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ORIGINAL ARTICLE

Microalbuminuria and Essential Hypertension: A Critical Evaluation

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Abstract

Background: Recent advancements in diagnostic modalities for microalbuminuria have shown that urinary excretion of albumin is more in hypertensive patients as compared to subjects with normal blood pressure. Microalbuminuria is known to be associated with certain complications like dyslipidemia, cardiac complications, atherosclerosis and kidney disease. **Purpose:** To analyze the prevalence of microalbuminuria and its clinical correlation with essential hypertension. **Material and Methods:** The study was of cross-sectional design, which was carried out in outpatient and inpatient departments of Medicine in DY Patil Medical School and Hospital, Nerul, Navi Mumbai. **Results:** Out of total 190 study participants 96 were normotensive controls, while 94 were hypertensive patients. Mean age in control group was 48 ± 9.4 years, while that in hypertensive group, it was 49.2 ± 10.2 years. The 24 hours mean urinary excretion of albumin in hypertensive patients with microalbuminuria was found to be 80.21, while it was 12.91 and 7.89 in hypertensive patients without microalbuminuria and control groups, respectively. **Conclusion: E**arly screening to detect microalbuminuria in early stages will help to initiate appropriate treatment regimen and prevent the risk of complications and thus improvement in prognosis.

Key Words

Cardiac, Microalbuminuria, Hypertension, Kidney

Introduction

Globally, hypertension (HTN) is one of the major causes of morbidity and mortality. More than 1/10th of Indian population is affected by HTN on annual basis (1). Essential HTN is defined as hypertension wherein no obvious cause can be detected. HTN is known to increase the risk of cardiovascular complications like myocardial infarction, angina, heart failure, peripheral arterial disease, and stroke (2). It also causes multiple other complications, of which renal complications are one of the commonest. Proteinuria and deterioration in functions of kidneys is detected in around 20% of the hypertensive patients (3). Microalbuminuria is the excretion of albumin in urine in the range of 30-300 mg in 24 hours (4).

Augmented afferent glomerular hydrostatic pressure, accentuated permeability of basal membrane of glomerulus, defects in tubular functions are some of the pathogenic changes in essential hypertension which are implicated in increased urinary excretion of albumin (4). Despite numerous studies have tried to find the prevalence of microalbuminuria in patients with essential hypertension, the precise prevalence rates are not known.

After analyzing the published studies, there was wide range in prevalence rates, which might be attributed to

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certain factors like difference in inclusion and exclusion criteria, smaller sample size, different grades of hypertension, etc. This prevalence ranges from 5 to 60% (5,6).

Recent advancements in diagnostic modalities for microalbuminuria have shown that urinary excretion of albumin is more in hypertensive patients as compared to subjects with normal blood pressure. Microalbuminuria is known to be associated with certain complications like dyslipidemia, cardiac complications, atherosclerosis, kidney disease, etc. (7). Whenever there is rise in urinary excretion of albumin by 10 units, the risk of stroke increases by 1.5 times. When compared to normal subjects, there is increased risk of stroke in patients with microalbuminuria. Microalbuminuria is also known to cause neuropsychiatric diseases like cerebral vasculopathy, Alzheimer's disease, memory loss, etc. It is also known to be associated to metabolic derangement which are considered to be an indicator of end organ damage, and thus bad prognosis in patients with essential hypertension (8).

It becomes logical to detect microalbuminuria as early as possible through screening of hypertensive patients, so that appropriate treatment regimens can be started quickly in pursuit of preventing end organ damage and improving the prognosis in these patients. Keeping the above findings in mind the present study was initiated to analyze the prevalence of microalbuminuria and its clinical correlation in patients with essential hypertension.

Material and Methods

The present study was of cross-sectional design, which was carried out in outpatient and inpatient departments of Medicine in DY Patil Medical School and Hospital, Nerul, Navi Mumbai. Study was initiated after obtaining approval from Institutional Ethics Committee (IEC).

Inclusion criteria: Out of total 190 study participants, 94 were diagnosed with essential HTN according to JNC 8 and these were of the age group 18-60 years with creatinine clearance of >80 ml/minute/1.73 m^2 (9). 96 age matched normotensive individuals were used as a control group. All the study participants were enrolled only after taking their informed written consent.

Exclusion criteria: Patients with hypertension other than essential type were excluded from the study. Also, pregnant patients, patients taking drugs altering urinary excretion of albumin like calcium channel blockers, beta blockers, angiotensin receptor II blockers, etc., patients with diseases known to affect urinary excretion of albumin like diabetes mellitus, urinary tract infection and patients with macroalbuminuria were excluded from the study.

