Prevalence of Microalbuminuria and its Association with Left Ventricular Hypertrophy (LVH), Ischemic Heart Disease (IHD), Retinopathy, and Stroke in Hypertension

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Abstract

Background:
Hypertension is a growing issue of public health problem of the adult population in both developed as well as developing world, is a serious medical condition that significantly increases the risks of heart, brain, kidney, and other diseases. There is a strong association between Microalbuminuria (MA) and hypertension. Microalbuminuria (MA) is the independent risk factor for developing cardiovascular and cerebrovascular morbidity and mortality in hypertension, suggesting that microalbuminuria (MA) could be a useful marker to assess the risk management of cardiovascular disease and renal disease.

Objective:
To assess the frequency of microalbuminuria in hypertension and to evaluate its association with left ventricular hypertrophy (LVH), ischemic heart disease (IHD), retinopathy, and stroke.

Methods:
This cross-sectional descriptive study was conducted at the Hypertension & Research Centre, Rangpur from January 2010 to January 2012. A total of 75 hypertensives without diabetes mellitus and/or other conditions causing microalbuminuria were purposively selected. Urine albumin was assessed and microalbuminuria was defined as albumin excretion between 20-200 microg/min. The relationship of microalbuminuria with the duration, severity, body mass index (BMI), lipid profile, and target organ damage (TOD) like left ventricular hypertrophy (LVH), ischemic heart disease (IHD), hypertensive retinopathy, and stroke was assessed by univariate analysis.

Results:
The patients were in between the age of 20-79 years with mean age of 52.98±12.2. Out of 75 subjects, 47 (62.7%) patients were male and 28 (37.3%) were female. Of the study group, 53 patients had stage 1 and 22 patients had stage 2 hypertension. Among the stage-1 hypertensive (53), 5 patients had microalbuminuria and 6 patients had microalbuminuria in stage-2 hypertensive (22) (p=0.047). Microalbuminuria was significantly higher in those with longer duration and greater severity of hypertension (p =0.039). Older age (p =0.008), and adverse lipid profile (p =0.003) were the other identifiable risk factors for microalbuminuria. Stroke (OR=9.77), echocardiography-proven LVH (OR=6.25), ECG and/or echocardiography-proven IHD (OR=8.71) and hypertensive retinopathy (OR=4.14) were significantly higher in those with microalbuminuria.

Conclusion:
The prevalence of microalbuminuria in hypertensive subjects is high and patients with microalbuminuria have high odds of developing TOD like stroke, LVH, IHD, and hypertensive retinopathy. So the early detection of microalbuminuria in hypertensive as well as prompt treatment may reduce the burden of TOD.

Keywords: Hypertension, Microalbuminuria, LVH, IHD, retinopathy, stroke

Introduction:

Hypertension has become one of the most challenging concerns for world public health due to its pivotal role in the rising global burden of disease and disability.[1] The number of people of 30–79 years age with hypertension doubled from

1990 to 2019, from 331 (95% credible interval 306–359) million women and 317 (292–344) million men in 1990 to 626 (584–668) million women and 652 (604–698) million men in 2019.[2] Hypertension, along with pre-hypertension and other hazardously high blood pressure, is responsible for 8·5 million deaths from stroke, ischaemic heart disease, other vascular diseases, and renal disease worldwide.[3,4] Hypertension has been attributed to be responsible for 13% of global deaths, with the projection of a 30% increase in the worldwide prevalence of this condition by the year 2025.[1]

