

# Prevalence and Risk Factors of Microalbuminuria in Hypertensive Patients of Tertiary Care Hospital

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**ABSTRACT- Background:** Microalbuminuria in hypertension has been described as an early sign of kidney damage and a predictor for end stage renal disease and cardiovascular disease. More specifically, it is seen amongst patients suffering from hypertension.

**Methods:** This study was conducted at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India in the department of emergency medicine and 84 subjects were included in the evaluation in the age of more than 30 years. All patients were diagnosed by clinical examination, anthropometric measurement, blood pressure, urinary microalbumin, and urinary creatinine. Statistical analysis was done by using SPSS, version 16.0 p-values were calculated by chi-square test and ANOVA unpaired t-test. The p<0.05 was considered statistically significant.

**Results:** It was found that microalbuminuria among hypertensive patients increased steadily with the advancing age and the duration of hypertension. The features of high urinary microalbumin 52.09±8.62 mg/24 hr and the urinary creatinine 2.37±0.86mg/dl were prevalent in hypertensive patients and it increased in both male and female patients.

**Conclusion:** The prevalence of microalbuminuria in hypertensive individuals is high, and it revealed strong association between microalbuminuria and hypertension. Our findings suggest that microalbuminuria could be a useful marker to assess risk stratification and management of cardiovascular disease and renal disease.

**Key words:** Hypertension, Cardiovascular disease, Renal disease, Risk factors, Age factors, Urinary creatinine, Urinary microalbumin

## INTRODUCTION

Hypertension is one of the most common cardiovascular disorders and is a major public health problem all over the world. A recent report on the global burden of hypertension indicates that nearly 1 billion adults (more than a quarter of the world's population) had hypertension in 2000, and this is predicted to increase to 1.56 billion by 2025. <sup>[1]</sup> Hypertension induced cardiovascular diseases (CVD) and cerebrovascular stroke <sup>[2]</sup> attributes to about 13.5% of all deaths associated with hypertension related deaths. Recent studies indicate that the prevalence of hypertension is rapidly increasing in developing countries and is one of the leading causes of mortality and disability. <sup>[3]</sup>

The incidence of hypertension is increasing year after year and the prevalence of hypertension is increasing day by day due to increased life expectancy and aging population. The incidence of hypertension in India is 5–15% of the adult population against 10–12% in the West. However, the Jaipur heart watch study and the Chennai Urban, Rural Epidemiology study (CURES) reported the prevalence of hypertension to be 37% and 20% respectively using the JNC-VII guidelines which was found to be higher the national average. By the time most of the individuals are diagnosed with hypertension they have already progressed into severe stage and many of them have already developed target organ damage like fatal stroke or myocardial infarction or irreversible renal failure. <sup>[4]</sup>

Microalbuminuria has a major impact on cardiovascular risk. <sup>[5]</sup> The association between microalbuminuria and hypertension was described by Parving *et al.* <sup>[6]</sup> during the past few years microalbuminuria has emerged as a prognostic marker for cardiovascular disorders. In essential hypertension, an increased transglomerular passage of albumin may result from several mechanisms such as hyperfiltration, glomerular basal membrane

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abnormalities, endothelial dysfunction and nephrosclerosis [7]. Microalbuminuria which represents albumin excretion rate (AER) of 30 to 300 mg/24 hours or 20–200 micrograms/minute [8] or 30-299 mg/g creatinine [9] defined as elevated urinary albumin excretion below the level of clinical albuminuria [8], undetected by Albustix and can only be detected by special methods such as immunochemical [10] and is reversible with euglycaemic control.

Several epidemiological studies were shown that proteinuria as well as micro-albuminuria is independent predictors of cardiovascular morbidity [11,12] and mortality in patients with essential hypertension. Moreover, 25% of patients with end stage renal disease have hypertension as the primary diagnosis [13]. It becomes paramount importance to study Urinary Albumin Excretion (UAE) and progression of nephropathy in hypertensive patients. Resting heart rate, respiratory rate and blood pressure were higher in overweight and obese children compared to normal children; indicates a lower level of cardiovascular efficiency in overweight and obese boys compared to normal weight boys. [14]

Antioxidant/pro-oxidant imbalance in hypertension can lead to detrimental consequences and long term adverse effects like atherosclerosis and cardiovascular disease. More extensive study is required to check the association between hypertension and oxidative stress. [15]

The purpose of this study was to evaluate the incidence of microalbuminuria in a large population with mild to moderate hypertension and its relation to the severity of hypertension and renal function.

