Original Article

Microalbuminuria and its associations with clinical profile and complications of type 2 Diabetes Mellitus

Sanjay Shrestha[1*], Rajesh Kumar Mandal[2], Kijan Maharjan[1]

[1]Department Of Internal Medicine, Sukraraj Tropical and Infectious Disease Hospital, Teku,Kathmandu, Nepal
[2]Department of Internal Medicine, Bheri Hospital, Nepalgunj, Nepal

Keywords: Prevalence; Diabetes mellitus; Microalbuminuria

Abstract

Background and Aims: Microalbuminuria is an early marker of diabetic nephropathy, which accounts for a significant reduction in life expectancy of diabetic patients. Timely detection of microalbuminuria facilitates appropriate preventive and therapeutic approaches to minimize risks. The aim of this study is to determine the prevalence and association of microalbuminuria with clinical profile and complications of type 2 diabetes mellitus.

Methods: This study was a descriptive, cross sectional study involving 100 diabetic subjects between July 2018 to January 2019 at Bir Hospital. Microalbuminuria (mg/dl) was defined as spot urine albumin to creatinine ratio of 30-300 mg/g (Kidney Disease Improving Global Outcomes guidelines) in a single spot urine sample. Statistical analysis was done using Statistical package for the social sciences version 20.

Results: Microalbuminuria was found in 35% of the sample and the rate was significantly higher among males (P =0.027). Microalbuminuria was significantly related to Body mass index (P = 0.018), duration of diabetes (P =0.000), retinopathy (P = 0.000) and stroke (P = 0.043). No statistically significant relation was found between microalbuminuria and age (P = 0.366), hypertension (P = 0.208), HbA1c (P = 0.098), dyslipidemia (P = 0.171) and ischemic heart disease (P = 0.651).

Conclusions: This study shows high prevalence of microalbuminuria in Nepalese Type 2 diabetes mellitus. Screening for microalbuminuria should be done for all the type 2 diabetes mellitus patients for early detection and management of complications of diabetes mellitus.

Introduction

Type 2 Diabetes Mellitus (T2DM) constitutes 90 to 95% of diabetes in the adults and is characterized by a combination of insulin resistance and insulin secretory defect.[1] Complications from diabetes mellitus can be microvascular (retinopathy, neuropathy, nephropathy) and macrovascular (acute myocardial infarction, peripheral vascular disease, stroke) that result in significant morbidity and mortality.[2]

Diabetic nephropathy is characterized by persistent albuminuria, progressive decline in glomerular filtration rate and raised arterial blood pressure.[3] Microalbuminuria is defined as detection of 30-300 mg of albumin in 24 hour urine collection or 30-300 mcg of albumin/mg creatinine in spot collection.[4] It affects 20 to 40 percent of patients after 10 to 15 years of the onset of diabetes.

Early recognition increases the chance to prevent the progression from incipient to overt nephropathy.[5] The aim of this study is to determine the prevalence and association of microalbuminuria with clinical profile and complications of type 2 diabetes mellitus.

*Corresponding Author:
Dr. Sanjay Shrestha,
Department of Internal Medicine,
Sukraraj Tropical and Infectious Hospital, Teku, Kathmandu, Nepal,
Email: shrestha834@gmail.com

METHODS

The study was a descriptive, crosssectional study conducted at National Academy of Medical Sciences (NAMS), Bir Hospital, from Jan 2018 to Jan 2019. The Ethical clearance for this study was taken from Institutional Review Board of NAMS .Ref. No. 596

Sample size: The sample size was calculated using the following formula

$n=z^2p(1-p)/d^2$ where, n=required sample size, z=statistical value for a level of confidence (for 95% level of confidence=1.96), p=estimated proportion of T2DM in the population, d=precision or maximum tolerable error, the prevalence of microalbuminuria in diabetes is 39.6 %.[6] Hence considering z=1.96, p=0.33, and d=0.1(precision of 10%), total sample size of 92 has been estimated. For convenience, 100 samples has been taken.

Inclusion Criteria : Diabetic individuals of age 20 to 70 years

Exclusion criteria : Known Type 1 diabetic patients, terminally ill diabetic patients, Type 2 DM with overt proteinuria, Urinary tract infections with Pus cells in urine >=5/ high power field, Pregnant ladies, febrile patients, obstructive uropathy and nephrolithiasis.

Consecutive sampling technique was applied. Patients fulfilling the inclusion criteria were enrolled after taking informed and written concent. 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. Laboratory results of fasting plasma glucose (FPG), 2hrs post-prandial glucose, and HbA1c, lipid profile panel and, Thyroid Function Test were recorded. Urinary creatinine and microalbumin were measured by enzymatic and immunoturbidimetric methods, respectively (using ERBA XL 300 machine at Bir Hospital). Patients were asked to avoid exercise prior to collection . Urine examination was done in women in non menstrual phase.

