Nephrourol Mon. 2017 January; 9(1):e40031. doi: 10.5812/numonthly.40031.

Published online 2016 December 13. **Research Article**

Risk Factors of Microalbuminuria and Macroalbuminuria in Type 2 Diabetic Patients in North of Iran - Rasht

Malek Moien Ansar,[1,2,*] Reyhaneh ShahrokhiRad,[3] and Mohammad Kazem Lebady[4]

[1]Department of Biochemistry, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[2]Neuroscience Research Center, Department of Biochemistry, Poursina Hospital , School of Medicine, Guilan University of Medical Sciences , Rasht , Iran
[3]School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[4]Department of Nephrology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

[*]*Corresponding author*: Malek Moien Ansar, Department of Biochemistry, School of Medicine, Guilan University of Medical Sciences, P.O. Box: 3363, Rasht, Iran. Tel: +98-136690884, Fax: +98-1316690036, E-mail: ansar_moien@yahoo.com

Received 2016 September 26; **Revised** 2016 October 24; **Accepted** 2016 December 06.

Abstract

Background: Higher urinary albumin excretion has been suggested as a predicting diabetic nephropathy.
Objectives: The present study aimed at determining the prevalence and risk factors associated with albuminuria in patients with Type 2 diabetes mellitus in north of Iran, Rasht.
Methods: Two hundred and four patients who referred to a diabetes center in north of Iran were enrolled in the current study. Urinary albumin excretion (UAE) was measured by immunoturbidimetric assay. Microalbuminuria and macroalbuminuria were considered as a UAE rate of 30 to 300 mg /24-h and more than 300 mg/24-h, respectively. Risk factors associated with albuminuria were evaluated by backward stepwise logistic regression.
Results: The prevalence of micro and macroalbuminuria was 17.2% and 17.6%, respectively. Microalbuminuria was significantly associated with longer diabetes duration, increased fasting plasma glucose, and diastolic blood pressure. It was also found that higher plasma glucose and BUN (blood urea nitrogen) were risk factors for macroalbuminuria.
Conclusions: Prevalence of both micro- and macroalbuminuria was high in the patients of this study. Therefore, it seems that controlling blood glucose and lowering blood pressure, even in the absence of hypertension-prehypertension, should be considered for patients with microalbuminuria.

Keywords: Albuminuria, Iran, Type 2 Diabetes, Risk Factors, Diabetic Nephropathy

1. Background

One of the long- term complications of diabetes mellitus (DM) is diabetic nephropathy (DN), and it is the leading cause of end-stage renal disease worldwide (American Diabetes Association, 2012) (1). Microalbuminuria is the first clinical detectable sign of DN and is considered as an independent predictor of diabetic nephropathy (2). In addition, microalbuminuria is a marker of the increase of cardiovascular disease (1).

Different epidemiological studies revealed marked variation in the prevalence of microalbuminuria in Type 2 diabetic patients, ranging from less than 10% in the United Kingdom (3), 36.3% in Southern India (4), 40.8% in Albania (5), and to more than 41% in China (6).

The prevalence of diabetes is increasing worldwide, particularly in developing countries (7). Among the developing countries, Iran is a leading country with the highest number of diabetic patients. Moreover, further rising is expected in this country in the coming years (8). Hence, studies on diabetes related complications are essential to reduce preventable burden of diabetes. To our knowledge, no report had been published on the prevalence and risk factors of micro- and microalbuminuria in patients with Type 2 diabetes in north of Iran at the time of this study.

2. Objectives

The present study aimed at assessing the prevalence and risk factors associated with albuminuria in Iranian patients with Type 2 diabetes who referred to a diabetes center in north of Iran.

3. Methods

This cross - sectional study was conducted on patients with Type 2 diabetes who referred to the diabetes clinic of Razi hospital in Rasht - north of Iran- from August 2008 to January 2009. Type 2 diabetes were diagnosed and then confirmed according to American diabetes association criteria (9). Data including age, gender, duration of DM, most recent level of fasting plasma glucose (FPG), systolic (SBP), diastolic blood pressure (DBP), blood urea nitrogen (BUN),

and serum creatinine were collected from patients' medical records. Hemoglobin A1c (HbA1c) was recorded as national Glycohemoglobin standardization program (NGSP), and international federation of clinical chemistry (IFCC) units. Moreover, the extent of albumin in urine was routinely measured and recorded. The study protocol was approved by the Guilan University of Medical sciences, School of medicine research and ethics committee.

