# PREVALENCE OF MICROALBUMINURIA AND OVERT PROTEINURIA IN HYPERTENSION AND THEIR RELATIONS WITH RENAL FUNCTION IN A RURAL POPULATION OF BANGLADESH

ANME KARIM[1], D DAS[5], M SALAHUDDIN[6], GA MARJAN[4], MN ISLAM[2], AK SHAHA[2], RD GUPTA[2], SM ISLAM[6], R AMIN[3], HU RASHID[7]

**Summary:**

*Hypertension is the third leading cause of chronic kidney disease (CKD) in Bangladesh. Microalbuminuria and overt proteinuria are the markers of the CKD. So detection of microalbuminuria and overt proteinuria in hypertensive subjects will help to identify the patient at risk of developing progressive renal impairment. This cross sectional study was carried out in a rural area of Bangladesh.1134 adult population (age between 18 and 65 years) were screened. A total of 217 (19.1%) were detected hypertensive; spot urine dipstick test was done among them. Those who where dipstick negative further studied for presence of microalbumin [ mg/L ]. Blood glucose level, serum creatinine, and estimated glomerular filtration rate (eGFR) were evaluated. A group of normotensive people (n=245) taken as comparison group. Microalbuminuria and overt proteinuria were present in 26.4% and 9.7% of the hypertensive subjects, respectively. Correlation between microalbuminuria and eGFR showed that two variables exhibited a tendency for negative relationship, although correlation was not statistically significant (P=0.186, r=-0.064). Overt proteinuric subjects showed no statistically significant deterioration of eGFR (81.6+_21.1). Microalbuminuria and overt proteinuria are prevalent among the hypertensive rural Bangladeshi people. So early detection of microalbuminuria and overt proteinuria will help to prevent or delay the development of end stage renal disease.*

***Key words:*** *Hypertension, microalbuminuria, overt proteinuria, prevalence*

**Introduction:**

Demographic transition leads to changes in the epidemiological transition, shifts the global mortality and morbidity from communicable to non communicable diseases. While heart disease, cerebrovascular disease and cancer are the major causes of mortality resulting from chronic diseases, chronic kidney disease (CKD) also now appeared as global epidemic[1]. One of the major causes of end stage renal disease (ESRD) in North America and in many countries is hypertension, which together accounts for almost 26% of all dialysis patient[2]. Next to glomerulonephritis and diabetes mellitus, hypertension is the third most common cause of chronic kidney disease, and accounts for 11% of the primary disease causing end stage renal disease (ESRD) in Bangladesh[3].

The relationship between the kidney and hypertension is interesting because the kidney can be affected by the hypertension or it can also cause hypertension. Eighty to ninety percent of patient with CKD experience hypertension during the course of their disease[4]. Uncontrolled hypertension accelerates the rate of progression regardless of the cause of renal failure. Clinical and epidemiologic studies indicate that hypertension is a major risk factor for progression of renal disease. Essential hypertension produces overt proteinuria and a significant reduction in renal

1. Assistant Professor, Department of Nephrology, Rangpur Medical College.
2. Associate Professor, Department of Nephrology, Dhaka Medical College.
   Assistant Professor, Department of Nephrology, Dhaka Medical College.
   Assistant Professor, Department of Nephrology, Dhaka Medical College.
3. Associate Professor, Department of Medicine, Dhaka Medical College.
4. Department of Radiology and Imaging, Dhaka Medical College.
5. MAG Osmani Medical College, Sylhet.
6. Chittagong Medical College.
6. Chittagong Medical College.
7. Ex- Professor and Chairman, Department of Nephrology, BSMMU.

function in 5-15% of patients[5], 40% of poorly controlled hypertensive individuals have microalbuminuria and its prevalence increases with duration and severity of the hypertension[6]. Hypertensive individuals had significantly higher levels of urea, creatinine and lesser levels of creatinine clearance compared to control subjects[7]. The dipstick method of measuring albumin in urine only detects protein excretion that exceeds 30mg/dl, which is a range that is currently denoted as overt proteinuria or macroalbuminuria. It has been used to screen renal disease in community based screening[8]. If dipstick for protein is negative then next step is to measure the albumin excretion, for which a spot urine collection is needed.

The population of Bangladesh is around 140 million. The population density is over 9000 per sq. kilometer. About 80% of the population of Bangladesh lives in rural area. So our study was designed to detect the prevalence of overt proteinuria and microalbuminuria in hypertensive subjects and whether these are associated with renal functional impairment in the rural area of Bangladesh. Microalbuminuria is a potentially reversible condition; overt proteinuria is an established risk marker for progressive loss of renal function, so effort should be given for detection of hypertension and early stage of hypertensive nephropathy, and take measures by optimum control of blood pressure.

