

Prevalence of Microalbuminuria in Newly Diagnosed T2DM Patients attending a Tertiary Care Hospital in North India and its Association with Various Risk Factors

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ABSTRACT

Introduction: The natural history of diabetic nephropathy has generally been viewed as a descending path from normoalbuminuria to end stage renal disease through an intermediate stage marked by microalbuminuria and overt proteinuria. For this reason, measurement of urine albumin is often used as a sensitive marker and predictor of overt nephropathy in patients with diabetes mellitus. Study aimed to determine the prevalence of microalbuminuria in newly diagnosed type 2 diabetes mellitus patients and to assess the probable risk factors associated with microalbuminuria.

Material and methods: A total of 155 newly diagnosed Type 2 Diabetes mellitus patients were included in our cross-sectional study. After the history, general physical examination and anthropometry, various biochemical investigations including kidney function test, plasma blood sugars, lipid profile and HbA1c. The detection of microalbuminuria was done by Micral Test (dipstick, Roche Diagnostic) method in a random spot urine sample. Microalbuminuria was diagnosed if the urinary albumin excretion was ≥ 20 mg/L of urine.

Results: The overall prevalence of nephropathy was 32.9% (51/155). There was significant association of albuminuria with the increase in age of the patients, increased BMI, high glycated haemoglobin, high fasting plasma glucose, and dyslipidemia.

Conclusion: A relatively high prevalence of microalbuminuria at the time of diagnosis in our study reconfirms that evaluation for microalbuminuria must be done at the time of diagnosis in all patients of T2DM.

Keywords: Diabetes mellitus, Microalbuminuria, Nephropathy

more than 50% of US patients receiving dialysis treatment have T2DM.² Microalbuminuria is often the first sign of renal involvement.³ Various studies have demonstrated that without specific interventions, 20–40% of T2DM patients with microalbuminuria progress to overt nephropathy.⁴ For this reason, measurement of urine albumin is often used as a sensitive marker and predictor of overt nephropathy in patients with diabetes mellitus.⁵

The development of diabetic nephropathy is determined by various risk factors and the level of glycemic control has been found to be the most dominant factor in the occurrence of microalbuminuria.⁶ Apart from such risk factors as hypertension, obesity and hypercholesterolemia, there are some genetic factors also which determine the incidence of nephropathy in these patients. More recently, genome-wide association studies identified several loci associated with an increased risk for diabetic nephropathy in both type 1 diabetes mellitus (T1DM) and T2DM.^{7,8} Diabetic nephropathy affects approximately 25% of patients with T2DM, and represents the leading cause of end-stage renal disease in high-income countries.^{9,10}

Diabetic nephropathy is a severe complication and is related to an increased risk of all-cause mortality, cardiovascular disease, and development of end-stage renal disease, requiring expensive renal replacement therapy in the form of dialysis or transplantation.^{11,12}

No systematic studies are available regarding the presence of microalbuminuria at diagnosis in Kashmiri patients with newly diagnosed T2DM. With this background we planned

INTRODUCTION

Diabetes mellitus is considered to be one of the most challenging health problems of the 21st century. Type 2 Diabetes Mellitus (T2DM) constitutes 90 to 95% of diabetes mellitus in the adults and is characterized by a combination of insulin resistance and insulin secretory defect. T2DM is characterized by an asymptomatic phase between the actual onset of hyperglycemia and clinical diagnosis. This phase has been estimated to last at least 4–7 years, and consequently 30–50% of T2DM patients remain undiagnosed.¹ Microvascular complications like diabetic nephropathy, diabetic retinopathy and diabetic neuropathy are major causes of morbidity in diabetes mellitus patients. Diabetic nephropathy is the single leading cause of end stage renal disease and

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How to cite this article: Sajad Rashid Mir, Moomin Hussain Bhat, Raiz Ahmad Misgar, Mir Iftikhar Bashir, Arshad Iqbal Wani, Humera Irshad Malik. Prevalence of microalbuminuria in newly diagnosed T2DM patients attending a tertiary care hospital in North India and its association with various risk factors. International Journal of Contemporary Medical Research 2019;6(4):D9-D13.

DOI: <http://dx.doi.org/10.21276/ijcmr.2019.6.4.40>

to conduct a study to determine the prevalence of diabetic nephropathy and its relation with various risk factors.