3.1. Urine Analysis

Urinary albumin excretion rate (UER) per 24 hours was measured by immunoturbidimetric assay using Dako (Glostrop, Denmark) kit. Microalbuminuria was defined as ranging from 30 to 300 mg in a 24-hour urine collection. Macroalbuminuria and normoalbuminura were defined as a urinary albumin excretion of more than 300 mg /24-h and less than 30 mg/24- h, respectively. Patients with hematuria, bacteriuria, acute febrile illness, congestive heart failure, and age under 30 years were excluded.

3.2. Statistical Analysis

The quantitative variables were assessed for normality using the Kolmogorov-Smirnov test. Descriptive statistics were expressed as mean $\pm$ standard deviation. Student's t test and Mann-Whitney test were used for continuous variables, and categorical variables were compared using the chi-square test. Risk factors associated with albuminuria were evaluated by backward stepwise logistic regression. The odd ratio and 95% confidence interval (95% Confidence Interval) were reported. Data were analyzed using SPSS Version 16, and statistical significance was set at $P < 0.05$.

4. Results

In the present study, out of the 225 eligible patients, 21 (9.3%) were excluded from the statistical analysis because of missing data. The mean age of 204 patients (154 females and 50 males) was 54.35 $\pm$ 0.7 years, and the duration of diabetes was 8.3 $\pm$ 0.45 years. The prevalence of microalbuminuria and macroalbuminuria were 17.2% (95% CI: 12 - 22.4) and 17.6% (95% CI: 12.4 - 22.8), respectively. The prevalence of microalbuminuria among females was 20.3%, but it was 22.5% in males.

4.1. Albuminuria and Its Associated Risk Factors

The microalbuminuric and macroalbuminuric patients had higher SBP ($P < 0.01$), DBP ($P < 0.05$), FPG ($P < 0.05$), HbA1c ($P < 0.01$), and longer duration of diabetes ($P < 0.01$) compared to the normoalbuminuric patients. Furthermore, the macroalbuminuric patients were older ($P < 0.01$), had higher BUN ($P < 0.001$) and serum creatinine ($P < 0.001$) than patients with normal albumin. The demographic and clinical characteristics of the patients are presented in Table 1.

4.2. Regression Analysis

Binary logistic regression with backward elimination of risk factors revealed diabetes duration (OR: 1.032, 95% CI: 1.006-1.141, P = 0.032), DBP (OR: 1.055, 95% CI: 1.014 - 1.098, P = 0.009), and FPG (OR: 1.007, 95% CI: 1.001 - 1.013, P = 0.023) to be associated with microalbuminuria. Higher FPG (OR: 1.013, CI: 1.005 - 1.022, P = 0.003), and BUN (OR: 1.143, CI: 1.072 - 1.218, P = 0.05) were picked as the main predicators for macroalbuminuria by stepwise regression based on backward elimination (Table 2).

5. Discussion

Based on the results of this cross- sectional study, the prevalence of microalbuminuria and macroalbuminuria in the patients with Type 2 diabetes was found to be 17.2% and 17.6%, respectively.

Many variations in the prevalence of albuminuria have been reported by different cross- sectional and epidemiological studies 10 - 16 .The prevalence of microalbuminuria was 19.7% and 25.5% in south and north of India, respectively (10, 11). A very high prevalence of microalbuminuria was found in those Indians newly diagnosed with Type 2 diabetes (54.09 %) (12). Studies in Hong Kong revealed a prevalence of 13.4% (13) and 22.7% in young diabetic patients (14). A study by Huraib et al. in Saudi Arabia denoted a prevalence of microalbuminuria of 16.8% (15). In Kuwaiti individuals with Type 2 diabetes, the prevalence of microalbuminuria was 27.3% (16). Furthermore, few studies on Iranian patients with Type 2 diabetes revealed the prevalence of microalbuminuria to be from 14.2% to 33% (17-19). Differences in populations, the definitions of microalbuminuria, method of urine collection, and method of measurement can explain the variation in the prevalence of microalbuminuria. Differences in the ethnic susceptibility to nephropathy may also be used to explain this variation.

