Original Article

Association of normoalbuminuria and microalbuminuria with the components of metabolic syndrome in Bangladeshi adults

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Abstract

Background: *Metabolic syndrome (MetS) is clustering of metabolic abnormalities characterized by obesity, hypertension, dyslipidemia and glucose intolerance that collectively increases the risk of diabetes mellitus, cardiovascular disease, stroke and overall mortality. Microalbuminuria is associated with diabetes mellitus, hypertention, obesity all are components of metabolic syndrome. Microalbuminuria and MetS have both been linked to chronic kidney disease and cardiovascular disease. Before development of microalbuminuria there is a wide normal range for urinary albumin excretion. By comparing the strength of the association between MetS and its components with normoalbuminuria and microalbuminuria, we can assess the risk of cardiovascular and renal diseases. This study aimed to evaluate the association of normoalbuminuria and microalbuminuria with the components of MetS in Bangladeshi adult subjects.*

Methods: *It was a cross-sectional analytical study, carried out in the Department of Biochemistry of Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh during the period of March 2017 to January 2018. Total 175 patients with MetS attending the outpatient department of Medicine and Endocrinology of Mitford Hospital were included. Collected data was checked, edited and analyzed with the help of software SPSS (Statistical Package for Social Sciences) version 22.*

Results: *This study showed, among the total 175 study subjects, 125 subjects were with normoalbuminuria (71.43%) and 50 subjects had microalbuminuria (28.57%). With an average age 42.4 years, female were 52% in this study. There was also female predominance among microalbuminuric subjects (13.71% vs 14.75%). Participants with microalbuminuria were more likely to have higher systolic blood pressure (SBP), diastolic blood pressure (DBP) and fasting blood glucose (FBG) than those with normoalbuminuria. The albumin creatinine ratio (ACR) of study subjects ranged from 3.00 to 270.39 mg/g and mean ACR was 27.14 mg/g. The mean ACR for participants with three (n=34), four (n=72) and five (n=69) components of MetS were 14.73, 19.94 and 40.77 mg/g respectively and corresponding prevalence of microalbuminuria was 10%, 32% and 58% respectively. Normal range of urinary albumin excretion rate (normoalbuminuria) were classified into four quartiles according to their ACR values and ranges for Q1, Q2, Q3 & Q4 were respectively Q1 = 3.00 to 5.1, Q2 = 5.1 to 8.2, Q3 = 8.2 to 13.89, Q4 = 13.89 to 28.1mg/g. The means of elevated DBP, SBP, FBG and tri-acyl glycerol (TAG) among the components of MetS showed increasing trend from lower to upper quartiles within normal range. Q1 was considered as base line in comparison to other quartiles. Odds of elevated WC, FBG, TAG, BP and low HDL-C were high across increasing quartiles of ACR (1.00 vs 1.33 vs 2.24 vs 1.79*

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respectively for central obesity; 1.00 vs 1.07 vs 1.97 vs 2.07 respectively for elevated fasting blood glucose; 1.00 vs 1.51 vs 1.69 vs 1.69 respectively for elevated TAG; 1.00 vs 6.86 vs 3.87 vs 2.88 respectively for elevated BP and 1.00 vs 1.35 vs 2.79 vs 2.79 respectively for low HDL-C; p-values <0.05 for all). Among the components of MetS, most significant relationship was observed between elevated BP and increasing ACR quartile within normal range.

Conclusions: *In conclusion, we demonstrated that microalbuminuria was strongly associated with MetS and its components. Microalbuminuria should be reconsidered as a component of MetS as it shows incremental effect with severity of MetS. Even upper normal range of albuminuria (higher normoalbuminuria) is strongly associated with elevated BP, FBG and TAG among the components of MetS. So, normal range of albuminuria should be rearranged after performing large scale population study in this regard.*

Key words: *Metabolic syndrome, albumin creatinine ratio, fasting blood glucose, high density lipoprotein, waist circumference.*

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Introduction

Metabolic syndrome (MetS) is a clustering of metabolic abnormalities characterized by obesity, hypertension, dyslipidemia and glucose intolerance that collectively increases the risk of diabetes mellitus, cardiovascular disease, stroke and overall mortality.[1,2] According to International Diabetes Federation (2006) approximately 20–25% of the world's adult population have metabolic syndrome. An increasing trend has also been observed in Asian countries.[3] Epidemiological studies showed an increased rate of MetS both in urban and rural areas in Bangladesh and this might be an important contributory factor for the increased prevalence of type 2 diabetes (T2DM) and cardiovascular disease in the Bangladeshi population.[4,5] The International Diabetes Federation estimated that 5.1 million people living in Bangladesh had diabetes in 2013.[6]