Statistical Analysis

Statistical package for the social sciences version 20 was used for data analysis. 95% confidence interval and p value of <0.05 was taken as significant. Descriptive statistics (frequency, percentage) were used and Chi-square test was used to assess association between microalbuminuria and clinical profile and complications of type 2 diabetes mellitus.

RESULTS

There were 100 patients enrolled in the study, 55 were females and 45 were males. Among 100 patients of type 2 Diabetes mellitus enrolled in the study, microalbuminuria was present in 35 patients. Thus the prevalence of microalbuminuria was 35%.

Microalbuminuria seems to increase with age but it is not statisticaly significant.While it is sig nificantly associated with male sex (p=0.27).

Table 1. Demographic distribution of microalbuminuria.

	parameters	Normo-albuminuric	Micro-albuminuric	Total	P value
Age	20-45	23	9	32	0.366
	46-55	18	8	26	
	>55	24	18	42	
Sex	Female	41	14	55	0.027
	Male	24	21	45	

Mean age in patients with microalbuminuria was 54.8 with standard deviation of 10.189.

The relation of microalbuminuria in type 2 diabetes mellitus with clinical data is shown in Table 2.

Table 2. Clinical data for microalbuminuric patients with type 2 diabetes mellitus

parameters		Normo-albumi-nuric	Micro-albumi-nuric	Total	P value
HTN	No	47	21	68	0.208
	Yes	18	14	32	
Duration	<5 yrs	40	7	47	0.000
	5-10 yrs	22	18	40	
	>10 yrs	3	10	13	
HbA1C	≤7	21	6	27	0.103
	>7	44	29	63	
Dyslipi-demia	No	39	16	55	0.171
	Yes	26	19	45	

Microalbuminuria increases with the duration of diabetes from 14.89% (7/47) to 76.92% (10/13) in group of patients of duration less than 5years of diabetes to duration of 10 years. Microalbuminuria shows positive association with duration of diabetes mellitus with p value 0.000. Similarly with BMI,microalbuminuria increases with increase in BMI, it increased from 10% (2/20) to 44.82% (26/58) from BMI (18.5-to 22.9)kg/m2 to BMI of ≥25 kg/m2. The study showed that BMI is significantly associated with microalbuminuria with p value 0.018. Microalbuminuria was present in 30.88% (21/68) patients without hypertension while 43.75% (14/32) hypertensive patients had microalbuminuria. It was present in 22.22% (6/27) patients with HbA1C ≤7 and microalbuminuria was present in 46.03% (29/63) patients with HbA1C >7. similarly, microalbuminuria was present in 29.09% (16/55) in patients without dyslipidemia while it was present in 42.22% (19/45) patients with dyslipidemia. However data showed that microalbuminuria was not statistically significant with hypertension,HbA1C and dislipidemia.

Type 2 Diabetes mellitus is associated with micro vascular complication like diabetic retinopathy and macrovascular complications like stroke and ischemic heart disease. The relation of microalbuminuria and complication is shown is table 3.

parameters	Normo-albuminuric	Micro-albuminuric	Total	P value	
Retinopaty	Absent	56	13	69	0.000
	Present	9	22	31	

Retinopathy Type and Grade	NPDR Mild	8	14	22	0.000
	NPDR Moderate	1	4	5	
	NPDR Severe	0	4	4	
	NPDR Very severe	0	0	0	
	PDR	0	0	0	
Stroke	Absent	64	28	92	0.001
	Present	1	7	8	
IHD	Absent	61	32	93	0.651
	Present	4	3	7	

Microalbuminuria was present in 18.84% (13/69) patients with out Retinopathy,while 70.96% (22/31) having retinopathy had microalbuminuria. Similarly, 4 out of 5 moderate NPDR and 4 out of 4 severe NPDR had microalbuminuria. Retinopathy had statistically significant relation with microalbuminuria with P value 0.000. Similarly 30.43% (28/92) patients without stroke had microalbuminuria while 87.55% (7/8) strokes patient had microalbuminuria. P value was 0.001 and hence stroke also had stastistically significant relation with microalbuminuria. However 34.44% (32/93) patients without ischemic heart disease had microalbuminuria while 42.85% (3/7) ischemic heart disease patients had microalbuminuria. It was not statistically significant.