MATERIAL AND METHODS

This cross-sectional hospital based observational study was conducted in the Department of Endocrinology at Sher-i-Kashmir Institute of Medical Sciences, Srinagar. The study was conducted according to the declaration of Helsinki and an informed consent was obtained from all the patients. One hundred fifty five recently diagnosed (within last six months) adult T2DM non pregnant patients aged 18 years and above, who attended the Endocrine OPD clinic or were admitted to the Endocrinology ward, and consented for the study, constituted the subject material for this study. Diagnosis of T2DM was made according to the American Diabetes Association criteria.¹³ Patients with T2DM diagnosed more than 6 months back, those with T1DM or secondary form of diabetes or having co-morbidities like cardiac failure, chronic liver and kidney disease, connective tissue disorder, or any known malignancy or using medications that could affect glucose tolerance were excluded from the study.

Clinical Assessment

A detailed history, physical examination and standard anthropometric data -height, weight, body mass index (BMI) and waist and hip circumference was obtained in all the patients. On the basis of BMI patients were classified as normal (BMI= 18.5 to 22.9 kg/m²), overweight (BMI = 23 to 24.9 kg/m²), or obese (BMI \geq 25 kg/m²).¹⁴ Waist circumference was measured, with patient in standing position, midway between the costal margin and the iliac crest in mid expiration; hip circumference was measured in standing position at the maximum circumference over the buttocks.¹⁵ Patients were labelled normotensive if systolic BP was less than 140 mmHg and diastolic BP less than 90 mmHg.¹⁶

Complete blood count and serum chemistry including liver function tests, kidney function tests, uric acid and lipid profile were obtained from all participants. Present glycemic status was assessed in every patient by obtaining pre- and

post-prandial plasma glucose and glycosylated hemoglobin (HbA1c). For the evaluation of microalbuminuria, Micral test strips (Roche diagnostic India Pvt. Ltd. GERMANY) were used and estimation of microalbuminuria was performed as directed by the manufacturer.

Sensitivity of the MICRAL test kit is 0.4 ng/ml and the measuring range is 0.8-10 ng/ml. Microalbuminuria was graded as mild (20 mg/L), moderate (50 mg/L), or severe (100 mg/L) depending on the colour change in the strip.¹⁷

All the patients also collected urine for 24 hours, and estimation of protein, creatinine was performed using colorimetric method. Proteinuric nephropathy was defined as daily urinary protein excretion of more than 150 mg in the absence of other obvious causes of proteinuria; protein excretion of 150-500 mg/day was classified as microproteinuria, and $>$ 500 mg/day as macroproteinuria.¹⁸

RESULTS

Overall, 155 study subjects fulfilling the inclusion criteria were enrolled. Age of the study patients ranged from 20 to 75 years with a mean (\pm SD) of 44.3 \pm 13.59 years. Majority of the study patients were in the age group of 35 to 49 years (37.4%), whereas the other two age groups of 20 to 34 years and 50 to 64 years had equal number of patients each i.e. 41(26.5%). There was a male preponderance among study patients with 88 males (56.8%) and 67 females (43.2%).

Microalbuminuria was present in 51 (32.9%) out of 155 study patients (Table 1) with 33 males and 18 females. But there was no statistically significant correlation between the two genders.

Most of the patients with microalbuminuria were having moderate to severe microalbuminuria (Table 1), whereas only 15.7% (8/51) were having mild microalbuminuria. Moreover, 12 out of 26 patients with severe microalbuminuria were detected to have proteinuria on 24 hour urinary protein estimation (\geq 150mg); 4 patients had microproteinuria and 8 patients had macroproteinuria (overt proteinuria).

The mean age of patients with microalbuminuria was 48.5 \pm 12.84 years which showed statistically significant difference when compared to the mean age of normoalbuminuric subjects who had mean age of 42.3 \pm 13.52. Moreover, the prevalence of microalbuminuria increased with age.

The mean BMI of microalbuminuric patients was 26.31 \pm 2.21 Kg/m² and was significantly greater than the BMI of normoalbuminuric patients (24.9 \pm 2.66 Kg/m²) with a p-value of 0.002. When compared with the BMI of normoalbuminuric

Microalbuminuria (mg/l)	No. of patients	Percentage
Mild (20mg/l)	8	15.7
Moderate (50mg/l)	17	33.3
Severe (100mg/l)	26	51
Total	51	100

