Microalbuminuria among type-2 diabetes mellitus patients in Pokhara, Nepal

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ABSTRACT

Microalbuminuria is considered to be an early stage of diabetic nephropathy as well as a marker of cardiovascular disease. The aim of this study was to see the prevalence of microalbuminuria in type 2 diabetic patients and assess its association with cardiovascular risk factors among them. A total of 143 type 2 diabetic patients with the mean age of 56.06±1.08 years were analysed. The prevalence of microalbuminuria and overt proteinuria was 45.5% and 11.2%, respectively. Prevalence of microalbuminuria in female was marginally higher than in male (p>0.05). Subjects with microalbuminuria had significantly higher blood pressure (p<0.001) and duration of diabetes (p<0.05) compared with normoalbuminuric subjects. High density lipoprotein was found to be significantly lower (p<0.05) in subjects with microalbuminuria whereas fasting blood sugar, triglyceride, total cholesterol and very low density lipoprotein were marginally higher in microalbuminuric than in normoalbuminuric subjects (p>0.05). High prevalence of microalbuminuria in diabetic patients and its positive association with blood pressure and altered lipid profile suggests that screening for microalbuminuria is essential for intervention and prevent further complications like end stage renal disease and cardiovascular diseases.

Keywords: Diabetic nephropathy, microalbuminuria, cardiovascular disease, renal disease.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. It is associated with long term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.[1] It is affecting almost 6.0 % of the world's population and prevalence of this chronic metabolic disease is increasing.[2] According to World Health Organization (WHO), 180 million people worldwide had diabetes in 2006 and this number is likely to double by 2030.[3] It has now been well known that diabetic nephropathy (DN) is the leading cause of premature deaths in diabetic patients, with deaths related to cardiovascular disease (CVD) as well as renal failure.[4] An early sign of impending nephropathy is microalbuminuria (MAU), which is defined as the urinary excretion of albumin at the rate of 30-299 mg/ 24 hr or 20-199 ìg/min.[5-7] This excretion of small amount of albumin in the urine has been documented to predict renal failure and cardiovascular morbidity as well as mortality in diabetics.[8,9] Study has predicted that up to 30.0 % of the people with newly diagnosed type 2 diabetes mellitus (T2DM) will already have abnormally high urinary albumin level and about 75.0% of these will have microalbuminuria.[10] Diabetes is also associated with dyslipidemia, a well recognized manifestation of uncontrolled DM.[11] Dyslipidemia associated with the metabolic syndrome and the insulin resistance syndrome increases the risk of premature coronary artery disease (CAD).[12] In diabetes, an unfavorable lipid profile is present at a very early stage of albuminuria, when glomerular filtration rate (GFR) is normal or slightly elevated.[13]

The prevalence of albuminuria or DN in Nepalese population has not been calculated. Moreover, the correlation of MAU in diabetics with lipid profile and body mass index (BMI) has not been investigated till date. So, our present aim was to investigate the prevalence of albuminuria (MAU and macroalbuminuria) in T2DM patients in prospectus of Western Region of Nepal and investigate the relationship of MAU with various demographic and biochemical parameters.

MATERIALS AND METHODS

A total of 153 confirmed diabetic patients with normal or abnormal lipid profile and controlled/uncontrolled hypertension, attending Fishtail Hospital and Research Centre, Pokhara from August to November 2007 were enrolled. Individuals with hematuria and/or pyuria, history of urinary tract infection within last one year or at present and individuals on menstruation period were not included in this study. Of the 153 subjects participating, only 143 met the inclusion criteria. Fasting blood samples and spot urine samples collected from

Table-1: Prevalence of various grades of albuminuria in type 2 diabetes mellitus (n=143)

	n	%
Normoalbuminuria	62	43.3
Microalbuminuria	65	45.5
Macroalbuminuria	16	11.2

each of the subjects were transported to the laboratory of The School of Pharmaceutical and Biomedical Sciences, Pokhara University, Pokhara, Nepal. Informed consent was taken from the each of the subjects. Blood sugar and lipid profile were determined by enzymatic method. Urinary creatinine and microalbumin were measured by enzymatic and immunoturbidimetric methods, respectively (using semi automated analyzer; Microlab 200). Anthropometric measurements were taken by standard instruments and techniques. Subjects were classified according to the urinary albumin to creatinine ratio (ACR): <30 mg/g, 30-299 mg/g, e"300 mg/g as normoalbuminuric, microalbuminuric and macroalbuminuric, respectively. Normoalbuminuric and microalbuminuric subjects as a whole were further divided into three groups according to their BMIs: <23, 23-24.9 and e"25, as non-obese, overweight and obese, respectively. Statistical analysis was performed using SPSS (version 11.0). Data were presented as mean ± standard error of mean (SEM). Two-tailed probability values were calculated, and $p<0.05$ was considered statistically significant.

