

Microalbuminuria and its Correlation with Left Ventricular Hypertrophy and Retinopathy in Non-diabetic Hypertensive Patients

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Abstract

Introduction: Hypertension is a very strong risk factor for cardiovascular disease and doubles the risk of coronary heart disease, congestive cardiac failure, stroke, chronic kidney disease, and peripheral vascular disease. Microalbuminuria (MAU) is more frequent among hypertensive patients presenting with target organ damage.

Aim: This study aims at detecting MAU in patients with essential hypertension and its relation to severity of hypertension, duration of hypertension, age, sex, and target organ damage such as hypertensive retinopathy (HRP) and left ventricular hypertrophy (LVH).

Methods: A total of 100 non-diabetic hypertensive patients of either sex were included in this study. MAU was estimated by immunoturbidimetry method. The relationship of MAU with the duration and the severity of hypertension, age, sex, and target organ damage such as HRP and LVH were studied.

Results: The prevalence of MAU among hypertensive patients was 69% in this study. The prevalence of LVH among hypertensive patients was 53% in this study. Hypertensive patients with LVH were found to have a higher prevalence of MAU (89%) which was statistically significant. Patients with MAU were more likely to have HRP than patients without it (87% vs. 13%) which was statistically significant.

Conclusion: MAU is more frequent among hypertensive patients presenting with target organ damage such as LVH and retinopathy. MAU is considered to be an early marker of cardiovascular damage and helps in identifying the hypertensive patients at increased risk of developing target organ damage and cardiovascular complications in the future.

Key words: Heart diseases, Hypertension, Microalbuminuria

INTRODUCTION

Hypertension is one of the leading causes of global burden of disease and is an increasingly important public health and medical issue. The probability for a middle-aged or elderly individual to develop hypertension in his or her lifetime is approximately 90%.¹ 20 lakh Indians are predicted to die due to ischemic heart disease which

constitutes 50% of all cardiovascular deaths² in 2020. Nearly 10% of all these deaths in India attributed to hypertension alone.³ Several regional small surveys in the past two decades with varying protocols have reported a prevalence which varies from 6.15% to 36.36% in men and 2-39.4% in women in urban areas and from 3% to 36% in men and 5.80-37.2% in women in rural areas.⁴ There is a continuous relationship between the level of BP and the risk of its complications. Hypertension is a very strong risk factor for cardiovascular disease and doubles the risk of coronary heart disease, congestive cardiac failure, stroke, chronic kidney disease, and peripheral vascular disease.⁵ Microalbuminuria (MAU) is a state of increased vascular endothelial permeability particularly in the kidney. It is an easily measured marker of endothelial dysfunction, low-grade inflammation,

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and vascular disease burden. MAU was found to be associated with increased risk for cardiovascular disease in hypertensive individuals. MAU was related to left ventricular hypertrophy (LVH) suggesting parallel cardiac damage and albuminuria in hypertensive patients.⁶ Although the hypertension is highly prevalent in India, the exact relationship between MAU and target organ damage in hypertensive patients is not well studied. MAU in primary hypertension has high prevalence rate and will increase the risk of developing cardiovascular damage such as retinopathy, LV hypertrophy, acute coronary syndrome, and stroke.

Aim

The aim of this study is to determine the prevalence of MAU in non-diabetic hypertensive patients and further to study the relationship between MAU and each of the following parameters - namely, LVH, retinopathy, age, gender, duration of hypertension, and severity of hypertension thereby to assess whether MAU can be used as an early marker of target organ damage in non-diabetic hypertensive patients.

MATERIALS AND METHODS

A cross-sectional study to be conducted among 100 non-diabetic primary hypertensive patients attending general medicine outpatient clinic and ward at Government Rajaji Hospital, Madurai. Inclusion criteria: Hypertensive patients, age more than 30 years. Exclusion criteria: Diabetic and pre-diabetic patients, chronic renal disease patients, chronic heart failure patients, ischemic heart disease, stroke.

A previously designed pro forma will be used to take a detailed history and general, systemic examination findings of cardiovascular, respiratory, gastrointestinal, and central nervous systems of patients diagnosed with essential hypertension. Necessary investigations was sent and correlated accordingly.

Clinical blood pressure was recorded using sphygmomanometer with standard cuff on two separate occasions at least 5 min apart. The higher of the two readings was taken as the subject blood pressure. MAU estimation was done using immunoturbidimetry two-point end assay. When a urine specimen is mixed with the reagents, albumin in the specimen combines with the anti-human albumin antibody in the reagent to yield an insoluble aggregate that causes increased turbidity in the solution. The absorbance (340 nm) of reaction turbidity is proportional to the concentration of albumin in the specimen and can be measured optically using

spectrophotometer. 12 lead ecg was taken. Transthoracic echocardiogram was done in study patients to detect the presence of LVH. Blood sugar (random, fasting and 2 h postprandial samples), urea, and creatinine were taken. Chest X-ray, ultrasonography of abdomen and pelvis, and computed tomography brain were taken as appropriate to the clinical presentation.

