

A Study on Microalbuminuria in Non-Diabetic Hypertensive Patients Attending a Tertiary Care Hospital in South India

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ABSTRACT

BACKGROUND

Essential hypertension represents 90 – 95 % of all instances of hypertension. Microalbuminuria was observed to be related to increased chances of coronary artery disease even in patients already on treatment for hypertension. Microalbuminuria was identified with left ventricular hypertrophy recommending equal heart harm and albuminuria in hypertensive patients. However, the pervasiveness of hypertension is high in India, the connection between microalbuminuria and target organ damage in hypertension isn't well studied. This study intended to decide the extent of microalbuminuria in non-diabetic patients with essential hypertension and concentrate on the relationship of microalbuminuria with the worsening of left ventricular hypertrophy (LVH) and hypertensive retinopathy (HRP).

METHODS

This was a hospital-based cross-sectional analysis conducted in a hospital from January 2019 to September 2019. Information was gathered from 93 patients fulfilling the consideration standards utilizing a formerly planned semi-structured questionnaire. Urine microalbumin level, echocardiography, ECG and fundus assessment were done. The study variables were recorded and dissected utilizing SPSS software.

RESULTS

The mean age of the group populace was 55 ± 8.89 years. Microalbuminuria was present in 68 %. There was a measurably critical relationship between the age group studied and the predominance of microalbuminuria. There was a huge factual affiliation between the presence of microalbuminuria and LVH in hypertensive patients ($P < 0.0001$), with microalbuminuria and HRP ($P < 0.0001$) and with microalbuminuria and long-standing hypertensives ($P < 0.0001$).

CONCLUSIONS

The larger part of microalbuminuria positives was found disseminated among higher ages. There was a positive relationship among patients with microalbuminuria and LVH, with retinopathy in hypertensive patients, with grade 2 hypertension and with long-standing hypertensives.

KEY WORDS

Hypertension, Microalbuminuria, LVH, Hypertensive Retinopathy.

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BACKGROUND

Primary hypertension accounts for almost all cases of hypertension.¹ Although, hypertension is often without any symptoms, the disease is related to multiple target organ damage manifestations and associated clinical conditions.² Cardiovascular risk rises steeply with different grades of hypertension. This risk increases further when additional risk factors accumulate. Microalbuminuria, hypertensive retinopathy and left ventricular hypertrophy (LVH) are important predictors of cardiovascular morbidity and mortality.² A significant proportion of the hypertensive population shows microalbuminuria in which there occurs a slight elevation in the urinary albumin excretion above a preset threshold. Microalbuminuria is one of the earliest markers of renal injury and vascular dysfunction. These people are more prone to develop cardiovascular and renal complications in later life.³ Microalbuminuria is defined as a persistent elevation of albumin in the urine from greater than 30 to less than 300 mg/day. This may not be detectable with routine protein dipstick assays.¹ Microalbuminuria is an index of increased renal endothelial permeability and diffuse endothelial dysfunction.^{4,5} Several studies show that a positive correlation exists between microalbuminuria and elevated blood pressure in hypertensive patients. As most hypertensive patients are almost always asymptomatic, they may be unaware of the consequent progressive damage to various target organs for as long as 10 to 20 years. If microalbuminuria is positively associated with hypertension, its presence calls for more strict control of blood pressure to prevent future cardiovascular risks. Evidence from the literature suggests that even very low levels of microalbuminuria with albumin excretion rates as low as 4.8 µg/min is associated with increased risk of cardiovascular and retinovascular disease, independent of the presence of other risk factors.⁴ So we intended to find the proportion of microalbuminuria in non-diabetic patients with essential hypertension and find if there was any association of it with the development of left ventricular hypertrophy and hypertensive retinopathy.

