1.00 to 1.07	.02	2.82	.005
Creatinine	1.73	0.72 to 4.16	.22	1.36	.18
Low-density lipoprotein cholesterol	1.00	0.99 to 1.01	.12	1.53	.13
Hemoglobin A1c	1.28	1.13 to 1.46	< .001	4.13	< .001
Duration of diabetes	1.00	1.00 to 1.00	.04	2.06	.04
Multivariate Analysis Model 2					
Blood urea nitrogen	1.05	1.01 to 1.08	.003	3.74	< .001
Hemoglobin A1c	1.03	1.015 to 1.48	< .001	4.52	< .001
Duration of diabetes	1.00	1.00 to 1.00	.046	2.04	.04

Table 6. Type 2 Diabetic Patients Who Achieved Optimal Treatment Goals for Modifiable Risk Factors

Optimal Treatment Goal	Number of Patients (%)
Hemoglobin A1c < 7%	69 (19.7)
Total Cholesterol < 200 mg/dL	235 (67.1)
High-density lipoprotein cholesterol > 40 mg/dL (men), > 50 g/dL (women)	167 (47.7)
Low-density lipoprotein cholesterol < 100 mg/dL	190 (54.3)
Blood Pressure < 130/ 85 mm Hg	257 (73.4)
Body mass index < 25 kg/m^2	83 (23.7)
Current nonsmoker	291 (83.1)

2 diabetic patients who had an average duration of DM 5 years. Albuminuria was significantly associated with the duration of DM in the patients. Blood urea nitrogen levels were higher among subjects with increased urinary albumin excretion, and albumin excretion was higher among those with uncontrolled glycemia (indicated by a higher Hb A1c level).

Several studies reported different prevalences for microalbuminuria. Nakhjavani and colleagues reported 20.3% microalbuminuria and 10.6% macroalbuminuria in Tehrani diabetic patients in 2002.[23] In another study carried out by this group in 2008, they showed 33% microalbuminuria and 5.8% macroalbuminuria.[24] In their study, increasing urinary albumin excretion was associated with dyslipidemia (low HDLC), DM duration, and poor control of blood glucose (high Hb A1c level), while age, systolic blood pressure, total cholesterol, LDLC, triglyceride, and GFR were not associated with increasing urinary albumin.

Shahbazian and colleagues showed a prevalence of 35.2% of microalbuminuria and 1.1% of macroalbuminuria in 2005 in Ahvaz.[25] Although microalbuminuria was more prevalent in their study than this study, we saw higher rates of macroalbuminuria and azotemia.[25] The prevalence of microalbuminuria was reported between 19% and 32% and macroalbuminuria between 5.2% and 17.5% in other countries.[26-28] Studies conducted in neighboring Asian countries reported different

prevalence rates of microalbuminuria ranging from 14.2% in Iran,[18-25,29] to 36.3% in India.[30,31] In the United Kingdom Prospective Diabetes Study,[7] the total prevalence of nephropathy was reported as 30.8%, while in other European countries, the total prevalence was observed as 47%.[32] The differences between these studies might be due to the study design, sample selection, and differences in population, genetic, race, duration of DM, age, sex, glycemic control, and other risk factors (hypertension and hyperlipidemia). The definition of albuminuria and diabetic nephropathy is another source of discrepancy, as well as the methods of measurement of albuminuria and urine collection. In present study, 24-hrs urine protein measurement was used but some studies are dependent on albumin-creatinine ratio.

In our study, there were significant relationships between albuminuria and blood urea nitrogen, creatinine, total cholesterol, LDLC, Hb A1c, systolic and diastolic blood pressure, GFR, and duration of DM. These findings were similar to some other studies in terms of duration of DM,[12,28,32-35] hypertension,[36] Hb A1c,[24,36] cholesterol,[26] LDLC,[26] and creatinine.[28,32] In our study, there was no relationship between albumin excretion and smoking, history of heart disease, body mass index, age, sex, and albuminuria, but some studies have shown these associations.[11,25-28,32-34]

The present study results showed an independent association between increased urinary albumin excretion and poor glycemic control (high Hb A1c), as well as long duration of DM and high blood urea nitrogen. Some other studies were in agreement with the correlation of Hb A1c level with albuminuria,[24,28] but not the other factors. Meisinger and coworkers found the Hb A1c, duration of DM, systolic blood pressure, creatinine level, smoking, and waist circumference as independent risk factors for albuminuria.[28] However, Nakhjavani and colleagues showed that only the duration of DM, HDLC, and Hb A1c were the independent risk factors.[24]

In our study, women with abnormal urinary albumin excretion had greater amounts of blood urea nitrogen, creatinine, LDLC, and Hb A1c and longer duration of DM than those with normal urinary albumin excretion. The men with abnormal urinary albumin excretion only had greater Hb A1c levels. However, in Nakhjavani and colleagues' study,[24] urinary albumin excretion correlated with HDLC, Hb A1c, and DM duration in women, while no correlation was found between variables and urinary albumin excretion among men.

