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Essential Hypertension is Associated with Higher Prevalence of Microalbuminuria - A Cross - Sectional Study

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Abstract

Background: Hypertension is a major public health problem. The incidence in India is 5-15% in adult population. Essential hypertension produces proteinuria and a significant reduction in renal function in 5-15% of patients. UAE (urine albumin ratio), of higher frequency (25-100%) found in patients with hypertension than in normotensive population.Microalbuminuria has been described as an early sign of vascular damage and renal disease. Endothelial dysfunction has been proposed to be a plausible pathophysiological mechanism of microalbuminuria. Microalbuminuria is a consequence of an augmented intraglomerular capillary pressure; intrinsic glomerular damage and tubular alterations also account for increased urinary albumin excretion. Microalbuminuria was associated with the presence of target organ damage, electrocardiographic abnormalities and retinal vascular changes. **Material and Methods:** A cross sectional observational study was conducted on 100 subjects including 50 cases diagnosed with essential hypertension and 50 healthy normotensive age and gender matched subjects as control taken from the Medicine OPD of GMC, Patiala. These patients were evaluated for microalbuminuria by ELISA kit method. **Results:** Prevalence of micro albuminuria in essential hypertensive subjects was 48% as compared to, no microalbuminuria in normotensive people.Microalbuminuria was strongly associated with increased systolic blood pressure in our study, SBP (155.58±9.36 mmHg) in microalbuminurics and SBP (148.76±7.2 mmHg) in normoalbuminurics. **Conclusion:** This study confirmed that increased urinary albumin excretion is associated with increased systolic blood pressure.

Keywords: Microalbuminuria, Essential Hypertension.

INTRODUCTION

Hypertension is a major public health problem worldwide. The incidence of hypertension in India is 5 –15% in the adult population against 10–12% in the West.[1] Essential hypertension produces proteinuria and a significant reduction in renal function in 5-15% of patients.[2] The advent of more sensitive methods to quantitate the urine albumin excretion (UAE) has revealed higher frequency (15-100%) of microalbuminuria in patients with hypertension than in normotensive population.[3]

The kidney is both a target and a causative organ of hypertension. Proteinuria is a reliable parameter to

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evaluate kidney function and predict disease progression.

Microalbuminuria is defined as urinary albumin excretion 30-300 mg/24 hour or albumin/creatinine ratio 30-300 mg/g.[4] The published prevalence of microalbuminuria in hypertensive subjects ranges from 4.7% to 58.4%.[5-8]Microalbuminuria is a consequence of an augmented intraglomerular capillary pressure; intrinsic glomerular damage and tubular alterations also account for increased urinary albumin excretion. Microalbuminuria has been postulated to represent the renal manifestation of generalized, genetically conditioned vascular endothelial dysfunction that may underlie the link between an increased UAE and an elevated risk for cardiovascular disease.[9] There is direct relationship between high blood pressure and microalbuminuria.[10] Combining eGFR and albuminuria screening identify hypertensive subjects at high risk of cardiovascular morbidities and mortalities.[11] Patients who develop chronic renal insufficiency are more likely to have microalbuminuria at baseline and reduction of urine albumin excretion is associated with better renal outcomes.[12] Therefore, routine checks for those at high risk for chronic disease should include albuminuria screening in order to prevent or delay possible progression to ESRD.

Microalbuminuria is independently associated with hypertensive retinopathy. Incidence and severity of hypertensive retinopathy is reported to be higher among microalbuminuric hypertensive patients as compared to normoalbuminuric hypertensives; independent of severity of hypertension.[13]

Existing literature highlights that there is high prevalence of microalbuminuria in hypertensive patients and it is associated with a cluster of metabolic and non-metabolic risk factors which is also a marker of target organ damage. Early screening for microalbuminuria in patients of essential hypertension and thereby early initiation of treatment might help in reducing ongoing target organ damage. In this sense; early microalbuminuria detection is a cheap and easily accessible commodity which may save our resources and patient lives by preventing further target organ damage and thus obviating the need of expected future interventions. Hence the present study was planned.

Aims and Objectives

1. To evaluate the frequency of microalbuminuria in patients with essential hypertension.
2. To study the correlation of microalbuminuria with severity and duration of hypertention.

