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Association between Microalbuminuria and Hypertension in Type 2 Diabetic Patients

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This study aimed to investigate the relationship between microalbuminuria and hypertension in type 2 diabetic patients.
Study Design: It was a descriptive type of cross-sectional study.
Place and Duration of Study: The study was conducted in collaboration at a diabetic clinic and Hypertension and Research Centre, Rangpur, Bangladesh from January to March 2018.
Methodology: A total of 180 diabetic patients were selected purposively age ranges 30-75 years. Anthropometric as well as biochemical measurement was done. Data was collected by a semi-structured questionnaire through face to face interview and analyzed by SPSS-20.
Results: Study subjects were separated into two groups. Group 1, those with normoalbuminuria (n=49) and Group 2, those having microalbuminuria (n=131). The prevalence of microalbuminuria was 72.8%. Group 2 or microalbuminuric patients showed higher blood pressure values (113.50±8.90 mm of Hg) as compared to Group 1 (101.88±9.80 mm of Hg). The results were statistically significant ($P \leq 0.05$). Further this study showed fasting blood sugar, duration of diabetes,

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systolic blood pressure and high level of sCreatinine were independently associated with microalbuminuria in the study subjects. The results were also statistically significant ($P \leq 0.05$).
Conclusion: Our study revealed high prevalence of microalbuminuria in diabetic patients and has an optimistic association with blood pressure. This study suggests the need to screen for microalbuminuria early and the active management of modifiable risk factors in particular fasting blood sugar, sCreatinine, hypertension for intervention and prevention of further complications like end stage renal disease and cardiovascular diseases.

Keywords: Normoalbuminuria; microalbuminuria; macroalbuminuria; hypertension; type 2 diabetes mellitus.

1. INTRODUCTION

A worldwide public health problem is diabetes mellitus (DM) especially type 2 diabetes mellitus (T2DM) [1]. The number of people with diabetes worldwide is projected to increase from 171 million in 2000 to 366 million by 2030. From recent statistics of World Health Organization reveals DM is more prevalent in developing countries. According to the International Diabetes Federation, in Bangladesh the prevalence of DM will be 13% by 2030 which was 9% in 2006 [2]. Hypertension (HTN) is also a worldwide medical and public health problem. In Bangladesh, approximately 20% of adult and 40–65% of elderly people suffer from HTN. High incidence of metabolic syndrome and lifestyle-related factors like obesity, high salt intake, and less physical activity may play important role in the pathophysiology of HTN [3]. In recent year T2DM and HTN are two important public health challenges, and both are linked to increased risk of cardiovascular events. In the diabetic individual HTN markedly increases the risk and precipitates the course of cardiac disease, peripheral vascular disease, stroke, retinopathy, and nephropathy [4]. In most of the T2DM patients may be hypertensive for years preceding to the onset of overt diabetes. About 70-80% patients have HTN at the time of diagnosis of T2DM. Still blood pressure rises further in those patients who subsequently develop diabetic nephropathy (DN) [5].

Diabetic nephropathy is an important cause of end stage renal disease (ESRD) worldwide [6]. It also responsible for a third of all patients requiring renal replacement therapies, The most important causes for the development of DN are progressive increase in the excretion of protein, particularly albumin, an early and continuing rise in systolic blood pressure (SBP), and a late decline in glomerular filtration rate (GFR), leading eventually to end stage renal failure. SBP may be particularly important and in the UKPDS (United Kingdom Prospective Diabetes Study), higher blood pressure (HBP) was associated with a higher risk of macro vascular and micro vascular disease [7]. HTN and Microalbuminuria commonly coexist. The mechanism is still controversial. But it is thought to be a renal manifestation of generalized vascular endothelial dysfunction and strongly linked with increased cardiovascular risk. It is well appreciated both that coexisting hypertension exacerbates DN and that DN somehow results in a markedly increased risk of HTN [6]. Microalbuminuria is a marker of the increase of cardiovascular disease [7]. In addition to, microalbuminuria is the first clinical detectable sign of DN and is considered as an independent predictor of DN [8]. National Kidney Foundations (NKF), defines microalbuminuria as excretion of 30-300 mg of albumin in a 24 hour urine collection sample (equivalent to albumin creatinine ratio (ACR) 30-300 mg/g without regard to age & sex in a random or spot sample of urine), on the other hand with values >300 mg/24 hour being defined as macroalbuminuria (equivalent to (ACR) > 300 mg/g without regard to age & and sex in a random or spot sample of urine [9,10]. Microalbuminuria is also characterized by increased prevalence of arterial hypertension, proliferative retinopathy, and peripheral neuropathy [11]. In T2DM patients prevalence of microalbuminuria ranges from 8-47% [12,13]. Studies in the Western literature have documented the linear relationship of degree of microaluminuria with body mass index (BMI), blood pressure (BP), and duration of diabetes. Gender correlation of microalbuminuria was not seen in T2DM [10,14].