Similar to the study in north of India (11) and Kuwait (16), the results of the present study showed higher prevalence of macroalbuminuria than others (5, 19). This may reflect the prolonged periods of undetectable subclinical hyperglycemia, or poor diabetes control.

Although the prevalence of microalbuminuria was slightly more in males than in females, the difference was not statistically significant. Our results were similar to the findings of Varghese et al. (4) and Afkhami-Ardekani et al. (18). In contrast, some studies reported an increased prevalence of microalbuminuria in males compared to females

Table 1. The Demographic and Clinical Characteristics among the Normo, Micro, and Macroalbuminuria Groups[a]

Parameters	Normoalbuminuria	Microalbuminuria	Macroalbuminuria
Number	133	35	36
Age (years)	53.1 ± 10	55.3 ± 10.4	58.1 ± 8.5[b]
Female/total	102/133	26/35	26/36
Duration (years)	7.1 ± 6.2[c]	9.6 ± 5.3	11.5 ± 7.7
SBP (mmHg)	130.5 ± 19.1[c]	138.8 ± 18	145.4 ± 23.5
DBP (mmHg)	77.5 ± 9.3[c]	82 ± 9.9	83.9 ± 12
FPG (mg/dL)	165 ± 62.2[c]	195.2 ± 68.5	200.1 ± 80.5
BUN (mg/dL)	12.9 ± 8.1	17.1 ± 9.2	27.4 ± 14.8[b]
Serum creatinine (mg/dL)	1.1 ± 0.7	1.3 ± 0.8	1.4 ± 0.7[b]
Cholesterol (mg/dL)	189.3 ± 63.9	202.4 ± 46.1	209.8 ± 66.1
Triglyceride (mg/dL)	180 ± 104.3	199.5 ± 83	193 ± 80.1
LDL (mg/dL)	108.5 ± 36	112 ± 45.9	128 ± 45.2
HDL (mg/dL)	44.9 ± 11	43.2 ± 8	42.8 ± 9.6
HbA1c			
%	7.4 ± 2.2[c]	8.4 ± 2.4	8.6 ± 2.8
mmol/mol	57 ± 23[c]	68 ± 26	70 ± 30

[a] Data were presented as mean ± SD.
[b] Significantly different from normoalbuminuria groups ($P < 0.01$).
[c] Significantly different from micro and macroalbuminuria groups ($P < 0.05$).

Table 2. Backward Stepwise Logistic Regression Analysis of Micro and Macroalbuminuria Considering the Dependent Covariates

Covariates	Odd Ratio	95% CI	P Value
Microalbuminuria as a dependent variable			
DBP (mmHg)	1.053	1.014 - 1.098	0.009
FPG (mg/dL)	1.007	1.001 - 1.013	0.023
Duration (years)	1.071	1.006 - 1.141	0.032
Macroalbuminuria as a dependent variable			
FPG (mg/dL)	1.013	1.005 - 1.022	0.003
BUN (mg/dL)	1.14	1.072 - 1.218	0.000

(9, 20). Moreover, we faced a problem when using albumin creatinine ratio to compare the prevalence across genders because females had lower creatinine excretion than males and this might have affected the results (21). Therefore, we used a daily excretion rate to evaluate microalbuminuria.

In the present study, backward stepwise logistic regression analysis revealed duration of diabetes, DBP, and FPG as the independent risk factors for microalbuminuria. John et al. reported male sex, older age, longer duration of diabetes, higher plasma glucose, and raised blood pressure as risk factors of microalbuminuria (10). Age, diabetes duration, SBP, and serum creatinine were selected as predicators in a regression model by Lutale et al. (22). Various studies have found a strong association between glycemic control and microalbuminuria (23, 24), but two other studies did not find any association (17, 19). Sheng et al. revealed that microalbuminuria mainly attributed to elevated DBP and plasma glucose (25). Unlike one study (11), but similar to others (4), we did not find a significant association between HbA1c and microalbuminuria. Other factors, which had been reported to be associated with microalbuminuria, were alcohol intake (23), smoking, and HDL (19).