**Materials and methods:**

This was a cross sectional study carried out at Bangaon union, a rural area of Savar upazilla 30 km away from Dhaka metropolitan city, over the period of August 2006 to April 2009. Data were collected by using a structured questionnaire. Adult rural population age between 18 to 65 year, both male and female were included in this study. Persons having fever, urinary tract infection, menstruation and pregnant women were excluded from the study. The study was done in the nephrology department, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Kidney Foundation, Dhaka, Bangladesh. 1134 adult participants were screened. Particulars of the participants including age, sex, occupation, marital status, height, weight; risk factor assessment including smoking habit, medical history including hypertension, diabetes & chronic kidney disease were taken. Physical examination was performed and blood pressure was recorded. Laboratory investigation was done eg. blood glucose, serum creatinine and detection of protein in urine by Dipstick. Microalbumin estimation in urine was done in hypertensive subjects who were negative in dipstick urine test.

Operational Definitions:

Hypertension and diabetes mellitus:

Participants were categorized for hypertension according to the JNC 7 Report[9] and for diabetes mellitus we consider ADA: clinical practice recommendations 2005[10].

Body mass index (BMI):

BMI was categorized as Malnutrition: BMI <18.5 kg/ $m^2$, Normal: BMI 18.5-24.9 kg/ $m^2$, Overweight: BMI 25.0-29 kg/$m^2$, Obese: BMI >30.0 kg/m >40.0 kg/$m^2$

Kidney function:

Kidney function was stratified according to NKF:K/ DOQI[11].

e-GFR done by Cockcroft-Gault prediction[12] and MDRD equation[13] from serum creatinine.

Data collection procedure:

Data were collected from all respondents by direct interview and using structured questionnaire after taking informed consent. In order to collect data and sample, there was a fixed centre where respondents would come every Friday from 9:00 am to 2:00 pm. Age, occupation, marital status, addresses were recorded as per statement of the participants at the time of interview; height and weight were measured. Blood pressure (BP) was measured after five minutes rest being relaxed in a chair with a support on the back keeping arm on a table at heart level. The average of the two readings separated by two minutes was taken who were hypertensive.

**Laboratory Method:**

Blood samples were collected on the spot for estimation of blood glucose and serum creatinine. The serum was then taken in appendrops and carried to kidney research laboratory of nephrology department at BSMMU keeping in icebox. Serum creatinine and blood glucose were estimated by Hospitex Screen Master, Techno-168 (ISE SRL, Italy). Spot urine sample was collected and dipstick test was done using Uric 2V GP reagent strip (Bayer, Germany) for detection Urinary protein. Presence of proteinuria was labeled as + (30mg/dl), ++ (100mg/ dl), +++ (300 mg/dl), ++++ (1000mg/dl). Hypertensive subjects, who are found dipstick negative for urine albumin on spot sample, further studied for urine microalbumin; for this urine was taken to Kidney Foundation keeping in icebox. Urine microalbumin is measured by NycoCard® U-Albumin a solid phase, sandwich-format, immunometric assay. Measuring range of albumin: 5-200 mg/L, Increased values (Microalbuminuria present): 20-200 mg/L, equivalent

to 30-300 mg/24 hours or 20-200 µgm/min. Overt proteinuria: >200 mg/L.

Data were processed and analyzed using computer software, SPSS version 11.5. The descriptive statistics were frequency, mean and standard error of mean. The test statistics used to analyze the data were descriptive statistics, Chi-square test, Fisher's exact probability test, Student's t-test. P-value <0.05 was considered significant.

**Results:**

A total of 1134 participants of 18 to 65 yrs of age were enrolled in this study with mean age of (37.2 ± 14.0) yrs. Among these participants <40 yrs of age were 56.9% (645), female 66%(753), married 86%(972), housewife 58.6%, farmer 11.1%, student 8%, service-holder 7.7%, businessman 5.7% and others 8.9%. Risk factors among the participants showed 23.8% of underweight, 56.1% of normal weight, 17.2% of overweight, 2.8% of obese in terms of BMI. Over 20% of the participants were smoker, 19.1% hypertensive, 7.1% diabetic 3.5% had both diabetes and hypertension. Family history of hypertension, diabetes and chronic kidney diseases were 8.6%, 9.1% and 0.6% respectively (Table-1)

