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RESEARCH ARTICLE

PREVALENCE AND PREDICTORS OF MICROALBUMINURIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL OBSERVATIONAL STUDY IN BANGLADESH

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ABSTRACT

Background: Microalbuminuria is considered to be an early stage of diabetic nephropathy as well as marker of cardiovascular disease. **Objective**: The aim of the study was to estimate the prevalence and predictors of microalbuminuria in type 2 diabetic subjects of Bangladesh. **Subjects and methods**: A total of 578 type 2 diabetic patients (male 308, female 270) with the mean age of 51.00±7.0 years were analyzed. Different biochemical parameters e.g. Serum glucose, triglyceride (TG), total cholesterol (TC), serum creatinine, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, and HbA1c were measured using available commercial kits. Microalbuminuria was measured by strip. **Results:** The prevalence of microalbuminuria among type 2 diabetic patients was 43.07%. Prevalence of microalbuminuria was marginally higher in male than in female (male 47.54%, female 38.51%). Subjects with microalbuminuria had significantly higher blood pressure, body mass index, fasting blood sugar (FBS), LDL cholesterol, serum creatinine, HbA1c, triglycerides ($p<0.001$), duration of diabetes ($p<0.05$) and significantly lower HDL cholesterol ($p<0.001$) than microalbuminuria absent group. Significant predictors for the development of microalbuminuria included age, diastolic blood pressure, triglycerides, LDL cholesterol, hypertension and retinopathy. **Conclusion**: Screening of microalbuminurea and its risk factors is urgent to alleviate cardiovascular complications of type 2 diabetic patients of Bangladesh.

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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 (ADA, 2007). It is affecting almost 6.0 % of the world's population and prevalence of this chronic metabolic disease is increasing (Adeghate *et al*, 2006). 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 (Marshall *et al*, 2004). Microalbuminuria defined as urinary albumin excretion rate of 20-200 µg/min or urinary protein excretion rate of 30-300 µg/min predicts future development of overt nephropathy (Graziella *et al*, 2003).

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Microalbuminuria is also considered to be a predictor for cardiovascular disease both among diabetic and nondiabetic subjects, (Yudkin *et al*,1988, Haffner *et al* 1990, Damsgaard *et al*, 1990) and is one of the components of the metabolic syndrome (insulin resistance syndrome) (Groop *et al*,1993, Niskanen *et al*, 1993). As microalbuminuria can be reversed and the future development of overt diabetic nephropathy significantly reduced, screening for microalbuminuria and timely therapeutic intervention has become standard of care worldwide. We conducted a cross sectional retrospective study to elucidate the prevalence of microalbuminuria in Bangladeshi type 2 diabetics and to find out the putative risk factors for the development of microalbuminuria.

Subjects and Methods

A total of 578 confirmed diabetic patients with normal or abnormal lipid profile and controlled/uncontrolled hypertension, attending Diabetic Hospital, Chittagong from August 2009 to June 2010 were enrolled. Individuals with hematuria and/or pyuria, history of urinary tract infection within last one year or at the period of data collection and individuals on menstruation period were not included in this study.

In all study patients, a complete clinical work up was done including height, weight, and body mass index. The body mass index was calculated and expressed as kg/m^2. The blood pressure was recorded in the right upper arm in the sitting posture, after a five minute rest. Clinical details of each subject were recorded in a specified proforma especially designed for this study. The variables that were recorded included age, gender, haemoglobin A1c, creatinine, systolic and diastolic blood pressures, patients' weight, height and the presence of hypertension. Subjects were defined as hypertensive if they had a systolic blood pressure more than 130mmHg or diastolic blood pressure more than 85 mmHg (Mogensen, 1998). A fasting sample of blood was drawn after an overnight fast of 10 hours and the following investigations were done: serum glucose, serum cholesterol, serum triglycerides, high density lipoprotein-cholesterol, serum creatinine and HbA1c. Type-2 diabetes was diagnosed based on the WHO study group report criteria (Albert *et al*, 1998). The fundus was examined using Vista 20 direct ophthalmoscope by a diabetologist. The retinopathy was taken as positive if there was evidence of microdots, hard exudates, soft exudates, new vessels or maculopathy.