MATERIAL AND METHODS

This cross-sectional study was conducted in Department of Medicine and Department of Biochemistry on 100 subjects including 50 cases diagnosed with essential hypertension and 50 healthy normotensive age and gender

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matched subjects as control taken from the Medicine OPD of GMC, Patiala.

Inclusion Criteria

Group A: Study group: 50 diagnosed cases of essential hypertension according to JNC (Joint National Committee) VII criteria (4)
Stage 1: Systolic = 140 to 159 mm Hg and diastolic 90 to 99 mm Hg.
Stage 2: Systolic ≥ 160 mm Hg and diastolic ≥ 100 mm Hg.

Group B: control group: 50 controls without hypertension which are age and gender matched patients presenting with minor ailments.

Exclusion Criteria

1. Patients with a diagnosis of secondary hypertension due to causes such as chronic kidney disease, renal artery stenosis, coarctation of aorta, cushing's syndrome, pheochromocytoma.
2. Drugs known to cause hypertension and other known causes of hypertension (Acetaminophen, Alcohol, Amphetamines, Corticosteroids, Cyclosporine, Erythopoietin, etc.)
3. Pregnant women.
4. Known case of diabetes mellitus or newly diagnosed case of diabetes mellitus.
5. Patients with urinary tract infections.
6. Patients with kidney disease.
7. Macro albuminuria (Urine Albumin Excretion >200 µg/min OR >300 mg/ 24hours)

In all the cases and controls the following examinations were performed.

1. Clinical examination: Medical history taking (including history regarding hypertension and its familial occurence), physical examintion and accurate BP (Blood Pressure) measurement.
2. Blood Pressure recordings were taken thrice 15 minutes apart, after 5 minutes of rest, with patient seated in a chair, the back supported and arm bare and at heart level with mercury sphygmomanometer.
3. Laboratory Evaluation-

A. Routine Investigations-

- CBC (Hb, TLC, DLC, Platelet counts)
- Blood urea
- Serum Creatinine
- RBS
- ECG
- Urine complete examination
- Fundus Examination

B. Special Investigations:

- Urine Albumin Excretion (µg/ml) for microalbuminuria.
- GFR(ml/min/1.73m2) [measured by Cockcroft method]=(140-age) x mass(kg) [x0.85 if female] ÷72 x serum creatinine(mg/dl).
- Ultrasonography abdomen for B/L kidney size and echo texture whenever necessary.

RESULTS

This study was conducted on 50 patients with essential hypertension (group A) taken from the outpatient and inpatient Medicine department of GMC, Patiala. 50 healthy age and sex

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matched normotensive controls (group B) were also enrolled in the study. Detailed history was taken and baseline investigations were done in all subjects. Patients were then evaluated for the presence of microalbuminuria and its correlation with various clinical and laboratory parameters were made. It was a one point cross sectional study. Data obtained was analyzed statistically:

	(22-64)	(18-65)	
Gender Male Female	 25 25	 25 25	>0.05

As shown in [Table 1], age of patients in hypertensive group ranged from 22 - 64 years with mean age 49.52± 9.02 years and in control group from 18 - 65 years with mean of 43.76±14.29years (p value >0.05).

In both the groups, out of 50 patients, 50% were males and 50% were females with p value >0.05.

Table 1: Sociodemographic characteristics of study subjects.

Parameters	Group A (n=50)	Group B (n=50)	p value
Age (years) Mean ± SD	49.52 ± 9.02	43.76 ± 14.29	>0.05

Table 2 (a): Clinical characteristics of study subjects

Parameters	Group A(n=50)	Group B(n=50)	p value
BMI (kg/m2)	24.37 ± 3.15(18-32.70)	23.17 ± 1.85(18-27.10)	>0.05
Blood pressure Systolic blood pressure (mmHg) Diastolic blood pressure (mm Hg) Mean arterial pressure (mmHg)	 151.92 ± 8.09(138 - 174) 91.60 ± 5.55(80 - 110) 111.66 ± 5.81	 111.20 ± 8.17 (100 - 128) 71.84 ± 5.25 (60 - 80) 84.82 ± 5.86	 <0.001 <0.001 <0.001

Table 2 (b): Distribution of Group A according to stage of Hypertension

	Stage of Hypertension	
	Stage 1	Stage 2
Number of patients	44	6
Percentage of Patients (%)	88 %	12 %

Table 3: Laboratory characteristics of study subjects. 3 (a) - Routine Investigations (Hb, FBS, Blood Sugar, Serum Creatinine). 3 (b) - Special Investigations (eGFR and UAE).

