**Original Research Article**

# A study of microalbuminuria and central nervous system involvement in patients with hypertension in urban South Indian population

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## Abstract

**Background:** Microalbuminuria is an early marker of target organ damage in essential hypertension and an important predictor of vascular complications. Hypertensive individuals with microalbuminuria were found to have significantly higher prevalence of end organ damage such as coronary artery disease, cerebrovascular disease and hypertensive retinopathy. This study was intended to observe the correlation of microalbuminuria with CNS complications such as transient ischemic attack, stroke, early cognitive dysfunction in patients with essential hypertension.

**Materials and methods:** This was a cross sectional study of 200 patients with essential hypertension of varying durations who were attended the hypertension clinic and admitted also patients who were admitted to Medical wards during the period of August 2019 to October 2020 were analysed. Proper history taking was done including duration of hypertension, history suggestive of central nervous system damage, drug history and previous blood pressure recordings, detailed clinical examination had also been done.

**Results:** Out of 200 cases 38 had either CVA/TIA, in that 38 patients 27(71.05%) had MA, 11 patients (28.95%) had normoalbuminuria. In remaining 162 patients 51 (31.48%) had MA, 111(68.52%) had normoalbuminuria. This association is significant p 0.000, in 38 patients 20 had infarct, 10 had haemorrhage, 8 had TIA. In patients with haemorrhage 90% had MA. 10 patients had

cognitive dysfunction in that 5 had MA, 5 had normoalbuminuria but this association is not statistically significant.

**Conclusion:** There is high prevalence of microalbuminuria in essential hypertension in our study population. High prevalence of microalbuminuria is seen in hypertensives presenting with stroke. So early screening for microalbuminuria in patients with hypertension and aggressive and appropriate treatment of positive cases might reduce the morbidity and mortality due to central nervous system involvement.

## Key words

Cerebrovascular accident, Transient ischemic attack, Microalbuminuria, Hypertension.

## Introduction

An increased blood pressure is the one of most important public health problem in all countries especially in India. It is common, easily detectable, often asymptomatic, usually readily treatable and if left untreated usually leads to lethal complications. Even though the basic pathophysiology of elevated arterial pressure has been well understood, the etiology in 90 to 95% of cases is still largely unknown. Because of this in majority of cases of hypertension is treated inadequately and non-specifically which leads to a large number of minor side effects and high non-compliance rate [1]. Untreated as well as inadequate treatment of hypertension increases the incidence of early coronary events, heart failure, Stroke, renal failure and retinopathy.

Microalbuminuria has recently emerged as a marker of wide spread vascular & endothelial damage in essential hypertension [2]. Hypertensive individuals with microalbuminuria were found to have significantly higher prevalence of end organ damage such as coronary artery disease, cerebrovascular disease and hypertensive retinopathy when compared to their normoalbuminuric counter parts [3]. Microalbuminuria is an early marker of target organ damage in essential hypertension and an important predictor of vascular complications [4]. According to results of various studies the prevalence rate of microalbuminuriain essential hypertension ranges between 4.7% to 46%. Various studies prove that the microalbuminuria also predicts development of proteinuria, decline in renal function and vascular complications in hypertension.

## Aim and objectives

- To determine the prevalence of microalbuminuria in patients with essential hypertension.
- To study, the correlation of microalbuminuria with CNS complications such as transient ischemic attack, stroke, early cognitive dysfunction in essential hypertension.

## Materials and methods

**Study centre:** Government Medical College, Omandurar Govt. Estate, Chennai.

**Study period:** From August 2019 to October 2020

**Sample size:** 200 Patients with essential hypertension.

**Inclusion criteria**

- Patients with essential hypertension who attended the hypertension clinic and also patients admitted to Medical ward of Government Medical College, Omandurar Govt. estate, Chennai.

**Exclusion criteria**

- Patients with diabetes mellitus, secondary hypertension, pregnancy induced hypertension, chronic kidney disease, urinary tract infection, patient on long term analgesics, Macroproteinuria and Serum creatinine >1.5 mgs%.

**Study design:** Cross sectional study

**Patient data collection:**

200 Patients with essential hypertension of varying durations who were attended the hypertension clinic and admitted also patients who were admitted to Medical wards during the period of August 2019 to October 2020 were analyzed. Proper history taking was done including duration of hypertension, history suggestive of central nervous system damage, drug history and previous blood pressure recordings, detailed clinical examination had also been done.