Results from randomized clinical trials demonstrated that control of glucose level as well as blood pressure and cholesterol level can delay or prevent the macrovascular and microvascular complication of DM.[36-39] Despite these guidelines, in the present study only some of patients with type 2 DM achieved the recommended levels of controls. Only 19.7% patients achieved the target Hb A1c less than 7%, indicating that in some cases the management of glycemic was less aggressive than desired. Among those with the highest Hb A1c, many patients were not started on insulin therapy may be due to fair of insulin injection. This is in accordance with results from other studies.[40-43]

Our study had some limitation. First, the present study was cross sectional in design, thus longitudinal trends in the management of DM and modified risk factors could not be under taken into account. Second, we did not collect certain important variable such as: diet, anemia and drug history, which might impact on the results. However, ignored confounding factors are likely to cause false positive correlations rather than false negative results. Also we did not collect the history of retinopathy in our patients. Third, renal biopsy that is the gold standard diagnostic investigation for diabetic nephropathy was not performed. Therefore, a long-term cohort study recommends addressing these limitations.

CONCLUSIONS

This study showed that microalbuminuria and macroalbuminuria had high prevalence rates in type 2 diabetic patients. There were no significant differences in age, sex, smoking, and history of heart disease between the groups with normal urinary albumin excretion, microalbuminuria, and macroalbuminuria, but the people who had microalbuminuria or macroalbuminuria had higher levels of blood urea nitrogen, creatinine, total cholesterol, LDLC, Hb A1c, and systolic and diastolic blood pressure, and longer duration of DM than those with normal urine albumin excretion. In multivariable regression analysis, increased urinary albumin excretion was associated with increasing blood urea nitrogen, Hb A1c and longer

duration of DM independent of other variables. Control of DM and cardiovascular risk factors was not optimal in our patients.

ACKNOWLEDGMENTS

This paper is a report of the research project of Dr Mehrnoosh Zakerkish's fellowship of endocrinology (registration no. D-8808) and financial support was provided by the Diabetes Research Center, Ahvaz Jundishapur University of Medical Sciences. The authors wish to thanks Ms M Salemzadeh, from Golestan Hospital clinical research development unit for her valuable help and contribution to this manuscript.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. World Health Organization. The Diabetes Program 2004. Available from: http://www.who.int/diabetes/en
2. Panzram G. Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia. 1987;30:123-31.
3. Tsalamandris C, Allen TJ, Gilbert RE, et al. Progressive decline in renal function in diabetic patients with and without albuminuria. Diabetes. 1994;43:649-55.
4. Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. Diabetes Care. 1992;15:815-9.
5. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW. The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. J Gerontol. 1976;31:155-63.
6. Parving HH, Gall MA, Skott P, et al. Prevalence and causes of albuminuria in non-insulin-dependent diabetic patients. Kidney Int. 1992;41:758-62.
7. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 2003;63:225-32.
8. Rossing P, Hougaard P, Borch-Johnsen K, Parving HH. Predictors of mortality in insulin dependent diabetes: 10 year observational follow up study. BMJ. 1996;313:779-84.
9. Stephenson JM, Kenny S, Stevens LK, Fuller JH, Lee E. Proteinuria and mortality in diabetes: the WHO Multinational Study of Vascular Disease in Diabetes. Diabet Med. 1995;12:149-55.
10. Molnar M, Wittmann I, Nagy J. Prevalence, course and risk factors of diabetic nephropathy in type-2 diabetes mellitus. Med Sci Monit. 2000;6:929-36.
11. Turner RC, Millns H, Neil HA, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). BMJ. 1998;316:823-8.
12. Yokoyama H, Sone H, Oishi M, Kawai K, Fukumoto Y, Kobayashi M. Prevalence of albuminuria and renal insufficiency and associated clinical factors in type 2 diabetes: the Japan Diabetes Clinical Data Management study (JDDM15). Nephrol Dial Transplant. 2009;24:1212-9.
13. Pan CY, Ho LT, Soegondo S, et al. Prevalence of albuminuria and cardiovascular risk profile in a referred cohort of patients with type 2 diabetes: an Asian perspective. Diabetes Technol Ther. 2008;10:397-403.
14. Afkhami-Ardekani M, Modarresi M, Amirchaghmaghi E. Prevalence of microalbuminuria and its risk factors in type 2 diabetic patients. Indian J Nephrol. 2008;18:112-7.
15. Shekiba M, Afkhami- Ardekani M, Orafa AM. The prevalence of micro and macroalbuminuria in diabetic patients referring to diabetes research center. J Shahid Sadoughi Univ Med Sci Health Service. 2003;10:20-4.
16. Azizi F. Diabetes mellitus in Islamic Republic of Iran. Tehran: WHO-EMRO; 1996.
17. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. Geneva: World Health Organization; 2006.
18. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42:1206-52.
19. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499-502.
20. [No author listed]. Standards of medical care in diabetes. Diabetes Care. 2005;28 Suppl 1:S4-S36.
21. [No author listed]. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens. 2003;21:1011-53.
22. Parving HH, Mauer M, Ritz E. Diabetic nephropathy. In: Brenner BM, editor. The kidney. 8th ed. Philadelphia: WB Saunders; 2008. p. 1265-98.
23. Nakhjavani M, Azmoodeh AA, Mazooji A. Frequency of microalbuminuria in type 2 diabetic patients referred to Imam Khomeini Diabetic clinic. Iran Diabet and Lipid J. 2002;1;153-8.
24. Nakhjavani M, Esteghamati A, Esfahanian F, et al. Albuminuria and its correlates in an Iranian type 2 diabetic population. Lipids Health Dis. 2008;7:28.
25. Shabazian HB, Shahbazian H. Prevalence of diabetic nephropaty among type 2 diabetic patients in Ahvaz diabetic clinic. Proceeding of the 7th Endocrinology Congress, 6-8 Dec, 2004, Tehran, Iran.
26. Bruno G, Cavallo-Perin P, Bargero G, et al. Prevalence and risk factors for micro- and macroalbuminuria in an Italian population-based cohort of NIDDM subjects. Diabetes Care. 1996;19:43-7.
27. Standl E, Stiegler H. Microalbuminuria in a random cohort of recently diagnosed type 2 (non-insulin-dependent)