**Table-I**

*Distribution of risk factors among the participants*

| Risk factors | Frequency | Percentage |
|---|---|---|
| BMI (kg/m$^2$) | | |
| < 18.5 (Underweight) | 270 | 23.8 |
| 18.5 – 24.9 (Normal) | 636 | 56.1 |
| 25 – 29.9 (Overweight) | 195 | 17.2 |
| 30 – 39.9 (Obese) | 32 | 2.8 |
| e" 40 (Morbid) | 01 | 0.1 |
| Smoking habit | 228 | 20.1 |
| Hypertension | 217 | 19.1 |
| Diabetes | 81 | 7.1 |
| Combined hypertension and diabetes | 40 | 3.5 |
| Family history hypertension | 97 | 8.6 |
| Family history of diabetes | 103 | 9.1 |
| Family history of chronic kidney disease | 07 | 0.6 |

* Total will not correspond to 100% because multiple response

Among the participants, a total of 217 (19.1%) were hypertensive (Stage-I + Stage-II)**.** Distribution of blood of blood pressure level among the participants showed 44.3% were within normal blood pressure range, 36.6% pre-hypertensive, 11.3% in stage-I and 7.8% in stage-II (Table II)

**Table-II**

*Distribution of patients by staging of hypertension*

| Staging of hypertension | Frequency | Percentage |
|---|---|---|
| Normal | 519 | 45.8 |
| Pre-hypertension | 415 | 36.6 |
| Stage-I | 119 | 10.5 |
| Stage II | 81 | 7.1 |
| Total | 1134 | 100 |

Staging of chronic kidney disease based on estimated GFR (eGFR) reveals that stage-III kidney disease formed the main bulk (17.5%) followed by stage-II (2.5%), stage-I (0.9%), stage-IV (0.4% each) and stage-V the least (0.1%). Thus a total of 21.3% participants had CKD (Table III)

**Table III**

*Distribution of participants by CKD staging*

| Staging of CKD | Frequency | Percentage |
|---|---|---|
| Total CKD | 242 | 21.3 |
| Stage-I | 10 | 0.9 |
| Stage-II | 28 | 2.5 |
| Stage-III | 198 | 17.5 |
| Stage IV | 05 | 0.4 |
| Stage-V | 01 | 0.1 |
| Normal | 892 | 78.7 |
| Total | 1134 | 100 |

Hypertensive participants had a significantly higher proportion of CKD (28.1%) compared to their non-hypertensive counterpart (19.7%) (p = 0.007)(Table IV).

**Table-IV**

*Association of CKD with hypertension*

| CKD | Hypertension | | p-value# |
|---|---|---|---|
| | Present (n = 217) | Absent (n = 917) | |
| Present | 61(28.1) | 181(19.7) | 0.007 |
| Absent | 156(71.9) | 736(80.3) | |

Figures in the parentheses denote corresponding percentage

Hypertensive participants had a significantly higher frequency of proteinuria (9.7%) compared to that of the non-hypertensive group (3.1%) (p < 0.001) (Table V).

**Table-V**

*Association between proteinuria and hypertension*

| Proteinuria | Hypertension | | p-value# |
|---|---|---|---|
| | Present (n = 217) | Absent (n = 917) | |
| Present | 21(9.7) | 28(3.1) | < 0.001 |
| Absent | 196(90.3) | 889(96.9) | |

Figures in the parentheses denote corresponding percentage

Over one-quarter (26.4%) of the hypertensive participants had microalbuminuria (20–200 mg/L) compared to 13.5% of the participants who did not have hypertension (p = 0.001) (Table VI).

**Table -VI**

*Association between microalbuminuria and hypertension*

| Microalbumin in urine (mg/L) | Hypertension | | p-value# |
|---|---|---|---|
| | Present (n = 178) | Absent (n = 245) | |
| < 20 | 131(73.6) | 212(86.5) | 0.001 |
| 20 – 200 | 47(26.4) | 33(13.5) | |

Figures in the parentheses denote corresponding percentage

The data on eGFR of proteinuric and non-proteinuric participants revealed that proteinuria of either sexes was not found to have any impact on eGFR (p=0.751and p=0.207 respectively (Table VII).

**Table-VII**

*Impact of overt proteinuria on eGFR*

| Overt proteinuria | eGFR | | p-value |
|---|---|---|---|
| | Mean | SD | |
| Male | | | |
| Proteinuric | 81.6 | 21.1 | 0.751 |
| Non-proteinuric | 83.2 | 21.8 | |
| Female | | | |
| Proteinuric | 71.5 | 23.2 | 0.207 |
| Non-proteinuric | 76.3 | 20.7 | |

Correlation between microalbumin in the urine and eGFR shows that the two variables exhibit a negative relationship, although the relationship was not statistically significant (r = -0.064, p = 0.186)(Fig-1).