METHODS

This study was approved by the Institutional review board and Institutional ethics committee and was conducted from January 2019 to September 2019 at a tertiary care medical college catering for nearly 10000 inpatients daily. It was a hospital-based cross-sectional study done among non-diabetic essential hypertensive in-patients with blood pressure above 140/90 mm of Hg and aged more than 30 years of either gender and admitted in general medicine ward of a tertiary care teaching institution in South India. Unwilling patients, diabetic patients, patients with renal disease, heart failure, macroalbuminuria and those with a positive history or clinical signs of ischaemic heart disease were excluded from the study. The sample size was calculated according to the formula $4PQ/L^2$ where; P is the prevalence, Q is 100-Prevalence, and L is an allowable error. From a study conducted by Sharan Badiger,⁶ where the prevalence of microalbuminuria in hypertensive patients was 63 %, the

sample size was calculated to be 93. All consecutive patients who satisfied the selection criteria were selected. The study tool used was a previously designed semi-structured questionnaire. Study variables included microalbuminuria, left ventricular hypertrophy (LVH), hypertensive retinopathy (HRT), duration of hypertension and sociodemographic variables like age and gender. Informed written consent was taken from the study patients before they were enrolled for the study. Relevant details of the patients were collected using a semi-structured questionnaire. Urine microalbumin was tested in a urine spot sample. Echocardiography, ECG interpretation and fundus examination were done in the Department of Internal Medicine.

Hypertension is defined as office systolic BP (SBP) values > 140 mmHg and/or diastolic BP (DBP) values > 90 mmHg. The 2018 ESC/ESH Guidelines for the management of arterial hypertension⁷ state that there are 3 grades of hypertension -

- Grade 1: SBP 140–159 mm of Hg and/or DBP 90–99 mm of Hg.
- Grade 2: SBP 160–179 mm of Hg and/or DBP 100–109 mm of Hg.
- Grade 3: SBP > 180 mm of Hg and/or DBP > 110 mm of Hg.

A person is said to have microalbuminuria if his albumin to creatinine ratio is in the range of 30 - 300 mg/g creatinine in a urine spot sample.⁸

Left ventricular hypertrophy was diagnosed by echocardiography when left ventricular posterior wall or interventricular septal thickness was greater than 1.3 mm⁹

All the patients were subjected to direct fundoscopy to assess retinal vasculature. It was also used to examine the optic disc for signs of hypertensive retinopathy. Keith Wagener Barker classification¹⁰ was used for grading of retinopathy. Grade 1 and 2 were considered as early retinopathic changes whereas grades 3 and 4 were considered as advanced retinopathy.

Statistical Analysis

Data collected were entered in SPSS software. Quantitative variables were expressed as means. Qualitative variables were expressed as proportions. Association of outcome variables like left ventricular hypertrophy and hypertensive retinopathy were analysed using the chi-square test.

RESULTS

During the eight months, 93 patients who were admitted for various reasons and had a blood pressure reading above 140/90 mm of Hg were enrolled for the study after careful analysis of the exclusion criteria. Most of them were above 50 years and the mean age of the group studied was 55 ± 8.89 years. Of this, the mean age in the males was 56.6 ± 8.9 years and that of the females was 52.6 ± 7.0 years. The majority of the cases with microalbuminuria was found in the higher age group, 59.75 ± 16.32 years in males versus 57.9 ± 17.58 years in females. There was male sex preponderance in our study with 65 % (60 patients) of them being males and 35 % (33 patients) females.

In the study population, 63 patients (68 %) had associated microalbuminuria. Of this, 44 patients (47 %) were males and 19 patients (21 %) were females. Although the prevalence of microalbuminuria was more in males when compared to females (47 % Vs 21 %), no significant association was present between gender and microalbuminuria (P-value 0.0924) (Table 1).

Gender	MAU Positive	MAU Negative	Total
Male	44	16	60 (65%)
Female	19	14	33 (35%)
Total	63 (68%)	30 (32%)	93 (100%)

Table 1. Baseline Gender Characteristics

Footnote: MAU: Microalbuminuria (P value 0.0924)

LVH was present in 49 people. Of this, 43 people (88 %) had associated microalbuminuria. The association of LVH with microalbuminuria was studied. A significant statistical association was noted between the presence of microalbuminuria and LVH (P < .0001) which is discussed in table 2.