RESULTS

Among 143 type 2 diabetic patients analysed, the prevalence of microalbuminuria and overtproteinuria was 45.5% and 11.2%, respectively (Table-1). Prevalence of MAU in female was marginally higher than in male (36 females and 29 males out of total 65 microalbuminuric subjects) ($p>0.05$). High values of mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and duration of diabetes was found in microalbuminuric than in normoalbuminuric subjects (Table-2). Low values of HDL were observed in microalbuminuric than in normoalbuminuric subjects (Table-3). Similarly, though insignificant, higher values of fasting blood sugar (FBS), triglyceride (TG), total cholesterol (TC) and very low density lipoprotein (VLDL) were found in microalbuminuric than in normoalbuminuric subjects (*$p>0.05$)* (Table-3). Also, higher values of SBP, DBP, waist to hip ratio (WHR), TG and VLDL were observed in obese when compared with non-obese subjects (Table-4).

DISCUSSION

This study indicated that 45.5% (nearly half) of the patients have MAU and 11.2% have macroalbuminuria where the mean duration since the diagnosis of diabetes was 4.94±0.48 years. This is higher than the prevalence rates reported in population-based studies in diabetic patients of western countries, which ranges from 17-20 percent.[10] However, earlier studies on Asians, Asian-immigrant Indians and native Indians have suggested a high prevalence of MAU. Wu *et al*, reported a high prevalence of microalbuminuria with 39.8% and macroalbuminuria with 18.8% in Asian population,[14] while in another Asian study, MAU was detected in 36.3% of T2DM at diabetes center in south India.[15] This marked variation in prevalence in albuminuria might be due to sample selection, race, study design, sample size, duration of diabetes, poor management of diabetes and the age/sex structure of study population.

Higher values of SBP and DBP in microalbuminuric than in normoalbuminuric patients suggest that hypertension is associated with microalbuminuria. The absence of significant difference in TG and TC values between microalbuminuric and normoalbuminuric patients, which is similar to that reported in many previous literatures,[9,15,16-20] suggests that microalbuminuria is independent of plasma TG and TC values to predict renal as well as CV risk.

Table-2: Demographic details of study group

Parameters	**Normoalbuminuria (n=62)**	**Microalbuminuria (n=65)**
Age (yrs)	53.05±1.41	56.11±1.66NS
BMI (kg/m2)	25.18±0.57	25.83±0.51NS
WHR	0.91±0.01	0.91±0.01NS
SBP (mmHg)	127.29±2.18	130.77±2.36**
DBP (mmHg)	85.88±1.38	87.83±1.53**
Duration since onset of diabetes (yrs)	3.40±0.57	5.01±0.58*

Values expressed as mean ± SEM

*p<0.05; **p=<0.001; NS: non significant when compared with normoalbuminuric subjects.

Table-3: Biochemical characteristics in normoalbuminuric and microalbuminuric subjects

Parameters	Normoalbuminuria (n=62)	Microalbuminuria (n=65)
FBS (mg/dl)	117.45±4.31	131.04±5.76NS
TG (mg/dl)	131.39±7.83	151.95±8.23NS
TC (mg/dl)	179.19±5.62	180.20±5.11NS
HDL (mg/dl)	45.13±1.32	42.24±1.05*
LDL (mg/dl)	107.65±5.22	107.14±4.96NS
VLDL (mg/dl)	26.36±1.59	30.65±1.66NS
ACR (mg/g)	20.38±0.87	71.31±10.03**

Values expressed as mean ± SEM
*p<0.05; **p=<0.001, NS: non significant when compared with normoalbuminuric subjects.

When BMI of normoalbuminuric and microalbuminuric group were compared, there was no significant difference, strongly supporting the numerous previous findings,[15,16,18,20] which suggested that MAU may remain independent of BMI as a risk factor. However, strong and positive association of the BMI with SBP, DBP and TG among the non-obese and obese groups may suggest that increase in BMI is associated with the increasing risk of atherogenesis and coronary as well as peripheral vascular resistance.[21]

Higher values of SBP, DBP, TG and VLDL levels in obese patients compared with non-obese patients are similar to those as described in previous studies.[22-24] This suggests that blood pressure increases with obesity. Also, increase in triglycerides in obese patients may be due to hyperinsulinemia and insulin resistance states contributing to characteristic alterations in lipid profile associated with obesity.[25]

From all the findings, it can be concluded that screening for MAU in diabetic patients should be done on a regular basis so that by following the intervention methods such as therapy and tight control over blood sugar and pressure, further complications can be prevented at an earlier stage.