The final data were entered onto Microsoft excel sheet 2007 version. Statistical analysis was performed using SPSS software and Chi-square test. The results of qualitative analysis were expressed as mean and standard deviation. The Chi-square test was used for the qualitative values and tests of significance. The results were considered very significant with $P < 0.01$ and significant with $P < 0.05$.

RESULTS

Among the 100 hypertensive cases taken up for study, mean age group was 55 years. Mean age group in the females was 52.6 years. Mean age group in the males was 56.6 years. Among the total 100 cases, 65 cases (65%) were male and 35 cases (35%) were female (Table 1).

The prevalence of MAU in this study was 69%. Among which 48% of cases were males and 21% were females. 53 cases were found to have LVH (53%). 47 cases did not have LVH (47%). Among 53 cases of LVH, 47 cases were MAU positive (89%) and 6 cases were MAU negative (11%). There was significant statistical association present between the presence of MAU and LVH ($P < 0.0001$). Out of 100 cases, 52 cases were found to have hypertensive retinopathy (HRP) (52%). 48 cases did not have HRP (48%).

Among 52 cases of HRP, 45 cases were MAU positive (87%) and 7 cases were MAU negative (13%). Among 45 cases of MAU positive HRP, 34 cases were found to have early retinopathy (Grade 1 or 2) and 11 cases found to have advanced retinopathy Grade (3 or 4). Among 7 cases of MAU negative HRP, 6 cases were found to have early retinopathy (Grade 1 or 2) and 1 case found to have advanced retinopathy Grade (3 or 4). There was a significant statistical association present between the presence of MAU and prevalence of HRP ($P < 0.0001$) (Table 2).

Table 1: Prevalence of MAU in hypertensive patients

MAU	Male	Female	Total
Positive	48	21	69
Negative	17	14	31

MAU: Microalbuminuria

Hypertensive patients were divided into two groups based on the duration of hypertension. One group with duration of hypertension <15 years and another group with duration of hypertension >15 years and its relationship with the presence of MAU were studied.

In <15 years duration group, only 12 patients were found to have MAU positive and 25 cases were MAU negative. In >15 years duration group, 54 cases were MAU positive and 9 cases were MAU negative (Table 3). There was a significant statistical association present between the presence of MAU and patients with duration of hypertension more than 15 years ($P < 0.0001$).

In this study, the relationship between severity of hypertension and MAU were studied. Out of 32 patients with Grade - 1 hypertension, 17 patients have MAU (53%) and 15 patients does not have MAU (47%). Out of 60 patients with Grade - 2 hypertension, 45 patients have MAU (75%) and 15 patients does not have MAU (25%). Out of 8 patients with Grade - 3 hypertension, 7 patients have MAU (87.5%) and 1 patients does not have MAU (12.5%) (Table 4).

There was a significant statistical association present between the presence of MAU and patients with Grade 2

Table 2: Relationship between presence of MAU and retinopathy in hypertensive patients

Retinopathy	Early	Advanced	Total
MAU positive	34	11	45
MAU negative	6	1	7
Total	40	12	52

MAU: Microalbuminuria

Table 3: Relationship between presence of MAU and duration of hypertension in hypertensive patients

Duration of hypertension	MAU positive	MAU negative
<15 years	12	25
>15 years	54	9
Total	66	34

MAU: Microalbuminuria

Table 4: Relationship between presence of MAU and severity of hypertension in hypertensive patients

Severity of hypertension	MAU positive	MAU negative	P value
Grade 1	17	15	0.942
Grade 2	45	15	0.002
Grade 3	7	1	0.181

MAU: Microalbuminuria

hypertension ($P = 0.002$). In this study, systolic blood pressure (SBP), diastolic blood pressure, pulse pressure, and its relationship with the prevalence of MAU were studied. Mean SBP was similar and there was no statistical difference ($P = 0.051$) between patients with MAU (156.23 ± 11.09 mmHg) and without MAU (151.81 ± 8.32 mmHg). Mean diastolic blood pressure was similar and was no statistical difference ($P = 0.534$) between patients with MAU (95.1 ± 6.73 mmHg) and without MAU (94.19 ± 6.72 mmHg). Mean pulse pressure was similar and was no statistical difference ($P = 0.534$) between patients with MAU (61.45 ± 11.71 mmHg) and without MAU (57.61 ± 8.36 mmHg). Thus, there was no statistical difference between SBP, diastolic blood pressure, pulse pressure, and the presence of MAU in our study.

DISCUSSION

Hypertension is the most common condition leading to target organ damage and systemic complications. In an attempt to improve the outcome in hypertensive patients presenting with MAU, we analyzed their history including age, sex, blood pressure, and screened for the presence of LVH and retinopathy. Our study group consisted of 100 cases attending our hospital, and they are selected on the basis of inclusion and exclusion criteria.

