

## Microalbuminuria and Its Risk Factors in Type 2 Diabetic Patients

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### ABSTRACT

**Background:** Diabetic nephropathy is one of the dreaded complications of diabetes leading to chronic kidney disease and end stage renal failure globally. Microalbuminuria is the most sensitive marker of early recognition of the diabetic nephropathy. This study was carried out to find out the prevalence and potential risk factors of microalbuminuria which is the marker of diabetic nephropathy among diabetes patients in Nepal.

**Methods:** A cross-sectional study was conducted on a random sample of 227 in T2DM patients in private diabetic clinics and Bir hospital in Kathmandu. Data were collected using standard questionnaire format to collect demography, anthropometry, and laboratory assessment of, HbA1c, post prandial, fasting glucose and micro albumin in urine. Micro albuminuria was measured using early morning urine specimen. Micro albuminuria was considered positive when urinary albumin to creatinine ratio was found to be 30–300 mg/g creatinine in preferably an early morning or a spot urine sample. The entire lab test was done by applying the internationally accepted standards of tools and techniques. Those that were reported >30mg/l of micro albumin were considered as positive.

**Results:** Out of total 217 diabetic patients, 56.2% (122/217) were male and 43.8% (95/217) were female. Among all age groups, maximum patients enrolled were between the age group 41 to 80 (95%). Of the total, 20% (44/217) patients were MA positive. A statistical significant association was seen between MA and BMI ( $p=0.029$ ), duration of DM ( $p<0.001$ ), hypertension ( $p<0.001$ ), smoking ( $p<0.001$ ) and physical activity ( $p<0.001$ ).

**Conclusions:** Diabetic patients in Nepal have prevalence of 20.3% microalbuminurea. Hypertension, obesity, sedentary lifestyles, duration more than 5 years of illness are found the most important risk factors for the development of microalbuminurea in diabetes.

**Keywords:** Microalbuminurea; type 2 diabetes Mellitus

### INTRODUCTION

Diabetes is managed with glycemic control and risk reduction.<sup>1</sup> worldwide it is a major public health problem.<sup>2</sup> Around 10-20% of T2DM has end stage renal failure and reduction in life expectancy.<sup>3</sup>

WHO defines diabetes as symptoms suggesting diabetes and Fasting blood sugar >7.0 mmol/l (>126mg/dl) and/or 2 hrs after glucose load >11.1mmol/l (>200mg/dl) or a random plasma glucose of  $\geq 200$  (mg/dl).<sup>4</sup>

Random spot urine sample for urine albumin to-creatinine ratio (UACR) in patients with 5-yr diabetes duration should be checked.<sup>5</sup>

Diabetic nephropathy (DN) leads to chronic kidney disease requiring dialysis life long.<sup>6</sup> Halting the progression is important in management.<sup>7</sup> Microalbuminuria (MA) is the most sensitive marker of the diabetic nephropathy.<sup>8</sup> Ahmad et al in Pakistan found 31.56% prevalence of microalbuminuria in T2DM.<sup>9</sup> T2DM patients, 20-40% with MA progress to overt nephropathy and 20 years later, approximately 20% develop end stage renal disease (ESRD).<sup>8</sup>

Intensive control of blood pressure, hyperglycemia and lipid levels needed.<sup>10</sup> Monitoring microalbuminuria and associated factors are important to prevent overt nephropathy.<sup>11</sup> Persoon et al, states that early intervention with ACEIs or ARBs reduces

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microalbuminuria.<sup>12</sup> Urine albumin level is the main marker of DN.<sup>13</sup> Microalbuminuria should be monitored once or twice a year.<sup>14</sup> Screening of microalbuminuria to modify risk factors are essential to reduce end-stage renal disease.<sup>15</sup>

Study was to done to find out prevalence of microalbuminuria and associated risk factors in T2DM.

## METHODS

This study was approved by the ethical review committee of the Bir hospital, Kathmandu. A cross-sectional study was conducted on Diabetes type 2 patients aged 20 years above who attended Annapurna Neurological Institutes and Allied Sciences, Global Hospital, Lagankhel Poly Clinic and Bir hospital, Kathmandu, Nepal from September 2017 to May 2018. A total of 217 patients were enrolled in this study after taking informed consent based on the set inclusion and exclusion criteria. Inclusion criteria were; diabetes type 2 patients aged 20 years and above who attend diabetic clinics in Kathmandu.

Exclusion criteria were presence of overt proteinuria, urinary tract infection, hematuria, ketonuria, pregnancy, heart failure, and use of systemic steroids in the past four weeks.