According to the American Diabetes Association (ADA) patients with T2DM are tested for albuminuria at the time of preliminary diabetes diagnosis and yearly afterward [15]. It can help to prevent more severe renal involvement. Blood pressure control is at least as important as glucose control, especially after the onset of

renal damage [16]. The present study was aimed to determine the prevalence of microalbuminuria in T2DM patients as well as to see the correlation between microalbuminuria and hypertension in those diabetics and its association with other risk factors.

2. MATERIALS AND METHODS

2.1 Place of the Study

The study was conducted in collaboration at an outdoor-based diabetic clinic, Rangpur Diabetic Association (RDA) and Hypertension and Research Centre, northern Bangladesh.

2.2 Study Population

Patients with T2DM of duration four years or more attending both at RDA and HTRC were included in this study. The inclusion criteria of the study subjects were: a) Adult subjects (male and female) aged 30-75 years. b) Subjects with both abnormal and normal blood glucose level, c) Subjects voluntarily agreed to participate in the study, and d) Subjects who have history of Diabetes mellitus either hypertensive or not. Exclusion criteria were: Diabetic patients suffering from any other medical problem like chronic heart disease, renal and liver diseases such as history of ischemic heart disease; history of renal disease or disturbed blood Urea Nitrogen (BUN); history of liver disease such as hepatitis B or C positive or disturbed liver function tests, urinary tract infection, acute febrile illness, menstruation or vaginal discharge. Besides, those subjects involved exercise within 24 hours, having marked hyperglycemia, marked hypertension and high protein diet were excluded from the study. Further, pregnant subjects were excluded in the study.

2.3 Study Design

This descriptive type of cross-sectional was carried out 1st January to 30th March 2018 to investigate the correlation between microalbuminuria and hypertension among T2DM patients.

2.4 Sample Size and Sampling Technique

2.4.1 Sample size determination

Sample size was determined by using following formula:

$n=z^2pq/d^2$

Here, n=sample size
z=standard normal deviation, the value is 1.96 at 95% confidence level
p= Estimated prevalence rate of micralbumnuria was 41.0% [16].
p=0.41
q= Estimated non-prevalence rate was 59.0%
= 1-p
=1-0.41=0.59
d=degrees of precision or allowable error. Here we set it at 5%
d=5% =0.05

So, our sample size, $n = \frac{z^2 \times p \times q}{d^2} = (1.96^2 \times 0.41 \times 0.59)/0.05^2$

$=371.71 \cong 372$

However, due to time and resources constraint, 180 T2DM patients were enrolled in the study as a sample. The selection of this study subjects was purposive.

2.5 Measurement

BP was recorded for each patient. BMI was calculated as weight (Kg) divided by height (m^2). BP was measured using Barometric Sphygmomanometer. It was measured in sitting position, with calf at the level of the heart. After 10 minutes of rest a second reading was taken and average was recorded. Recorded Korotkoff sound I (the first sound) and V (the disappearance of sound) denoted the SBP and DBP [1]. The mean arterial pressure (MAP) is defined as an approximation of a time-weighted average of blood pressure values in large system arteries during the cardiac cycle. It was calculated using following equation.

MAP= 1/3 * SBP + 2/3 * DBP

High blood pressure or hypertension was defined as SBP of ≥140 mm (Hg) and DBP of ≥90 mm (Hg) or use of anti-hypertensive medications [1]. Blood samples were obtained for test of serum glucose, serum creatinine. All assays were performed according to the guideline of the manufacturers. Fasting blood sugar (FBS) was measured by enzymatic colorimetric (GOD-POD) method in the Humalyzer 3000. Estimation of creatinine was done by modified Jaffe method in the humalyzer 3000 using reagents Randox CREA R1a and R1b.

Morning urine sample was used to calculate albumin to creatinine ratio (ACR) in mg/g. Micro albumin was carried out using ELISA assay whereas creatinine was done by calorimetric methods using Fortress kit. This test was funded by National Science and Technology (NST) Fellowship Scheme, Bangladesh. If the ACR was <30 mg/g, the patient was normoalbuminuric, ratios between 30-300 mg/g were indicative of microalbuminuria and above 300 mg/g revealed macroalbuminuria.

2.6 Data Collection Tools and Technique

A semi-structured questionnaire was used as a data collection tools regarding the demographic data such as age, gender, height, body weight while wearing light weight clothing, without shoes and family history of DM, habit of smoking. Data were collected through face to face interviewing technique.