The overall pooled prevalence of hypertension in Bangladesh is 20% and an increasing trend of hypertension was also observed.[1] The heart, kidney, brain, and arterial blood vessels are prime targets of hypertensive damage. Uncontrolled hypertension accelerates the damage to these organs and eventually causing organ failure and cardiovascular death and disability.[5] Manifestations of target organ damage are: in kidneys – proteinuria, nephrosclerosis, chronic kidney disease & end-stage renal disease, in heart – left ventricular hypertrophy, coronary artery disease, angina, myocardial infarction, systolic dysfunction, diastolic dysfunction, chronic heart failure, atrial fibrillation & ventricular fibrillation, in the brain- transient ischaemic attack & stroke, in the eye- retinopathy.[6] The study of microalbuminuria in hypertension has been of increasing interest in recent years, since this abnormality has proved to be a strong predictor of cardiovascular morbidity and mortality. [7] Great importance has been given to microalbuminuria as a prognostic marker of cardiovascular and /or renal risk in diabetes and hypertension.[8] Variations in the prevalence of microalbuminuria ranged from 7 to 40 % depending upon the age and ethnic group.[9-16] This is probably due to differences in the techniques used for the detection of microalbuminuria and in the criteria used for patient selection. Microalbuminuria has been shown to be a marker of systemic endothelial dysfunction, considered to be an early stage of the atherosclerotic process. In patients with hypertension with or without diabetes and/or existing nephropathy, microalbuminuria is an independent risk marker for cardiovascular and cerebrovascular events such as ischemic heart disease, stroke, left ventricular hypertrophy, retinal vascular lesions, increased carotid artery wall thickness, and glomerular hyperfiltration, as well as all-cause of mortality.[7,8,17] Studies have shown an ongoing association of microalbuminuria with cardiovascular events and kidney lesions, the higher the microalbuminuria, the higher the risk of developing these conditions.[15] Screening for microalbuminuria is a sensitive, reliable, and accessible test for renal disease and cardiovascular morbidity or mortality. Because microalbuminuria has been shown to predict cardiovascular events-both in patients with hypertension with or without diabetes – the 2007 ESH/ESC guidelines recommend screening for microalbuminuria in all patients with hypertension.[18] The JNC-7 report states that the presence of albuminuria, including microalbuminuria, even in the setting of normal GFR, is also associated with an increase in cardiovascular risk and recommends annual screening for microalbuminuria in high-risk groups, such as those with diabetes or renal disease and optional in other hypertensives.[19] Hypertensive patients with microalbuminuria have a high risk for target organ damage resulting in a stroke, retinopathy, and adverse cardiovascular events. So the early detection of microalbuminuria in hypertensive is very important to reduce the progression of TOD. Microalbuminuria is simple, easy to perform, and annual screening is recommended by international treatment guidelines and should be implemented in general practice.[17] It is seen that aggressive treatment with antihypertensive agents that provide complete renin-angiotensin system blockade reduces the risk of cardiovascular damage in patients with microalbuminuria.[17] This study is undertaken to detect microalbuminuria in hypertensive patients in the northern zone of Bangladesh and its association with target organ damage. We feel that the present study will improve the awareness of physicians and hypertensive patients in planning the proper management of hypertension.

Methods:

This cross-sectional descriptive study was conducted at the Hypertension & Research Centre, Rangpur during the period of January 2010 to January 2012. A total of 75 hypertensive patients were purposively selected. Patients less than 18 years, diabetes mellitus, serum creatinine level higher than 2 mg/dl, with overt albuminuria, with fever, urinary tract infection (UTI), overnight exertion, pregnancy, and those who were on ACEI or ARB as antihypertensive were excluded.

Hypertension was defined as systolic blood pressure (SBP) greater than or equal to 140 mm Hg and/or diastolic blood Pressure (DBP) greater than or equal to 90 mm of Hg (or taking antihypertensive medication) in adults 18 yrs of age or older. According to the latest kidney foundation guidelines, when the urine albumin excretion is persistently elevated to 30-300 mcgram/24 hrs (microalbuminuria) – it gives the urinary concentration of albumin 20-200 microgm/L. A thorough clinical examination with special attention to the measurement of blood pressure was done. After ethical clearance and informed written consent, a detailed history was taken from patients.

The target organ damage of hypertension like left ventricular hypertrophy (LVH), ischemic heart disease (IHD), hypertensive retinopathy, and stroke was confirmed by clinical evaluation and relevant investigation. Blood and urine samples were collected from all subjects and urinary MA, serum lipid profile, Blood glucose, and serum creatinine were measured. In all subjects, ECG and Echo and in selected individuals CT scans were also done. Test for microalbumin in urine was performed by NycoCard U –Albumin method. Patients with total cholesterol levels higher than 200 mg/dl or triglyceride levels higher than 150 mg/dl , LDL higher than 130 mg/dl , HDL less than 50 mg/dl in female and less than 40 mg/dl in male , or who were receiving lipid- lowering drugs were considered dyslipidemic. All the data generated was recorded in a pre-designed data sheet. Study subjects were classified into two groups on the basis of the presence or absence of microalbuminuria as follows Group A: Subjects with microalbuminuria and Group B: Subjects without microalbuminuria. The relationship of microalbuminuria with the duration, severity, body mass index (BMI), lipid profile, and TOD by univariate analysis.

Results:

Table-I showed the different sociodemographic and clinical characteristics of both groups. A total of 75 hypertensive patients were studied in between the age of 20–79 years with a mean age of 52.98± 12.2 years and the majority (53.8%) were in the age range 40–59 years. Among the study subjects, 47 (62.7%) patients were males and 28 (37.3%) were females, and the male-female ratio was 1.7:1.

