Prevalence of Microalbuminuria with Relation to Glycemic Control in Type-2 Diabetic Patients in Mymensingh

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Abstract

Diabetes is one of the most common endocrine disorders characterized by hyperglycaemia. Diabetic nephropathy is a consequence of long standing diabetes. The prevalence of microalbuminuria predicts progression to diabetic nephropathy. The present study was conducted to determine the prevalence of microalbuminuria in relation to duration of diabetes, BMI, Serum Creatinine and HbA1c in an ethnic group of Type 2 diabetes mellitus residing in Mymensingh, Bangladesh. This descriptive cross-sectional study was carried out in a community based medical college hospital, located at Winnerpar, Mymensingh from July to December 2012. Fasting verious blood and morning urine sample was collected for analysis of creatinine, Bb Alc and microalbumin uria respectively. One hundred twenty known Type 2 diabetic patients with age 30 years and above were included in the study. Pearson correlation was applied to observe association of microalbuminuria with different parameters. Microalbuminuria had a highly significant correlation with duration of diabetes ($p<0.001$), serum creatinine , HbA1c ($p<0.001$) and BMI (p 0.001). The correlation demonstrates that with the increase in age, raised serum creatinine significantly bearing a perfect positive correlation as evident by $r = 0.878$, $p < 0.001$. The present study found an early onset of microalbuminuria in the selected community which could be due to poor glycaemic control (high HbA1c >7%) or heredity factors. Screening for microalbuminuria and HbA1c test should be done in both newly and already diagnosed Type 2 diabetic patients as an early marker of renal dysfunction and glycaemic control.

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Introduction

Diabetic nephropathy is characterized by proteinuria and is the leading cause of end-stage renal disease worldwide. It constitutes the major work load of dialysis centers. The estimated cost for dialysis per diabetic subject in Pakistan is around $30000/year[1]. Diabetic subjects on dialysis and transplant recipients also have higher morbidity and mortality rates than their non diabetic counterparts[2]. Progression to established diabetic nephropathy occurs through several stages. Microalbuminuria (MA) is an earliest marker of nephropathy and cardiovascular disease (CVD) in patients with diabetes[3]. Microalbuminuria defined as urinary albumin excretion rate of 20-200 g/min or urinary protein excretion rate of 30-300 g/min predicts future development of overt nephropathy[4]. 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 world wide. Although microalbuminuria

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is predictive of worsening microvascular disease in the kidney (5-10% per year progress to overt diabetic nephropathy), an increased albumin excretion rate (AER) reflects a generalized abnormality of vascular function and is associated with 2-4 fold increases in cardiovascular and all-cause mortality[5].

Microalbuminuria requires ultrastructural changes rather than alterations in glomerular pressure or filtration rate alone Microalbuminuria requires ultrastructural changes rather than alterations in glomerular pressure or filtration rate alone[6]. There is some evidence that irrespective of the duration and type of diabetes the damage to the kidney can be avoided if good glycemic control is achieved[7].

Measurement of HbA1c is used to determine average glycemic control over an 8-12 week period, and HbA1c level has been linked to development of microvascular complications[8]. The Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetic Study (UKPDS) have demonstrated that intensive glycemic control significantly reduces the risk for development of microalbuminuria in type 2 diabetics. According to DCCT strict glycemic control (HbA1c < 7) had a relative risk reduction for development of Microalbuminuria by 34%. In the UKPDS, a difference in HbA1c of 0.9% reduces the risk for development of microalbuminuria by 30%. Therefore, a target HbA1c <7 should be recommended in all patients with type 2 diabetes[9].

A cross sectional study was conducted in Mymensingh, Bangladesh was designed to determine the frequency of microalbuminuria in patients with type 2 diabetes and compare this among those with good and poor glycemic control.