Anthropometric measurements were taken by standard instruments and techniques. Serum glucose levels were estimated by GOD-/POD method in micro well plate described by Kunst et al.(Kunst *et al*, 1984) on Elisa reader at 515 nm and calculated with respect to standard calibration curve (Randox Laboratories LTD Ardmore, Diamond Road, Crumlin, Co. Antrim,United Kingdom BT294QY). Serum lipid profile (Cholesterol, triglycerides, HDL- cholesterol) were estimated by GOD-/PAP method in Elisa reader at 500 nm (Siedel *et al*, 1983. McGown *et al*.1983) (Randox Laboratories LTD Ardmore, Diamond Road, Crumlin, Co. Antrim,United Kingdom BT294QY). Serum LDL- cholesterol was calculated by the Friedwald formula: LDL-cholesterol = Total cholesterol – (1/5 TG + HDL cholesterol). Serum creatinine was estimated in all patients by modified kinetic method of Jaffie (Randox laboratories, UK). Glycated haemoglobin (HbA1c) was estimated by high pressure liquid chromatography using the Variant machine (Bio Rad, Hercules, CA, USA). Urine samples were collected in the early morning after an overnight fast. Microalbuminuria was defined as urinary albumin 50 mg/l or higher. Microalbuminuria was checked by using semiquantitative dry immuno chemical screening strips. (Micral Test II Strips, Accu-Check product, Roche Diagnostics, Australia.)

Statistics: Statistical analyses were performed using Statistical Package for Social Science (SPSS) for Windows version 12. Student's *t* test was used to compare the means of continuous variables and $\chi 2$ was used to compare proportions. Backward stepwise multiple logistic regression analysis was done using microalbuminuria as the dependent variable and age, body mass index, retinopathy, hypertension, duration of diabetes, fasting blood sugar, HbA1c, HDL, LDL, serum creatinine, systolic and diastolic blood pressure as independent variables.

RESULTS

The baseline characteristics of the subjects are summarized in Table 1. Mean age of subjects was 51.00±7.0 years. Mean Body Mass Index (BMI) was 24.83±2.82 kg/m². The mean duration of diabetes was 9.58±5.06 years. 53.28% of the subjects were males while 46.72% were females, 70.42% of the subjects had systolic blood pressure 130 mmHg or more. Among the study subjects, 47.06% had diastolic blood pressure more than or equal to 85 mm Hg. In our study we found that prevalence of microalbuminuria was 43.07%. Prevalence of microalbuminuria among males was higher than female (47.54% and 38.51% respectively). Table 2 presents the clinical and biochemical characteristics of the normoalbuminuric and microalbuminuric patients. The microalbuminuric patients were older and had a longer duration of diabetes compared with the normoalbuminuric group (p=0.000). The microalbuminuric patients had significantly increased systolic and diastolic blood pressure compared to normoalbuminuric subjects (p=0.000). Fasting glucose and HbA1c were also significantly higher in the microalbuminuric group compared with the normoalbuminuric subjects (p=0.001 and 0.000 respectively). Serum creatinine and triglycerides values were found to be significantly higher in the microalbuminuric group (p=0.000). Serum total cholesterol values were not significantly differ between groups whereas LDL value were significantly higher (p=0.000) and HDL value were significantly lower (p=0.009) in microalbuminuric patients than normoalbuminuric patients.

The backward stepwise multiple logistic regression analysis model indicated that significant predictors for the development of microalbuminuria include age (>50 years; OR: 25.44; CI: 14.121-45.839; p=0.000), diastolic blood pressure (85- 90 mmHg; OR: 2.894; CI: 1.356-6.175; p=0.006), Triglycerides (>150 mg/dl; OR: 2.751; CI: 1.491-5.075; p=0.001), LDL (>100 mg/dl; OR: 2.315; CI: 1.049-5.109; p=0.038), presence of hypertension (OR: .244; CI: 0.120-0.492; p=0.000) and retinopathy (OR: .463; CI: .279-.768;p= 0.003) (Table 3). No significant association was observed between microalbuminuria and gender, HDL, total cholesterol (p< 0.07), systolic blood pressure, serum creatinine, HbA1c, duration of diabetes and BMI.