Essential hypertension was diagnosed and the severity of hypertension has been classified according to the Joint National Committee (JNC) VII report on prevention detection, evaluation and treatment of high blood pressure [5].

Two or more readings separated by 2 minutes interval were measured and averaged. In newly detected hypertensives, the diagnosis was made based on the average of two or more readings taken at each of two or more visits after an initial screening.

**Investigations done:**

Complete urine analysis, Complete hemogram, Biochemistry (urea, creatinine, FBS), Serum electrolytes, ECG, Echo, Fasting lipid profile, CT scan brain (when specifically indicated) and Urine albumin creatinine ratio.

Microalbuminuria was assessed by urine albumin creatinine ratio based on the recommendations of National Kidney foundation and the American Diabetic Association. 5 ml of first voided, single early morning sample was used. Urine albumin was measured by turbidimetry. The patients were asked to avoid exercise prior to urine collection. In women, urine examinations were done during non-menstrual phase of their cycles. ACR values between 30-300 mg / gram were taken as MA.

## Results

**Prevalence of microalbuminuria:**

In our study out of 200 patients 78 people had microalbuminuria. The prevalence was 39%.

**Age and sex distribution:**

In our study, 7 out 30 patients in 30-39 years age group had MA, 19 out of 50 Patients in 40-49 years age group had MA, 28 out of 50 patients in 50-59 years age group had MA, 14 out of 40 in 60-69 years age group had MA, 10 out of 20 patients in >70 years age group had MA. The prevalence of MA was increasing with age. This association was statistically significant p 0.044.

Out of 200 essential hypertensive cases, there were 120 males and 80 females in our study group. Out of which 57 males and 21 females had microalbuminuria. The remaining 63 males and 59 females had normoalbuminuria, which was statistically significant and there was no correlation between microalbuminuria and sex of the hypertensive cases other studies. Association of BP with microalbuminuria was as per **Table – 1**.

**Table – 1:** Association of BP with microalbuminuria.

| Microalbuminuria | BP | | Total | P VALUE |
|---|---|---|---|---|
| | Stage 1 | Stage 2 | | |
| >30 mg/g | 31 | 47 | 78 | <0.01 |
| | 39.74% | 60.25% | 100.0% | |
| <30 mg/g | 89 | 33 | 122 | |
| | 72.95% | 27.05% | 100.0% | |
| Total | 120 | 80 | 200 | |
| | 60.0% | 40.0% | 100.0% | |

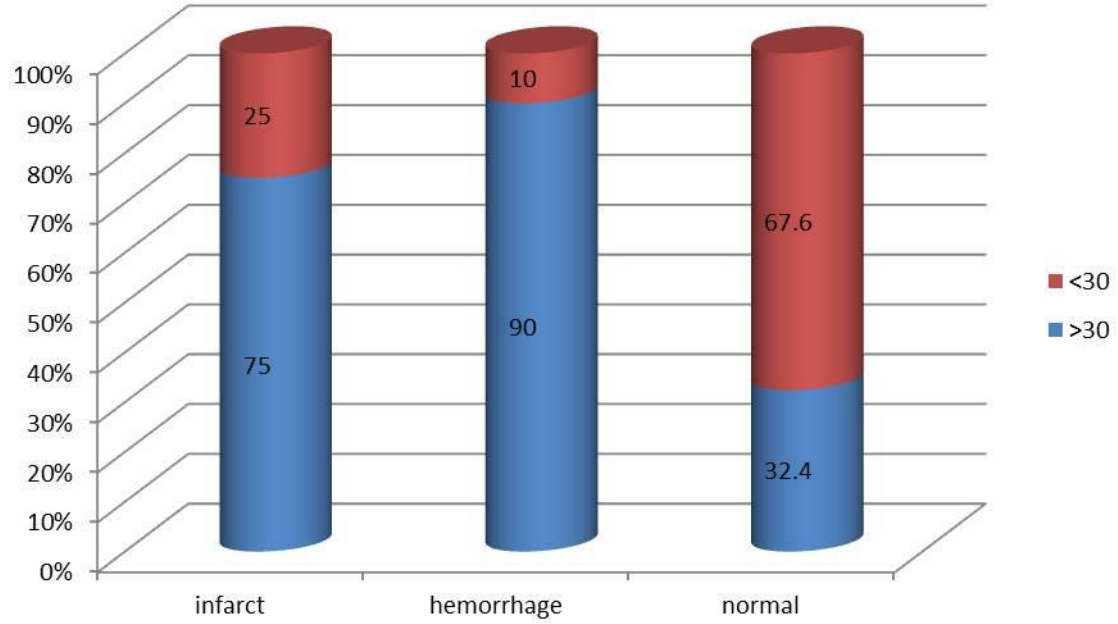
**Table – 2:** Stage of hypertension and degree of microalbuminuria.

