

# Study of Correlation Between Microalbuminuria and Ischemic Stroke

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## ABSTRACT

**Introduction:** Microalbuminuria has been extensively studied in the western countries and has been co related to Hypertension and diabetes. Aims and Objectives of the study were to study the profile of microalbuminuria in cases of acute non hemorrhagic stroke i.e less than 24 hours, to study the correlation between microalbuminuria and other risk factors for non hemorrhagic stroke and to study the prevalence of microalbuminuria in major subtypes of non hemorrhagic stroke.

**Material and Method:** A total number of 104 cases were studied. The patients with possible kidney disease, endocrine disease, Liver disease, NSAID abusers etc were excluded from the study. The 24 hour urine sample was collected and sent for microalbuminuria estimation and the values were expressed in mg/dl. At the end results the patients were grouped into 2. The Group A consisted of the patients with microalbuminuria and the Group B were the patients without microalbuminuria. Then the 2 groups were correlated with respect to the age, gender, GCS, Lipid profile, ECG and smoking history.

**Results:** There were total of 104 cases included in the study according to the inclusion criteria, and out of which the patients with microalbuminuria were 47 (45.19%) and the number of patients were 57 (54.81%). These patients were divided into Group A (Microalbuminuria Positive) and Group B (Microalbuminuria Negative). The mean age in the Group A were (61.9±15.9), and the mean in Group B was (64.14±12.8). In the Group A the number of males were 31(66%) and females were 16 (34%), and in the Group B the males were 39 (66.4%) and females were 18 (31.6%). These two groups compared for the mean urine microalbumin excretion in group-A (110.7 ± 65.4), mean UAE in group-B (13.3 ± 8.6) and mean GCS in group-A (13.8 ± 1.5), in group-B (14.82 ± 0.3). Among them the number of Smokers were (14) in group A, and in group B were (9). The mean triglycerides levels were (95.49) in both the groups, the mean total Cholesterol levels were (139.23) in both groups whose correlation to microalbuminuria were insignificant.

**Conclusion:** There was no significant correlation between the levels of the total cholesterol and the triglyceride levels and the microalbuminuria among both the group and also there was no significant co relationship between the presence of microalbuminuria and the in patients with or without microalbuminuria. There was no significant correlation between the presence of ECG changes and the presence and absence of microalbuminuria.

**Keywords:** Diabetic, Acute ischemic stroke, Microalbuminuria, Prevalence, GCS, ECG, Smoking, Triglyceride, Total cholesterol, Lacunar.

## INTRODUCTION

Microalbuminuria is excretion of the albumin in minute quantity which is not detected with normal dipstick method. it is estimated to be excretion of 30 - 300 micrograms of albumin in urine and has been called as microalbuminuria.

Microalbuminuria is defined as levels of albumin between 30 - 300 mg per day (equivalent to 20 to 200 µg/minute in a timed overnight urine collection, 20-200 mg/L on spot urine specimen or ACR 2.5 to 25 mg/mmol in males or 3.5 to 25 mg/mmol in females).<sup>1</sup>

Ischemic stroke is defined as the acute onset in neurological deficit following sudden occlusion of blood supply to the brain tissue due to any cause. Many studies have been published in the past demonstrating the interaction between the microalbumin excretion and the small vessel damage. which would have manifested and involving the heart, the kidneys and the brain. This cerebro-renal interaction has been implicated with small vessel damage, the cerebral and glomerular small vessels might have a common soil of pathogenesis, as these organs are closely connected to each other through anatomic and vaso-regulatory similarities since small vessel disorder is a systemic disorder information about damage in one organ may be provided by damage through another organ.<sup>2,3</sup>

As in kidneys the prime markers of damage would be proteinuria and microalbuminuria and also reducing estimated glomerular filtration rate. where as in the central nervous system the imaging studies like MRI etc has been the mainstay for diagnosis as in small vessel ischemic changes. Advancing age and the Male predominance has been exhibited for the prevalence of microalbuminuria. And the population of Great Britain has shown wide spectrum in the levels of microalbumin. It has also been proven to show increase in the microalbumin excretion in the African-American population.<sup>4,5</sup> One of the western studies the prevalence was found to be 46.7% in acute stroke, 16% of the patients has a history of stroke and 16.7% of control.<sup>6</sup> Whereas in an Indian studies it has been found out that the incidence of microalbuminuria was found to be about 68% which is