Table-I: Frequency distribution of microalbuminuria (MA) in patients with hypertension according to different variables

Variables	Number of cases n=75 (%)	MA present (n=11) (%)	p-value
Age group (in year)			
20-29	3(4)	0(0)	
30-39	7(9.3)	1(9.1)	
40-49	21(28)	1(9.1)	
50-59	19(25.4)	1(9.1)	0.017
60-69	15(20)	3(27.3)	
70-79	10(13.3)	5(45.4)	
Advancing age 50-79	44(58.6)	9(81.8)	0.017
Mean Age	52.98±12.2		
Sex			
Male	47(62.7)	7(14.9)	1.00
Female	28(37.3)	4(14.3)	
Smoking history			
Smoker	22(29.3)	4(18.2)	0.409
Non smoker	53(70.7)	7(13.2)	
Stage of hypertension			
Stage 1	53(70.7)	5 (9.4)	0.047
Stage 2	22(29.3)	6 (27.3)	
Duration of hypertension			
Less than 5 years	8(10.7)	1(12.5)	0.039
More than 5 years	67(89.3)	10(14.9)	
Treatment history			
No treatment	19(25.3)	3(15.8)	0.425
With Treatment	56(74.7)	8(14.3)	
Treatment details			
Irregular	30(40)	6(20)	0.177
Regular	26(34.7)	2(7.7)	
BMI			
18.5-24.9	40(53.4)	5(12.5)	0.404
25-29.9	28(37.3)	4(14.3)	
≥ 30	7(9.3)	2(28.6)	
Dyslipidemia			
Present	23(30.7)	8(34.8)	0.003
Absent	52(69.3)	3(5.76)	

Out of 75 patients,11(14.7%) subjects had MA whereas 64 (85.3%) had no MA (Figure 1). Among the 11 patients who had MA, 7 were males (63.6%) and 4 were females (36.3%), and there was no statistically significant difference in the risk for MA between the two sex groups (p =0.612). In the age range of 20–49 years, MA was present in 2 patients (6.45%) and MA was present in 9 cases (20.5%) in the 50–79 years of age and the result was statistically significant between the two age groups (p =0.017). In our study, 22 (29.3%) patients were smokers and 53 (70.7%) patients

were nonsmokers, among the 22 smokers, 4 (18.2%) had MA and among the 53 nonsmokers, 7 (13.2%) had MA, but these differences were not significant on univariate analysis (p =0.05). Of the study group, 53 patients had stage-1 hypertension (systolic BP 140-159 mmHg and or diastolic BP 90-99mmHg) and 22 patients had stage-2 hypertension (systolic BP ≥160 mmHg and or diastolic BP ≥100 mmHg). Among 53 stage-1 hypertensives, 5 patients had MA and 22 stage-2 hypertensives 6 patients had MA and the result was significant (p=0.047).

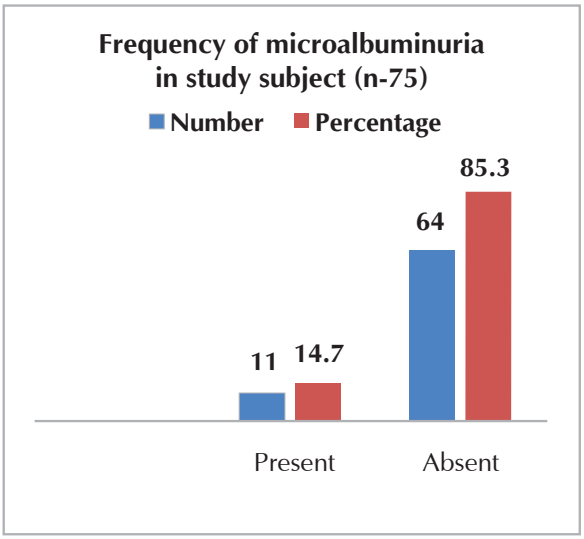

Figure-1: Frequency of microalbuminuria in study subject (n=75)

Among the 75 patients, 8 patients had hypertension for less than 5 years and 1 had MA, on the other hand, 67 patients had hypertension for more than 5 years and among them 10 patients had MA. The result was statistically significant. (p =0.039). Of the study subjects, 19 (25.3%) patients did not receive treatment previously, among them 3 patients had MA and out of 56 (74.7%) patients who were on treatment 8 patients had MA and this difference was not found to be statistically significant (p=0.425). Out of these 56 patients, 30(53.6%) patients received treatment irregularly and 26 (46.4%) patients received treatment regularly. In our study, 28 patients were overweight, 7 were obese and the remaining 40 had normal weight. MA was detected among 4 patients (14.3%) with overweight, 2 patients (28.6%) with obesity, and 5 (16.7%) with normal weight, and this difference was not found to be statistically significant (p=.404) (Table 13). Among the 23 patients with dyslipidemia, MA was detected in 8 (30.8%), whereas MA was detected in only 3 (6.1%) of the 52 patients with normal lipid profiles, and the difference was found to be statistically significant (p= .003). (Table-I)

In the study subjects the most common target organ lesion of hypertension was retinopathy 34.7% (26/75); next common was cardiac in the form of IHD 30.7% (23/75), LVH 28% (21/75), and least common was stroke 17.3% (13/75) (Figure-2).

