

## ORIGINAL ARTICLE

### Microalbuminuria in Non-diabetic Hypertensive Individuals: A Cross Sectional Observation in Dhaka Medical College Hospital

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#### Abstract:

*The study was conducted to assess the prevalence of microalbuminuria in non-diabetic hypertensive individuals with or without antihypertensive medication(s), attending medicine outpatient department of Dhaka Medical College Hospital. Non-diabetic hypertensive individuals without a history of pre-existing kidney diseases participated in this cross-sectional study. A questionnaire was used for collecting information on demographics, life style and family history of cardiovascular and kidney disease. Spot morning urine samples were collected for albumin estimation. Albuminuria thresholds were evaluated and defined using albumin-creatinine ratio (ACR). A total of 500 non-diabetic hypertensive individuals (310 males, 190 females) aged 52.25±7.99 years were enrolled in this study. After excluding 08 persons with macroalbuminuria, microalbuminuria was found in 51 cases (10.37%) [7.68%-13.06%]. The prevalence was higher in females than males, ie 11.89% [7.23%-16.55%] and 9.45% [6.18%-12.72%] respectively. There was no statistical significant difference between the sex groups. Duration of blood pressure showed statistical significant association with the occurrence of microalbuminuria. This suggests that, in Bangladeshi hypertensive individuals microalbuminuria is not uncommon. Further prospective studies with large sample size in different areas of the country are needed to confirm the prevalence of microalbuminuria in such individuals. The causative factors as well as prognostic value of the occurrence of microalbuminuria in this population remain to be determined in prospective cohort studies.*

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#### Introduction:

The term microalbuminuria (MA) is a relative misnomer: it implies 'small size' but actually refers to the presence of a relatively 'quantity' of protein in the urine. The term was first used nearly 30 years ago when referring to urinary protein excretion of 30-300mg per day, which was below the detection threshold of a standard urine dip stick.<sup>1</sup> It is also considered when albumin/creatinine ratio (ACR) lies between 30-300mg/gm creatinine in random spot urine sample.<sup>2</sup>

Microalbuminuria has been shown to be associated with an increased risk of cardiovascular<sup>3</sup> and

progressive kidney diseases<sup>4</sup> not only in diabetes but also in nondiabetic subjects. Many patients with essential hypertension may present with overt or subclinical target organ damage involving heart, kidneys and central nervous system as well as peripheral arteries. Assessment of subclinical target organ damage has become the key element in evaluating hypertensive patients.<sup>5</sup> Clinically microalbuminuria may be an indicator of early vascular complication of hypertension.<sup>6</sup> It has been reported that 11% to 40% of persons of hypertension have microalbuminuria<sup>7</sup> and appears to correlate with both the severity and duration of hypertension.<sup>8</sup>

In essential hypertension, MA results from renal hemodynamic changes due to the direct transmission of increased systemic pressure to the glomeruli,<sup>9</sup> selective changes of the glomerular filter and/or insufficient tubular reabsorption of albumin<sup>10</sup> and structural damage to the glomeruli and arteries.<sup>11</sup> Systolic blood pressure has been shown to be one of the most relevant determinants of MA in the early stages of hypertensive disease.<sup>12</sup> Patients with elevated UAE have higher left ventricular mass<sup>13</sup>, a higher prevalence of hypertensive retinopathy<sup>14</sup> and an increased thickness and presence of plaques in the carotid artery<sup>15</sup>.

Reduction of UAE with drug regimes (such as angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists) correlates with a decrease in the rate of decline of renal function that is independent of the antihypertensive effect of these agents<sup>16</sup>. The Seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of high blood pressure 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 group, such as those with diabetes or renal disease and optional in other hypertensives<sup>17</sup>. Therefore, routine screening to detect patients at risk of developing microalbuminuria is critical to patient care and long term outcomes.

## Materials and Method:

### *Study population*

A cross-sectional study was performed from January 2011 to December 2011 at medicine outpatient department of Dhaka Medical College Hospital, Dhaka. Non-diabetic essential

Hypertensive individuals, age  $\geq 18$  years, without a history of preexisting kidney diseases participated in this study. The major inclusion criteria were individuals with essential hypertension (defined by sitting blood pressure (BP)  $\geq 140/90$  mmHg not previously diagnosed with hypertension or those

were previously diagnosed with hypertension and reported current use of antihypertensive medications.) Exclusion criteria were those with previously diagnosed diabetes mellitus or random blood glucose  $\geq 11.1$  mmol/L, impaired kidney function (serum creatinine  $> 1.4$  mg/dl in male or  $> 1.2$  mg/dl in female), urine albumin creatinine ratio (ACR)  $> 300$  mg/gm, false positive albuminuria (fever, menstruation, urinary tract infection and past exercise) or those suffering from chronic debilitating illness such as malignancy, autoimmune disease, congestive heart failure, pregnant women and individuals unwilling to give consent are also excluded from this study. This study was approved by the Ethical Committee of Dhaka Medical College.