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much more than the incidence compared to that of the western population, there was a positive correlation between the incidence and stroke in the patients of age >60 years with male predominance (72.72%).<sup>7</sup>

There is plenty of documented evidence that not only the albumin excretion but also microalbumin excretion which is associated with a higher incidence of cardiovascular mortality and morbidity. It is also important to note that not only the diabetics but also the hypertensive patients and also the general population as well, that MA is the early marker for future cardiovascular events and target for early detection and intervention to prevent long term morbidity.<sup>8</sup> Although several studies have attempted to define the prevalence of microalbuminuria in essential hypertension, the exact figure is still unclear. The published prevalence of microalbuminuria in hypertensive subjects ranges from 4.7% to 58.4%.<sup>9,10</sup> In more recent studies of hypertensive subjects without established cardiovascular disease or renal impairment suggested that microalbuminuria, measured on a single occasion by 24-hour collection, is present in 23-27% of the studied population while less than 1% of the subjects had gross proteinuria.<sup>11-13</sup> Levels of albumin in the urine can be expressed as a concentration or as a ratio of albumin-creatinine. Albumin in the urine at levels exceeding 300 mg/day (> 200 mg/L in a spot specimen or albumin-to-creatinine ratio (ACR) > 25 mg/mmol) is regarded as macroalbuminuria (or gross proteinuria). This state of increased excretion of proteins in the urine usually reflects deterioration of kidney function.<sup>14,15</sup> There are also some of the confounding factors which might affect the levels of microalbuminuria like Exercise, UTI, protein diet, Infections and inflammations, pregnancy renal impairment, hypertension etc which needs to be ruled out.<sup>16-18</sup>

Many of the western studies have evidently proven the association of urine albumin excretion and cerebral ischemia. Whereas there is lacking Indian data in the same subject.<sup>19</sup> Aims and Objectives of the study were to study the profile of microalbuminuria in cases of acute non hemorrhagic stroke i.e less than 24 hours, to study the correlation between microalbuminuria and other risk factors for non hemorrhagic stroke and to study the prevalence of microalbuminuria in major subtypes of non hemorrhagic stroke.

## MATERIALS AND METHODS

The study was done on the patients presenting with history of Acute ischemic stroke to Hanagala Shri Kumareshwar Hospital And Research center, Bagalkot. The patients who present with history of acute ischemic stroke within 24 hours of the onset of symptoms, and the diagnosis confirmed by the CT scan. It was the Case series Study done for the period of 1 year, From November 2013 to October 2014.

**Selection of study groups:** The patients with history of acute ischemic stroke presenting within 24 hours of the onset of symptoms and the diagnosis being compared by computed tomography scan of brain, and also subjected to stroke protocol wherever necessary will be included in the study.

The Exclusion criteria included: Kidney disease with etiolo-

gy of both acquired and congenital, Liver disorders, Chronic inflammatory gastrointestinal disorder, Neoplasm, Endocrine Disorders, Dyslipidemias, Those on NSAIDs or other immunosuppressant and other Nephro-toxic drugs, Fever, or any other focus of infection, Inflammatory Rheumatic disease, Hypertension etc.

All the patients were screened for the presence of symptoms that gives a clue of possible CVA especially were attended and the detailed history was taken regarding the time of onset and the progression of the disease with respect to the neurological deficits.

The detailed neurological examination was done to access the extent of the neurological deficits on the patients. On arrival the baseline sugars were taken with Glucometer and monitored further throughout the course in the hospital as and when required, and also the Electrocardiogram was also taken.

The diagnosis of the Ischemic stroke was confirmed by the computed tomography of brain or even followed with the stroke protocol as and when required. And the size of infarct was differentiated into Lacunar or major artery involvement (non Lacunar) as per the diagnostic criteria of Department Radiology. Most patients with poor GCS or with extensive neurological deficits were cauterized with Foley's catheter and the 24 hour urine collection was subjected to the microalbuminuria estimation. The microalbumin is estimated using Erba 5X Chem Semi Auto analyzer, by Kinetic method and is expressed in ....mg/day. The kits were also supplied by Erba Pvt Ltd.