Blood and urine investigations were done using automated analyzer machine. Microalbuminuria was defined as urinary excretion of albumin in the range of 30-300 mg/24 hours (10). All the relevant data entered into predesigned format in Microsoft Excel. This data was analyzed with the help of SPSS version 21.0. Statistical tests used were unpaired t test, and one-way analysis of variance. A p-value of < 0.05 was considered as statistically significant.

Results

In the present study, out of total 190 study participants 96 were normotensive controls, while 94 were hypertensive patients. Mean age in control group was 48 ± 9.4 years, while that in hypertensive group, it was 49.2 ± 10.2 years. There was no statistically significant difference in age, sex and BMI between the 2 groups *(Table 1).* Amongst the 94 hypertensive patients, microalbuminuria was detected in 32 patients (34%), while it was not found in 62 patients (66%) *(Figure 1).*

On analyzing the blood pressure parameters in hypertensive group, it was found that systolic BP was higher in patients with microalbuminuria as compared to those without microalbuminuria and this difference was found to be statistically significant ($p < 0.05$). There was no statistically significant difference in diastolic BP between both sub-groups ($p = 0.236$). Mean arterial pressure (MAP) was more in patients with microalbuminuria as compared to those without it. This difference was statistically significant ($p = 0.01$) *(Table 2)*.

The fasting blood sugar was comparable in both the sub-groups of hypertensive patients i.e. groups with and without microalbuminuria. On analysis of lipid profile in both sub-groups of hypertensive patients, it was found that all the parameters including serum cholesterol,

Table 1: Showing Demographic and Body Mass Index (BMI) Details of Normotensive and Hypertensive Groups

	Normotensive	Hypertensive	*p*-value
Age	48 ± 9.4	49.2 ± 10.2	0.102
Sex:			
Male	51	53	0.124
Female	45	41	
BMI (kg/m2)	21.56 ± 4.32	23.67 ± 5.61	0.196

Table 2: Showing Systolic and Diastolic Blood Pressure (BP), Mean Arterial Pressure (MAP) in Hypertensive Patients with Respect to Microalbuminuria

Blood pressure	Hypertensive patients		*p*- value
	Microalbuminuria	No Microalbuminuria	
Systolic BP	152.13 ± 3.47	143.27 ± 5.31	< 0.05
Diastolic BP	92.24 ± 5.42	91.01 ± 4.78	0.236
MAP	114.37 ± 4.98	109.81 ± 3.96	0.01

Table 3: Showing Laboratory Investigations in Hypertensive Patients With/Without Microalbuminuria

Sr. No.	Profile	Test/s	Control	Hypertensive		*p*-value
				No Microalbuminuria	Microalbuminuria	
1	FBS		87.54 ± 9.8	86.12 ± 7.8	88.47 ± 6.5	0.194
2	Sr. Lipid Profile	TG	104.21 ± 11.1	109.46 ± 8.9	126.48 ± 13.1	0.001
		Cholesterol	176.35 ± 9.8	179.29 ± 9.4	198.62 ± 9.47	0.04
		HDL	46.41 ± 3.6	44.26 ± 9.6	43.95 ± 6.8	0.001
		LDL	112.46 ± 7.8	120.39 ± 11.4	136.15 ± 10.1	0.001
		VLDL	23.52 ± 4.2	23.16 ± 3.6	24.37 ± 5.1	0.124
3	KFT (Serum Values)	Blood urea	18.71 ± 2.1	20.41 ± 2.3	28.12 ± 5.6	0.001
		eGFR	99.12 ± 9.87	99.92 ± 10.4	90.42 ± 11.2	0.05
		Creatinine	0.71 ± 0.02	0.78 ± 0.05	0.83 ± 0.07	0.04
		Uric acid	3.67 ± 1.4	3.98 ± 1.9	5.01 ± 2.0	0.001
		Na^+	140.56 ± 0.9	141.14 ± 2.1	141.8 ± 1.7	0.316
		K^+	3.86 ± 0.8	3.99 ± 1.1	4.03 ± 1.0	0.198
		Ca^{++}	8.98 ± 0.31	9.09 ± 0.2	9.04 ± 0.12	0.276
		PO_4^{3-}	3.24 ± 0.31	3.37 ± 0.51	3.31 ± 0.39	0.413
		Protein	6.97 ± 0.21	6.91 ± 0.32	6.99 ± 0.41	0.225
		Albumin	4.08 ± 0.22	3.92 ± 0.37	4.04 ± 0.17	0.293