The following variables were obtained using a questionnaire filled through direct interview with the study participants: age, sex, level of education, marital status, smoking habit, family history of hypertension and diabetes mellitus, comorbid illnesses, and type of diabetes therapy. Body mass index (BMI) and blood pressure were measured using standard methods.

Body mass index (BMI) was divided into underweight, Normal weight, over weight and obese with BMI of <17.50, 17.50-22.9, 23.00-27.99, and >28 for Asian population. Patients were categorized as hypertensive if the systolic/diastolic blood pressure was >140/90 mmHg. Micro-albumin (MA) was defined as micro-albumin $\geq$ 30-300 mg/L on urine specimen. While on diabetes treatment, Glycated hemoglobin (HbA1c) <7%; post prandial and fasting blood glucose below 180 mg/dl and 120 respectively were considered a good control of sugar.

Distributions, percentage and frequency of diabetes patients having micro albuminuria, internal group comparison and Pearson's chi-square test was used to assess intergroup significance at 95% confidence interval by using standard formula. BMI calculation-calculated applying the formula, i.e., BMI = (Weight in Kilograms/ (Height in Meters x Height in Meters)

## RESULTS

A total of 217 diabetic patients were analyzed for the micro albuminuria; 56.2 %(122/217) weremale and 43.8% (95/217) were female. Among all age groups maximum patients were between ages 41 - 60 years 49.8% (108/217). 61-80, 21-40 and 81-100 as 49.8% (108/217), 46.1% (100/217), 2.8% (6/217) and 1.4% (3/217) respectively. There were 66.6% (145/217), 21.7% (47/217) and 11.5% (25/217) over weight, obese and normal weight respectively. The majority of the patients (84.3%) were <5 years duration of diabetes illness since diagnosed and physically active were found (64.1%). Whereas 30% (65/217), 30% (65/217), and 12% (26/217) had hypertension, good sugar control and smoking respectively (Table 1).

Table 1. Diabetics' sociodemographic features and disease related variable characteristics.

Variables	Frequency (%)
<b>Gender</b>	
Male	122 (56.2)
Female	95 (43.8)
<b>Age</b>	
21-40	6 (2.8)
41-60	108 (49.8)
61-80	100 (46.1)
81-100	3 (1.4)
<b>BMI</b>	
Normal weight	25 (11.5)
Over weight	145 (66.6)
Obese	47 (21.7)
<b>Sugar Control</b>	
Yes	65 (30)
No	152 (70)
<b>Duration of DM</b>	
<5	183 (84.3)
>5	34 (15.7)
<b>Hypertension</b>	
Yes	65 (30)
No	152 (70)
<b>Smoking</b>	
Yes	26 (12)
No	191 (88)
<b>Physical Activity</b>	
Active	139 (64.1)
Sedentary	78 (35.9)

The overall prevalence of MA was found to be 20.3%, the prevalence of MA was higher in male 52.3% than female 47.7% and there was no statistically different % (p=0.554). Similarly, higher prevalence was observed in age group 61-80 (52.3%) and lower at 81-100 (2.3%) years and there were no any significant difference among others age groups (p=0.517). MA was statistically significantly associated (p=0.029) with the BMI of overweight (61.4%) and obese (15.9%) than the normal weight (22.7%). A significantly difference association (p=0.056) was found between the prevalence of MA and status of sugar control (18.2%) and uncontrolled (81.8%) (Table 2).

**Table 2. Relation of microalbuminuria with sociodemographic features and disease related variables.**

Variables	Microalbumin		P Value
	Positive	Negative	
<b>Sex</b>			
Male	23 (52.3%)	99 (57.2%)	0.554
Female	21 (47.7%)	74 (42.8%)	
<b>Age</b>			
21-40	2 (4.5%)	4 (2.3%)	0.517
41-60	18 (40.9%)	90 (52.0%)	
61-80	23 (52.3%)	77 (44.5%)	
81-100	1 (2.3%)	2 (1.2%)	
<b>BMI</b>			
Normal weight	10 (22.7%)	15 (8.7%)	0.029
Over weight	27 (61.4%)	118 (68.2%)	
Obese	7 (15.9%)	40 (23.1%)	
<b>Sugar Control</b>			
Yes	8 (18.2%)	57 (32.9%)	0.056
No	36 (81.8%)	116 (67.1%)	
<b>Duration of DM</b>			
<5 Years	10 (22.7%)	173 (100.0%)	0.00
>5 Years	34 (77.3%)	0 (0.0%)	
<b>Hypertension</b>			
Yes	24 (54.5%)	41 (23.7%)	0.00
No	20 (45.5%)	132 (76.3%)	
<b>Smoking</b>			
Yes	12 (27.3%)	14 (8.1%)	0.00
No	32 (72.7%)	159 (91.9%)	
<b>Physical Activity</b>			

Active	10 (22.7%)	129 (74.6%)	0.00
Sedentary	34 (77.3%)	44 (25.4%)	

Higher prevalence of MA was observed in >5 years (77.3%) and lower in <5 years (22.7%) of diabetics period, which was significantly associated with each other (p=<0.001). Similarly, there was significant association of MA with hypertension (p=<0.001); yes (54.5%) and no (45.5%), smoking (p=<0.001); yes (27.3%) and no (72.7%), and physical activity (p=<0.001); active (22.7%) and sedentary (77.3%)(Table 2).