The most frequently utilized techniques for detection of microalbuminuria are *The immunoassays*. Non-immunological techniques for quantifying microalbuminuria have also been used. These tests are mainly chromatographic techniques such as size-exclusion *high performance liquid chromatography* (HPLC).<sup>20,21</sup>

The patients urine protein excretion value between 30 and 300 per day was taken to be positive for Microalbuminuria.

The ECG changes were studied with respect to standard criteria to identify the ischemic changes. The Glassgow coma scale was also accessed according to the standard scaling. Taking Eye Opening, Verbal and Motor responses into consideration.

A fully informed consent was obtained from all the study subjects, having been explained regarding the study the patients involved and the bearable expenses. Study was proceeded only on obtaining a fully informed consent.

The parameters of the study were confined to only the estimation of MA, the functional outcome and death or further follow up could not be obtained during the study. Since this is a tertiary center there is a possibility of a anticipated selection bias especially with the seriously ill patients. For which the study settings may have had to be widened.

## STATISTICAL ANALYSIS

Statistical analysis was done using SPSS Software, version 18. Percentages and proportion were used for qualitative data, Chi square for association. Mean and standard deviation for

quantitative data, unpaired student 't' test for differences. P value <0.05 was considered as statistically significant.

**RESULTS**

As per the minimum sample sizing a total of 104 patients of Acute ischemic stroke were studied. Among these patients 47 patients had the presence of Microalbuminuria and the rest of the 57 had no Microalbuminuria. Since for comparison purposes the entire study group was divided into two groups:

*Group A:* Patients with Microalbuminuria

*Group B:* Patients without Microalbuminuria.

Hence the Group A consisted of a total number 47 patients and the Group B consisted a total of 57 Patients of all the age groups and gender.

All the baseline characteristics of both Group A and Group B was observed and the mean was calculated and was presented on the following table.

These two groups compared for the mean urine microalbumin excretion in group-A (110.7 ± 65.4), mean UAE

	Group B MA Negative (mean SD)	Group A MA Positive (mean SD)	t	p
Age	64.14 ± 12.8	61.9 ± 15.9	0.78	0.43
Pulse	84.3 ± 11	80.7 ± 10.5	1.68	0.09
Sys.BP	130.39 ± 13.2	130.55 ± 11.6	0.06	0.94
Dia.BP	82.9 ± 9.8	82.2 ± 7.8	0.37	0.71
GCS	14.82 ± 0.3	13.8 ± 1.5	4.68	0.0001
RBS	132.1 ± 28.8	129.4 ± 27.6	0.48	0.62
S Creat.	1.0 ± 0.29	1.01 ± 0.28	0.19	0.84
B Urea	30.8 ± 13.5	35 ± 14.3	1.52	0.13
Trigly	94.4 ± 21.1	86 ± 27.5	1.75	0.08
T Chol	151.2 ± 35.6	141.0 ± 43.7	1.3	0.196
MA	13.3 ± 8.6	110.7 ± 64.4	11.11	0.0001
Hb%	11.6 ± 1.4	11.7 ± 1.52	0.47	0.63

