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Research Article

Correlates of microalbuminuria in hypertensive patients of a tertiary care teaching hospital of Central India

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ABSTRACT

Background: Although the prevalence of hypertension is high in India, the relationship between micro-albuminuria and target organ damage in hypertension is not well studied. Hence this study aims to study the prevalence of micro-albuminuria in patients of hypertension and its correlation with other cardiovascular risk factors.
Methods: This cross-sectional study was done in 112 essential hypertension non-diabetic patients presented at a tertiary care hospital of Madhya Pradesh, India who fulfilled inclusion criteria and exclusion criteria during a calendar year. The diagnosis of essential hypertension was made by the study physician after complete medical history, physical examination and routine biochemical analysis of blood and urine. The data was analysed using SPSS version 20 and Mann Whitney U and Chi-square test was used for quantitative and qualitative data respectively.
Results: The total number of patients having micro-albuminuria was 26 and the prevalence came out to be 23.21%. The mean age of micro-albuminuric patients was less compared to non-microalbuminuric patients ($p<0.05$). The systolic, diastolic blood pressure and cholesterol levels were found to be higher but was statistically insignificant whereas body mass index (BMI) and duration of disease was statistically higher ($p<0.05$) amongst the cases having micro-albumin in their urine.
Conclusions: The prevalence of micro-albuminuria increases with the increase in duration, stages /severity of hypertension. Micro-albuminuria may be considered as a marker of adverse cardiovascular risk profile such as LVH and hyperlipidemia. High BMI, smoking and advanced stages of retinopathy are also the risk factors of micro-albuminuria.

Keywords: Essential hypertension, Micro-albuminuria, Target organ damage, Cardiovascular risk factors

INTRODUCTION

Hypertension is a disease that affects about one billion individuals worldwide.[1] It increases the risk for development of cerebral, cardiac, and renal events. Although our understanding of the pathophysiology of the elevated arterial pressure has increased, in 90-95% of cases the etiology is still largely unknown. Patient with arterial hypertension and no definable cause are said to have primary, essential or idopathic hypertension. Micro-albuminuria, a biomarker of endothelial dysfunction, is associated with increased cardiovascular, renal, and cerebrovascular morbidity and mortality. Its presence in hypertension, even in the setting of normal renal function, confers additional risk for cardio-vascular disease. Micro-albuminuria is a common finding in diabetes and hypertension, respectively, the first and second leading causes of end-stage renal disease.

Micro-albuminuria (MA) is one of the earliest indications of kidney injury in patients with diabetes mellitus and hypertension and is associated with high incidence of cardiovascular morbidity.[2] Micro-albuminuria possibly reflects a state of increased renal endothelial permeability and is considered an early marker of diffuse endothelial dysfunction.[3] Micro-albuminuria is the excretion in urine

of small quantities of albumin, insufficient to be demonstrated by ordinary laboratory methods. It has been suggested that micro-albuminuria may represent the renal manifestation of generalized, genetically conditioned vascular endothelial dysfunction.[4-6]

Since micro-albuminuria is associated with poor control of hypertension, its presence may indicate the need for improvement in control of hypertension and careful follow-up for detection of complications. This study has been undertaken with the concept of detecting micro-albuminuria, as the early marker of intra renal vascular dysfunction in essential hypertension and to illustrate the correlation with the severity of HTN, duration of HTN and other cardiovascular risk factors such as age, smoking, obesity and target end organ damage.

METHODS

The study was a hospital based cross-sectional study conducted during September 2008 to September 2009 in a tertiary care teaching hospital of Madhya Pradesh. It caters to both rural and urban population of its own and nearby districts of Uttar Pradesh, India.

Sample size calculation

Considering prevalence of micro-albuminuria to be 30%, a sample size of 84 study subjects was calculated for this study at 5% confidence interval and 10% allowable error using the formula $N=4PQ/L^2$.

In the study, patients with essential hypertension (old and new) was taken from OPDs and wards of the hospital and investigated for the presence of micro-albuminuria. A total of 112 (also includes patients who voluntarily requested to be included in the study) hypertensive patients according to Joint National Commission on the Prevention, Detection, Evaluation and treatment of Hypertension (JNC) VII i.e Systolic ≥140mm Hg and diastolic ≥90 mm Hg were included considering the following inclusion and exclusion criteria.[7]

Inclusion criteria

- All known hypertensives (on regular or irregular treatment)
- All newly detected hypertensives

Exclusion criteria

Patient with

- Diabetes
- Pregnant women
- Positive Urine Analysis including hematuria, leucocyturia, proteinuria, glycosuria.
- Chronic heart failure
- Hepatic and renal insufficiency
- Clinical and laboratory signs of infection
- Neoplastic diseases

The study was carried out on patients from OPD and wards by random selection after taking their written consent. The diagnosis of essential hypertension was made by the study physician after complete medical history, physical examination and routine biochemical analysis of blood and urine.