Table-1: Quantitative analysis of microalbuminuria in study patients

HbA1c (%)	microalbuminuria		Normoalbuminuria		p-value
	No.	% age	No.	% age	
<7	4	7.8	7	6.7	0.034*
7.0-7.9	4	7.8	28	26.9	
8.0-9.9	16	31.4	32	30.8	
\geq 10.0	27	52.9	37	35.6	
Total	51	100	104	100	

Table-2: Correlation of albuminuria with HbA1c in study subjects

Parameter	Normoalbuminuria	Microalbuminuria	p-value
Age (Years)	42.3 ± 13.52	48.5 ± 12.84	0.007*
BMI	24.9±2.66	26.31±2.21	0.002*
HbA1c	7.62±1.68	8.69±1.96	0.034*
FBG	216.4±78.67	255.6±85.36	0.011*
RBG	344.5±85.7	386.5±132.31	0.213
PPBG	268.74±84.4	277.3 ±96.31	0.619
Cholesterol	183.4±34.24	221.9±19.24	<0.001*
LDL	113.9±25.51	148.8±17.5	<0.001*
HDL	39.8±7.83	36.9±8.92	0.039*
Triglycerides	192.3±122.43	227.6±79.68	0.042*

*indicates p value of < 0.05

Table-3: Clinical and biochemical characteristics of the study population

patients, 24.9±2.66 Kg/m², BMI of albuminuric patients was significantly greater with a p-value of 0.002. With increase in BMI, there was also a corresponding increase in the prevalence of microalbuminuria.

The study also revealed that the majority of the study patients (84.3%) having albuminuria had HbA1c level ≥ 8% (Table 3). There was a significant correlation when it was compared to that among normoalbuminuria patients in which only 66.4% had HbA1c ≥ 8%. It also depicts that with increase in the absolute value of HbA1c, there is relative increase in the prevalence of microalbuminuria when compared to normoalbuminuric subjects and this association is statistically significant with a p-value of 0.034.

The mean cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG) level in microalbuminuria patients was 221.9 ± 19.24 mg/dl, 148.8 ± 17.5mg/dl, 36.9 ± 8.92mg/dl and 227.6 ± 79.68 respectively. These values were statistically significant when compared to those of normoalbuminuric subjects whose mean cholesterol, LDL, HDL and TG level was 183.4±34.24, 113.9± 25.51, 39.8± 7.83, 192.3± 122.43mg/dl respectively (table 3).

The mean values of random blood glucose (RBG), fasting blood glucose (FBG) and post prandial blood glucose (PPBG) in microalbuminuria subjects were slightly more than those in normoalbuminuria subjects. But only FBG of subjects with albuminuria (255.6±85.36) had statistical significance (p-value 0.011), table 3.

DISCUSSION

We included a total of 155 adult patients (M:F- 88:67) with mean age of 44.3± 13.59 (age range of 20 to 75years). Majority of the patients (63.9%) were clustered between 35 to 65 years of age and most of the patients were from a younger age group of 35-49 years (37.4%). Other studies from developing countries have also reported that the majority of patients with diabetes are in the age range of 45-64 years, whereas age at diagnosis is higher (>65 years) in the developed countries.^{19,20} Younger age of onset implies that these patients develop diabetes in the most productive years of their life and have a greater chance of developing complications. Both environmental and genetic factors might explain the younger onset of age along with high prevalence of diabetes in the Indian population.²¹

Several studies conducted to ascertain the nephropathy in new onset T2DM patients have reported the prevalence ranging from 16.2% to 56.2%.^{17,22,23} The present study has shown that the prevalence of nephropathy in newly diagnosed T2DM patients is 32.9% (51/155). However, low prevalence rate of 8% only has been reported by Thompson, whereas Unuigbo reported a high prevalence rate of 50%.^{24,25} The variation in prevalence of albuminuria can be attributed to factors such as different methods of estimation of microalbuminuria, ethnic differences in the study populations, definitions of microalbuminuria, adopted method of urine collection, etc. Two third (64.7%) of the subjects with nephropathy were males. But the male preponderance was statistically insignificant as compared to that in normoalbuminuric patients. In an Indian study, gender-wise correlation analysis of microalbuminuria showed significantly higher prevalence of microalbuminuria in males.¹⁷ Among 51 patients with nephropathy, 8 patients had mild microalbuminuria, 17 had moderate microalbuminuria, 26 had severe microalbuminuria. Out of 26 patients with severe microalbuminuria, 12 had overt proteinuria (>500mg/day).