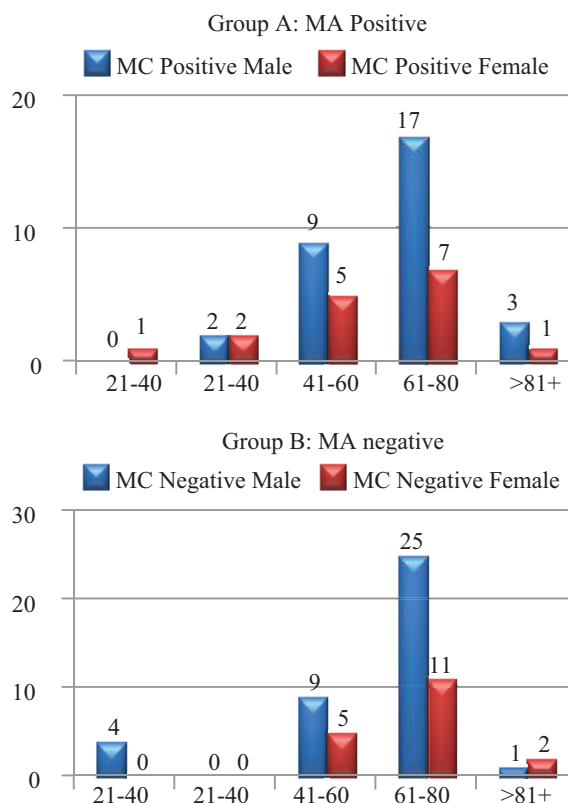
**Table-1:** Baseline characteristics of all the basic components of the studies.

Age (Years)	Group B: MA Negative		Group A: MA Positive	
	Male (No%)	Female (No%)	Male (No%)	Female (No%)
21-40	4(100%)	0	0	1(100%)
21-40	0	0	2(50%)	2(50%)
41-60	9(64.3)	5(35.7%)	9(64.3%)	5(35.7%)
61-80	25(69.4%)	11(30.6%)	17(70.8%)	7(29.2%)
>81+	1(33.3%)	2(66.7%)	3(75%)	1(25%)
Total	18(31.6%)	39(68.4%)	16(34%)	31(66%)

**Table-2:** Age wise distributions of the studies subjects.

Study	Sample size	Prevalence in %	Year of Study
Muralidhara N et al	116	47.91%	2015
Muhammad Ahsan et al	195	48.2%	2013
PC Mathur et al	50	68%	2005

**Table-3:** Showing the comparison of the prevalence from the previous studies in the Indian settings.



**Figure-1:** Genderwise distribution of the studies subjects in Group A and Group B.

in group-B (13.3 ± 8.6) and mean GCS in group-A (13.8 ± 1.5), in group-B (14.82 ± 0.3). There was a clear statistical significance of the GCS <0.0001 and the Presence or absence of the microalbuminuria. Which was taken to be a prognostic index for the survival of the patients and the neurological outcome of the same. The Lower the GCS and the presence of the microalbuminuria the poor was the outcome the disease state.

The age and sex wise distribution of the studied subjects was estimated that the maximum number of male and female patients of both the Group A and Group B were in the age group of 61-80 years. and there was a demonstrable male preponderance among the presence of the microalbuminuria as depicted in the following tables.

With the group A and group B patients there was a obvious male preponderance and also there was demonstrable incidence of ischemic stroke which was more in the males.

The Subjects were also subjected to comparison with respect to other parameters like the dylipidemia, the presence of ischemic changes in on ECG, and the history of smoking. It was also observed for the patterns of the microalbuminuria in the patients with 2 major subsets of ischemic stroke i.e Lacunar strokes and Non lacunar stroke( Large vessel involvement) and Combined stroke.

The Triglyceride values and the values of the Microalbuminuria for both Group A and Group B was estimated, the mean triglycerides levels were (95.49) in both the groups, the mean total Cholesterol levels were (139.23) and statistical significance was not significant with the p value being 0.17.



Total cholesterol with the Microalbuminuria of both Group A and Group B patients, since the p value being 0.86 it was thought to have no significance. Some of the patients had ischemic changes in ECG, among both the Group A and Group B and was compared with the estimated microalbuminuria, with the p value of 0.48 it was proved not significant hence the presence of ECG changes had no correlation with the presence of microalbuminuria. The smoking being one of the risk factor for stroke, all the patients were asked about the history of smoking, the smoking group of patients were present in both group A and B and the number of Smokers were (14) in group A, and in group B were (9) they were compared with the presence and absence of microalbuminuria and the p value was estimated to be 0.08 hence was declared to be of no statistical significance.