| Stage | MA grading (mg/g) | | | | Total | P VALUE |
|---|---|---|---|---|---|---|
| | 30-100 | 101-200 | 201-300 | <30 | | |
| S1 | 18 | 12 | 1 | 89 | 120 | < 0.01 |
| S2 | 5 | 30 | 12 | 33 | 80 | |
| **Total** | **23** | **42** | **13** | **122** | **200** | |

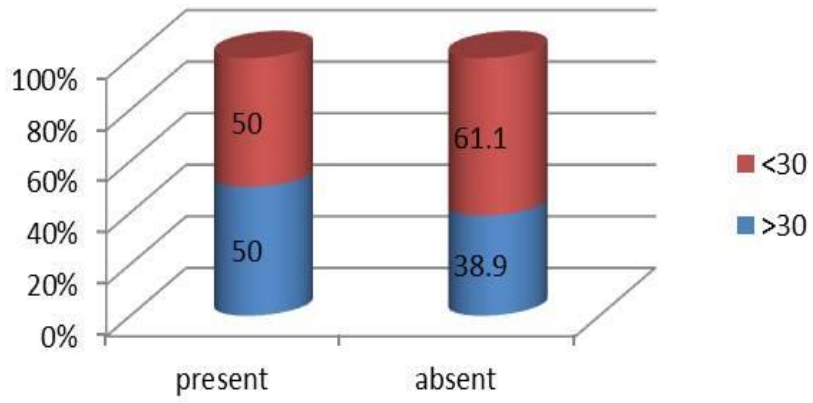
**Table – 3:** Association of CVA/TIA with microalbuminuria.

| CVA/ TIA | MA grade(mg/g) | | | | Total | P value |
|---|---|---|---|---|---|---|
| | 30-100 | 101-200 | 201-300 | <30 | | |
| Present | 3 | 19 | 5 | 11 | 38 | < 0.01 |
| Absent | 20 | 23 | 8 | 111 | 162 | |
| **Total** | **23** | **42** | **13** | **122** | **200** | |

**Graph – 1:** Association of type of CVA With microalbuminuria.




**Graph – 2:** Association of MA with cognitive dysfunction.



Out of 200 essential hypertensive cases in present study, 120 cases belong to stage I hypertension out of these 120 cases, 31 cases (25.83%) were microalbuminuric, and (74.17%) cases were normoalbuminuric. The remaining 80 cases belong to stage II hypertension, out of these 80 cases, 47 cases (58.75%) were microalbuminuric and 33 cases (41.25%) were normoalbuminuric .This shows that the quantity of the microalbuminuria increases with severity of hypertension i.e. the quantity of microalbuminuria is more in patients with stage II hypertension as compared to stage I hypertension, which is statistically significant (**Table – 2**).

**Association of duration of hypertension with MA:**

Out of total 200 essential hypertension cases in present study, 78 cases had microalbuminuria. In that 7 out of 40 cases (17.5%) belong to newly detected hypertension patients, 14 out of 45 cases (23.72%) were belong to 0 to 4 years duration of hypertension, 37 out of 60 cases (61.66%) were belong 5 to 10 years duration of hypertension, 20 out of 41 cases (48.78%) were belong to >10 years duration of hypertension . The remaining 122 cases were found to have normoalbuminuria, in that 33out of 40 cases (82.5%) belong to newly detected hypertension patients, 45 out of 59 cases (76.28%) were belong to <5 years duration of hypertension, 23 out of 60 cases (38.34%) were belong 5 to 10 years duration of hypertension and 21 out of 41 cases (51.22%) with > 10 years duration. This showed that, as duration of hypertension increases, the number of cases having microalbuminuria also increases.