DISCUSSION

Microalbuminuria (MAU) is the first clinical detectable sign of involvement of the kidney. It affects between 20-40% of subjects 10-15 years after the onset of diabetes. Once microalbuminuria is present, it progresses over 5-10 years to proteinuria in 20-50% subjects. With microalbuminuria, the decline in renal functions varies but average reduction in glomerular filtration is around 10-12 ml/min/year (Ritz *et al*, 1999). This study indicated that 43.07% of the type 2 diabeic patients of Bangladesh have MAU. This is higher than the prevalence rates reported in population-based studies in diabetic patients of western countries, which ranges from 17-20 percent (Tobe *et al*, 2002). However, earlier studies on Asians, Asian immigrant Indians and native Indian diabetic patients have suggested a high prevalence of MAU. Wu et al. (Wu *et al*, 2005) reported a high prevalence of microalbuminuria with 39.8% and macroalbuminuria with 18.8% in Asian diabetic population while in another Asian study, MAU was detected in 45.5% of type 2 diabetic patients in Nepal (Sigdel *et al*, 2008). 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. However, this could also reflect true differences in the ethnic susceptibility to nephropathy. Earlier studies by Vijay et al. (Vijay *et al*, 1993) from Madras (Chennai, India) have demonstrated a familial clustering of diabetic

Table 1. Baseline characteristics of study subjects

Variables	No. or Mean (% or SD)
Gender(n=578)	
Male	308(53.28)
Female	270(46.72)
Smoking(578)	
Yes	166(30)
No	411(70)
Retinopathy(578)	
Yes	197(34.08)
No	381(65.02)
Hypertension(578)	
Yes	411(71)
No	167(29)
Systolic Blood pressure(578)	
<130	171(29.58)
≥130	407(70.42)
Diastolic blood pressure(578)	
<85	306(52.94)
≥85	272(47.06)
Age(in years)	51.00(7)
Duration of diabetes(in years)	9.58(5.06)
Body mass index(BMI)	24.83(2.82)

Data are expressed as No (%) or mean (SD)

Table 2. Clinical and biochemical characteristics of the study subjects

Parameter	Microalbuminuric Group (n-249)	Normoalbuminuric Group (n-329)	P value
Age(years)	56.14(4.35)	47.25(6.10)	0.000
BMI(Kg/m2)	25.44(3.1)	24.36(2.44)	0.000
Cystolic BP(mmHg)	138.67(11.87)	129.54(10.1)	0.000
Diastolic blood pressure(mmHg)	88.58(10.41)	82.92(9.1)	0.000
Duration of Diabetes(years)	12.97(4.52)	6.99(3.75)	0.000
No. with Retinopathy	120(48.2)	77(23.4)	0.000
Fasting blood sugar(mmol/l)	11.55(4.5)	9.76(7.5)	0.001
After break fast sugar(mmol/l)	17.51(3.8)	15.18(4.47)	0.000
HbA1c(%)	9.29(1.63)	8.82(1.5)	0.000
Serum creatinine(mg/dl)	2.16(0.73)	1.07(0.46)	0.000
Total Cholesterol(mg/dl)	197.94(37.7)	194(69.56)	NS
HDL	36.96(8.4)	38.72(7.52)	0.009
LDL(mg/dl)	138.32(33.62)	124.82(32.70)	0.000
TG(mg/dl)	217.14(62.07)	180.05(58)	0.000
No. with hypertension	233(93.57)	177(53.80)	0.000

Data expressed as No (%) or mean (SD).Students t test was done for comparison of variables between groups and chi square test was done for proportion between groups. P<0.05 were considered as test of significance.
BP- blood pressure, HDL- High density lipoprotein, LDL-Low density lipoprotein, BMI- Body mass index.
NS- not significant

Table 3. Odds ratio and its confidence interval for microalbuminuria using backward logistic regression analysis

Predictors	Frequency	Odds ratio(OR)	95% CI[a] for odds ratio(lower- upper)	P value
Age> 50 years	328	25.441	14.121-45.839	0.000
Hypertension	411	.244	.120-.494	0.000
Diastolic blood pressure				
85-90	181	2.894	1.356-6.175	0.006
>90	91	1.677	0.790-3.558	0.178
Serum Cholesterol	372	.534		
> 180 mg			.271-1.052	0.070
LDL> 100mg/dl	462	2.315	1.049-5.109	0.038
TG>150 mg/dl	437	2.751	1.491-5.075	0.001
Retinopathy	197	.463	.279-.768	0.003