Parameters	Group A(n=50)	Group B(n=50)	p value
Hemoglobin (g/dl)	13.5 ± 0.96	13.7 ± 0.87	>0.05
Fasting blood glucose (mg/dl)	90.02 ± 9.26	88.94 ± 6.31	>0.05

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Blood urea (mg/dl)	30.32 ± 5.87	25.84 ± 4.65	<0.001
Serum creatinine (mg/dl)	0.862 ± 0.124	0.814 ± 0.104	<0.001
Parameters	**Group A (n=50)**	**Group B (n=50)**	**p value**
eGFR (ml/min/1.73m2)	91.74 ± 8.18	105.42 ± 11.92	<0.001
UAE (µg/mL)	54.44 ± 56.49	6.85 ± 5.68	<0.001
Normal values of UAE=0-25 µg/mL Average estimated GFR was significantly lower (p value <0.001) in hypertensive group than control group. Average urine albumin excretion was 54.44±56.49 in hypertensive group which was significantly higher (p value <0.001) as compared to control group (6.85±5.68).			

Table 3 (c): Micro albuminuria in Study Subjects

Micro albuminuria	Group A (n=50)	Group B (n=50)	p value
Number of subjects	24	Nil	<0.001
Percentage of subjects	48 %	Nil	
Out of 50 subjects in hypertensive group, 24 subjects manifested microalbuminiuria and none of the subjects was microalbuminuric in control group with significant p value (p<0.001).			

Table 4: Distribution of hypertensive microalbuminuric subjects according to stage of hypertension

Parameter	Total number	No. of subjects with microalbuminuria	Percentage
No. of subjects with stage 1 hypertension	44	19	43.18 %
No. of subjects with stage 2 hypertension	6	5	83.33%
Total	50	24	48 %

Table 5: Age distribution of microalbuminuric and normoalbuminuric hypertensive patients

Age group	Microalbuminuric(n=24)	Normoalbuminuric(n=26)	Total(n=50)
18-29 years	0 (0%)	2 (100%)	2
30-39 years	1 (25%)	3 (75%)	4
40-49 years	9 (52.94%)	8 (47.05%)	17
50-59 years	10(50%)	10 (50%)	20
≥ 60 years	4 (57.14%)	3 (42.85%)	7

Table 6: Correlation of severity of hypertension with urine albumin excretion

Parameter	Pearson correlation coefficient	R2	p value
Hypertension and microalbuminuria	0.368	0.135	0.008

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On a scatter plot between severity of hypertension and urine albumin excretion we observed that there was a positive relation between the two variables but it seemed to be weak. On regression analysis we found R2 = 0.135, thus severity of hypertension explained approximately 13.5% of the variability in microalbuminuria. Further, the Pearson correlation coefficient between severity of hypertension and microalbuminuria was found to be 0.368 which was weak but statistically significant (p value 0.008) thus indicating a positive correlation between severity of hypertension and microalbuminuria.

These observations reveal that prevalence of microalbuminuria in essential hypertensive patients was 48%. Out of these, 79.16% (n=19) were stage 1 hypertensives and rest 20.83% (n=5) belonged to stage 2 hypertension. Microalbuminuria was directly correlated with increasing age and hypertension. Both severity of hypertension and increasing microalbuminuria were associated with increased end organ dysfunctions including, decreased GFR and increased serum creatinine.

DISCUSSION

Microalbuminuria and vascular dysfunctions are known to occur early in the course of essential hypertension. Microalbuminuria is a consequence of an augmented intraglomerular capillary pressure; intrinsic glomerular damage and tubular alterations also account for increased urinary albumin excretion. Systolic blood pressure has been shown to be one of the most relevant determinants of microalbuminuria in early stages of hypertensive disease.

The purpose of this study was to assess the prevalence of microalbuminuria in essential hypertensive subjects attending outpatient and inpatient departments at tertiary care centre. It was carried out on 50 hypertensive patients and 50 age and sex matched normotensive controls as per the inclusion criteria. Apart from assessing the prevalence of microalbuminuria in essential hypertensive subjects we also studied the correlation of microalbuminuria with severity of hypertension.

Table 7: Comparison of microalbuminuria in Hypertensive Subject.