Methods

This cross sectional study was conducted in the Medical Unit of Community Based Medical college Hospitals, Mymensingh, Bangladesh from July 2012 to December 2012. 120 known type 2 diabetic patients more than 30 years of age were included in the study. Subjects were excluded from the study if they came to the hospital after vigorous exercise, had any serious illness such as history of heart failure, Urinary Tract Infections or were known patients of nephropathy. Clinical details of each subject was recorded in a specified proforma especially designed for this study. This included height, weight and body mass index. Type-2 diabetes was diagnosed based on the WHO study group report criteria. Subjects were identified as hypertensive if they were on antihyperterisive medication or if they had a systolic blood pressure more than 130mmHg or diastolic blood pressure more than 85 mmHg. A subject was labeled as smoker if he/she was smoking actively or was an active smoker in the last 6 months. The fundus was examined using Vista 20 direct ophthalmoscope by a diabetologist. The retinopathy was taken as positive if there was evidence of either microdots, hard exudates, soft exudates, new vessels or maculopathy. Peripheral neuropathy was defined as absent touch or vibratory sensations of the feet. Touch was assessed by 10 gm monofilament and vibration sensation by 128 Hz tuning fork.

According to WHO criteria diabetes type 2 was diagnosed if fasting blood sugar was more than 126 mg/dl or random blood sugar was more than 200 mg/dl and not insulin dependent. Venous blood was collected after 12 hours fasting for HbA1c. Twenty-four hours urine was collected for estimation of microalbuminuria. In order to measure urinary albumin concentration accurately, patients were given necessary instructions regarding the collection of urine samples. When no evidence of infection and/or haematuria was found in the urinalysis, urine samples were examined for microalbuminuria. Urinary albumin was measured with an autoanalyzer (analyzer medical system, Italy) using Randox kits (urinary albumin measured with immunoturbidimetry method, UK). A second 24-hours urine sample was obtained and examined for microalbuminuria, if the first measurement exceeded 30mg of albumin. The diagnosis of microalbuminuria was confirmed when >30 mg/dl albumin was found in the second sample. Twenty four hours

urinary albumin concentration of <30 mg were considered as normal (normoalbuminuria), 30–300 mg as microalbuminuria. HbA1c was carried out and labeled good glycemic control when found less than 7 and greater than or equal to 7 were considered poor glycemic control. Patients with hypertension and urinary tract infection were excluded because these are the confounders. All the investigations were done by single pathologist to control the confounder and to make the study results unbiased. SPSS version 16 was used for the analysis of data. Mean and standard deviation was calculated for age, and duration of diabetes. Frequency and percentage was calculated for gender. HbA1c and microalbuminuria stratifications were done with regards to age, gender and duration of diabetes to see the effect of these on outcomes. Chi-square test was applied between microalbuminuria and HbA1c and cross tabulation tool was used to see the relation between HbA1c and microalbuminuria. P Value <0.05 was considered as significant.

Results

One hundred and twenty type-2 diabetic patients with mean age 57.8 ± 14.7 years were evaluated and male to female ratio was roughly 3:1. Family history of diabetes, hypertension, chronic disease and renal disease were present in 56.7%, 55%, 30% and 31.7% of patients respectively. Majority (84.2%) of patients was hypertensive (Systolic blood pressure >130 mmHg in 41.7% and diastolic blood pressure >85 mmHg in 49.2%). Over 48% of patients had diabetic retinopathy and 50% smoking habit. The mean body mass index and duration of diabetes were 25.7 ± 6.2 kg/m^2 and 9.2 ± 4.7 years respectively (Table I). Table II demonstrates binary logistic regression analysis of Odds Ratios for characteristics of the patients likely to be associated with positive microalbuminuria. The variables were significant associated with microalbuminuria ($p < 0.05$) by univariate analyses were all entered into the model directly. Of the 6 variables, age >50 years, family history of renal disease, body mass index >23 kg/m^2 and diabetic retinopathy were found to be the independent predictors with odd ratios being 1.6, 0.3, 1.3 and 2.4 respectively ($p = 0.048$, $p = 0.025$, $p = 0.040$, $p = 0.031$ respectively).

Among the studied patients microalbuminuria was found 76.9% of male and 23.1% of female ($p = 0.869$) (Table III). The present of microalbuminuria was higher between age 50 – 60 years and 60 years of patients, however lower those who were less than 50 years ($p = 0.122$) (Table IV). Figure 1 shows the comparative statement of good and poor glycemic control between microalbuminuria groups. A higher percentage of patients with microalbuminuria was observed in the both good glycemic control and poor glycemic control group (55% and 54% respectively). Table V summaries the correlations between duration of diabetes, body mass index, HbA1c, serum creatinine and microalbuminuria of Type-2 diabetic patients. All the components were observed to be positively correlated with microalbuminuria ($r = 0.363$, $p < 0.001$; $r = 0.295$, $p = 0.001$; $r = 0.441$, $p<0.001$ and $r = 0.266$, $p = 0.003$ respectively). The correlation demonstrates that with the increase in age, serum creatinine raise significantly bearing a perfect positive correlation as evident by $r = 0.878$, $p<0.001$(Figure2).