Table 4: Showing Complications in Hypertensive Patients and Urinary Excretion of Albumin

Sr. No.	Complications		No. of pts. (n=94)	Urinary excretion of albumin	*p*-value
1	Cardiac ischemia	Yes	19	133.56 ± 8.1	< 0.001
		No	75	55.18 ± 4.4	
2	Hypertrophic LV	Yes	27	121.52 ± 7.3	0.001
		No	67	63.38 ± 5.1	
3	Retinopathy	Yes	44	119.35 ± 4.7	0.001
		No	50	59.21 ± 6.3	

triglycerides (TGs), low density lipoproteins (LDL), and very low density lipoproteins (VLDL) were raised and high density lipoproteins (HDL) were reduced more in hypertensive patients with microalbuminuria, and this difference was highly statistically significant. Amongst the kidney function tests (KFT), blood urea, eGFR, serum creatinine and uric acid levels raised in hypertensive patients with microalbuminuria and the difference was statistically significant. Although differences were found in other parameters of KFT between 2 subgroups of hypertensive patients, it was not statistically significant *(Table 3)*.

The 24 hours mean urinary excretion of albumin in hypertensive patients with microalbuminuria was found to be 80.21, while it was 12.91 and 7.89 in hypertensive patients without microalbuminuria and control groups,

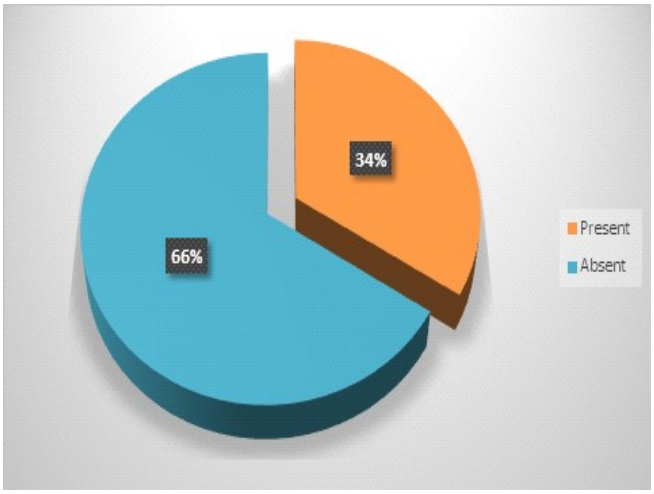

Figure 1: Showing Presence or Absence of Microalbuminuria in Hypertensive Patients

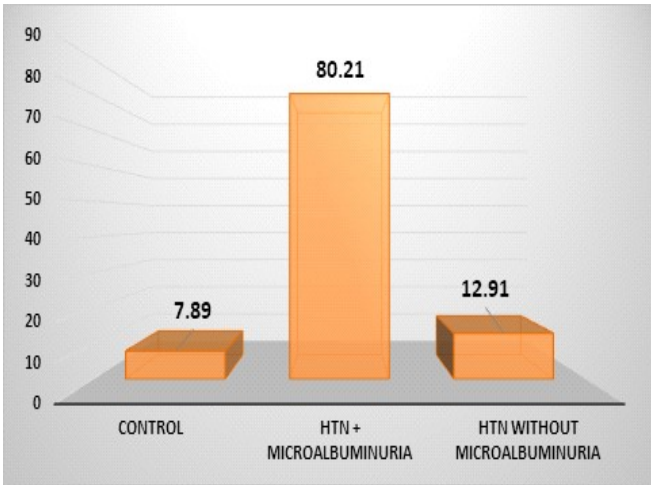

Figure 2: Showing Mean 24 Hours Urinary Excretion of Albumin in Subgroups of Study Participants

respectively *(Figure 2)*.

On analysis of complications and urinary excretion of albumin in hypertensive patients, it was found that cardiac ischemic changes were seen in 19 patients, left ventricular hypertrophy was seen in 27 patients, and hypertensive retinopathy was seen in 44 patients. Urinary excretion of albumin was raised more in hypertensive with these complications as compared to those without complications, and this difference was highly statistically significant *(Table 4)*.

Discussion

Derangements in vascular functions and microalbuminuria are some of the complications seen in patients of essential hypertension. Increased urinary excretion of albumin and microalbuminuria are linked to vascular endothelial dysfunction in these patients (11). Published literature suggests that risk of cardiovascular complications is augmented in patients of essential hypertension who encounter reduction in kidney function (12).