## MATERIALS AND METHODS

In this study, collected morning urine samples of clinically documented hypertensive patients attending Department of Emergency Medicine of Dr Ram Manohar Lohia Institute of Medical Sciences Lucknow, were screened for albuminuria by using turbidimetric immunoassay. Urine samples centrifuged at 2000 rpm for 3-5 minutes were used for quantitation of urine creatinine whereas the corresponding urine sample collected in sterile plastic urine container were sent to Pathology. After weight and height were measured, the body mass index (BMI) was calculated. Individuals with a BMI equal to or higher than 25 were considered over-weight and those with a BMI equal to or higher than 30 were considered obese. Waist circumference was measured and considered increased when higher than 80 cm for women or higher than 90 cm for men. An albumin/creatinine ratio higher than 30 in a spot morning urine sample was considered microalbuminuria.

## ASSESSMENT

**Clinical evaluation:** Detailed information, including medical history, personal information, and Family history of the subjects were taken.

- Blood pressure assessments
- BMI assessment

BMI was calculated using the formula,

$$\text{BMI} = \text{weight (kg)} / \text{height (m}^2\text{)}$$

## Biochemical Assessment

- ❖ Urinary microalbumin by ImmunoTurbidimetry
- ❖ Urinary creatinine by Jaffe's reaction

## SELECTION OF CASES

### Inclusion criteria

1. Subject diagnosed with Hypertension as per the joint national committee-VIII definition
2. Age group more than 30 years
3. Subject or subject's representative has signed the consent form

### Exclusion criteria

1. Subjects suffering from any chronic diseases or acute infections
2. Alcoholic and smoker

## SELECTION OF CONTROL

### Inclusion criteria

1. Age group more than 30 years
2. Subjects diagnosed as a normal healthy person

### Exclusion criteria

1. Subjects suffering with any chronic diseases or acute infections
2. Alcoholic and smoker

## Joint National Committee VIII Hypertension diagnosis, selection criteria

Hypertension was categorized according to blood pressure readings by JNC-VIII definitions: Normal (systolic <120 mm Hg and diastolic <80 mm Hg), prehypertension (systolic 120 to 139 mm Hg or diastolic 80 to 89 mm Hg), hypertension stage I (systolic 140 to 159 mm Hg or diastolic 90 to 99 mm Hg), and hypertension stage II (systolic  $\geq 160$  or diastolic  $\geq 100$  mm Hg). [16]

In spot urine sample albumin was measured quantitatively and adjusted to creatinuria then interpreted as an albumin creatinine ratio (ACR) <3.4 mg albumin/mmol creatinine as normal albuminuria,  $\geq 3.4$ -33.9 mg albumin/mmol creatinine as microalbuminuria, and >33.9 mg albumin/ mmol creatinine as macroalbuminuria. [17]

The formula of Cockcroft and Gault equation was used to calculate estimated glomerular filtration rate (eGFR) [18].

Calculation of eGFR in males-

$$\text{eGFR} = [140 - \text{age (yrs)}] \times \text{weight (kg)} \times 88.4 / [72 \times \text{serum creatinine } (\mu\text{mol/L})]$$

A companion equation for women, based on their 15% lower muscle mass (on average)-

$$\text{eGFR} = [140 - \text{age (yrs)}] \times \text{weight (kg)} \times 88.4 \times 0.85 / [72 \times \text{serum creatinine } (\mu\text{mol/L})]$$

**STATISTICAL ANALYSIS**

The results are presented in mean±SD (standard deviation) and percentage. The chi-square test was used to compare the categorical variables between cases and controls. The unpaired t-test was used to compare the study parameters between cases and controls. The Pearson correlation coefficient was calculated among the study parameters. The p-value<0.05 was considered significant. All the analysis were carried out by using the SPSS 16.0 version (Chicago, Inc., USA).