Table I. Distribution of patients by baseline characteristics (n=120)

Baseline characteristics	Frequency (%)	Mean ± SD
GenderMale Female	93(77.5) 27(22.5)	-
Family H/O DM	68(56.7)	
Family H/O hypertension	66(55.0)	-
Family H/O chronic disease	36(30.0)	-
Family H/O renal disease	38(31.7)	-
Hypertension	101(84.2)	-
Systolic blood pressure <130 mmHg >130 mmHg	 70(58.3) 50(41.7)	-
Diastolic blood pressure <85 mmHg >85 mmHg	 61(50.8) 59(49.2)	-
Diabetic retinopathy	58(48.3)	-
Smoking habit	60(50.0)	-
Age (years)	-	57.8 ± 14.7
BMI	-	25.7 ± 6.2
Duration of DM	-	9.2 ± 4.7

Table II. Association between micoalbuminuria and disease related variables (n = 120)

Variables of interest	Univariate analysis (p-value)	Multivariate analysis	
		Odds Ratio (95% CI of OR)	p-value
Age (> 50 years)	0.040	1.6(0.5 – 6.0)	0.048
Family H/O renal disease	0.010	0.3(0.1 – 0.9)	0.025
Hypertension	0.031	2.2(0.5 – 9.7)	0.294
Systolic blood pressure	0.028	1.1(0.4 – 2.9)	0.922
BMI (>23 kg/m^2)	0.001	1.3(0.4 – 4.6)	0.040
Diabetic retinopathy (fundoscopy)	0.001	2.4(0.8 – 7.1)	0.031

Table III. Sex wise distribution of microalbuminuria

Sex	Microalbuminuria		p-value
	Yes (n = 65)	No (n = 55)	
Male	50(76.9)	43(78.2)	0.869
Female	15(23.1)	12(21.8)	

Data were analysed using x^2 Test

Table IV. Age wise distribution of microalbuminuria

Age	Microalbuminuria		p-value
	Yes (n = 65)	No (n = 55)	
<50	20(30.8)	27(49.1)	
50 – 60	18(27.7)	11(20.0)	0.122
60	27(41.5)	17(30.9)	