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Table-4: Demographic and biochemical characteristics of normoalbuminuric and microalbuminuric subjects classified according to obesity

Parameters	Non-obese (n=32)	Overweight (n=21)	Obese (n=74)
Age (yrs)	55.65±2.49	54.80±2.73	54.10±1.35NS
Duration since onset of diabetes (yrs)	5.37±1.10	4.42±0.72	3.67±0.47NS
WHR	0.86±0.01	0.92±0.01	0.94±0.01**
SBP (mm Hg)	124.37±3.38	128.57±3.96	131.24±2.04*
DBP (mm Hg)	80.31±1.85	84.90±2.32	90.28±1.29**
FBS (mg/dl)	135.90±8.34	126.57±10.06	118.81±4.22NS
TG (mg/dl)	125.38±12.03	140.01±12.30	149.60±7.53*
TC (mg/dl)	167.94±6.35	176.40±8.61	185.70±5.26NS
HDL (mg/dl)	44.42±1.57	42.47±2.22	43.65±1.13NS
LDL (mg/dl)	98.07±6.98	105.20±8.00	112.04±4.82NS
VLDL (mg/dl)	24.49±2.25	28.73±2.63	30.26±1.55*
ACR (mg/g)	39.66±5.74	44.19±8.84	50.02±8.98NS

Values expressed as mean ± SEM
*p<0.05;**p=0.001; NS: non-significant compared with non-obese.

REFERENCES

1. ADA. Diagnosis and classification of diabetes mellitus (Position statement). *Diabetes Care* 2007 (Suppl); 30: 42-7.
2. Adeghate E, Schattner P, Dunn E. An update on the etiology and epidemiology of diabetes mellitus. *Ann New York Acad Sci* 2006; 1084: 1-29.
3. WHO. Diabetes facts 2006. Fact sheet 312.
4. Marshall WJ, Bangert SK, editors. Clinical Chemistry (5th ed.). Elsevier Limited, London 2004.
5. Burtis CA, Ashwood ER, Bruns DE, editors. Teitz Textbook of Clinical Chemistry and Molecular Diagnosis (4th ed.). Elsevier Limited, New Delhi 2006.
6. ADA. Nephropathy in diabetes (Position Statement). *Diabetes Care* 2004 (Suppl); 27: 79-83.
7. de Boer IH, Sibley SD, Kestenbaum B *et al*. Central obesity, incident microalbuminuria and change in creatinine clearance in the epidemiology of diabetes interventions and complications study. *J Amer Soc Nephrol* 2007; 18: 235-43.
8. Naidoo DO. The link between microalbuminuria, endothelial dysfunction and cardiovascular disease in diabetes. *Cardiovasc J South Africa* 2002; 13: 194-9.
9. Romundstad S, Holman J, Hallman H, Kvenild K, Ellekjaer H. Microalbuminuria and all cause mortality in treated hypertensive individuals: Does sex matter? The nord-trondelag health study (HUNT), Norway. *Circulation* 2003; 108: 2783-9.
10. Tobe SW, McFarlan PA, Naimark DM. Microalbuminuria in diabetes mellitus. *Canadian Med Assoc J* 2002; 167: 499-503.
11. Siraj ES, Seyoum B, Saenz C, Abdulkadir J. Lipid and lipoprotein profiles in Ethiopian patients with diabetes mellitus. *Metabol Clin Expt* 2006; 55: 706-10.
12. Brunzell JD, Ayyobi AF. Dyslipidemia in metabolic syndrome and type 2 diabetes mellitus. *Amer J Med* 2003 (Suppl); 115: 24-8.
13. Roberto T, Alessandro RD, Giuseppe L. Lipids and renal disease. *J Amer Soc Nephrol* 2006 (Suppl); 17: 145-7.
14. Wu AYT, Kong NCT, Leon FA *et al*. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: The microalbuminuria prevalence (MAP) study. *Diabetologia* 2005 (Suppl); 48: 17-26.
15. 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.
16. Lu B, Wen J, Song XY *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: 184-92.
17. Haffner SJ, Cassels H. Hypertension as a cardiovascular risk factor. *Amer J Med* 2003 (Suppl); 115: 6-11.
18. Bahia L, Gomes MB, Da Cruz PD, Goncalves MDF. Coronary artery disease, microalbuminuria and lipid profile in patients with non insulin dependent diabetes mellitus. *Arq Bras Cardiol* 1999; 73: 17-22.
19. Kim YI, Kim CH, Choi CS *et al*. Microalbuminuria is associated with the insulin resistance syndrome independent of hypertension and type 2 diabetes in Korean population. *Diabetes Res Clin Pract* 2001; 52: 145-52.
20. Liu JE, Robbin DC, Bella JN *et al.* Association of albuminuria with systolic and diastolic left ventricular dysfunction in type 2 diabetes. The strong heart study. *J Amer Coll Cardiol* 2003; 41: 2022-8.
21. Haslam DW, James WP. Obesity. *Lancet* 2005; 366: 1197-209.
22. Despres JP, Moorjani S, Tremblay A *et al* . Relation of high plasma triglyceride levels associated with obesity and regional adipose tissue distribution to plasma lipoprotein-lipid composition in premenopausal women. *Clin Invest Med* 1989; 12: 374-80.
23. Freedman DS, Jacobsen SJ, Barboriak JJ *et al.* Body fat distribution and male/female differences in lipids and lipoproteins. *Circulation* 1990; 81: 1498-506.
24. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG. Diet, lifestyle and the risk of type 2 diabetes mellitus in women. *New Engl J Med* 2001; 345: 790-7.
25. Kopelman P. Health risk associated with overweight and obesity. *Obes Rev* 2007; 8: 13-7.