**RESULTS**

As per the statistical analysis (Total 42 study cases and 42 control cases were included in this study).

**Table 1:** Distribution of the cases and controls according to age group

Age (years)	Cases (n=42)		Controls (n=42)	
	No.	%	No.	%
30-40	9	22.1	5	11.9
41-50	16	39	18	45.8
51-60	8	17.2	8	19.0
>60	5	16.0	7	19.5
<b>Mean±SD</b>	48.98±9.76		51.02±9.90	

p=0.56 (Chi-square test)

In this study, Table 1 was shown that the distribution of the cases and controls according to age. The mean age of cases and controls was 48.43±9.76 and 51.02±9.90 years respectively. More than one third of the cases (39%) and controls (45.8%) were between 41–50 years. There was no significant (p>0.05) difference in the age between cases and controls shown the comparability of the groups.

**Table 2:** Distribution of the cases and controls according to sex

Sex	Cases (n=42)		Controls (n=42)	
	No.	%	No.	%
Male	19	45.2	16	38.1
Female	23	54.8	26	61.9

p=0.50 (Chi-square test)

Table 2 was shown that the distribution of the cases and controls according to sex. More than half of the cases (54.8%) and controls (61.9%) were females. There was no significant (p>0.05) difference in the sex between cases and controls showing comparability of the groups.

**Table 3:** Distribution of the cases and controls according to anthropometric parameters

	Cases (n=42)	Controls (n=42)	p-value
<b>Height (cm)</b>	149.63±5.82	174.83±5.67	0.002*
<b>Weight (kg)</b>	64.60±9.94	54.35±3.72	0.350
<b>BMI</b>	31.22±5.62	27.57±2.26	0.030

Unpaired t-test, \* statistically significant

Table 3 was shown, the distribution of the cases and controls according to anthropometric parameters. The height was significant (p=0.02) lower among the cases (149.63±5.82) compared to controls (174.83±5.67). However, weight was significantly (p=0.350) higher among the cases (64.60±9.94) compared to controls (54.35±3.72). BMI was also observed to be significant (p=0.030) higher among the cases (31.22±5.62) than controls (27.57±2.26).

**Table 4:** Comparison of the cases and controls according to family history of hypertension

Family history of hypertension	Cases (n=42)		Controls (n=42)	
	No.	%	No.	%
<b>Present</b>	27	71.2	18	45.1
<b>Absent</b>	11	28.8	20	54.9

p=0.01 (Significant) (Chi-square test)

Table 4 was shown, the comparison of the cases and controls according to family history of hypertension. The family history of hypertension was found to be significant (p=0.01) higher among the cases (71.2%) compared to controls (45.1%).

**Table 5:** Comparison of the cases and controls according to blood pressure level

	Cases (n=42)	Controls (n=42)	p-value
<b>SBP</b>	130.59±4.96	110.86±3.53	0.0001*
<b>DBP</b>	89.92±5.93	69.52±2.09	0.0001*

Unpaired t-test, \*Statistically significant

SBP= Systolic blood pressure, DBP= Diastolic blood pressure

Table 5 was shown that the SBP comparison of the cases (130.59±4.96) and controls (110.86±3.53) according to Systolic blood pressure level were found to be significant (p=0.0001\*) higher among the cases compared to controls.

DBP comparison of the cases (89.92±5.93) and controls (69.52±2.09) according to Systolic blood pressure level were found to be significant (p=0.0001) higher among the cases compared to controls.

**Table 6:** Comparison of the cases and controls according to Urinary micro albumin level

Urinary micro albumin level (mg/mmol)	
<b>Cases</b>	32.09±8.62
<b>Controls</b>	26.92±5.19
<b>p-value</b>	0.002*

Unpaired t-test, \*statistically significant

Table 6 was shown, the comparison of the cases and controls according to urinary micro albumin level. Urinary micro albumin level was found to be significant (p=0.002) higher among the cases (32.09±8.62) compared to controls (26.92±5.19).