*Sample size:* There was no known prevalence of microalbuminuria in non-diabetic hypertensive subjects in Bangladesh. So, to calculate the sample size in the present study, the prevalence of neighboring country (27%) was used as mean, using statistical formula  $n = z^2 pq/d^2$ , calculated sample size was 261. For better precision the study was performed by taking 500 samples.

*Data collection and evaluation:* A questionnaire was used for collecting information on demographics, life style, current medical illness and family history of cardiovascular and kidney disease. All participants have their blood pressure measured after 10 minutes rest with a standard aneroid sphygmomanometer. Height and weight of individuals were measured to calculate BMI. Biochemical profiles like- random blood glucose (RBS), serum creatinine were also estimated.

*Laboratory methods:* Blood sample was collected from hypertensive individuals for estimation of random plasma glucose and serum creatinine. Glucose was estimated enzymatically by 'glucose oxidase' method and serum creatinine was estimated by 'Jaffe reaction method'.

All participants gave a spot morning urine sample for analysis after making him/her clear about the purpose. Before collection patients were asked to avoid exercise or exertion and took rest for at least

15minutes.Urine was collected in two different tubes- one for estimating albumin and another for estimating creatinine to calculate urinary albumin creatinine ratio(ACR). Albuminuria measured as urine albumin concentration (UAC) by the method of immunoturbidimetric technique with fully automated Olympus Au 400 chemistry analyzer. Urine creatinine was measured using Jaffe's method using the same analyzer for albumin. Microalbuminuria was considered when ACR lies between 30-300mg/gm creatinine<sup>2</sup>. ACR of 08(eight) cases were more than 300mg/gm creatinine. As such, out of 500 study subjects 492 cases were valid for analysis.

*Statistical analysis:* An overall prevalence and specific population prevalence were estimated along with their 95% confidence interval(CI).Categorical variants were summarized using frequency and percentages  $\pm$  standard error (SE) while continuous variables were summarized using mean  $\pm$  standard deviations (SD) unless otherwise indicated. To compare two percentages between two groups Z-test of proportion were done where applicable.

Pearson bivariate correlation was seen among the variables (as appropriate).All the tests were two tailed and  $p < 0.05$  was considered statistically significant. All analysis were performed using SPSS statistical package version 17.0

### Results:

A total of 500 non-diabetic hypertensive individuals aged  $52.25 \pm 7.99$  years were enrolled in this study. Among 310 males and 190 females, 59 subjects ( both male & female) were found to have increased albumin-creatinine ratio giving a prevalence of 11.8%. After excluding 08 persons with macroalbuminuria, microalbuminuria was found in 51 cases (10.37%).We are 95% confident that the prevalence lies within 7.68%-13.06%. Among male subjects, 9.45% (95% CI; 6.18%-12.72%) and 11.89% (95% CI; 7.23%-16.55%) female have got microalbuminuria. Mean age with microalbuminuria was  $51.47 \pm 6.87$  and that among the individuals without microalbuminuria was  $52.34 \pm 8.11$ .There was negative correlation of urinary albumin to creatinine ratio (ACR) with age ( $r = -0.034$ ,  $p > 0.05$ ).

**Table I :** Distribution of study group according to age groups

Age distribution	Total, n=492	Non-diabetic HTN with MA	Non-diabetic HTN without MA	Prevalence of MA at 95% CI
18-39 years	77	10.39%	89.61%	3.57-17.21
40-59 years	134	11.19%	88.81%	5.85-16.53
>60 years	281	9.96%	90.04%	8.17-11.25

Results are expressed as frequency (percentage) n: Number of study population

MA: Microalbuminuria

HTN: Hypertension

**Table II :** Distribution of study group according to duration of hypertension

Duration	Total, n=492	Non-diabetic HTN with MA	Non-diabetic HTN without MA	Prevalence of MA at 95% CI	p-value
$\geq 5$ years	214	16.35%	83.65%	11.39-21.31	p<0.05
< 5 years	278	5.76%	94.24%	3.04-8.48	

In the setting of duration, individuals having  $\geq 5$  years duration of hypertension,35 (16.35%; 95% CI; 11.39% - 21.31%) have microalbuminuria whereas those having <5 years duration 16 (5.76%; 95% CI;

3.04% - 8.48%) cases showed microalbuminuria.