Microalbuminuria, defined as a urinary albumin-creatinine ratio (UACR) of ≥30 mg/g of creatinine, originally has been used as an early warning sign of chronic kidney disease and diabetic nephropathy.[1] Additionally, it has been known as a useful predictor of cardiovascular events in adults.[7,8] In light of these reports, it has been suggested that microalbuminuria screening should be added to the assessment of the cardiovascular disease risk profile, in addition to lipids and blood pressure.[7]

The prevalence of microalbuminuria varies widely from 5% to 40% among non-diabetic persons who have essential hypertension.[9] The prevalence of microalbuminuria in people who have type 2 DM is about 20% and it affects about 30% of people who have type 2 DM and older than age 55.[10]

Several epidemiological studies have been conducted globally to determine the relationship between microalbuminuria and MetS by an early morning or random spot urine sample and a significant positive correlation was found between them.[11-13] However, studies on the association between various components of MetS and microalbuminuria to some extent were conflicting. A positive correlation was reported between microalbuminuria and elevated blood pressure, reduced high density lipo-protein (HDL-c), elevated tri-acyl glycerol (TG)– in a cross sectional study among United States (US) adults[14] whereas another national survey in US adults revealed that among all MetS components blood pressure and fasting blood glucose (FBG) demonstrated a strong association with microalbuminuria. A study in Japan among general population reported a positive association between microalbuminuria and high fasting blood glucose, high blood pressure, obesity among MetS components.[15] However two other studies in China demonstrated that microalbuminuria was associated with all components of the MetS.[16,17] Another study in China identified both microalbuminuria and higher normal value of 24 hour urinary albumin excretion as stronger risk factor for MetS.[18] They concluded from their study findings that prevalence of MetS and its components were increased even in normal range of albuminuria (normoalbuminuria). There is limited information regarding the relationship of normoalbuminuria and microalbuminuria with the components of MetS in our population. This study has been designed to evaluate the association of normoalbuminuria and microalbuminuria with the components of MetS in Bangladeshi adult subjects with MetS.

Methods

It was a cross-sectional analytical study carried out in the Department of Biochemistry of Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh during the period of March 2017 to January 2018. One hundred and seventy-five subjects who fulfilled the modified The United States National Cholesterol Education Programme Adult Treatment Pannel- III (NCEP ATP III) criteria for MetS within the age range of 19 to 59 years were included. Sociodemographic as well as other relevant data were taken and recorded in data collection sheet with prefixed questionnaire, after taking necessary approval from institutional ethical committee and informed written consent from study subjects. Blood was collected from antecubital vein after all aseptic precautions. Five ml of venous blood was taken by sterile disposable syringe. One ml of collected blood was taken in a test tube coated with dried sodium fluoride and plasma was separated after centrifugation at 3000 rpm for five minutes. The remaining 4 ml blood was taken in a clean and dry test tube without anticoagulant and kept 30 minutes for clot formation. Plasma and serum were taken in labeled ependroff. FBG was measured on the day of collection. Fasting lipid profile was measured after storing at 2-8ºC and batch analysis was done within a week. In duplicate labeled ependroff serum was preserved at -70 ºC for future analysis. Five ml spot urine sample was collected in a test tube from each study subject after giving instruction for taking midstream urine properly. The study subjects were instructed neither to take excess fluid nor doing excess exercise before giving urine. Urine was then preserved at 2-8ºC for batch analysis within a week. In a duplicate labeled ependroff, urine was preserved at -70ºC for future analysis.

Collected data was checked, edited and analyzed with the help of software Statistical Package for Social Sciences (SPSS) version 22. Categorical values were expressed as percentage and continuous data were expressed as mean (±SD). Unpaired student t-test was performed to show any significant difference between the mean values. Then continuous values of the components of MetS were converted into categorical values as defining criteria for MetS. Logistic regression analysis was done to show the relationship of microalbuminuria with the components of MetS. After dividing the values of ACR within normal range into four quartiles, Odds ratio of each component of MetS was estimated at 95% confidence level and 5% level of significance to show their risk in normal range of ACR quartiles. The p value of <0.05 was considered statistically significant.