**Table 7:** Comparison of the cases and controls according to Urinary creatinine level

	Urinary creatinine level (mg/dl)
Cases	1.37±0.86
Controls	1.00±0.38
p-value	0.018*

Unpaired t-test, \*statistically significant

Table 7 was shown, the comparison of the cases and controls according to urinary creatinine level. Urinary creatinine level was found to be significant ( $p=0.018^*$ ) higher among the cases ( $1.37\pm 0.86$ ) compared to controls ( $1.00\pm 0.38$ ).

## DISCUSSION

The present study was conducted among 84 patients (42 study cases and 42 control cases) with the objective to evaluate the association of microalbuminuria in hypertensive patients and healthy subjects. There was no significant difference in the age and sex between the cases and controls in this study showing the comparison of the groups (Table 1, and 2).

High blood pressure is an important modifiable risk factor for coronary heart diseases (CHD). Evidence from several epidemiological studies suggests that the risk of developing CHD increases with the increase of blood pressure. For instance, the Multiple Risk Factor Intervention Trial, which involved 361,662 men, revealed a strong association between hypertension and CHD.<sup>[19]</sup> Among subjects with CHD, the prevalence in hypertension has been estimated to be 32%.<sup>[20]</sup> Studies conducted in the United States indicated that reduction in Systolic Blood Pressure (SBP) was the second most important factor (after total cholesterol), which attributed to reduction in CHD-related mortality.<sup>[21]</sup>

Microalbuminuria is known to be a risk factor for cardiovascular disease; however, it is not known whether this association results from an effect of microalbuminuria in the development of subclinical atherosclerosis or whether microalbuminuria destabilizes subclinical atherosclerosis, thus leading to clinical events. Cao *et al.*<sup>[22]</sup> evaluated a population of 3312 participants in the "Cardiovascular Health Study" in regards with Microalbuminuria (MA). The participants were divided into three groups: individuals without diabetes or hypertension (33%), individuals with hypertension (52%), and diabetic individuals with or without hypertension (15%). For each one of the three groups, the relative risk of cardiovascular disease in the presence of MA increased by 1.7 to 1.8 times. However, MA was not associated with risk of subclinical atherosclerosis in the absence of hypertension or Diabetes mellitus (DM), which may lead to a conclusion that the mechanism of association of MA with cardiovascular disease involves destabilization of the vascular system, thus leading to clinically overt disease<sup>[22]</sup>.

The prevalence of microalbuminuria in different populations with the same clinical condition varies

significantly. This variability might be due to several factors such as the threshold used, measurement methods, instruments or extent of co-morbidities in the study population (e.g. in hypertension; mild, moderate or severe). The prevalence of microalbuminuria varies according to ethnicity. Microalbuminuria is more common in black and Asian populations compared with whites.<sup>[23]</sup>

In the present study, the BMI was observed to be significantly ( $p=0.093$ ) higher among the cases ( $23.22\pm 3.62$ ) than controls ( $23.57\pm 2.26$ ). In a study, compared with a BMI of 18.5-24.9 kg/m<sup>2</sup>, a BMI of 25-30 kg/m<sup>2</sup> and a BMI of >30 kg/m<sup>2</sup> were associated with an increased risk of hypertension occurrence.<sup>[24]</sup>

In the present study, the urine creatinine level was found to be significantly ( $p=0.018$ ) higher among the study group ( $1.37\pm 0.86$ ) compared to controls ( $1.00\pm 0.38$ ). Hasit *et al.*<sup>[25]</sup> observed that the urinary albumin creatinine ratio was lesser than the established microalbuminuric range of 30-300 mg/g, in both study and controls irrespective of the values obtained for lipid profile and anthropometric indices.

## CONCLUSIONS

This study demonstrates a strong and significant association between Microalbuminuria and hypertension. This study indicated that Microalbuminuria is a useful marker to assess risk management of renal and cardiac involvement by early screening of patients with hypertension for microalbuminuria. Planned and aggressive management of positive cases might reduce the burden of chronic kidney diseases and cardiovascular diseases. This may be an early marker for end-organ damage susceptibility.

The findings of this study reinforce the JNC-VIII recommendations for lifestyle modification and also suggest that proper BMI and sleep duration are applicable for young patients with hypertension to manage their blood pressure.

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