The detailed history was recorded with particular emphasis on knowledge of hypertension and regularity of treatment including family history and addiction if any. The individuals found suitable for the study were subjected to the following investigations.

- ***Blood:*** Hemogram, total leukocyte count, differential leukocyte count, ESR.
- ***Urine:*** Proteinuria (heat concentration test), nitrite reaction, Benedict's test for glycosuria and microscopic examination (esp. For hematuria and leukocytosis).
- Blood sugar (fasting and post prandial).
- Blood urea, serum creatinine, serum electrolytes.
- Lipid profile was obtained after 12 hours of fasting.
- ECG was done in every case to detect atrial fibrillation, ischaemic heart disease and left ventricular hypertrophy
- ***Micral test*** for micro-albuminuria (MA) was done on all the study subjects. Micro-albuminuria was defined as micro-albumin in urine in range of 30-300 mg/L. Micral Test (Roches Diagnostics Ltd) is an immunological, semi-quantiative method for the in vitro determination of urinary albumin. The patient was advised to avoid any physical strenuous exercise prior to urine collection and 5 ml of first voided early morning midstream urine was used for testing.[8-9]

The data was compiled in Microsoft excel 2010 and was analysed using SPSS version 20. The quantitative data was analysed using Mann Whitney U test and qualitative data using Chi-square test. The data were expressed as mean, standard deviation and percentages wherever possible. The p value was calculated and <0.05 was considered to be statistically significant.

RESULTS

A total of 112 patients of hypertension who fulfilled the inclusion and exclusion criteria were taken in the study. Out of them 66 (58.9%) were females and 46 (41.1%) were males. The total number of patients having micro-albuminuria was 26 and the prevalence came out to be 23.21%. The percentage of patients having micro-albuminuria in the range of 20-50mg/l, 50-100mg/l and 100-200mg/l was 15.40, 42.30 and 42.30 respectively. The mean age of micro-albuminuric patients was less compared to nonmicro-albuminuric patients ($p<0.05$). The systolic, diastolic blood pressure and cholesterol

levels were found to be higher but was statistically insignificant whereas Body Mass Index (BMI) and duration of disease was statistically higher ($p<0.05$) amongst the cases having micro-albumin in their urine. (Table 1).

Table 1: comparison of different variables with presence and absence of micro-albuminuria.

Independent variables (Mean±SD)	Microalbuminuria		P value (Mann Whitney U test)
	Positive (n=26)	Negative (n=86)	
Age (years)	50.34 ± 9.61	55.90 ± 11.59	0.026**
Systolic blood pressure (mm Hg)	162.69 ± 10.41	160.86± 19.86	0.653
Diastolic blood pressure (mm Hg)	98.46 ± 14.33	95.56 ± 11.89	0.085
Body mass index (kg/m^2)	28.91±4.04	26.89±3.34	0.031**
Cholesterol (mg/dl)	211±57.62	186±29.08	0.104
Duration of disease (hypertension) (in years)	4.77±1.3	1.01±0.26	0.008**

** indicates statistically significant

Table 2: Association of different variables with micro-albuminuria.

Independent variables		Micro-albuminuria		P value (Chi-square test)
		Present (N=26)	Absent (N=86)	
Sex	Females	15 (22.7)	51 (77.3)	0.884
	Males	11(23.9)	35 (76.1)	
Treatment	No	4 (7)	53 (93)	<0.001**
	Yes	22 (40)	33 (60)	
Smoking	No	23 (23)	77 (77)	0.877
	Yes	3 (25)	9 (75)	
Retinopathy	Absent	14 (14.3)	84 (85.7)	<0.001**
	Present	12 (85.7)	2 (14.3)	
JNC stages	Stage 1	5 (12.2)	36 (87.)	0.036**
	Stage 2	21(29.6)	50 (70.4)	
Left ventricular hypertrophy	Absent	22 (21.2)	82 (78.8)	0.063
	Present	4 (50)	4 (50)	

*Figures in parentheses show percentages; ** indicates statistically significant

It was also observed that the patients having hypertension diagnosed for more than 10 years are likely to have micro-albuminuria and least likely in newly diagnosed cases. The association with other variables was also qualitatively observed.

