

Frequency and association of microalbuminuria with target organ damage in hypertensive patients

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Abstract:

Background: Hypertension has become as an important cause of premature mortality and morbidity due to its major etiologic role in the development of coronary artery disease, stroke and renal failure. Majority of the patients died due to any of the hypertension related complications.

Subjects and Methods: This was a descriptive cross sectional study, carried out in Hypertension & Research Centre, Rangpur. Assuming 5% prevalence of microalbuminuria in hypertensive patients

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a sample size of 73 was calculated. In this study we have taken 75 patients.

Results: *During the study period, we have studied over 75 patients of both sexes. Mean age of the victims were 52.98 ± 12.2 years. Males were more common than female (62.7% vs 37.3%. Among the study patients MA was present in 11(14.7%). MA was more in stage 2 hypertensive patient than stage 1 hypertensive patients (vs 9.43%) ($p = 0.047$). Among the study population 7 (9.33%) were obese. MA was more in obese patients than overweight and normal body weight patients ($p=0.404$). In the study among the target organ lesion retinopathy was 34.7%, IHD 30.7%, LVH 28% and least common was stroke 17.3%. A statistically significant association was found between LVH and microalbuminuria ($p=0.009$) (OR=6.25), between IHD and microalbuminuria ($p=0.003$) (OR=8.71) and between microalbuminuria and retinopathy ($p = 0.035$) (OR=4.14).*

Conclusion: *In our study frequency of MA was 14.7% and a significant association was found between microalbuminuria and target organ damage of hypertension (LVH, IHD, and retinopathy).*

Key words: Microalbuminuria, target organ, retinopathy

INTRODUCTION

Bangladesh has been experiencing an epidemiological transition from communicable disease to NCDs¹ due to economic development and increased level of control and treatment of infectious diseases.² Among the common noncommunicable diseases hypertension is emerging as a public health problems worldwide. It is now spreading in epidemic fashion in developing countries as well.³ A marked increase in prevalence of hypertension (from 11.3% to 17.9%) was observed in Bangladesh from 1999 to 2010.^{4,5} In Rangpur division (Northern part) of Bangladesh prevalence of hypertension and pre-hypertension is 33.3% and 29.9% respectively.⁶ The adverse effects of hypertension principally

involve the blood vessels, central nervous system, retina, heart & kidneys and can often be detected clinically. Thus these organs are treated as target organ of hypertension.⁷ 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 brain- transient ischaemic attack & stroke, in eye- retinopathy.⁸ Microalbuminuria is defined as an abnormal urinary excretion of albumin between 20 and 200µgm/min (i.e 30-300 mg/day) a value below the detection threshold of conventional test but which can be accurately measured by several widely available sensitive methods (ELISA, RIA etc). Urinary albumin: creatinine ratio (UACR) of 2.5-30 mg/mmol in men, 3.5-30mg/mmol in women is also defined as microalbuminuria.⁹ The incidence of microalbuminuria seen in patients with hypertension is similar to that seen in patients with diabetes.¹⁰ The study of Microalbuminuria in hypertensive subjects has been of increasing interest in recent years, since this abnormality has proved to be a strong predictor of cardiovascular morbidity and mortality.¹¹ Great importance has been given to microalbuminuria as prognostic marker of Cardiovascular and /or renal risk in diabetes and hypertension.¹² Microalbuminuria is a marker of early organ damage in hypertensive subjects namely left ventricular hypertrophy, retinal vascular lesions, increased carotid artery wall thickness, and glomerular hyperfiltration.¹¹ Microalbuminuria in addition to being an early sign of kidney damage, is often found in patients with hypertensive subjects suggesting that it may reflect early vascular abnormalities.¹³ Early identification of a patient at risk of cardiovascular events provides an opportunity for early treatment, to slow the

progression of disease. 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.¹⁴

Therefore this study was undertaken to see the frequency of microalbuminuria in hypertensive patients and its association with different TOD.