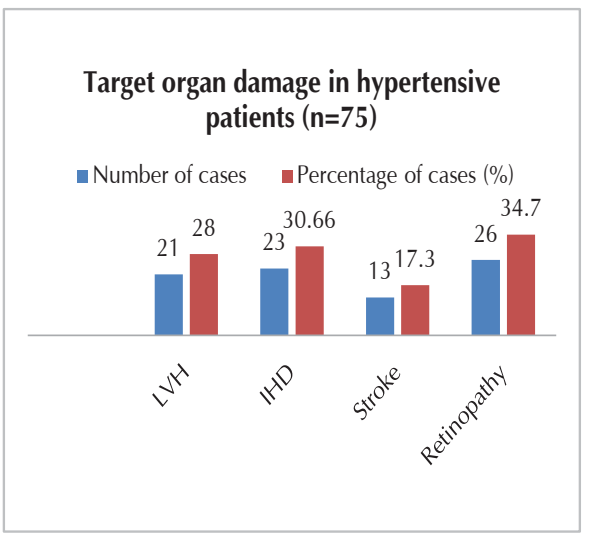

Figure-2: Various target organ damage (TOD) in hypertensive patients

A statistically significant association was found between LVH and microalbuminuria (p=0.009) (OR=6.25). Among 11 patients with MA 7(63.6%) had LVH and 4 (36.4%) had normal study. Among 64 patients without MA 14 (21.8%) had LVH and 50 (78.2%) had no LVH. A statistically significant association was found between IHD and microalbuminuria (p=0.003) (OR=8.71). Among 11 patients with MA 8 (72.7%) had IHD and 3 (27.3%) had normal study. Among 64 patients without MA 15 (28.8%) had IHD and 49 (71.2%) had no IHD.CT scans were performed on 17 patients with neurological symptoms and/or signs and 13 scans were abnormal (9 had cerebral infarcts and 4 had hemorrhages). Among the 13 patients, 6 (46.1%) had MA, these differences were also significant on univariate analysis (p =0.002) (OR=9.77). Among the 75 patients retinopathy was present on 26, among them 7(20.8%) had MA, and 19(79.2%) had no MA whereas among 49 had no retinopathy only 4 (11.8%) had MA. These differences were significant on univariate analysis (p = 0.035) (OR=4.14). (Table-II).

Table-II: The risk for various target organ damage (TOD) in hypertensive patients with microalbuminuria (MA)

Target organ damage		Number of cases n=75 (%)	MA present n=11(%)	p-value	OR	95% CI
LVH	Present	21(28)	7(33.3)	0.009	6.25	1.598-4.448
	Absent	54(72)	4(7.4)			
IHD	Present	23(30.7)	8(34.8)	0.002	8.71	2.049-37.043
	Absent	52(69.3)	3(5.76)			
Stroke	Present	13(17.3)	6(46.2)	0.002	9.77	2.355-40.544
	Absent	62(82.7)	5(8)			
Retinopathy	Present	26(34.7)	7(26.9)	0.041	4.14	1.085-15.835
	Absent	49(65.3)	4(8.2)			

Discussion:

The frequency of microalbuminuria in hypertension in our study was 14.7%, a value which is consistent with other studies like 14.4% of 5359 non-diabetic hypertensives in HUNT study in Norway,[20] 11.5% was reported from PREVEND study in the Netherlands[9] and 13.0% was reported from MAGIC study in Italy[21] but the study by Pudota PN et[15], Sabharwal K et al[22] showed prevalence was 30% and 33.3% respectively. A large study (MAGIC: Microalbuminuria A Genoa Investigation on Complications) conducted in the Genoa area on 787 patients with mild or moderate hypertensive subjects yielded a 6.67% prevalence of persistent microalbuminuria.[23] There is a difference in prevalence in these studies owing to the different methods to evaluate MA, and different times of urine collection.