Although there seems no obvious sex predilection as well as history of smoking, ECG changes suggestive of left ventricular hypertrophy (LVH) but males, smokers and persons with LVH were found to have more micro-albuminuria. The subjects with retinopathy, stage II hypertension of JNC VII and antihypertensive treatment are positively associated with micro-albuminuria ($p<0.05$) (Table 2).

DISCUSSION

Micro-albuminuria is known to occur in early essential hypertension and considered to be a biomarker of endothelial dysfunction. Hypertensive nephropathy is a known cause of chronic kidney disease but may remain under recognized sometimes. In the present study, out of total 112 hypertensive patients, 26 patients were found to have MA (30-300mg/l), hence the prevalence of MA is 23.21%. This is in concordance with some studies.[10-16] The prevalence of MA is described in Table 3.

The high prevalence of MA in patients with essential hypertension in this part of country must raise an alarm amongst the health professionals about the rising subclinical chronic kidney diseases (CKD). The prevalence in males and females is approximately same which differs from the findings of some studies.[17-19]

There are studies where micro-albuminuria was higher in females as observed by Jones et al.[20] Jacobein C et al also concluded that there is a possible difference in mechanisms and significance of micro-albuminuria between genders.[19] There was a statistical difference between MA and duration of hypertension (p=0.008) and longer the duration, the more possibility of micro-albuminuria in urine. It is a well-known fact that larger

the duration of hypertension, more severe will be the vascular changes in the kidney and hence the incidence of micro-albuminuria should increase with the duration of hypertension. Various other studies supported this finding.[12,21] Also there is statistically difference between severity of hypertension and MA (p=0.036). The percentage of patients of Stage II hypertension having micro-albuminuria is approximately 30% and of Stage I hypertension is only 12%.

Table 3: Comparison of prevalence rate of micro-albuminuria in various studies.[9-16]

	Total Number of patients	Prevalence of Micro-albuminuria
Present study	112	23.21%
Roberto Begazzi et al[10]	123	40%
Albert Mimran et al[11]	106 (Never treated mild to moderate hypertensive)	24.5%
Pontremoli et al (MAGIC study)[12]	787 (18-72yr age, discontinued treatment for 4wk.)	8%
Jalal et al[13]	288	37.5%
Wachtell et al (LIFE study)[14]	8029 (55-80yr. age) stage II or greater, discontinued treatment for 4wk.	26%
Palatini et al[15]	1041 (18-45yr age) untreated mild hypertension	6%
Hitha et al[16]	150	26.67%

The findings of the studies done by Jalal et al and Mimran et al were also in concordance with our study.[11,13] The study found out a highly significant difference between MA and the presence/absence of hypertensive retinopathy (p<0.0001). It is already established fact that long standing hypertension, produces retinopathy. Vascular changes in retina are reflection of similar changes in kidney, hence it is expected that there should be significant positive correlation between hypertension retinopathy & microalbuminuria.[12,16]

Although BMI is high in both the groups but group having micro-albuminuria is having significantly higher BMI (p=0.031) which supports the already proven fact that high BMI among hypertensives are at high risk of micro-albuminuria. There is a positive correlation between micro-albuminuria and obesity which was also found in other studies.[16,22] Many studies have reported that lipoprotein profiles of all micro-albuminuric hypertensives are significantly deranged when compared to non-albuminuria hypertensive patients.[12,21] In the present study mean serum cholesterol in micro-albuminurics was higher but was statistically insignificant (p=0.104).

Smoking is associated with excessive urinary albumin excretion in hypertensive subjects.[23,11] But there is insignificant association between smoking and micro-albuminuria in this study (p=0.877) and this may be attributed to less smokers in the study contributing to only <10% of the total sample size. It is also observed that MA is associated more with the Left ventricular hypertrophy (LVH) but the association is insignificant (p=0.063). The present study concludes that MA in HTN is a marker of wide spread vascular damage and is associated with adverse cardiovascular risk profile.

CONCLUSION

The prevalence of micro-albuminuria increases with the increase in duration, stages /severity of hypertension. Micro-albuminuria may be considered as a marker of adverse cardiovascular risk profile such as LVH and hyperlipidemia. High BMI, smoking and advanced stages of retinopathy are also the risk factors of micro-albuminuria.

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