METHODOLOGY

This was a descriptive cross sectional study, carried out in Hypertension & Research Centre, Rangpur from January 2009 – December 2010. Hypertensive patients presenting in Hypertension and Research Centre, Rangpur was included in this study.

Sample Size: Assuming 5% prevalence of microalbuminuria¹⁵ in hypertensive patients a sample size of 73 was calculated. For this study we have taken 75 patients. Hypertensive patient age less than 18 years, having DM, creatinine level higher than 2 mg/dl, overt albuminuria, fever, UTI, overnight exertion, pregnancy and taking ACEI or ARB were excluded from the study.

Sampling technique

Purposive sampling technique was applied to select study subject. The patient who fulfilled both the inclusion and exclusion criteria was enrolled in this study. Evaluation of the patient was based on history, physical examination and laboratory investigation.

Procedure of data collection

A detailed history was taken and clinical examination was done. Urine R/M/E, urine heat coagulation test, X-ray chest PA view, ECG, blood sugar (RBS), blood urea, serum creatinine, fasting lipid profiles and echocardiogram was done in all patients. For selected patients USG of KUB, serum Electrolytes, uric acid, CRP, CT scan of brain and MRI of brain was done. Study subjects was classified into two groups on the basis of presence or absence of microalbuminuria as follows- group A: Subjects with microalbuminuria and group B: Subjects without microalbuminuria. Presence & extend of target organ damage was assessed in both the groups. Test for microalbumin in urine was performed by NycoCard U – Albumin method.

Measurement of blood pressure and anthropometry:

During the course of the interview, two measurements of blood pressure on each study participant were made with an aneroid sphygmomanometer in auscultatory method. Study participants were instructed to refrain from drinking any caffeinated beverage and from smoking during the half-hour preceding the interview. Both blood pressure measurements were obtained after the subject taking rest for at least 5 min in a seated position. The first blood pressure measurement was recorded after obtaining socio-demographic information from the study subject, while the second was recorded after a brief clinical examination.

All blood pressure measurements were made on the left arm to maintain uniformity of each study subject, using a cuff of appropriate size at the level of the heart. The cuff pressure was inflated 30 mm Hg above the level at which the radial pulse was disappeared then deflated slowly at the rate of about 2 mm per sec and the readings recorded to the nearest 2 mm Hg. The first (appearance) and the fifth (disappearance)

Korotkoff sounds were recorded as indicative of the systolic (SBP) and the diastolic blood pressure (DBP) respectively. The average of two readings of SBP and DBP to describe the blood pressure of the participant was used. In cases where the two readings differed by over 10 mm of Hg, a third reading was obtained, and the average of the three reading was recorded. Body weight & height were expressed in Kg & meter respectively.

OPERATIONAL DEFINATION

Hypertension:

Systemic hypertension is currently 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.

Stage-1 hypertension:

Systolic BP 140-159mmHg and or diastolic BP 90-99mmHg

Stage-2 hypertension:

Systolic BP ≥ 160 mmHg and or diastolic BP ≥ 100 mmHg¹⁶

Microalbuminuria:

Microalbuminuria is defined as excretion of 30–300 mg of albumin per 24 hours (or 20–200 mcg/min or 30–300 mcg/mg creatinine) on 2 of 3 urine collections.¹⁷

Target Organ Damage:

Manifestations of target organ damage was detected in the following ways –

1. Heart: Clinical evaluation and ECG findings like T Inversion, ST Depression / Elevation, Q Wave, LVH. In

echocardiogram LVH and LVD. In chest X-ray cardiomegaly, pulmonary oedema.

2. CNS: Clinical evaluation (TIA, Stroke) and infarction / haemorrhage in brain imaging (CT scan or MRI of brain).

3. Kidney: Clinical evaluation and increased s. creatinine, blood urea, USG of KUB kidney Size.

4. Retina: Fundoscopic examination, grade 1 to grade 4 hypertensive retinopathy.

5. Peripheral vessel: Clinical evaluation and doppler Study.

Dyslipidemia: Patients with 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.