diabetic patients living in the greater Munich area. Diabetologia. 1993;36:1017-20.

28. Meisinger C, Heier M, Landgraf R, Happich M, Wichmann HE, Piehlmeier W. Albuminuria, cardiovascular risk factors and disease management in subjects with type 2 diabetes: a cross sectional study. BMC Health Serv Res. 2008;8:226.
29. Alrawahi AH, Rizvi SG, Al-Riyami D, Al-Anqoodi Z. Prevalence and risk factors of diabetic nephropathy in omani type 2 diabetics in Al-dakhiliyah region. Oman Med J. 2012;27:212-6.
30. Vijay V, Snehalatha C, Ramachandran A, Viswanathan M. Prevalence of proteinuria in non-insulin dependent diabetes. J Assoc Physicians India. 1994;42:792-4.
31. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgrad Med J. 2001;77:399-402.
32. Gall MA, Rossing P, Skott P, et al. Prevalence of micro- and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in European type 2 (non-insulin-dependent) diabetic patients. Diabetologia. 1991;34:655-61.
33. Tapp RJ, Shaw JE, Zimmet PZ, et al. Albuminuria is evident in the early stages of diabetes onset: results from the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab). Am J Kidney Dis. 2004;44:792-8.
34. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgrad Med J. 2001;77:399-402.
35. Chan JC, Cheung CK, Swaminathan R, Nicholls MG, Cockram CS. Obesity, albuminuria and hypertension among Hong Kong Chinese with non-insulin-dependent diabetes mellitus (NIDDM). Postgrad Med J. 1993;69:204-10.
36. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet. 1998;351:1755-62.
37. [No author listed]. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ. 1998;317:703-13.
38. Pyorala K, Pedersen TR, Kjekshus J, Faergeman O, Olsson AG, Thorgeirsson G. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. A subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). Diabetes Care. 1997;20:614-20.
39. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med. 2003;348:383-93.
40. Liebl A, Mata M, Eschwege E. Evaluation of risk factors for development of complications in Type II diabetes in Europe. Diabetologia. 2002;45:S23-S28.
41. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA. 2004;291:335-42.
42. Charpentier G, Genes N, Vaur L, et al. Control of diabetes and cardiovascular risk factors in patients with type 2 diabetes: a nationwide French survey. Diabetes Metab. 2003;29:152-8.
43. Beaton SJ, Nag SS, Gunter MJ, Gleeson JM, Sajjan SS, Alexander CM. Adequacy of glycemic, lipid, and blood pressure management for patients with diabetes in a managed care setting. Diabetes Care. 2004;27:694-8.

Correspondence to:
Hajieh Shahbazian, MD
Diabetes Research Center, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran, Post Code: 61357-15794
Tel: +98 611 336 9539
Fax: +98 611 336 9539
E-mail: hjb_shahbazian@yahoo.com

Received January 2012
Revised July 2012
Accepted January 2013