Results

One hundred and seventy five subjects were included in this study with mean age 42.4(±8.11) years and majority were (52%) female. Base line characteristics of the study subjects were shown in table I and their status of albuminuria were demonstrated in table II.

Table I Base line characteristics of the study subjects

	Mean (± SD)
Age (years)	42.4 (± 8.11)
BMI (kg/m^2	27.32 (±3.40)
WC (cm)	93.937 (±7.1198)
SBP (mmHg)	136.5 (±21.91)
DBP (mmHg)	88.3 (± 10.1)
FBG (mmol/L)	9.38 (± 3.28)
TAG (mg/dl)	197.69 (± 80.652)
HDL-C (mg/dl)	37.33 (± 6.013)
UcrC (mg/dl)	182.6 (± 96.101)
UAC (mg/L)	45.942 (± 55.591)
ACR (mg/g)	27.147 (± 38.149)

BMI- body mass index, WC- waist circumference, SBP- systolic blood pressure, DBP – diastolic blood pressure, FBG- fasting blood glucose, TAG- tri-acylglycerol, HDL-C-high density lipoprotein cholesterol, UAC- urinary albumin concentration, UcrC- urinary creatinine concentration, ACR- albumin creatinine ratio.

Table II Albuminuric status of the study subjects (N=175)

	Sex		Total
	Male	Female	
Normoalbuminuria	60 (34.28%)	65 (37.14%)	125 (71.43%)
Microalbuminuria	24 (13.71%)	26 (14.85%)	50 (28.57%)

Mean (±SD) of anthropometric and biochemical parameters of study subjects between the groups with

microalbuminuria and normoalbuminuria were shown in table III. Statistically significant difference was observed for elevated blood pressure and fasting blood glucose between these two groups.

Means of components of MetS in ACR quartiles within normal range were demonstrated in table IV. Subjects with normoalbuminuria were classified into four categories according to their ACR values with cut off values for quartiles were 5.1, 8.2 and 13.88 mg/g of ACR respectively for Q1, Q2 and Q3 (Q1 = 3.00 to 5.1, Q2 = 5.1 to 8.2, Q3 = 8.2 to 13.89, Q4 = 13.89 to 28.1mg/g) .Means of elevated DBP, SBP, FBG and TAG were found increasing in upper ACR quartiles within normal range.

Table III Characteristics of participants according to status of microalbuminuria (n=175)

	Microalbuminuria		P-values
	Yes	No	
No. of subjects	50	125	
Age (years)	44.30 (1.16)	41.77 (0.71)	>0.05
WC (cm)	94.96 (1.05)	93.64 (0.62)	>0.05
SBP (mmHg)	145.8 (3.30)	132.14 (1.80)	<0.01
DBP (mmHg)	92.18 (1.57)	86.61 (0.85)	<0.01
FBG (mmol/L)	10.60 (0.49)	9.01 (0.27)	<0.05
TAG (mg/dl)	215.34 (16.43)	190.15 (5.41)	>0.05
HDL-C (mg/dl)	37.94 (0.93)	37.22 (0.53)	>0.05
UAC (mg/L)	109.58 (8.75)	20.49 (2.08)	<0.01
UcrC (mg/dl)	184.00 (15.33)	182.17 (8.16)	>0.05
ACR (mg/g)	69.28 (7.10)	10.29 (0.60)	<0.01

Table IV Characteristics of the study subjects according to ACR quartiles within normal range (n=125)

	Q1	Q2	Q3	Q4
No. of participants	31	32	31	31
Age (years)	41.28 (1.48)	41.29 (1.46)	41.45 (1.43)	43.06 (1.37)
WC (cm)	95.00 (1.07)	92.87 (1.15)	92.64 (1.16)	94.09 (1.57)
SBP(mmHg)	122.09(2.59)	133.03 (3.02)	135.97 (3.77)	133.51 (4.33)
DBP (mmHg)	82.42 (1.31)	87.64 (1.57)	87.90 (1.38)	88.54 (2.19)
FBG (mmol/L)	8.27 (0.52)	8.67 (0.52)	9.26 (0.65)	9.70 (0.50)
TAG (mg/dl)	184.8 (9.55)	185.18(11.32)	196.60 (5.2)	197.06(10.51)
HDL-C (mg/dl)	38.35 (1.12)	35.43 (1.09)	36.16 (0.82)	37.7 (0.92)
UAC (mg/L)	9.29 (2.64)	11.18 (1.02)	18.35 (1.89)	43.41 (5.99)
UCrC(mg/dl)	184.47 (10.2)	169.65(15.14)	169.17 (15.99)	205.77(21.77)
ACR (mg/g)	3.73 (0.15)	6.59 (0.17)	10.82 (0.29)	20.13 (0.83)