Smokers: Individuals who had smoked any amount of cigarettes in the past year were considered smokers.

Obesity: Individuals with a BMI 18.5 to 24.9 Kg/m² were considered normal, and those with a BMI 25 Kg/m² to 29.9 Kg/m² were considered overweight and BMI 30 Kg/m² or higher than 30 Kg/m² were considered obese.

Ethical issues

The eligible patient and or family were informed about the purpose of research and informed consent was taken.

Statistical analysis

The data were analyzed by SPSS windows version 17.0. The socio-demographic data of the study population were expressed in frequency distribution and their observed difference was tested by one sample 't' test and 'chi square' test. P value <0.05

was and two tailed t test were considered as statistically significant with the 95% confidence interval.

Result

During the study period, we have studied over 75 patients of both sexes. Mean age of the victims were 52.98 ± 12.2 years, majority (50.7%) were in the age range 40-59 years. Males were more common than female (62.7% vs 37.3%. Among the study patients MA was present in 11(14.7%). Among them 7 were male (63.6%) and 4 were female (36.3%), and there was no statistically significant difference in the risk for MA between the two sex groups ($p = 0.612$). MA was more in 50-79 year age group (20.5%) than 20-49 year age group (6.45%) ($p = 0.017$). Among the study subjects 22 (29.3%) patients were smoker and 53 (70.7%) patients were non smoker. Among the smokers 4 (18.2%) had MA and among the non-smokers 7 (13.2%) had MA. ($p = 0.05$).

Among the study population 53 patients had stage-1 hypertension and 22 patients had stage-2 hypertension. MA was more in stage 2 hypertensive patient than stage 1 hypertensive patients (vs 9.43%) ($p = 0.047$). In the study 8 (10.67%) patients had hypertension for less than 5 years, among them 1 (12.50%) had MA and 67 (89.33%) patients had hypertension more than 5 years of whom 10 (14.92%) patients had MA ($p = 0.039$). 19 (25.3%) patients was newly diagnosed (did not receive treatment previously), among them 3 (15.78%) patients had MA and 56 (74.7%) patients who were on treatment 8 (14.28%) patients had MA ($p = 0.425$). Among the patients on treatment 30(53.6%) patients received treatment irregularly and 26 (46.4%) patients received treatment regularly. Among the study population 7 (9.33%) were obese. MA was more in obese patients than overweight and normal body weight patients ($p = 0.404$) (Table 1).

Table-1: Frequency distribution of BMI of the hypertensive patient and MA (n = 75)

BMI (kg/m ²)	Number of cases	MA present (% of cases)	P value
18.5-24.9	40	5(12.5%)	p=.404
25-29.9	28	4(14.3%)	
≥ 30	7	2(28.6%)	

In this study dyslipidaemia was present in 23 (30.67%) patients, among them MA was detected in 8 (30.8%), whereas MA was detected in only 3 (6.1%) of the 52 patients with normal lipid profile. (p= .003) In the study among the target organ lesion retinopathy was 34.7%, IHD 30.7%, LVH 28% and least common was stroke 17.3%. A statistically significant association was found between LVH and microalbuminuria (p=0.009) (OR=6.25), between IHD and microalbuminuria (p=0.003) (OR=8.71) and between microalbuminuria and retinopathy (p = 0.035) (OR=4.14). (Table 2)

Table-2: Target organ damage of hypertension and microalbuminuria

Target organ damage	Microalbuminuria (n=11)	No microalbuminuria (n=64)
LVH	7(63.6%)	14 (21.8%)
IHD	8 (72.7%)	15 (28.8%)
Retinopathy	7 (63.63%)	19 (29.69%)

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.