2.7 Statistical Analysis

Data were analyzed using SPSS-20 (Chicago, IL, USA). Results are presented as mean ± standard deviation (SD) for continuous variables, and as frequencies and proportions for categorical variables*;* Independent *T*-test was used for continuous variables. Both the univariate and multivariate analysis was done to measure the association between dependent and independent variables. A *P*-value of 0.05 or less than 0.05 was used as a level of significance with a 95% confidence level.

2.8 Ethical Issues

Study was approved by the institutional ethics committee and written informed consent was taken from all the patients.

3. RESULTS

3.1 Prevalence of Microalbuminuria among Study Subjects

Out of 180 DM patients 27.2% (49) and 72.8% (131) were normoalbuminuric and microalbuminuric respectively.

Patients were divided into two Groups: Group 1 or Normalbuminuric: (n=49; those patients with ACR <30 mg/g) and Group 2 or Microalbuminuric (n=131; those patients with ACR between 30-300 mg/g) for comparison.

3.2 Baseline Characteristics of Normoalbuminuric (Group 1) and Microalbuminuric (Group 2)

A total of 180 patients, 79 males and 101 females, were included in the study. In group 1, 27.1% and in group 2, 72.9% had positive family history of DM. The mean age and BMI was higher among group 2 or microalbuminuric than Group 1 or normoalbuminuric. But there was no significant statistical difference in case of age (Group 1:55.71±9.58; Group 2: 54.31±8.83), BMI (Group1:23.38±3.79k g/m²; Group 2:24.14±3.68 kg/m²) between these two group. Age at onset of DM (Group 1:47.62±10.07; Group 2:47.05±9.03) between two groups also statistically insignificant (Table 2). Mean FBS in group1 was 7.37±3.37 (mmol/L) while in group 2 it was 9.9±2.71 (mmol/L). These results were statistically significant (Table 2). Mean sCreatinine in group 1 was 91.05±32.71 (µmol/L) while in group 2 it was 175.03±38.90 (µmol/L) as well as mean duration of DM were 6.51±3.90 years and 8.49±4.06 years in group 1 and group 2 respectively. These results were also statistically significant (Table 2).

3.3 Difference of Blood Pressure between Two Groups

The two groups were also assessed for difference of BP that included SBP, DBP and MAP. Group 2 or microalbuminuric showed higher MAP than group 1 or those with normoalbuminuric that was statistically significant (*P*<0.05). Similarly group 2 showed mean diastolic pressure (MDP) and mean systolic pressure (MSP) higher than group 1 as evidenced by *P*<0.05 that was again statistically significant. These results showed significant statistical difference (*P*-value≤0.05). So, microalbuminuric had higher BP values as compared to normoalbuminuric patients [Table 3].

Table 1. Prevalence of microalbuminuria among study subjects

Albuminuria status	Frequency	Proportion (%)
Normoalbuminuric (<30mg/g)	49	27.2
Microalbuminuric (30-300mg/g)	131	72.8

3.4 Multiple Logistic Regression Analysis

Table 4 shows the univariate and multivariate analysis using microalbuminuria as the dependent variable as well as age, duration of diabetes, FBS, SBP, DBP, sCeratinine as the independent variables. By univariate analysis, duration DM (*P*= 0.005), FBS (*P*= 0.002), sCreatinine (*P*= 0.002), SBP (*P*= 0.000), and DBP (*P*= 0.000) were found to be significantly associated with microalbuminuria, in T2DM patients. After incorporating all significant (p<0.05) and non-significant variables in the univariate analysis, multivariate logistic regression was performed to identify risk factors independently associated with microalbuminuria. According to multivariate analysis, duration of DM (adjusted OR =1.149, CI: 1.013-1.281), FBS (adjusted OR= 0.887, CI: 0.790-0.995), sCreatinine (adjusted OR = 0.352, CI: 0.148-0.837), SBP (adjusted OR = 1.084, CI: 1.037-1.132) were independently associated with microalbuminuria (Table 4).

Table 2. Baseline characteristics of two groups

Variables	Group1	Group 2	*P*-value
Sex(n=180)			
Male=79	20(25.3%)	59(74.7%)	-
Female=101	29(28.7%)	72(71.3%)	
Age in years	55.71±9.58	54.31±8.83	0.356
BMI in kg/m²	23.38±3.79	24.14±3.68	0.224
Duration of DM in years	6.51±3.90	8.49±4.06	0.004
Age at onset of DM in years	47.62±10.07	47.05±9.03	0.626
FBS(mmol/L)	7.37±3.37	9.9±2.71	0.001
sCreatinine(µmol/L)	91.05±32.71	175.03±38.90	0.030
Family history of DM			
Yes	9(27.1%)	51(72.9%)	
No	30(27.3%)	80(72.7%)	-
Smoking habit			
Yes	2(11.1%)	16(88.9%)	-
No	47(29.0%)	115(71.0%)	