MAU	LVH Present	LVH Absent
MAU Positive	43	20
MAU Negative	6	24
Total	49 (52.7 %)	44 (47.31 %)

Table 2. Left Ventricular Hypertrophy (LVH) and Microalbuminuria

Footnote: MAU: Microalbuminuria P<0.0001

48 patients (51.7 %) had evidence of retinopathy. Of this, 87.5 % had microalbuminuria. Microalbuminuria was higher in patients with early retinopathy (66.7 %) than in those with advanced retinopathy (20.8 %) (32 patients Vs 10 patients). A significant statistical association was also noted between people with microalbuminuria and those with hypertensive retinopathy (P < 0.001). This has been documented in Table 3.

MAU	Early Retinopathy (Grade 1 and 2)	Advanced Retinopathy (Grade 3 and 4)	Total N (%)
MAU positive	32(66.7%)	10(20.8%)	42 (87.5%)
MAU negative	5 (10.4%)	1(2.1%)	6 (12.5%)
Total	37 (77.1%)	11 (22.9%)	48

Table 3. Hypertensive Retinopathy and Microalbuminuria

Footnote: MAU: Microalbuminuria.(P<0.0001)

Microalbuminuria and its association with the duration and severity of hypertension were studied. For comparing the duration of hypertension, the study population was divided into two groups - Long-standing hypertensives (i.e. > 15 years) and those of short duration (i.e. < 15 years). We found that 12 patients (12.9 %) with a shorter duration of hypertension had microalbuminuria whereas 51 (54.8 %) long-standing hypertensives had microalbuminuria. As the duration of hypertension increases, the prevalence of microalbuminuria also increases (54.8 % Vs 12.9 %). A significant statistical and clinical association was also established between the duration of hypertension and the presence of microalbuminuria. P < 0.0001.

Duration Since the Detection of Hypertension	Microalbuminuria	No Microalbuminuria
< 15 years	12(12.9%)	22(23.7%)
> 15 years	51(54.8%)	8(8.6%)
Total	63	30

Table 4. Microalbuminuria and Duration of Hypertension

Footnote: MAU: Microalbuminuria (P<0.0001).

Hypertension severity and its association with microalbuminuria were studied. The study population was divided based on the severity of hypertension into three groups i.e., Grade 1-3. Of the 58 people with grade 2 hypertension, 42 patients (45.2 %) had associated microalbuminuria. Most of the people in the study group (i.e., 58 patients) had grade 2 hypertension and there was a positive association between microalbuminuria and grade 2 hypertensives (P = 0.002). (Table 5). This association was not noted in grade 1 and grade 3 hypertension. (P = 0.942, 0.118)

Hypertension Severity	Microalbuminuria (%)	No Microalbuminuria (%)	P Value
Grade 1	15 (16.1%)	13 (13.9%)	0.942
Grade 2	42 (45.2%)	16 (17.2%)	0.001
Grade 3	6 (6.5%)	1 (1.1%)	0.118

Table 5. Microalbuminuria and Hypertensive Severity

DISCUSSION

Our study correlated well with other studies on many levels. Most of the people were middle-aged and the mean age was 55 ± 8.89 years. Our study continues to show that there is still an increased prevalence of essential hypertension in middle-aged people although there is upcoming evidence of young hypertensives in other parts of India. Gender-wise, our study suggests that females are developing hypertension at early ages compared to men (52.6 years Vs 56.6 years) probably due to the early onset of menopause in females. There was slightly increased age preponderance in males. In spite of this, gender did not pose any higher risk for the presence of microalbuminuria.