DISCUSSION

The frequency of microalbuminuria in hypertensive individuals in our study was 14.7%, a value which consistent with other studies like 14.4% of 5359 non-diabetic hypertensive in HUNT study in Norway, 11.5% was reported from PREVEND study in

Netherlands¹⁸ and 13.0% was reported from MAGIC study in Italy.¹⁹ But it was lower than that found by other authors (26.67%)²⁰ and observed in the LIFE study (23%).²¹ The relative risk for development of MA was found to be higher among men in the Gubbio Population Study,²² our study found similar result, MA was more in male than female 63.6% vs 36.3%). Advancing age was found to be a risk factor for higher prevalence of MA in our study, was also observed in other studies.⁴ As expected, longer duration of hypertension was also associated with higher prevalence of MA in our cases. The frequency of MA was significantly greater in hypertensive subjects with higher BP values than lower BP values (27.3% vs 9.4%). The result was significant on univariate analysis ($p = 0.047$). It consistent with the other study ($p = 0.001$).²³ Low frequency of MA among the hypertensive on regular anti-hypertensive drug, points towards the role of drug therapy in hypertension in reducing the prevalence of CKD. Strict round the clock control of high BP is important in reducing the risk of MA in hypertensive because even isolated ambulatory hypertension is associated with higher risk for TOD.^{24,25} There was no statistically significant difference in the frequency of MA between smokers and non-smokers in our study in contrast to the observation made by the others. The small sample size of the present study might be one reason for this discrepancy. High BMI among hypertensive is an important and well-known risk factor for the development of MA.^{26,27,28} Valensi at all found prevalence of up to 12% of MA among obese individuals. In our study frequency of MA among our obese and overweight patients was of only 12.9%. But MA was more in normal body weight hypertensive than those who were overweight and obese. This may be due to small sample size. As observed in the Gubbio study²⁶, an adverse lipid profile was found to be associated with higher prevalence of MA in our study subjects as well. In our study frequency of HDL

abnormality is more in patients with MA which is consistent with other study.^{29,30}

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 patient 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 MA group versus 43.95 (58/132) in normoalbuminuria group (p=0.006).³¹ In patients with hypertension, LVH is one of the earliest TOD like MA⁸ and there is significant association between these two subtle TOD's as shown in many studies. ^{21,26,32,33} The frequency of LVH found in our study was 28%, though the prevalence of LVH reported in other studies was higher.^{34,35} But the higher odds for LVH in cases with MA (OR =6.25) implies higher risk for cardiovascular events in the study population with hypertension. 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%).³⁶

As regards peripheral arterial disease (PAD), a relationship between MA and this disease was also observed. Spanish researchers studied 141 patients with acute coronary syndrome and divided them into two groups according to the presence or absence of PAD, and observed that MA was significantly higher in the PAD group.¹⁸ In our study peripheral pulses were present in all patients clinically. 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. ^{8,23} MA was more prevalent among patients with stroke (46.1%) (OR=9.77) in the present study as well. In other study of our country prevalence of microalbuminuria in ischaemic stroke was 64% in study

subjects.³⁷ We observed significant association between hypertensive retinopathy and MA ($p=0.035$) (OR=4.14), like that of ETODH study.²⁶ The overall prevalence of CKD in USA is reported to have increased from 10 to 13% recently, and the major of these patients have early CKD in the form of persistent MA.³⁵ There are no studies reported from our country till date about the prevalence of MA among patients with hypertensive subjects. Our observation on the high prevalence of MA in patients with hypertensive subjects, must alert the clinicians regarding the high prevalence of subclinical CKD in this part of the world, especially in view of the observations made by Mani MK from South India.³⁶ On the preventive strategies for reduction of the burden of CKD by early detection and treatment of hypertension.

CONCLUSION:

In our study frequency of MA was 14.7% and a significant association was found between microalbuminuria and target organ damage of hypertension (LVH, IHD, and retinopathy).

Limitation

Sample size was small.

Future direction

A cohort study with large sample size will be needed to clarify association of microalbuminuria and its target organ damage.

Conflict of interest

There was no conflict of interest.

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