Traditionally, renal function in hypertensive patients is monitored by laboratory investigations like serum creatinine, blood urea nitrogen, etc. But these investigations detect deterioration in kidney function when the disease is already increased in severity. In the light of the above findings, quantifying urinary excretion of albumin in relation to hypertension severity has gained attention in recent times. Excretion of urinary albumin in the range of 30-300 mg/g is defined as microalbuminuria. Whether single measure or repeated measurements of urinary excretion of albumin should be done for the above purpose is a matter of debacle (13).

The socio-demographic findings in the present study were comparable to that of study done by Aggarwal *et al*. (14). In the present study, serum triglycerides, cholesterol, very low-density lipoproteins and low-density lipoproteins were raised in patients with hypertension and more so in those hypertensive patients who had microalbuminuria. Ghooschi *et al.* (15) and Choudhury *et al.* (16) reported similar trends in hypertensive patients in their clinical studies on correlation of lipid profile and hypertension complications. Similarly, an Indian study by Rekha and Prasad (17) reported increased derangements in lipid parameters in hypertensive patients. Wong *et al.* (18) had established correlation of hypertension and early development of coronary artery disease. Microalbuminuria is considered as an indicator of sub-clinical atherosclerotic thickening of blood vessels (19). Thus, multiple interventions like dietary and lifestyle modifications along with appropriate drug therapies to reduce the blood pressure as well as correcting lipid derangements are required to prevent development of coronary artery disease (17).

In the present study blood urea, creatinine and uric acid levels were raised in hypertensive patients and this was more pronounced in hypertensive patients showing microalbuminuria. Similar trends were reported by Jalal *et al.* (20) in their clinical study. In an Indian study done by Yadav *et al.,* (4) it was found that serum levels of urea, uric acid, and creatinine were raised in patients

with hypertension as compared to non-hypertensive. HTN is a risk factor for nephropathy and kidney failure, and this risk association continuously increases with each unit rise in blood pressure, more so with rise in systolic blood pressure as compared to diastolic blood pressure (17). Increased serum creatinine is thought to reflect derangement in endothelial structure and function or hyper coagulation state (4).

Microalbuminuria was seen in 34% of the hypertensive patients in the present study. As per the published literature, prevalence of microalbuminuria in hypertensive patients varies from 16 to 99% (21,22). Multiple factors might be responsible for such a huge range of prevalence rates, like different stages of hypertension, type of investigation method/ technique used to measure microalbuminuria, differences in race, gender, age, co-morbidities, etc.

The prevalence rates of microalbuminuria reported by Kumar *et al.* (7) and Hitha *et al.* (23) was in accordance with the present study findings, which reported prevalence rates of microalbuminuria in hypertensive patients to be 27 and 32%, respectively. However, study done by Aggrawal *et al.* (14) on prevalence of microalbuminuria in hypertensive to be 47%, while Rodila *et al.* (24) and Sharan Badiger *et al.* (25) had reported the prevalence rates of microalbuminuria to be 63% and 58%, respectively.

Various studies have shown a contributory association between increasing excretion of urinary albumin and advancements in intensity of hypertension, which is corroborated by the findings of the present study (7,10). Complications like ventricular hypertrophy, cardiac ischemic changes, retinopathy was more in hypertensive cases and that too more in patients with microalbuminuria. Interestingly, patients in whom complications were present, the urinary excretion of albumin was far more as compared to the patients without complications. Even the eGFR was reduced more in patients with microalbuminuria as compared to those without it. Rodicio *et al.* (8) had reported similar trends of increased complications in hypertensive patients who had microalbuminuria as compared to patients without microalbuminuria. Also, Crippa *et al.* (10) had cited in their study that microalbuminuria is an important prognosticator for cardiovascular complications in patients suffering from essential hypertension.

Conclusion

In the light of findings of the present study, it becomes amply clear that microalbuminuria is present in significant number of patients with essential hypertension and it carries increased risk of developing complications. The silent nature of hypertension/ microalbuminuria implies that patients will be unaware of the disease until diagnosed on routine testing or in worst scenario until complications develop. Thus, early screening to detect microalbuminuria in early stages will help to initiate appropriate treatment regimen and prevent the risk of complications and thus improvement in prognosis. The aim is to hit early and hit hard. However, more such studies need to be done with larger sample size and at multiple sites throughout the country to generalize the results.

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Conflicts of Interest
There are no conflicts of interest.

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