The mean age of the patients with microalbuminuria (48.5±12.84 years) was significantly higher than normoalbuminuria patients (42.3±13.52 years). Moreover, the results were suggestive of a steady increase in the prevalence of microalbuminuria with advancing age. In a study by Aggarwal, 22.36% of patients in 40-60 years age group had microalbuminuria at the onset of diabetes mellitus; it increased significantly with increase in age and was 30% in age group >60 years.²² Another study from India also observed that the mean age of patients with microalbuminuria was significantly higher than those without microalbuminuria.¹⁷

Mean BMI of patients with microalbuminuria was significantly higher than that of normoalbuminuric patients. Patients with a BMI of more than 26 Kg/m² had significant increase in the microalbuminuria. Agarwal reported a similar observation in their study. The authors observed that with increasing BMI, the prevalence of nephropathy increased; 30% of patients with BMI 25-29.9 developed nephropathy in their study.²² These findings are consistent with the studies that Indians are at increased risk of diabetes mellitus and its complications, at a relatively lower BMI, probably due

to an excess total body fat composition, and because they have high upper body obesity with high level of insulin resistance.²⁶ However, some Indian studies could not derive any significant correlation between BMI and albuminuria.¹⁷ In our study, majority of the patients with microalbuminuria (84.3%) had HbA1c level more than 8% and it was significantly higher when compared to normoalbuminuric patients (66.4%). There was a steady increase in the prevalence of albuminuria with increasing HbA1c%. Evidence of nephropathy at onset has been found to increase significantly with increase in HbA1c.²² UKPDS study showed that microvascular complications were benefitted by better control of blood glucose levels.²⁷ Studies of newly diagnosed type 1 and type 2 DM patients have shown a decrease in albumin excretion with improved glucose levels (28). In our study, assessment of patients for the presence of microalbuminuria was done at the time of initial contact only. However, attaining glycemic control may result in reversibility of albuminuria subsequently in some of the patients. In a study on newly diagnosed T2DM patients HbA1c concentrations were reported to be significantly higher in the microalbuminuria group compared with the normoalbuminuric patients ($p < 0.001$). The authors also observed that HbA1c value above 8% was associated with higher incidence (44%) of microalbuminuria.²⁹

Our study revealed that plasma glucose values (fasting, post-prandial and random) were higher among patients with microalbuminuria than among normoalbuminuric patients but only the fasting blood glucose level of patients with microalbuminuria (255.6 ± 85.36 mg%) achieved statistical significance when compared to that of patients without microalbuminuria (216.4 ± 78.67 mg%). Other studies also observed that average fasting blood glucose level in albuminuric patients was significantly higher than in normoalbuminuric ones.¹⁷

Dyslipidemia has been reported to be significantly related to microalbuminuria. In our study, the mean cholesterol, LDL and TG level was more in patients with microalbuminuria than in normoalbuminuric group. The differences were found to be statistically significant. HDL was also significantly lower in patients with microalbuminuria. Debbarma B, observed that serum total cholesterol and LDL values were significantly increased in albuminuric patients but triglyceride level was not significantly increased.²⁹ In one study, the prevalence of microalbuminuria was reported to be directly proportional to the severity of dyslipidemia.²² However, a Chinese study did not find any significant difference in cholesterol, triglyceride, HbA1c among normoalbuminuric, microalbuminuric, or overt proteinuric patients.³⁰

Our study didn't show any significant association between smoking history and family history with respect to microalbuminuria. Positive association between smoking cessation and amelioration of microalbuminuria in newly detected type 2 diabetes mellitus patients has been reported previously.³¹

Our study was a tertiary care hospital-based study and not a community-based study; selection bias cannot be ignored.

The sample size was relatively small

The findings of this study provide support for comprehensive screening for diabetes related complications especially microalbuminuria at the time of diagnosis of type 2 diabetes mellitus. Abnormal albumin excretion and other microvascular complications occur with considerable frequency before diabetes is diagnosed clinically. The relation between the development of microalbuminuria and degree of hyperglycemia indicates that early intervention towards attaining glycemic control might serve to help prevent the development of diabetic nephropathy.

CONCLUSION

A relatively high prevalence of microalbuminuria at the time of diagnosis in our study reconfirms that evaluation for this complication must be done at the time of diagnosis in all patients with T2DM. Also, there was a significant association of albuminuria with the increasing age, BMI, glycosylated haemoglobin, fasting plasma glucose, and dyslipidemia which impresses upon to address these risk factors also.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 11-03-2019; **Accepted:** 02-04-2019; **Published:** 29-04-2019