**All values were expressed as Mean±SD except sex and family history of DM, habit of smoking; Independent T-test; FBS: Fasting Blood Sugar, DM: Diabetes Mellitus; P≤0.05 was considered statistically significant*

Table 3. Difference of blood pressure between two groups

Variables	Group 1	Group 2	*P*-value
SBP (mm of Hg)	123.57±14.21	141.30±15.56	0.008
DBP (mm of Hg)	82.65±5.41	89.16±7.52	0.022
MBP (mm of Hg)	101.88±9.80	113.50±8.90	0.030

**All values were expressed as Mean±SD; Independent T-test; P≤0.05 was considered statistically significant*

Table 4. Univariate and multivariate regression analyses using microalbuminuria as the dependent variable

Factors	COR(95%CI)	*P*-value	AOR(95% CI)	*P*-value
Age	0.983(0.948-1.019)	0.354	1.013 (0.968-1.061)	0.568
Duration of DM	1.151(1.043-1.270)	0.005*	1.149(1.013-1.281)	0.012*
FBS	0.857 (0.779-0.943)	0.002*	0.887(0.790-0.995)	0.041*
sCreatinine	0.460 (0.216-0.977)	0.043*	0.352 (0.148-0.837)	0.018*
SBP	1.095(1.059-1.131)	0.000*	1.084(1.037-1.132)	0.000*
DBP	1.159(1.090-1.232)	0.000*	1.032(0.948-1.123)	0.473

**Statistically significant at ≤0.05 significance level, COR: Crude Odd Ratio; AOR: Adjusted Odd Ratio.*

4. DISCUSSION

The incidence of diabetes mellitus is significantly rising in last few decades [17]. This current global epidemic is associated with an increase of cardiovascular diseases that primarily accounts for the increase in morbidity and mortality seen in patients with diabetes [18,19]. This cross-sectional study presents data on prevalence and associations of microalbuminuria with various parameters inT2DM patients. Present study has shown prevalence of microalbuminuria at 72.8%, which is much higher when compared to the study by Ghai et al., Abougalambou et al. and Chowta et al. where prevalence was reported at 25% 25.4% and 37% respectively [20,21]. Studies in the white UK population revealed a prevalence of microalbuminuria of 7%–9% [22,23], while in Mexican Americans, it was 31% [22]. Pima Indians 26%, Nauruans and Hispanic Americans 35% [24-26]. In the present study, higher prevalence may be due to the fact that most of the patients were on irregular treatment with high FBS level and also may be due to the small sample size. Method of estimation of microalbuminuria as well as ethnical differences, method of urine collection, etc would have also played a role in giving higher prevalence in the present study. The level of blood glucose level seems to be the strongest factor influencing transition from normoalbuminuria to microalbuminuria [27].

A well-known United Kingdom prospective diabetes study (UKPDS) reported that the presence of hypertension is a risk factor for microalbuminuria and that reducing the incidence of chronic complications was significantly associated with the amplitude of SBP decrease, the lowest risk corresponding to a SBP below 120 mm(Hg) [5] which was also support our study. In our study, those with microalbuminuric had higher SBP, DBP and MAP than those were in normoalbuminuric and there was a statistically significant difference in case of these variables (P=0.008, P=0.022, P=0.30) between these two group. These result of our study similar to the study conducted in Lahore, Pakistan among T2DM patients where microalbuminuric had higher SBP, DBP and MAP than those were in normoalbuminuric that was statistically significant (P=0.001, P=0.001, P=0.001) [8].

Some studies have revealed duration of DM, male sex, and pre-existing retinopathy as major risk factors for microalbuminuria [28,29]. John et al. [30] reported male sex, older age, longer duration of diabetes, poor glycaemic control, and raised blood pressure as risk factors of microalbuminuria while Vijay et al. [31] reported duration of diabetes, systolic and diastolic blood pressure, age of the patient, and serum creatinine to be associated with proteinuria. Age was reported as one of the risk factors in the Wisconsin study which was comparable to our study [32]. The result of our study revealed that duration of DM, SBS, FBS and high level of serum creatinine were independently associated with microalbuminuria. But there was no significant association with age and DBP.

The limitations of our study must be further considered. As our study was not based on the general population and selection bias might have affected the outcome of the study. Larger sample size in general population may be required to confirm the results of the present study.

5. CONCLUSION

Our study revealed high prevalence of microalbuminuria in diabetic patients and has an optimistic association with BP. This study suggests the need to screen for microalbuminuria early and the active management of modifiable risk factors in particular FBS, sCreatinine, hypertension in T2DM for intervention and prevention of further complications like end stage renal disease and cardiovascular disease.

CONSENT

All authors declared that written informed consent was obtained from the patient (or other approved parties) for publication of this research article.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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