The results of the logistic regression analysis revealed

that higher plasma glucose and BUN were risk factors of macroalbuminuria. Similar to many other studies (26, 27), our results also revealed that controlling blood glucose and maintaining an optimal blood pressure might decrease the prevalence of albuminuria.

Being a clinical based study was one of the limitations of the present study, which could have introduced some degree of referral bias.

5.1. Conclusions

The prevalence of both micro- and macroalbuminuria was high in the patients with Type 2 diabetes. Therefore, the annual screening programme for microalbuminuria should be performed for these patients. Microalbuminuria is mainly attributed to high diastolic blood pressure, high fasting plasma glucose, and longer duration of diabetes. It seems that lowering blood pressure, even in the absence of hypertension- prehypertension, and controlling blood glucose should be considered for patients with microalbuminuria. Patients with significantly high plasma glucose and higher BUN were prone to develop macroalbuminuria.

Acknowledgments

The authors are grateful to all the staff and patients who participated in this project. Special thanks also go to Mr. Mostafa Haghiri (MA in English linguistics) for editing the manuscript.

Footnote

Financial Disclosure: We have no financial interests related to the material in the manuscript.

References

1. American Diabetes A. Standards of medical care in diabetes–2012. *Diabetes Care.* 2012;**35 Suppl 1**:S11–63. doi: 10.2337/dc12-s011. [PubMed: 22187469].
2. Alzaid AA. Microalbuminuria in patients with NIDDM: an overview. *Diabetes Care.* 1996;**19**(1):79–89. [PubMed: 8720542].
3. Gatling W, Knight C, Mullee MA, Hill RD. Microalbuminuria in diabetes: a population study of the prevalence and an assessment of three screening tests. *Diabet Med.* 1988;**5**(4):343–7. [PubMed: 2968883].
4. 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**(908):399–402. [PubMed: 11375456].
5. Pasko N, Toti F, Strakosha A, Thengjilli E, Shehu A, Dedej T, et al. Prevalence of microalbuminuria and risk factor analysis in type 2 diabetes patients in Albania: the need for accurate and early diagnosis of diabetic nephropathy. *Hippokratia.* 2013;**17**(4):337–41. [PubMed: 25031513].
6. Lu B, Wen J, Song XY, Dong XH, Yang YH, Zhang ZY, et al. High prevalence of albuminuria in population-based patients diagnosed with type 2 diabetes in the Shanghai downtown. *Diabetes Res Clin Pract.* 2007;**75**(2):184–92. doi: 10.1016/j.diabres.2006.06.024. [PubMed: 16893584].
7. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care.* 2004;**27**(5):1047–53. [PubMed: 15111519].
8. Haghdoost AA, Rezazadeh-Kermani M, Sadghirad B, Baradaran HR. Prevalence of type 2 diabetes in the Islamic Republic of Iran: systematic review and meta-analysis. *East Mediterr Health J.* 2009;**15**(3):591–9. [PubMed: 19731775].
9. Classification and diagnosis of diabetes. *Diabetes Care.* 2014;**38**(Supplement_1):S8–S16. doi: 10.2337/dc15-S005.
10. John L, Rao PS, Kanagasabapathy AS. Prevalence of diabetic nephropathy in non-insulin dependent diabetics. *Indian J Med Res.* 1991;**94**:24–9. [PubMed: 2071180].
11. Vijay V, Snehalatha C, Ramachandran A, Viswanathan M. Prevalence of proteinuria in non-insulin dependent diabetes. *J Assoc Physicians India.* 1994;**42**(10):792–4. [PubMed: 7876049].