[a]95% confidence interval. Multiple logistic regressions were done using microalbuminuria as the dependent variable. The following categories were taken as independent variables; age, body mass index, duration of diabetes, systolic blood pressure (BP), diastolic BP, fasting blood sugar (FBS), glycated haemoglobin (HbA1c), LDL, HDL, hypertension, retinopathy and serum creatinine.

ephropathy among south Indian type 2 diabetic subjects. Genetic susceptibility linked to angiotensin encoding gene as shown in Oji- Kree Indians could also be an important determinant for development of diabetes renal disease (Hegele *et al*, 1999). In our study, microalbuminuria was found to be more frequent in males (47.54% vs. 38.51%) as compared to females which have been observed in other studies (Ahmedani *et al*, 2005, Parchwani *et al*, 2011).

Again, the microalbuminuria positive group was older and had a longer duration of diabetes compared to the microalbuminuria negative group is in agreement with other study (Hashim *et al*, 2004). Our study also revealed that the microalbuminuria positive group had a higher BMI as compared to the microalbuminuria negative group. The microalbuminuria positive group had a higher systolic and diastolic blood pressure compared to the microalbuminuria

negative group (p=0.000) which has been observed by others (Hirano *et al*. 1999). Like other study (Gall *et al*, 1997) significant lipids abnormalities have also been observed in subjects with microalbuminuria. In our study, Backward stepwise multiple logistic regression analysis was done to find out the predictors of microalbuminuria which revealed age (>50 years), LDL (>100mg/dl), Triglycerides (>150mg/dl), diastolic blood pressure (85-90mmHg), hypertension and retinopathy as the significant risk factors for microalbuminuria. For diastolic pressure more than 90 mmHg we did not get any significant result which may be due to small sample size. Although we did not find cholesterol as significant predictor (at 5% level), it showed significancy at 10% level (p=0.07). Al- Futaisi et al. (Al- Futaisi *et al,* 2006) indicated HbA1c, creatinine and hypertension as the significant predictors for the development of microalbuminuria, Parving et al. (Parving *et al*, 2006) reported HbA1c, systolic blood pressure (BP), ethnicity, retinopathy, duration of diabetes, kidney function, body height, and smoking as independent risk factors of microalbuminuria while Unnikrishnan et al. (Unnikrishnan *et al*, 2007) reported duration of diabetes, HbA1c and systolic blood pressure, to be associated with both microalbuminuria and overt nephropathy. Age was reported as one of the risk factors in the Wisconsin study (Klein *et al*, 1993), in a Danish population study (Schmitz *et al*, 1987) and in the Pima Indians (Nelson *et al*, 1989).

Microalbuminuria was checked by using micral dip stick. Screening for microalbuminuria with micral test strips is relatively cheap, fast and has an acceptable sensitivity of 96.7% with a specificity of 71% (Mogensen *et al*, 1997). All positive tests should be rechecked and confirmed by more specific tests. Micral test strip is an optically-read immunoassay specifically for detection of microalbuminuria and the use of these strips has been widely advocated (Mogensen *et al*, 1997). Several studies have shown the overall high sensitivity (b/w 79-99%) of Micral strips but lower specificity (67- 87%) with higher negative predictive values than positive predictive values (Mogensen *et al*, 1997, Ritz *et al*, 1999, Bruce *et al*, 2003, Mogensen, 1984, Dinneen *et al*,1997, Fernandez Fernandez *et al* ,1998). Several studies comparing Micral test and laboratory methods of detecting albuminuria have concluded that it could be used as a screening tool but not as diagnostic tool.

Conclusion

The prevalence of microalbuminuria in Bangladesh was 43.07% and this study also identified age, triglycerides, LDL, diastolic blood pressure, hypertension and retinopathy to be significant predictors in our studied population. Because of the adverse impact of proteinuria on survival of subjects with type 2 diabetes, screening and intervention programs should be implemented early stage of microalbuminuria and risk factors should be treated aggressively.

Conflict of interest- There is no conflict of interest.

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