Table 4: Biochemical profile of the cases with and without microalbuminuria

Parameters	Microalbuminuria Present		Microalbuminuria Absent		P value
	Mean	Standard deviation	Mean	Standard Deviation	
Fasting Blood Glucose	156.7353	49.73768	150.4308	65.24377	0.623
PP Blood Glucose	262.8824	105.38350	225.9538	101.33660	0.093
HbA1c	8.1669	1.30941	8.0089	1.70224	0.634
HDL	41.8286	9.32576	45.9077	10.75541	0.061
LDL	88.5143	30.46249	88.6615	23.21319	0.978
Triglyceride	150.89	44.139	148.15	49.392	0.785
Creatinine	0.81	0.14	0.80	0.14	0.733
Creatinine Clearance	92.94	15.80	92.51	16.80	0.90

Table 4 shows the mean and standard deviations of various biochemical parameters among patients with presence and absence of microalbuminuria. On comparison of means by using t test ,none were found to be statistically significant.

DISCUSSION

The prevalence of microalbuminuria in this study was 35%, which is lower as compared to the study by Khadka B et al in Devdaha Medical College and Teaching Hospital, Rupandehi, Nepal[7] and by Acharya K et al at TUTH, Kathmandu.[6] Prevalence of microalbuminuria is found to vary in different studies done at different countries from 13.4 to 48.7%.[8-17] This variation in prevalence can be attributed to factor such as difference in populations, in the definition of microalbuminuria, method of urine collection, etc. However this could also reflects true differences in the ethnic susceptibility to nephropathy.

No significant statistical relation was found between the prevalence of microalbuminuria and the age of patients in our study. Mean age in patients with microalbuminuria was 54.8 with standard deviation of 10.189. It was in accordance with the result of study done at National Guard Hospital in Alhasa, which also showed no relation of age with microalbuminuria.[8] However, other studies done on Diabetic Centre, Teaching Hospital Jaffna[11], in Hong Kong[13] and in India[14,19] showed positive association of microalbuminuria with age. The logical explanation related to microalbuminuria in aged patients might be due to the poor glycemic control for longer duration in older age group or the presence of age related atherosclerotic changes in the glomeruli.

Our study has shown significant association of sex with prevalence of microalbuminuria with male dominance. Study conducted on Israeli patients also showed significant association of male sex with microalbuminuria and diabetic nephropathy.[15] In contrast to our study, study done at National Guard Hospital in Alhasa and in Hongkong showed that prevalence of microalbuminuria was significantly higher among females.[8,13] Gender had so significant association , as reported from study at Diabetic Centre, Teaching Hospital Jaffna.[11]

This study has shown positive association of microalbuminuria with duration of diabetes mellitus which is in accordance with many previous reports.[7,8,10-12,14,19] Mean duration of diabetes among patients with microalbuminuria with duration of diabetes was 7.57 years with standard deviation of 4.089 years. Study of Acharya K et al. supports our findings.[6] Duration of diabetes has significant contribution for the development microalbuminuria by prolonged exposure to hyperglycemia-induced advanced glycosylation end products accumulations. Control of diabetes with regular treatment also plays a significant role in the development of diabetic nephropathy.

Microalbuminuria and diabetic renal disease are closely linked and are found to be associated with increasing blood pressure and often antecedent hyperfiltration.[18] Presence of hypertension however showed no significant association with microalbuminuria, in contrast to previous studies.[7,8,9,13,14] Similar to our study, hypertension had no significant association in a study done at at Diabetic Centre, Teaching Hospital Jaffna.[11] Failure to show association might be because of the smaller sample size in the study and hence the result might have to be further justified with larger sample studies.

In the present study, no statistically significant correlation was found between the prevalence of microalbuminuria and HbA1c, which was similar to findings reported by Acharya K et al.6 However, Khadka B et al. reported a positive correlation of the prevalence of microalbuminuria with the with HbA1c levels.[7] The previous studies conducted at Alhasa, Oman, USA and Botswana also showed abnormalities of lipoprotein metabolism are one of the major factors contributing to cardiovascular risk in patients with type 2 diabetes. However in contrast to many studies, our study failed to show any correlation between dyslipidemia and microalbuminuria.[8,11,15]

The association of obesity with T2DM has been recognized for decades.[20] In present study, statistically significant association was found between body mass index and the prevalence of microalbuminuria, with P value 0.018, which was similar to the findings reported by Alfehaid AA et al.[8] In our study, mean body mass index among patients without microalbuminuria was found to be 24.96 with standard deviation of 3.17 and body mass index was found to have a mean of 26.29 with standard deviation of 2.28

among patients with microalbuminuria. However, Subunca R et al.[11] reported that microalbuminuria was not significantly related to body mass index (BMI).

Our study showed that stroke and retinopathy (p<0.000) were significantly associated with the presence of microalbuminuria. It was consistent with the previous study by Subunca R et al.[11], which showed that ischemic heart disease (p<0.008), retinopathy (p<0.002) and nephropathy (p<0.0001) , with corresponding P values were significantly associated with the presence of microalbuminuria. However ischemic heart diseases failed to show significant association with the prevalence of microalbuminuria in our study. It might be because of the smaller sample size and smaller population with ischemic Heart Disease, enrolled in the study.