Out of 200 cases 38 had either CVA/TIA, in that 38 patients 27(71.05%) had MA, 11 patients (28.95%) had normoalbuminuria. In remaining 162 patients 51 (31.48%) had MA, 111(68.52%) had normoalbuminuria. This association was significant p 0.000, in 38 patients 20 had infarct, 10 had hemorrhage, 8 had TIA. In patients with hemorrhage 90% had MA. 10 patients had cognitive dysfunction in that 5 had MA, 5 had normoalbuminuria but this association was not statistically significant (**Table – 3**, **Graph - 1**).

**Association treatment regularity and MA**

Out of 200 patients 130 patients were taking regular treatment, 70 patients were not under regular treatment. In patients taking regular treatment 43 (33.1%) had MA, 87 (66.9%) had normoalbuminuria. In patients under irregular treatment 35(50%) had MA, 35(50%) had normoalbuminuria. in patients who were not taking regular treatment had increased frequency of MA and this association was also significant p 0.000 (**Graph – 2**).

## Discussion

In the study it was found that, people with microalbuminuria at levels too low to detect with standard dipstick test are at increased risk not only for pre-clinical nephropathy but also for central nervous system morbidity and mortality. Microalbuminuria and Hypertension commonly co-exist. The mechanism is not well understood but is thought to be a renal marker of generalized vascular endothelial dysfunction and strongly associated with increased cardiovascular risk [6]. So the finding of microalbuminuria should in particular, trigger a careful search for evidence of end organ damage and other cardiovascular risk factors with appropriate investigations followed by aggressive intervention. According to Several retrospective and cross-sectional studies, to prevent the target organ damage there is a need for early detection of significant microalbuminuria in essential hypertension, Therefore our study was conducted systematically to determine the prevalence of microalbuminuria in cases with essential hypertension and to study the correlation of microalbuminuria with central nervous system damage of essential hypertension.

In the present study, out of 200 essential hypertensive cases, 78 cases had microalbuminuria. The prevalence of microalbuminuria in essential hypertension in present study was 39% as compared to

prevalence of microalbuminuria found in other literatures ranging from 4.7% to 46% like in other studies conducted by Pedrenelli R (27.4%) [7], Anil Vij (30%) [8], Yudkin (32.9%) [9], Jalal S (37.5%) [10], Bigazzi R (40%) [11]. It is clear from above that the prevalence of microalbuminuria in present study was comparable. The mean age of 200 essential hypertensive cases in present study population was years ranging from 31-81 years. Out of these, 39% cases found to have microalbuminuria with mean age of 59.65±11.49 years when compared to cases with normoalbuminuria, the mean age was 54.12±11.18 years (p 0.044). This observation in present study was comparable and near to most of other studies conducted by Ghai R [12] (62.38±5.6 years), Agrawal B [13] (57 years), Kadam NN [14] (52.0±7.0 years).

The data from 200 patients were analyzed. Among them microalbuminuria was present in 78 patients, and the prevalence was 39%. In our study out of 200 patients 120 were males and 80 were females. Out of 78 patients who had microalbuminuria 57 were males (47.5%), and 21 were females (27.5%) and there was statistically significant difference in the risk for MA between two sex groups ( p <). In other studies, conducted by Agrawal B [13], male were 32% and females were 28%, by Kadam NN [14], male were 22.07%, females were 21.56%. Microalbuminuria is not related to the sex of the patient. This difference has to be confirmed in a large population based study.

The prevalence of MA among hypertensive patients increased steadily with their advancing age. This association is statistically significant. The prevalence of MA among hypertensive patients decreases according to regularity of treatment. And their association was statistically significant (p 0.000).

Out of 200 essential hypertensive cases in present study, 120 cases belong to stage I hypertension out of these 120 cases, 31 cases (25.83%) were microalbuminuric, and (74.17%) cases were normoalbuminuric. The remaining 80 cases belong to stage II hypertension, out of these 80 cases, 47 cases (58.75%) were microalbuminuric and 33 cases (41.25%) were normoalbuminuric. This shows that the quantity of the microalbuminuria increases with severity of hypertension i.e. the quantity of microalbuminuria is more in patients with stage II hypertension as compared to stage I hypertension, which is statistically significant (p0.000). Thus the magnitude of microalbuminuria correlates with severity of hypertension, particularly with systolic blood pressure. Ghai R [12], Pedrinelli R [7], Sharan Badiger [15] also showed the similar significance.