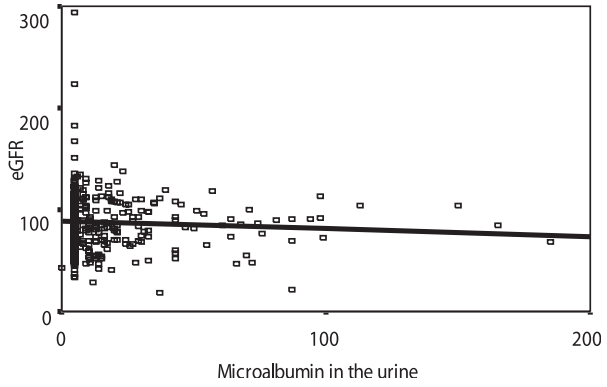


**Fig.1:** *Correlation between microalbumin in the urine and eGFR*

**Discussion:**

This study was conducted to know the prevalence of overt proteinuria and microalbuminuria in hypertensive subjects in a rural adult community. The relation of overt proteinuria and microalbuminuria with the renal function of these hypertensive individuals was also seen.

In the presenting study 19.1% were hypertensive; 36.6% pre hypertensive state and 44.3% were normal blood pressure. Among the hypertensive (19.1%), 11.3% stage 1 and 7.8% had stage 2 hypertension. In a study performed in the urban slum of Dhaka metropolitan city showed 11.6% of the participants were hypertensive[14]. According to NHANES 2003-2004, the prevalence of hypertension among the US adult population was 29.3%[15]. In China, from China National Nutrition and Health Survey 2002 among the adults, prevalence of hypertension was higher in urban compared with rural areas in men (23% versus 18%) and women (18% versus 16%)[16].

Prevalence of chronic kidney disease (CKD) in our study was 21.3%. In Bangladesh, the prevalence of CKD in adult disadvantage people in Dhaka was 16%[14]. In our study among the hypertensive subjects, 28.1% had been suffering from chronic kidney disease, compared to 19.7% in non hypertensive group. A prospective study among 8093 subjects, showed an increase in systolic blood pressure , pulse pressure and mean arterial pressure were associated with 12.8% subjects developed CKD over 12 years follow up[17]. In our study prevalence of diabetes mellitus was 7.1%, and 3.5% of the participants had both hypertension and diabetes.

Proteinuria is the cardinal manifestation of renal disease irrespective of etiology and persistence proteinuria is an independent risk factor for progression of renal disease. In our study, proteinuria was present in 9.7% of hypertensive subjects, but in non hypertensive prevalence of proteinuria was 3.1%. The prevalence of proteinuria in health service providers in a tertiary hospital in Dhaka was 2.4%[18]. In another study showed the prevalence of proteinuria was 7.7% in adult disadvantageous people in Dhaka Metropolitan city[14]. 'The AusDiab kidney study' found proteinuria in 2.4% of the participants by measuring protein creatinine ratio in a morning urine sample[19].

Among the hypertensive participants micro-albuminuria was present in 26.4%. Healthy general population as a control showed the prevalence of microalbuminuria was 13.5%. Hypertensive subjects were observed to be significantly older than non hypertensive counterpart (46.8±12.3 vs. 36.1±13.4 years, p<0.001). Age and obesity were found to be important predictors for a higher risk of having microalbuminuria. Overweight and obesity demonstrated their significant presence in hypertensive participants than that in the non-hypertensive counterparts (36% vs. 19.6%, <0.001).

Correlation between microalbuminuria and e-GFR showed that two variables exhibit a negative relationship, as patient having microalbuminuria their renal function declines. In a study among 141 hypertensive patients, 54 (38%) patients had microalbuminuria[20] and another study to determine the frequency of microalbuminuria in hypertensive subjects, 288 participants were screened, the prevalence microalbuminuria was 37.5%. In addition, hypertensive patients had significantly higher levels of urea and creatinine, and lesser levels of creatinine clearance compared to control subjects[7].To determine the prevalence of microalbuminuria in a large sample of Spanish hypertensive population, 7673 hypertensive subjects were screened. The prevalence of microalbuminuria was 25.3% and 2.6% showed overt proteinuria[21].

To see the prevalence of microalbuminuria and its relationship with target organ damage in patients with essential hypertension, a total of 150 hypertensive without diabetes mellitus and/or other conditions causing microalbuminuria were studied. 26.67% patients were found to have microalbuminuria and it was significantly higher in those with longer duration and greater severity of hypertension. Older age, adverse lipid profile, higher BMI were other identifiable risk factor for microalbuminuria[22].

In the present study proteinuria and microalbuminuria are prevalent among the hypertensive subjects which comparable to other studies. Other than hypertension increasing age, obesity, and diabetes are important risk factors for microalbuminuria. Hypertensive microalbuminuric subjects are prone to develop renal function deterioration. A large scale study should be conducted on both rural and urban population of different parts of Bangladesh to identify risk groups and initiate intervention so that future burden of CKD could be minimized.

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