The prevalence of MA was observed equally among males and females in our study subjects (14.9% and 14.3%). There was no significant difference in microalbuminuria among males and females in a study conducted by Pudota PN et[15], but MA was found to be higher among men in the Gubbio Population Study.[24]

Like the previous study,[15] longer duration of hypertension was also associated with a higher prevalence of MA in our cases. Advancing age was found to be a risk factor for a higher prevalence of MA in our study, as observed in other studies.[15,25,26] The frequency of MA was significantly greater in hypertensive subjects with higher BP values as among 53 stage 1 hypertensives patients 5 (9.4%) had MA and 22 stage 2 hypertensives patients 6 (27.3%) had MA in our study (p =0.047) consistent with the other study.[27] Agarwal et al[28] demonstrated an association with age, male gender, systemic hypertension duration, and treatment duration whereas Nakamura and associates, Clausen et al. and Redon et al. did not observe this relationship.[29] There was no statistically significant difference in the frequency of MA between smokers and non-smokers in our study similar to the study conducted by Pudota PN et,[15] in contrast to the observation made by the others.[24] The small sample size of the present study might be one reason for this discrepancy. High BMI among hypertensives is an important and well-known risk factor for the development of MA.[24,25,30] But the prevalence of microalbuminuria among our obese and overweight patients were of only 12.9% which is lower than that of the patients with normal weight at 16.7%. Valensi et al found a prevalence of up to 12% of microalbuminuria among obese individuals.[31] An adverse lipid profile was found to be associated with a higher prevalence of MA in our study subjects, as observed in the Gubbio study.[24]

In the present study, a statistically significant association was found between the target organ lesion and MA. The frequency of at least one target organ lesion was 34.7% and was greater in patients with MA group [26.9% (7/26)] versus normoalbuminuria [8.2 % (4/49)] which was statistically significant (p=0.035). In a study, the prevalence of at least one target organ lesion was 76.2% 16/21) in the A group versus 03.95 (58/132) in normoalbuminuria group (p=0.006).[8]

In patients with hypertension, LVH is one of the earliest TOD-like MA[6] and there is a significant association between these two subtle TOD as shown in many studies. [15,26,32-34] The frequency of LVH found in our study was 28%, though the prevalence of LVH reported in other studies was higher.[35,36] But the higher odds for LVH in cases with MA (OR =6.25) im□ plies a higher risk for cardiovascular events in the study population with hypertension.Redon et al[10] and later Cerasola et al[27] reported a correlation between albuminuria and left ventricular mass as assessed by echocardiography. In the Magic study, patients

with elevated albumin excretion rate showed a significantly higher prevalence of electrocardiographic changes compatible with left ventricular hypertrophy and/or ischaemia.[23]

A high frequency of microalbuminuria was found among our patients with coronary artery disease (34.9%) (p=0.003) (OR=8.712) which is similar to the other studies (33%),[37] MA had been reported to be three times more prevalent in patients with recent stroke, and the risk for future stroke had been found to be high among patients with MA. [6,26] MA was more prevalent among patients with stroke (46.1%) (OR=9.73 in the present study as well. The prevalence of MA was higher among the patients with stroke. MA is a cause of generalized atherosclerosis and can involve carotid vessels, patients with MA were 20 times more likely to develop carotid intima-media thickness.[15]

We observed a significant association between hypertensive retinopathy and MA (p=0.035) (OR=4.14), like that of previous studies.[15,33] The relationship between hypertensive retinopathy and microalbuminuria was studied by Biesenbach in a group of 84 patients with hypertensive subjects. Patients who were microalbuminuric despite effective antihypertensive treatment showed a significantly higher prevalence (85%) of hypertensive retinopathy (grades I and II) compared to patients with reversible microalbuminuria (36%) and to normoalbuminuric patients (31%). Results from the Magic study show a higher degree of albuminuria in patients with hypertensive retinopathy.

Conclusion:

The prevalence of microalbuminuria in hypertensive patients is high. Due to the endothelial damage to the glomerulus MA appear in urine which indicates the initial stage of atherosclerosis. Our study also showed a positive relation between MA and advancing age, duration of hypertension, severity of hypertension, and dyslipidemia. Since this was a cross-sectional study, we could not establish a causal relationship between microalbuminuria and target organ lesions. Patients with essential hypertension and MA have high odds of developing TOD in the form of LVH, IHD, hypertensive retinopathy, and stroke. So the measurement of urinary MA may be a new marker for the initial stage of atherosclerosis and also can relate the occurrence of target organ damage to hypertension with other established risk factors and early detection of microalbuminuria in hypertensive as well as prompt treatment may reduce the burden of TOD.

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