Mean age group in this study was 55 years. Mean age group in the females was 52.6 years. Mean age group in the males was 56.6 years. The majority of MAU cases were found distributed among higher age group in males (59.75 ± 16.32 years) and females (57.9 ± 17.58 years). Higher the age group, higher the prevalence of MAU which was statistically significant ($P < 0.0001$). This study was well correlated with the previous study done by Stalin *et al.*, in which majority of MAU cases were found distributed among higher age group (60.6 ± 10.53 years).⁷

The prevalence of MAU in our study was 69%. Among which 48% of cases were males and 21% were females. 31% of cases were MAU negative, among which 17% cases were males and 14 cases were females. In studies conducted by Poudyal *et al.*, out of 64 hypertensive patients 40 (62.5%) had MAU positive.⁸ Stalin *et al.* conducted a study and they found that the prevalence rate of MAU among hypertensives was 56%. This study reveals that gender did not pose high risk for the presence of MAU.⁷

Among 53 cases of LVH, 47 cases were MAU positive (89%) and 6 cases were MAU negative (11%). There was

significant statistical association present between presence of MAU and LVH in hypertensive patients ($P < 0.0001$). Kartik *et al.* conducted a study and they found that the frequency of MAU is higher in hypertensive patients with LVH (71.4%), and the difference is statistically significant ($P < 0.0001$).⁹ Stalin *et al.* conducted a study and they found that hypertensives with MAU were found to have significantly higher prevalence of hypertensive LVH (74.3%, $P = 0.003$).⁷

In our study, among 100 hypertensive patients, 52 cases were found to have HRP (52%). Among 52 cases of HRP, 45 cases were MAU positive (87%). Among 45 cases of MAU positive HRP, 34 cases were found to have early retinopathy (Grade 1 or 2) and 11 cases found to have advanced retinopathy Grade (3 or 4). There was a significant statistical association present between presence of MAU and prevalence of HRP ($P < 0.0001$).

Stalin *et al.* found that hypertensives with MAU were found to have significantly higher prevalence of HRP (69.8%, $P = 0.035$).⁷ Busari *et al.* conducted a study in 96 consecutive newly diagnosed hypertensive patients, and they found that patients with MAU were more likely to have HRP (71%) than patients without it (37%) ($P = 0.001$).¹⁰ Advanced HRP, i.e., Grade 3-4, was more common in patients with MAU than in those without it (22.6% vs. 1.5%). This shows that there is a significant association between MAU and target organ damage in primary HTN and MAU can be considered an early marker of target organ damage.

This study observed that hypertensive patients with MAU are more susceptible to target organ damage such as LVH and retinopathy than patients without it. Thus, hypertensive patients with MAU should be evaluated for the presence of LVH and retinopathy. These patients are more prone for the development of stroke, ischemic heart disease, and heart failure.

In our study, duration of hypertension and its relationship with the prevalence of MAU were studied. Hypertensive patients were divided into two groups based on the duration of hypertension. We found that only 12 patients were found to have MAU positive (12%) and 25 cases were MAU negative (25%) in patients with duration of hypertension <15 years. In >15 years group, 54 cases were MAU positive (54%) and 9 cases were MAU negative (9%). There was a significant statistical association present between presence of MAU and patients with duration of hypertension more than 15 years ($P < 0.0001$).

Kartik *et al.* conducted a study and they found that as the duration of hypertension increases there is an

increase in the incidence of microalbuminuria in the study group and this difference is statistically significant with a Chi-square value of 27.38 and a $P < 0.001$.⁹ Stalin *et al.* showed that cases with longer duration of HTN (8.44 ± 5.58 years) were found to have higher prevalence of MAU.⁷

In this study, severity of hypertension and its relationship with prevalence of MAU were studied. Hypertensive patients were divided into three groups based on the severity of hypertension into Grade 1-3. The prevalence of MAU is higher with patients with Grade 2 and 3 hypertension. There was a significant statistical association present between presence of MAU and patients with Grade 2 hypertension ($P = 0.002$).

In a previous study done by Stalin *et al.*, Stage 2 hypertension, higher SBP (169.96 ± 19.32 mmHg), and higher age group (60.6 ± 10.53 years) showed good correlation with the presence of MAU.⁷

CONCLUSION

The majority of MAU positive cases were found distributed among higher age group. Gender did not pose a greater risk for MAU in this study. There was a significant statistical association present between presence of MAU and LVH in hypertensive patients. In our study, patients with MAU were more likely to have HRP than patients without it. As the duration of hypertension increases, there is an increase in the incidence of MAU and this difference is statistically significant. There was a significant statistical association present between presence of MAU and patients with Grade 2 hypertension.

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