**Table III :** Distribution of study group according to BMI

BMI	Total, n=492	Non-diabetic HTN with MA	Non-diabetic HTN without MA	Prevalence of MA at 95% CI	p-value
Obese	222	14.41%	85.59%	12.05-16.77	p<0.05
Non-obese	270	7.04%	92.96%	5.48-8.60	

In aspect of BMI, 222 (45.12%) individuals were found to have BMI  $\geq 25$  kg/m<sup>2</sup>, of them 32(14.41%) have got microalbuminuria. Among the remaining 270(54.88%) cases have BMI < 25kg/m<sup>2</sup>, out of them 19 individuals were microalbuminuric and the rest them were the cases of non-diabetic

hypertension without microalbuminuria. Mean BMI among patients with microalbuminuria was 27.01 $\pm$ 2.87. There was positive correlation of urinary albumin to creatinine ratio (ACR) with BMI ( $r=0.379$ ,  $p<0.05$ ). At 95% CI the difference between the two mean was significant.

**Table IV :** Distribution of study group on the basis of severity of blood pressure

Status	Total, n=492	Non-diabetic HTN with MA	Non-diabetic HTN without MA	Prevalence of MA at 95% CI	p-value
$\geq 160/100$ mmHg	191	16.75%	83.25%	11.46-22.04	p<0.05
<160/100mmHg	301	6.31%	93.69%	3.75-9.05	

Among all cases of study group, 191 cases were found to have blood pressure  $\geq 160/100$ mmHg of which 32 (16.75% ; 95%CI;11.46%-22.04%) individuals have microalbuminuria. In the same way, out of 301 patients whose blood pressure was  $\leq 160/100$ mmHg, 19(6.31%; 95% CI; 3.75%-9.05%) patients were microalbuminuric and 282 (93.69%) were found to have normoalbuminuria. Analysis done by Z-test of proportion, result found statistically significant.

### Discussion:

Hypertension has long been associated with microalbuminuria<sup>18</sup>. Clinically it may be an indicator of early vascular complication of hypertension<sup>6</sup>. Microalbuminuria and vascular dysfunction are known to occur early in the course of essential hypertension.

In this study out of 500 non-diabetic hypertensive patients 08 persons were excluded because of higher than cut off value for microalbuminuria and microalbuminuria was found in 51 cases (10.37%) [7.68%-13.06%]. Among the study population, 307 persons were male of which 29 (9.45%) [6.18%-12.72%] found to have microalbuminuria and the remaining 185 females, 22(11.89%) [7.23%-

16.55%] were microalbuminuria positive. Though the prevalence of microalbuminuria was found to be high in females; there was no statistical significant difference in the risk for microalbuminuria ( $p>0.05$ ) between the two sex groups. A number of previous studies evaluated the prevalence of microalbuminuria in non-diabetic hypertensive patients has been published, which is varied from 16% in the USA<sup>19</sup> 11.50% to 30% in Europe<sup>20</sup> and 15.0% to 18.20% in Thailand<sup>21</sup>. This varying might be due to type of study base (ie, community versus hospital base), patient characteristics, urine sample collection and the methods of test used.

Regarding the duration and severity of hypertension, statistically significant result has been found in the study population. Longer the duration and more the severity of hypertension, more the possibility of microalbuminuria ( $p<0.05$ ). Similar findings for both duration and severity of hypertension were observed in several different studies done separately by Badiger S et al.<sup>22</sup> and Hitha B et al.<sup>5</sup>

High body mass index among hypertensives is an important and well-known risk factor for the development of microalbuminuria, in this study there was statistically significant difference between the microalbuminuria and the body mass



index ( $p < 0.05$ ). Significant positive correlation was also found between BMI and ACR ( $r = 0.379$ ). The same type of result was seen in study conducted in India by S. Badiger.<sup>22</sup> However, it has also been observed that development of microalbuminuria may represent the genetically determined renal vascular endothelial dysfunction and elevated risk of cardiovascular disease.<sup>23</sup> Furthermore, microalbuminuria in non-diabetic subjects might be part of insulin resistance syndrome. Many risk factors associated with microalbuminuria are well-known components of insulin resistance syndrome. So further study is required to find out association between the components of insulin resistance syndrome and microalbuminuria.

No significant association was found in respect to age in this study ( $p > 0.05$ ). A hospital based study performed in Thailand among non-diabetic hypertensive individuals showed no association of this factor with microalbuminuria.

It has been accepted that screening for microalbuminuria is cost-effective in the prevention of progressive kidney disease in diabetic patients.<sup>21</sup> However, there is still a debate concerning whether or not that benefit would be the same in other high risk groups such as hypertensive patients. According to the 2007 European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guidelines, microalbuminuria has been considered as a recommended test for risk stratification.<sup>24</sup>

### Conclusion:

This study documents that microalbuminuria is not uncommon in non-diabetic hypertensive subjects in Bangladesh. So hypertension should be treated as an independent risk factor in developing microalbuminuria. Early screening of patients with essential hypertension for microalbuminuria and aggressive management of positive cases might reduce the burden of chronic kidney diseases and cardiovascular diseases.

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