According to the study conducted by Ghai R [12] high percentage of hypertensives found to be microalbuminuric. The patients with microalbuminuria had a significantly longer duration of hypertension, and prevalence of microalbuminuria was significantly higher in patients with severe hypertension. This would probably explain that, with increasing severity and duration of hypertension, damage to blood vessel endothelium becomes significantly more in several organ systems and also in the kidneys and is probably presented as microalbuminuria. All hypertensive with microalbuminuria demonstrated a higher prevalence of cerebrovascular disease (71.05%), coronary artery diseases (94.07%), and hypertensive retinopathy (100 % above grade 1), as a reflection of wide spread vascular damage. Out of 200 essential hypertensive cases in present study, 120 cases belong to stage I hypertension, out of these 120 cases, 41 cases (34.16%) were microalbuminuric, with mean range of microalbuminuria of 72.19±36.48 mg / day and 79 (65.83%) cases were normoalbuminuric with mean range of normoalbuminuria of 19.64 ±6.15 mg/day. The remaining 80 cases belong to stage II hypertension, out of these 80 cases, 38cases (69.56%) were microalbuminuric with mean range of microalbuminuria of 132.1±92.6 mg / day and 14 cases (30.43%) were normoalbuminuric with mean range of

normoalbuminuria 17.89±5.99 mg/day. This shows that as the stage of hypertension increases the quantity of microalbuminuria also increases, which is statistically significant (p 0.000).

Present study also indicates that microalbuminuria correlates well with the duration of the disease. The incidence in newly detected hypertensives were 17.5%, quite constant for first 5 years at around 23.72%, peaks to 56.43% in patients having hypertension >5 years . In general, cases having less than 5 years duration of hypertension only 23.72% cases had microalbuminuria whereas cases having more than 5 years duration of hypertension, almost 57% cases had microalbuminuria. This indicates that longer the duration of hypertension more number of cases will be microalbuminuric and which is statistically significant (p 0.005). The mean duration of hypertension was 7.55±5.29 years were observed in total study population. Patients with microalbuminuria had mean duration of hypertension of 11.06±5.24 years and patients with normoalbuminuria had 4.12±2.22 years. Studies conducted by Kumar D [16] (microalbuminuria group and normoalbuminuria group mean duration of hypertension was 11.29 and 9.63 years respectively). Bianchi S [11] (in microalbuminuria group and normoalbuminuria group mean duration of hypertension was 10.15±2.93 and 7.93 ±1.03 years respectively) shows similar significance.

In this study 38 patients presented with history of stroke / TIA. Out of this 30 patient had CVA, 8 had TIA. In 30 cases of CVA 24 patients ( 80%) had microalbuminuria, remaining 6 cases 20% had normoalbuminuria. In 8 patients with TIA 4 cases had microalbuminuria and 4 cases had normoalbuminuria. Coming to 158 cases who had no history of stroke/TIA but all were hypertensives, 31.48% had microalbuminuria and 68.52%had normoalbuminuria. This clearly indicates microalbuminuria has more association with stroke or cerebrovascular pathology, which is statistically significant. P (<0.01) Study conducted by Maura Ravera [17] and others also showed the similar findings.

Out of 200 patients 130 patients were taking regular treatment, 70 patients were not under regular treatment. In patients taking regular treatment 43 (33.1%) had MA, 87 (66.9%) had normoalbuminuria. In patients under irregular treatment 35(50%) had MA, 35(50%) had normoalbuminuria. in patients who were not taking regular treatment had increased frequency of MA and this association is also significant p< 0.010.

## Conclusion

There is high prevalence of microalbuminuria in essential hypertension in our study population. High prevalence of microalbuminuria is seen in hypertensives presenting with stroke. So early screening for microalbuminuria in patients with hypertension and aggressive and appropriate treatment of positive cases might reduce the morbidity and mortality due to central nervous system involvement.

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