CONCLUSIONS

In our study prevalence of microalbuminuria in type 2 diabetes mellitus was 35%, which is the predictor for later development of diabetic nephropathy. Microalbuminuria was found to be more common with male sex with significant statistical association. Prevalence of microalbuminuria showed statistically significant association with BMI, duration of diabetes, retinopathy and stroke. However, no significant statistical relation was found between the prevalence of microalbuminuria and the age of patients, presence of hypertension, HbA1c level, dyslipidemia and ischemic heart disease in the present study. Larger trials with bigger sample size should be carried out to confirm this finding from our study.

Limitation of study:

The study being a cross-sectional study, single center, small sample size may not be able to generalize the entire population.

Conflict of Interest: None

ACKNOWLEDGEMENTS: none

REFERENCES

1.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

2. Karki PK, Timalsina S, Chalise S, Yadav A, Bhattarai AK. Prevalence of microalbuminuria and its association with glycemic control in type 2 diabetic patients: a cross sectional study at Kathmandu Medical College. Journal of Chitwan Medical College. 2019; 9 (27): 2-7.

3.Obineche EN, Adem A. Update in diabetic nephropathy. Int J Diabetes Metab. 2005;13:1–19.

4.Kidney Disease Outcomes Quality Initiative. Clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. Am J Kidney Dis. 2007;49:S62-73.

5.Remuzzi G, Schieppati A, Ruggenenti P. Nephropathy in patients with type 2 diabetes. N Engl J Med. 2002;2002(346):1145–1151

6. Acharya K, Regmi S, Sapkota AS, Raut M, Jha B. Microalbumin status in relation to glycated haemoglobin and duration of type 2 diabetes mellitus. Ann Clin Chem Lab Med. 2015;1:21-4.

7. Khadka B, Tiwari ML, Timalsina B, Risal P, Gupta S, Acharya D. Prevalence and Factors Associated with Microalbuminuria Among Type 2 Diabetic in An Institution. Journal of the Nepal Medical Association. 2018 Jan 1;56(209).

8. AlFehaid AA. Prevalence of microalbuminuria and its correlates among diabetic patients attending diabetic clinic at National Guard Hospital in Alhasa. J Fam Community Med 2017 ;24:1-5

9.Al-Futaisi A, Al-Zakwani I, Almahrezi A, Al-Hajri R, Al-Hashmi L, Al-Muniri A, et al. Prevalence and predictors of microalbuminuria in patients with type 2 diabetes mellitus: A cross-sectional observational study in Oman. Diabetes Res Clin Pract. 2006 May 1;72(2):212–5

10.Tabaei BP, Al-Kassab AS, Ilag LL, Zawacki CM, Herman WH. Does microalbuminuria predict diabetic nephropathy? Diabetes Care. 2002; 25(2):406-7.

11.Subunca R, Senthuran S, Kumaran S, Aravinthan M, Coonghe PA. Biochemical and clinical correlates of microalbuminuria among type 2 diabetes mellitus patients attending the Diabetic Centre, Teaching Hospital Jaffna.

12.Molefe-Baikai OJ, Cainelli F, Rwegerera GM, Mooketsi M. The prevalence of microalbuminuria and associated factors among patients with type 2 diabetes mellitus in Botswana.

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. Hongkong medical journal. 2004 Oct;10(5):307-11.

14.Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgraduate medical journal. 2001 Jun 1;77(908):399-402.

15.Ravid M, Brosh D, Ravid-Safran D, Levy Z, Rachmani R. Main risk factors for nephropathy in type 2 diabetes mellitus are plasma cholesterol levels, mean blood pressure, and hyperglycemia. Archives of internal medicine. 1998 May 11;158(9):998-1004.

16.Maiti A, Dey SK, Raychaudhuri P, Sinha PK, De J, Chatterjee A, Mukhopadhaya S. Changes in Microalbuminuria in Relation to Glycosylated Haemoglobin (HbAlc) and Duration in Type 2 Diabetes Mellitus.

17. Diouf NN, Lo G, Sow-Ndoye A, Djité M, Tine JAD, Diatta A. [Evaluation of microalbuminuria and lipid profile among type 2 diabetics]. Rev Med Brux. 2015 Feb;36(1):10–3.

18.Mogensen CE. Microalbuminuria, blood pressure and diabetic renal disease: origin and development of ideas. In The Kidney and Hypertension in Diabetes Mellitus 2000 (pp. 655-706). Springer US.

19. Chowta NK, Pant P, Chowta MN. Microalbuminuria in diabetes mellitus: Association with age, sex, weight, and creatinine clearance. Indian journal of nephrology. 2009 Apr;19(2):53.

20.Melmed S, Polonsky K, Larsen P, Kronenberg H. Williams textbook of endocrinology, Philadelphia: Saunders. Elsevier; 2011