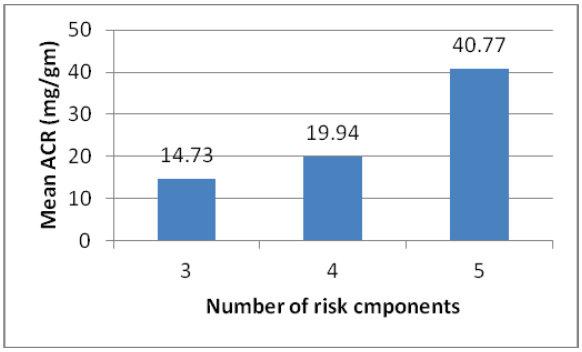

Figure 1(a) Showed mean ACR according to number of components of MetS

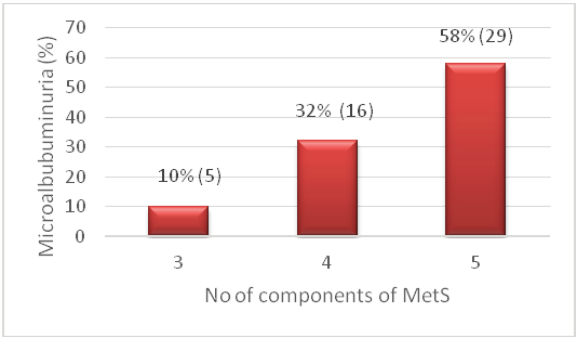

Figure 1(b) Showed Prevalence of microalbuminuria along with increasing number of components

Association between the components of MetS and microalbuminuria was shown in table V by setting up a binary multivariate logistic regression model after adjusting for age and sex. Normoalbuminuria was considered as base line. Risk of microalbuminuria for each components of MetS was expressed as OR (odds ratio). Odds ratio of microalbuminuria was significantly high for all the components of Mets except for raised WC and low HDL-c.

Association between each component of MetS in comparision to Q1with other quartiles within normal range had illustrated in table VI. Association was express by Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). Q1 was considered as base line in comparison to other quartiles. Odds of elevated WC, FBG, TAG, BP and low HDL-C were found high across increasing ACR quartiles. Among the components of MetS most significant relationship was observed between elevated BP and increasing ACR quartile within normal range.

Table V Logistic regression between microalbuminuria and components of MetS and adjusted OR with 95% CI

	No of cases	Coefficients	CI of Coefficients	P value	Odds ratio	CI of OR
WC	152	0.48	-0.70 , 1.66	>0.05	1.61	0.49 , 5.26
FBG	168	0.91	0.28 , 3.10	<0.01	2.49	0.29 , 22.28
TAG	134	0.51	-0.34 , 1.34	<0.05	1.66	0.72 , 3.86
HDL-C	155	0.07	-1.02 , 1.17	>0.05	1.07	0.36 , 3.24
BP	125	1.62	0.61 , 2.64	<0.01	5.07	1.84 ,13.98

(Model adjusted for age and sex.)

Table VI OR with 95% CI of components of MetS according to ACR quartiles within normal range (n=125)

	Q1	Q2	Q3	Q4
		OR (95% CI)	OR (95% CI)	OR (95% CI)
WC	1.00	1.33 (0.27 - 6.51)	2.24 (0.51- 9.91)	1.79 (0.39 - 8.27)
FBG	1.00	1.07 (0.14 - 7.84)	1.97 (0.13 - 7.59)	2.07 (0.18 - 24.07)
TAG	1.00	1.51 (0.51 - 4.46)	1.69 (0.67 - 4.64)	1.69 (0.67 - 4.64)
HDL-C	1.00	1.35 (0.33 - 5.56)	2.79 (0.50 -15.62)	2.79 (0.50 - 15.62)
BP	1.00	6.86 (2.18 - 21.55)	3.87 (1.34- 11.17)	2.88 (1.03 - 8.07)

Discussion

MetS, a disorder of energy utilization and storage, is a serious public health challenge in Bangladesh and worldwide. Several studies found that microalbuminuria is related with obesity, hypertension and diabetes, all are components of metabolic syndrome.[19,20] Recent studies showed positive association between MetS and its related components with microalbuminuria as well as normal range albuminuria. In present study 175 subjects who fulfilled the predefined enrollment criteria, 91 (52%) were female and 84 (48%) were male with average age 42.4 (±8.11) years and BMI 27.32 (±3.40) kg/m^2, had been investigated to find out the association of MetS and its components with both microalbuminuria and normoalbuminuria in our country.