12. Thakkar B, Arora K, Vekariya R. Prevalence of microalbuminuria in newly diagnosed type 2 diabetes mellitus. *NJIRM.* 2011;**2**(4):22–5.
13. Tam TK, Cheng LP, Lau DM, Lai TC, Lai WY, Ng KK, et al. The prevalence of microalbuminuria among patients with type II diabetes mellitus in a primary care setting: cross-sectional study. *Hong Kong Med J.* 2004;**10**(5):307–11. [PubMed: 15479958].
14. Ko GT, Chan JC, Lau M. Diabetic microangiopathic complications in young Chinese diabetic patients: a clinic-based cross-sectional study. *J Diabetes Complications.* 1991;**13**(5):300–6.
15. Huraib S, Abu-Aisha H, Sulimani RA, Famuyiwa FO, Al-Wakeel J, Askar A, et al. The pattern of diabetic nephropathy among Saudi patients with noninsulin-dependent diabetes mellitus. *Ann Saudi Med.* 1995;**15**(2):120–4. [PubMed: 17587920].
16. Al-Adsani A. Risk factors associated with albuminuria in Kuwaiti adults with type 2 diabetes. *Saudi J Kidney Dis Transpl.* 2012;**23**(4):860–5. doi: 10.4103/1319-2442.98189. [PubMed: 22805411].
17. Afkhami-Ardekani M, Modarresi M, Amirchaghmaghi E. Prevalence of microalbuminuria and its risk factors in type 2 diabetic patients. *Indian J Nephrol.* 2008;**18**(3):112–7. doi: 10.4103/0971-4065.43690. [PubMed: 20142916].
18. Iranparvar AM, Aminisani N, Bashardoost B. Prevalence and risk factors of microalbuminuria in type 2 diabetic patients in a diabetic clinic of Ardabil-Iran. *Int J Endocrinol Metab.* 2006;**4**:8–12.
19. Nakhjavani M, Esteghamati A, Esfahanian F, Aghamohammadzadeh N, Hamidi S, Meysamie A, et al. Albuminuria and its correlates in an Iranian type 2 diabetic population. *Lipids Health Dis.* 2008;**7**:28. doi: 10.1186/1476-511X-7-28. [PubMed: 18691434].
20. Mather HM, Chaturvedi N, Kehely AM. Comparison of prevalence and risk factors for microalbuminuria in South Asians and Europeans with Type 2 diabetes mellitus. *Diabetic Med.* 1998;**15**(8):672–7. doi: 10.1002/(sici)1096-9136(199808)15:8<672::aid-dia648>3.0.co;2-3.
21. Krolewski AS, Laffel LM, Krolewski M, Quinn M, Warram JH. Glycosylated hemoglobin and the risk of microalbuminuria in patients with insulin-dependent diabetes mellitus. *N Engl J Med.* 1995;**332**(19):1251–5. doi: 10.1056/NEJM199505113321902. [PubMed: 7708068].
22. Lutale JJ, Thordarson H, Abbas ZG, Vetvik K. Microalbuminuria among Type 1 and Type 2 diabetic patients of African origin in Dar Es Salaam, Tanzania. *BMC Nephrol.* 2007;**8**:2. doi: 10.1186/1471-2369-8-2. [PubMed: 17224056].
23. Klein R, Klein BE, Moss SE. Prevalence of microalbuminuria in older-onset diabetes. *Diabetes Care.* 1993;**16**(10):1325–30. [PubMed: 8269789].
24. Haffner SM, Morales PA, Gruber MK, Hazuda HP, Stern MP. Cardiovascular risk factors in non-insulin-dependent diabetic subjects with microalbuminuria. *Arterioscler Thromb.* 1993;**13**(2):205–10. [PubMed: 8427856].
25. Sheng CS, Hu BC, Fan WX, Zou J, Li Y, Wang JG. Microalbuminuria in relation to the metabolic syndrome and its components in a Chinese population. *Diabetol Metab Syndr.* 2011;**3**(1):6. doi: 10.1186/1758-5996-3-6. [PubMed: 21470432].

26. Nosadini R, Tonolo G. Relationship between blood glucose control, pathogenesis and progression of diabetic nephropathy. *J Am Soc Nephrol.* 2004;**15 Suppl 1**:S1–5. [PubMed: 14684663].
27. Krairittichai U, Potisat S, Jongsareejit A, Sattaputh C. Prevalence and risk factors of diabetic nephropathy among Thai patients with type 2 diabetes mellitus. *J Med Assoc Thai.* 2011;**94 Suppl 2**:S1–5. [PubMed: 21717870].