Data were analysed using x^2 Test

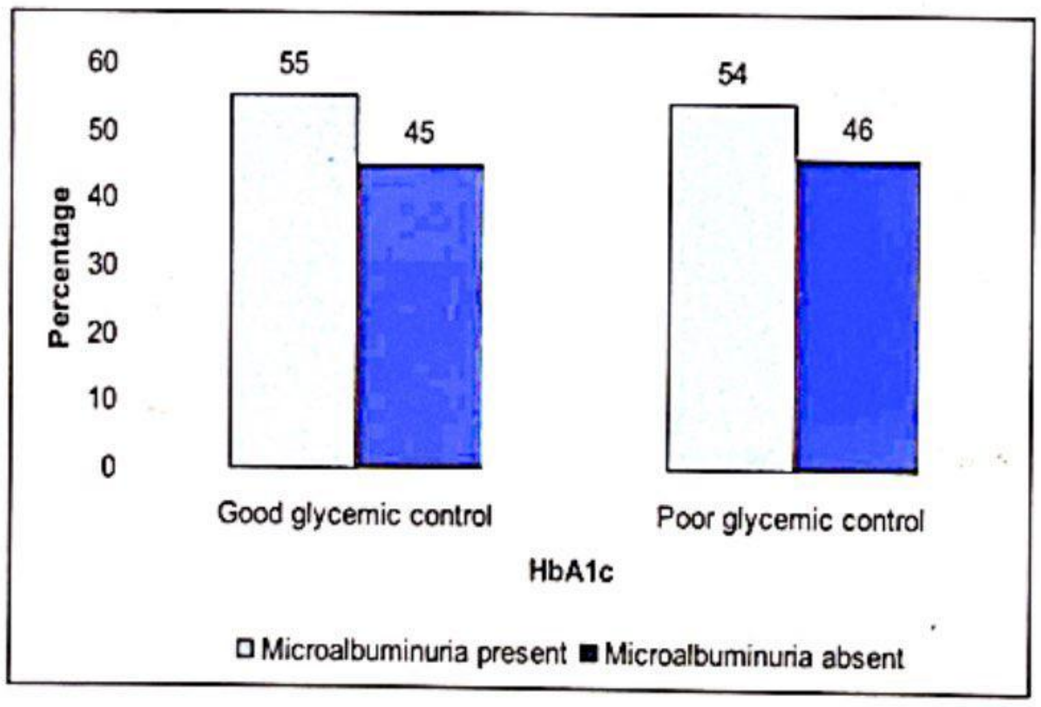
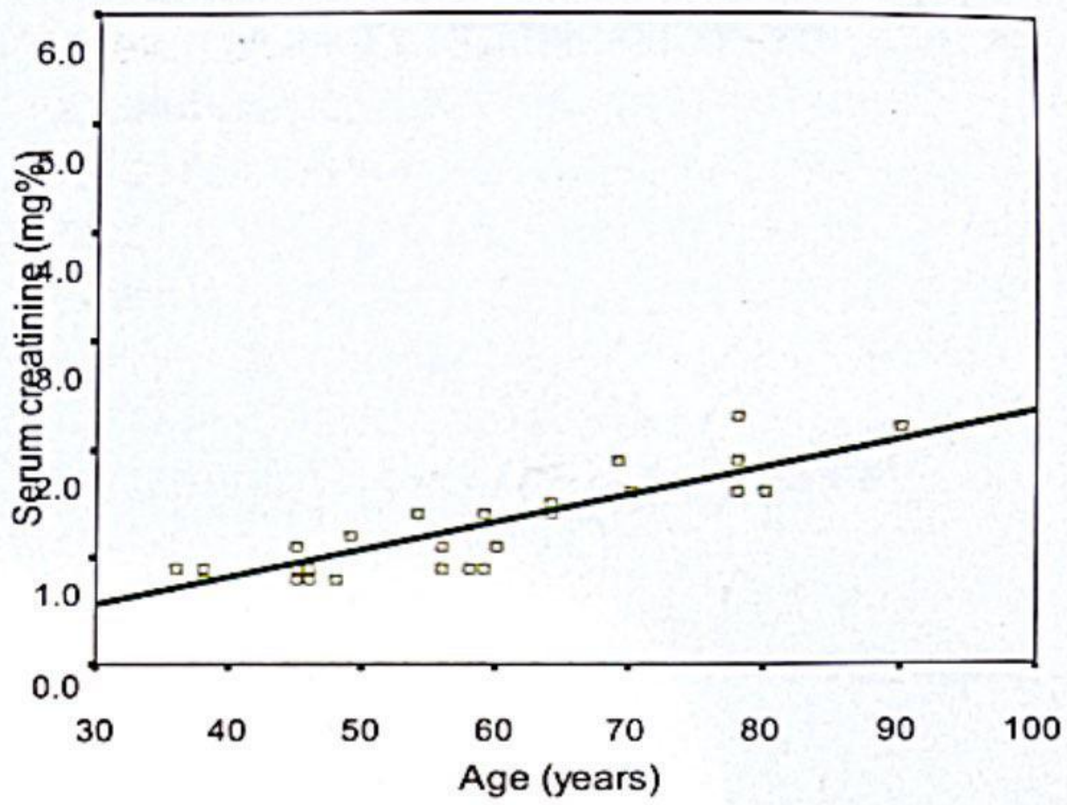


Fig 1: Comparison of HbA1c between microalbuminuria group (n = 120)

Table V. Correlation between microalbuminuria with duration of DM, BMI, HbA1c & serum creatinine

Correlated variables		Correlation coefficients (r)#	p-value
Duration of DM		0.363	<0.001
Body Mass Index	Microalbuminuria	0.295	0.001
HbA1c		0.441	<0.001
Serum creatinine		0.266	0.003



 # Pearson correlations were performed; * Correlation is significant at **0.01 level.**

Fig 2: Correlation between serum creatinine and age (n = 120)