Among the study subjects 28.57% were microalbuminuric. This result was consistent with a study carried out in Pakistan by Latif and Zafar[21] who found the frequency of microalbuminuria as 26.06% among patients with MetS. However, in a study conducted among Chinese population by Sheng et al.[12] reported overall prevalence of microalbuminuria as 12% among MetS. In this study prevalence of microalbuminuria were 13.71% vs 14.85% in male and female subjects respectively. It was consistent with a study in Korea where prevalence of microalbuminuria among Mets were 11% vs 14.4% among male and female respectively.[22] However, Li et al.[23] in China reported higher prevalence of microalbuminuria in male (48.2%) than female (36.2%) subjects with MetS.

In this study, subjects with microalbuminuria were older than those with normoalbuminuria (44.30±1.16 vs 41.77±0.71 years). Participants with microalbuminuria were more likely to have significantly higher SBP, DBP and FBG than those with normoalbuminuria. However, TAG and HDL-C did not differ significantly in subjects with microalbuminuria as compared to normoalbuminuria. These findings have similarity with the observation of the study among Chinese population by Ge, et al.[18] However, another study in China by Li, et al.[23] among aged population showed subjects with microalbuminuria also had lower levels of HDL-C.

The range of ACR of the study subjects was 3.00 to 270.39 mg/g with an average of 27.14 mg/g. Subjects with normoalbuminuria were classified into four categories according to their ACR values. Mean values of elevated DBP, SBP, FBG and TAG were increased across the increasing ACR quartiles within normal range. This observation was in agreement with two studies in China.[18,24] However, the latter investigators used 24 hour urinary albumin excretion (UAE) instead of ACR for categorizing the study subjects. In this study, subjects within higher ACR quartile had higher levels of SBP and DBP compared with the subjects in lower ACR quartile. Activation of renin angiotensin system (RAS) can explain the higher values of SBP and DBP in upper ACR quartile. The RAS activation, resultant oxidant stress and inflammation, might be responsible for microalbuminuria.[24]

It was observed from the study that both prevalence of microalbuminuria and mean ACR significantly increased with the increasing number of components of MetS. This observation was supported by several studies suggesting that higher ACR had association with severity of MetS.[13,15,23,24]

Adjusted Odds ratios (OR) of elevated BP, FBG and TAG were found to be significantly higher among participants with microalbuminuria than those with normoalbuminuria in this study which is in agreement with other studies with few variations. Sheng, et al.[12] found strong association between microalbuminuria with FBG and BP after adjusting for covariates. However, Ge, et al.[18] found strong association with elevated WC, BP and TAG, but not with FBG in Chinese adults. Third National Health and Nutrition Examination Survey conducted on US civilians found stronger OR for FBG and BP indicating even mild elevation of FBG and BP were associated with microalbuminuria.[14]

It was also observed that the ORs of central obesity, elevated FBG, TAG, BP and low HDL-C remained high across increasing quartiles of ACR within normal range. Among the components of MetS most significant relationship was observed between elevated BP and increasing ACR quartile within normal range. These findings were consistent with those of Ge, et al.[18] except for elevated FBG and low HDL-C. Moreover, several studies showed significant association between normal range ACR and hypertension.[13,26] Possible explanation behind this finding might be causal relationship of some components of MetS with albuminuria like obesity, glucose intolerance and hypertension individually and normal reference range for albumin excretion is quite large.

Conclusion

This present study finding demonstrates association of microalbuminuria with elevated BP, FBG and TAG among five defining components of MetS. Microalbuminuria is also prevalent among severely affected MetS subjects. Importantly significant association of all components of MetS was observed within normal range of albuminuria across increasing ACR quartiles.

Recommendation

As the study conducted in a single center and sample size was small, so large scale population study is required to rearrange the normal reference range for albuminuria.

Conflicts of interest: Nothing to declare.

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