### DISCUSSION

The risk factors found associated for microalbuminuria were raised blood pressure and poor glycemiconcontrol. Some studies have revealed duration of diabetes, male sex, and pre-existing retinopathyas major risk factors for microalbuminuria.<sup>4</sup> According to this model, blood pressure, duration of diabetes, BMI, smoking status and physical activity directly correlates with micro albuminuria.

In this study the prevalence rate of urinary microalbuminuria among diabetes patients was found to be 20.3%. which is quite higher than various epidemiological and cross-sectional studies of Afkhami-Ardekani et al (2008), Huraib et al ( 1995) and Vijay et al (1994) 14%, 16.8%, 18.7%), respectively.<sup>16-18</sup> However in some studies conducted in India and Nepal higher prevalence of microalbuminuria also reported as 36.3%, 45.5% respectively.<sup>19-20</sup> There was not any significant association with microalbuminurea and age (p=0.517) and sex (p=0.554). Similarly in the other studies also showed not statistically significant.<sup>17,18,20</sup> In contrast Varghese et al., and Chowta et al., reported a statistically significant correlation with age.<sup>19,21</sup>

In the present study, a good statistical significant correlation was found between appearance of microalbuminuria and body mass index of the patient with the p= 0.029. Similar findings were observed in a study conducted by Gall et al (1991) who reports higher BMI had higher albumin excretion.<sup>22</sup> A study conducted by Ko GT et al (1999) in China had also shown a correlation between obesity and appearance of MA in diabetics.<sup>6</sup> However, in many other studies showed no correlation with MA explaining poorly controlled diabetes induces weight loss and these patients with low body mass index are at higher risk for diabetic complications and microalbuminuria.<sup>18</sup> However, our findings can be supported with the fact that obesity is also associated with an increase in insulin resistance that further raises

the blood glucose level which in turn hastens glomerular arteriolar sclerosis promoting early onset MA. In the study similar to this study of Gupta et al (1991) reported high levels of HbA1c was associated with microalbuminuria.<sup>23</sup> Duration of diabetes has significant contribution for the development microalbuminuria by prolonged exposure to hyperglycemia-induced advanced glycosylation end products accumulations.<sup>21</sup> Present study has shown positive correlation of microalbuminuria with duration (>5 years) of diabetes mellitus (( $p < 0.001$ )) which is in accordance with many previous reports.<sup>17-18</sup> Similar findings have been observed with Idowu et al., and Varghese et al., who reported that the duration of diabetes and retinopathy were the major predictors of microalbuminuria.<sup>19,24</sup>

Blood pressure is one of the most important risk factor of micro albuminuria. High blood pressure may cause microalbuminurea by increasing glomerular filtration pressure and subsequent renal damage.<sup>25</sup> In this study, High blood pressure was statistically significant with microalbuminurea( $p=0.00$ ). Similarly, many studies have shown a positive correlation between these two variables.<sup>6,16-19,23</sup>

In established diabetic nephropathy, the rate of progression to renal failure amongst smokers is twice in both Type I and Type II diabetes.<sup>26</sup>

This study has also shown a positive correlation of MA with physical inactivity. Physical activity improves endothelial function and as we know endothelial dysfunction in the renal vasculature is associated with albuminuria.<sup>27</sup> This association held for both walking and strenuous activity. The patients who were physically active were negative for MA than those with a sedentary lifestyle which can in turn be supported by the positive correlation between BMI and MA in this study itself. Similar findings were reported by study conducted by where negative MA was associated with patients who were involved in aerobic exercise for 6 months without any change in variable.<sup>28</sup>

## CONCLUSIONS

There is a high prevalence rate 20.3% of urinary microalbuminuria among diabetes patients of Nepal. There are several risk factors/correlates associated with it. In this study, the most important risk factors found are obesity, 5 or more year duration of disease, smoking, hypertension and sedentary lifestyles. Early recognition and institution of risk control strategy along with early start of ARBs or ACEIs in these patients would halt the progression of diabetic nephropathy.

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