	Microalbuminuria percentage in Hypertensives
MAGIC Study (1997).[6]	6.7 %
B Hithal et al (2008).[8]	26.67 %
SEARCH global study (2007).[14]	58 %
Present Study	48 %

In our study; out of 50 hypertensive subjects; 24 had microalbuminuria as compared to none in control group. So the prevalence of microalbuminuria in essential hypertensive subjects was 48% in our study possibly pointing towards the subclinical and subtle changes happening in the glomeruli of these patients.

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Table 8: Comparison of age groups in microalbuminurics and normoalbuminurics

Age (years)			
	Microalbuminuric	**Normoalbuminuric**	**p value**
Jansen etal (2010)(15)	64.50±12.70	62.80±11.6	<0.05
Chowtaetal (2009)(17)	51.70±9.80	46±11.60	<0.05
Present Study	51.41±7.22	47.88±10.13	<0.05

Table 9: Comparison of Systolic Blood Pressure correlation with microalbuminuria

Systolic Blood pressure (mmHg)			
	Microa lbuminuria	**Normoalbum inuria**	**p value**
Lurbe etal (2002).[19]	109.9±11.3 to 114.9±11.7	106±8.8 to 106.4±14.8	<0.05
HK Aggarwal etal (2017).[20]	155.32±6.99	147.83±7.2	<0.05
Present study	155.58 ± 9.36	148.76 ± 4.70	<0.05

In hypertensive group subjects with microalbuminuria (51.41±7.22 yrs) were older than those with normal albumin excretion (47.88±10.13 yrs) with significant P value <0.05. This finding is in agreement with previous studies done by Janssen et al,[15] study by Klausen etal,[18] and study by Chowta etal in 2009.[17] In cross sectional study done by Janssen et al on 5241 nondiabetic and nonhypertensive subjects of age 28 to 75 years, microalbuminuria was found to be linearly correlated with age.

Study done by Klausen et al included 1734 men and women aged 30 to 70 years with hypertension and microalbuminuria was found significantly higher in older age groups.[18] [Table 8]

Microalbuminuria was strongly associated with increased systolic blood pressure in our study, SBP (155.58±9.36 mmHg) in microalbuminurics and SBP (148.76±7.2 mmHg) in normoalbuminurics with significant P value of <0.01, a finding that agrees with studies done by Moran et al and Lurbe et al.[16,19]

Table 10: Comparison of Serun Creatinine in Microalbuminuric and Normoalbuminurics Subjects

	Serum Creatinine (mg/dl)		
	Microalbuminuric	**Normoalbuminuric**	**P-value**
F Perticone etal (2007).[21]	1.00±0.22	0.88±0.16	0.004
Geetha P etal	1.13±0.38	0.89±0.19	<0.001

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(2017).[22]			
Present Study	0.88 ± 0.141	0.84 ± 0.106	<0.05

Subjects with microalbuminuria had poor renal function, manifested by significantly high serum creatinine and low eGFR. Subjects with microalbuminuria had serum creatinine (0.88±0.141 mg/dl) and subjects with normoalbuminuria had serum creatinine (0.84±0.106 mg/dl) with P value <0.05. eGFR (89.54± 7.27 ml/min/1.73m2) seen in subjects with microalbuminuria and eGFR (93.77 ± 8.57 ml/min/1.73m2) in normoalbuminuric subjects with P value <0.01. Further; eGFR declined with increasing degree of microalbuminuria indicating increasing renal dysfunction. Study done by Hallan etal,[11] showed that a combination of eGFR and albuminuria is a powerful predictor for progression to ESRD and mortality in the general population.

CONCLUSION

Therefore in this study it was observed that prevalence of microalbuminuria in essential hypertension was 48%. Risk factors for microalbuminuria included higher age, SBP and MAP. Major limitation of the study was small sample size of 50 cases and 50 controls. Early screening for microalbuminuria in patients of essential hypertension and thereby early initiation of treatment might help in reducing ongoing target organ damage. In this sense; early microalbuminuria detection is a cheap and easily accessible commodity which may save our resources and patient lives by preventing further target organ damage and thus obviating the need of expected future interventions.