Discussion

Diabetes mellitus has become a major health problem in Bangladesh. Some population-based studies conducted in Bangladesh in different time and have revealed the increasing trends of diabetes prevalence ranging from 1.5 to 3.8% in rural communities[10,11]. Usually the patients are asymptomatic until complications become obvious and among those affected one-third will eventually have progressive deterioration of renal function[12]. Among the diabetics 30% were undiagnosed and 25% already had developed micro-vascular complications at the time of diagnosis[13]. The present study was conducted on a group of One hundred and twenty type-2 diabetic patients with mean age 57.8 ± 14.7 years were evaluated and male to female ratio was roughly 3:1. Near about fifty seven percent had family history of diabetes showing that Type 2 diabetes has a strong genetic component and parental history of diabetes is significantly associated with microalbuminuria.[14] The American Diabetes Association (ADA) recommends screening adults 45 years of age and especially those with BMI 25 Kg/m2. Body mass Index 19–25 is taken as normal, while 25–30 is considered as overweight and BMI 30 is obesity.[15] Weight gain was significantly associated with diabetes[16]. The present study had diabetic patients with mean value of BMI 25.7±6.2

kg/m^2, indicating that the patients were overweight; this overweight could be due to their different dietary habits. The patients included in the study were overweight not obese according to the definition of obesity by ADA[15]. A study on Type 2 diabetes mellitus patients by Mokdad *et al* reported a correlation between obesity and microalbuminuria[17]. The present study also found a significant correlation(r = 0.295, p = 0.001) between microalbuminuria and BMI as shown in Table-5. Blood glucose is a continuous variable, rising and falling about two-fold throughout the day in people without diabetes, and up to some 10-folds in people with diabetes.[18] Earlier studies have reported glycosylated haemoglobin to be used as a diagnostic test for Type-2 Diabetes instead of relying only on fasting blood glucose[18]. In the present study as shown in Table 5 micro-albuminuria has a significant correlation with HbA1c (p<0.001), similar to the study reported by Kassab[19]. The complications of both Type 1 and 2 Diabetes do not develop or progress for 6–9 years when the average HbA1c level is kept at <7%[20]. A higher percentage of patients with microalbuminuria was observed in poor glycemic control group. The frequency of microalbuminuria increased with the increase in duration of diabetes[21]. Microalbuminuria had a highly significant correlation with duration of diabetes p<0.001 as shown in Table-5. Population in the present study had an early onset of microalbuminuria, similar to that reported in an earlier study[21]. In a study on Type 2 diabetic subjects having poor metabolic control a prevalence of microalbuminuria approximates 20% and is associated with components of the metabolic syndrome[19]. Microalbuminuria is related to hyperglycaemia and control of blood glucose level has been shown to prevent the development of nephropathy in Type 1 & 2 diabetes[22]. The measurement of serum creatinine concentration is widely used clinically as an index of renal function[23]. Serum creatinine concentration is widely affected by age, sex, and body weight[23]. Microalbuminuria and serum creatinine increase significantly in Type 2 diabetes as reported in an earlier study[23]. Table V showed the correlations between serum creatinine and microalbuminuria of Type-2 diabetic patients. Serum creatinine concentration were observed to be positively correlated with microalbuminuria (r = 0.266, p = 0.003). The correlation demonstrates that with the increase in age, serum creatinine raise significantly bearing a perfect positive correlation as evident by r = 0.878, p < 0.001 (Figure 2). Serum creatinine measurement is a convenient and inexpensive method of assessing renal function and a consistently elevated level indicates chronic kidney disease, but however some patients have a substantial decrease in glomerular filtration rate, while their serum creatinine concentration remains within the normal range and thus it is a poor screening test for mild kidney disease[24]. A rapid decline in renal function can be predicted for patients having poor glycaemic control and microalbuminuria[25,26]. In adults, a diagnosis of microalbuminuria can precede Type 2 diabetes and is a component of the World Health Organization's definition of the metabolic syndrome[27]. The present study found that a high prevalence of microalbuminuria, a higher BMI and an increase in serum creatinine concentration as age increases in Type 2 diabetic patients belonging to an ethnic group could be of genetic origin. Minimizing microalbuminuria and having a tight glycaemic control is an important treatment goal for patients with diabetes[28].

Conclusion

The screening for microalbuminuria is not yet consistently done in Bangladesh. Being a developing country; there is a dire need that microalbuminuria and HbA1c testing should be done in both, newly diagnosed as well as already diagnosed Type 2 diabetic patients as an early marker of cardiovascular and renal risk factor. Strict glycaemic control, having a healthy lifestyle, maintaining standard body weight is especially important for diabetic patients and for those with a family history of diabetes.

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