All the cases were divided according to the 2 major subtypes of the ischemic stroke as Lacunar or Small vessels ischemic changes and Large vessels involvement or the non Lacunar infarct according to the Radiological protocol with CT or MRI brain findings. Among the patients with positive microalbuminuria the ratio to Lacunar and non lacunar were 23:28, and among the negative Microalbuminuria group the number of lacunar and non lacunar were 18 and 21, and with combined CT findings the number was 6 and 8 among the microalbuminuric and non microalbuminuric cases respectively. The correlation was tabulated with the p value of 0.97 and was not statistically significant.

## DISCUSSION

The prevalence and the association of the microalbuminuria in the event acute ischemic stroke has been successfully proven with statistical significance in many of the western studies and in a few recent Indian studies. Keeping this in mind this study was taken up with Study sample of 104 patients for having filtered them using the exclusion criteria.

Also there was a well anticipated selection bias especially considering the seriously ill patients, and also the prognosis of those patients and the functional outcome of the neurological deficit and even the possibility of the death could not be followed up. And the patients on follow up visits were also not re-estimated for MA, to know the disease process and the behavior of the albumin excretion in urine.

### Prevalence of Microalbuminuria

In our study the prevalence of microalbuminuria was 47 among the 104 patients, which is about 45.19 %. Which was also confirmed about by some previous Indian studies. as depicted in the following table.

In the above studies the patients had the same risk factors profiles and it depicts a slightly higher prevalence of Microalbuminuria in acute ischemic stroke.<sup>7,22,23</sup>

With different study samples the total percentage prevalence was estimated for them to be higher compared to our studies. And also these studies have show significant correlation statistics to other risk factors like hypertension and diabetes etc.

### Prognostic significance of microalbuminuria

In our study the mean GCS was 13.8±1.5 among the MA positive patients, and it was 14.82±0.3 among MA negative patients. Which clearly states that the GCS was significantly lower in patients with MA when compared to patients without MA. p value of 0.0001.

Hence presence of microalbuminuria proves to be an important marker for prognosis in ischemic stroke. It May serve as a assessment marker in case patients requires aggressive medical intervention.

### Age Gender and MA

In this study microalbuminuria we have compared Age Gender and presence of MA. In many of the studies it has been significantly proven to have correlation between age and MA.

No significant correlation was found between the age and the extent of MA among the group A and group B. Furthermore the age was divided into < 60 years and > 60 years. In both the groups it was found out that the number of patients were significantly high in the age group of more than 60 years, than below 60 years.

Whereas other studies also inferred that there is significant male preponderance and more number of patients in the age group of more than 65 years. But does not give any significance regarding the prognostic value or the outcomes of the same when compared to the age and the gender. In our study we did not establish any significant correlation between the age and the GCS. Similarly there was no correlation between the sex and GCS as well. Some of the studies have suggested the severity of the age and GCS and the extent of neurological deficits. In our study there was no significant correlation established between the patients with ECG changes s/o IHD. Both Group A and Group B there were patients with e/o ECG changes, but no conclusion could be drawn about the correlation with MA.

Also the patients of group A and Group B were had patients with history of Smoking, although no correlation was established with respect of GCS and MA. The Sizes of the infarcts of all the patients was studied according to the radiological protocol, as lacunar(Small vessel ischemic changes) and non lacunar(Major vessel involvement). Among the Group A the number of patients with lacunar infarcts was 23 and the non lacunar infarcts were 18 and some of the patients had both changes combined were 6 in number. And the Group B had the Lacunar infarct cases of 28, and the Non lacunar changes of 21 patients, and combined changes of 8 patients. The statistical analysis was done and the no significant correlation was inferred. Hence the size of the infarct had no correlation in patients with or without MA.

## CONCLUSION

Presence of MA was significantly correlated to the Glasgow coma scale for assessing the prognostic significance. Lower the GCS the prevalence and the values of the MA were more. There was no significant correlation between the Age and the presence of MA, even among the subdivided age groups with

60 years as a demarcation. There was no significant gender discrepancy with the presence of MA. There was no significant correlation between the presence of ECG changes and the presence and absence of MA. But the prevalence was still high among the patients with ECG changes. No significant correlation was withdrawn from the presence of smoking history and the presence of MA, but the prevalence was high among the males. Also there was no significant relationship was established between the lipid parameters and MA.

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