REFERENCES

1. Datey KK, Kumar M, Goyal BK. Recent advances in the management of hypertension. Indian Heart Journal 1982;34:349-55.
2. Bigazzi R, Bianchi S, Campese VM, Baldari G. Prevalence of microalbuminuria in a large population of patients with mild to moderate hypertension. Nephron 1992;61:94-7.
3. Giaconi S, Levan C, Fommei E, Innocen F, Seghieri G, Palla L, et al. Microalbuminuria and casual and ambulatory blood pressure monitoring in normotensives and in patients with borderline and mild hypertension. Am J Hypertens 1989;2:259-61
4. Ruilope LM, Rodicio JL. Clinical relevance of proteinuria and microalbuminuria. CurrOpinNephrolHypertens 1993;2:962-7.
5. Summerson J, Bell R, Konen J. Racial differences in the prevalence of microalbuminuria in hypertension. Am J Kidney Dis 1995;26:577-9.
6. Pontremoli R, Sofia A, Ravera M, Nicolella C, Viazzi F, Tirotta A, et al. Prevalence and clinical correlates of microalbuminuria in essential hypertension:The MAGIC Study. Hypertension 1997;30:1135-43.
7. Bigazzi R, Bianchi S, Campese VM, Baldari G. Prevalence of microalbuminuria in a large population of patients with mild to moderate hypertention. Nephron 1992;61:94-7.
8. Hithal B, Pappachan JM, Balachandran Pillai H, Sujathan P, Ramakrishna CD. Microalbuminuria in patients with essential hypertension and its relationship to target organ damage: An Indian experience. 2008;19:411.
9. Pedrinelli R, Giampietro O, Carmassi F, Melillo E, Dell'olmo G, Catapano G, et al. Microalbuminuria and endothelial dysfunction in essential hypertension. Lancet 1994;344:14–8.

10. Parving HH, Jensen HAE, Mogensen CE, Evrin PE. Increased urinary albumin excretion rate in benign essential hypertension. Lancet 1974; 21:1190-92.
11. Levey A, Coresh J, Balk E, Kausz A, Levin A, Steffes M, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139,:137-47.
12. Hallan S, Ritz E, Lydersen S, Romundstad S, Kvenild K, Orth S. Combining GFR and albuminuria to classify CKD improves prediction of ESRD. J Am SocNephrol 2009;20:1069-77.
13. Goos JD, Kester M, Barkhof F, Klein M, Blankenstein M, Scheltens P, et al. Patients with Alzheimer disease with multiple microbleeds. Stroke 2009;40:3455-60.
14. Bohm M, Thoenes M, Danchin N, Bramlage P, La Puerta P, Volpe M, et al.Association of cardiovascular risk factors with microalbuminuria in Hypertensive individuals: the i-SEARCH global study. J Hypertens 2007; 25:2317-24.
15. Metcalf P, Baker J, Scragg R, Dryson E, Scott A Wild C. Dietary nutrient intakes and slight albuminuria in people at least 40 years old. ClinChem 1993;39:2191-8.
16. Bonnet F, Marre M, Halimi J, Stengel B, Lange C, Laville M, et al. Waist circumference and the metabolic syndrome predict the development of elevated albuminuria in non-diabetic subjects: the DESIR Study. J Hyperten 2006; 24:1165-71.
17. Chowta N K, Pant P, Chowta M N. Microalbuminuria in diabetes mellitus: Association with age, sex, weight, and creatinine clearance. Indian J Nephrol [serial online] 2009 [cited 2018 Nov 20]; 19:53-6.
18. Wachtell K, Ibsen H, Olsen M, Borch K, Lindholm L, Mogensen C, et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE Study. Ann Intern Med 2003; 139:901-6.
19. Lurbe E, Redon J, Kesani A, Pascual JM, Tacons J, Alvarez V, et al. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. N Engl J Med 2002;347:797-805.
20. HK Aggarwal, Deepak Jain, SudhirMor, RK Yadav, Promil Jain. Prevalence and Clinical Correlates of Microalbuminuria in Patients with Essential Hypertension - A Tertiary Care Center Cross Sectional Study. Journal of Physicians of India, May 2018, Vol. 66.
21. Perticone F1, Maio R, Tripepi G, Sciacqua A, Mallamaci F, Zoccali C. Microalbuminuria, endothelial dysfunction and inflammation in primary hypertension. J Nephrol. 2007 Nov-Dec;20Suppl 12:S56-62.
22. Geetha P, Shanmugasundaram P. Correlation of microalbuminuira with age, duration, glycated hemoglobin, blood sugar levels, blood pressure and renal parameters of type 2 diabetes patients. Asian Journal of Pharmaceutic.

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