In our study, microalbuminuria was seen in 68 % of the patients. This was similar to studies conducted by Poudyal et al. (62.5 %),¹¹ Rameez et al.¹² (69 %) but much higher than the study by Stalin et al.¹³ (24.3%) and Hitha et al. (26.67 %).¹⁴ Studies from Nigeria as in Busari et al.¹⁵ showed a lower prevalence of microalbuminuria (32.2 %) and a study in the Iranian population by Hemmati et al.¹⁶ showed a much lower prevalence of 5.6 %. Variations in different studies conducted could be due to different criteria used in selection, inpatients versus outpatients in the study population, differences in the methods used for detecting microalbuminuria, the severity of hypertension, different age, population and ethnicity, and coexistent comorbidities.

People with increasing age are more likely to have microalbuminuria in our study also, as observed in other studies like Wachtell et al.³ (beta = .095, P < .01) and Stalin et al.¹³ As expected, we noticed that long-standing high blood pressure patients with or without treatment were associated with an increased prevalence of microalbuminuria. We also studied the association of microalbuminuria with the severity and duration of hypertension. We noticed that there was a positive association between microalbuminuria and long-standing hypertensive patients (P < 0.0001). This study had similar findings as the study conducted by Kartik et al.¹⁷ (Chi-square value of 27.38 and a P < 0.001) and Stalin et al.¹³ According to Stalin et al. long-standing hypertensives (8.44 ± 5.58 years) had more increased incidence of microalbuminuria.

There was a huge factual affiliation between the presence of microalbuminuria and patients with grade 2 hypertension

($P = 0.001$). This affiliation was not noted in patients of grade 1 and 3 hypertension. This could be because over 60 % of our study populace had hypertension with grade 2 severity. Comparative discoveries were additionally seen in the review by Stalin et al.¹³

LVH, like microalbuminuria, occurs very early in patients with hypertension¹⁸ and there is a huge relationship between these two entities - LVH and microalbuminuria as displayed in numerous studies.^{3,19,20,21} The prevalence of LVH found in our study was 52.7 % and is similar to the studies by Kartik et al.¹⁶ and Stalin et al.¹³ Be that as it may, the prevalence (52.7 %) is much more than in a study conducted in 2008 in South India by Hitha et al.¹⁴ (29.33%). The reason for the higher prevalence in our study could be because the study by Hitha et al. involved both outpatients and inpatients whereas our study group included only in-patients who were already admitted because of their poorly controlled blood pressure. A better comparison would have been obtained if the cohort included equal number of inpatients and outpatients.

In opposition to the observations made in the ETODH study,²² we noticed a strong relationship between hypertensive retinopathy and microalbuminuria. The predominance of microalbuminuria was higher among those with hypertensive retinopathy in this review (51.7 %). The higher predominance of microalbuminuria in patients with hypertensive retinopathy correlated with the study by Stalin et al.¹³ In the review by Busari et al.¹⁵ advanced hypertensive retinopathic changes, i.e., Grades III-IV were more often seen in patients with microalbuminuria than in those without microalbuminuria (22.6 % versus 1.5 %). This shows that there is a critical relationship between microalbuminuria and target organ damage in essential hypertension and microalbuminuria can be viewed as an early forerunner of target organ damage.

Consequently, this review saw that hypertensive patients with microalbuminuria were more prone to develop target organ damage like LVH and retinopathy than patients without it. Microalbuminuria would thus be able to serve as a marker of subclinical cardiovascular injury and may account for the worse outcome that is usually associated with increased urinary albumin excretion in essential hypertension. In this way, hypertensive patients with microalbuminuria ought to be assessed for the presence of LVH and retinopathy. These patients are inclined to develop stroke, coronary artery disease, and heart failure. Therefore, aggressive administration of positive cases with drugs that decline microalbuminuria might decrease their higher supposition for development of severe CKD, and adverse cardiovascular events as displayed in numerous studies.^{18,19,21,23,24}

CONCLUSIONS

Most of microalbuminuria positive cases were found appropriated among higher ages. In this study, gender didn't represent a more serious danger for microalbuminuria. There was a huge measurable affiliation present between the microalbuminuria and span and the seriousness of hypertension. There is also a huge measurable affiliation

present between microalbuminuria and target organ damage like LVH and retinopathy in hypertensive patients.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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