

## ORIGINAL ARTICLE

# Microalbuminuria as A Probable Predictor of Severity and Prognosis in Non Diabetic Acute Non-Hemorrhagic Stroke Patients

AnuragSharma\*,RNYadav\*\*,RajendraKumarKasana\*\*\*,Manoj Sharma\*\*\*\*

### ABSTRACT

**Background and Objectives:** Microalbuminuria is considered to be a marker of widespread vascular damage. It's association with increased mortality in diabetes mellitus, hypertension, and acute myocardial infarction is well documented but data regarding association with cerebrovascular accident is sparse. The present study is aimed to assess Microalbuminuria to predict severity and prognosis of non-diabetic acute non-haemorrhagic stroke patients using National institutes of Health Stroke Scale (NIHSS).

**Materials and Method:** This study was carried out at SMS Medical College and attached group of Hospitals, Jaipur. A total of 120 patients admitted with recent ischemic stroke presenting within 7 days and confirmed with CT / MRI Brain were recruited in the study. The microalbuminuria was assayed. The stroke severity and prognosis was assessed by NIH Stroke Scale. P value less than 0.05 was considered the level of significance.

**Results:** Patient with MA positive have more severe stroke according to NIHSS score (P value < 0.005). MA positive patients had NIHSS score  $17.32 \pm 7.20$  and MA negative patients have NIHSS score  $12.15 \pm 6.56$  with  $P < 0.05$ , it was statistically significant that patient with microalbuminuria present with more severe stroke than patient without microalbuminuria.

Change in NIHSS score (from admission day 0 to follow up on day 28) in MA positive patients was  $4.54 \pm 2.14$  while in MA negative was  $5.72 \pm 2.27$  ( $P < 0.05$ ). MA positive patients have satisfactory outcome in comparison with MA negative patients (P value < 0.05) that prognosis is poor in MA positive patients than MA negative patients.

**Conclusion:** In the present study, we found that non-diabetic acute nonhemorrhagic stroke patients with microalbuminuria presented with increased severity and poor prognosis according to NIHSS, thus opening a window of opportunity to predict the cerebro-atherovascular disease by regularly screening the urine for microalbumin.

**Key Words:** Microalbuminuria, Ischemic stroke, NIHSS scale

### INTRODUCTION

WHO defines stroke as rapidly developing clinical signs due to focal disruption in cerebral function, which lasts for more than twenty four hours or which can cause death without any apparent reason other than vascular origin<sup>1</sup>. Stroke or cerebrovascular disease accounts for the largest number of death and disabilities worldwide<sup>2</sup>. The lack of awareness programmes, regarding prevention and early medical management is also improper. This leads to an increase in prevalence and incidence of stroke, thus increasing the economic burden. All this can be

\* Medical Officer CHC, Chomu Jaipur.

\*\* Senior Professor, Department of Medicine, SMS Medical College Jaipur

\*\*\* Assistant Professor Department of Medicine, SMS Medical College, Jaipur

\*\*\*\* Junior Resident, Department of Medicine, SMS Medical College, Jaipur

#### Corresponding Author

Dr. R NYadav

Senior Professor, Medicine, SMS Medical College Jaipur

Email: drarnaranyadav@gmail.com, Mob. 9414408713

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prevented by assessing well defined modifiable risk factors and take preventive measures<sup>3</sup>.

Risk factors or risk markers for stroke are classified according to their potential for modification. Modifiable risk factors are hypertension, exposure to cigarette smoke, diabetes mellitus, atrial fibrillation etc<sup>4</sup>. The realization that atherosclerosis is an inflammatory disease has led to a search for new stroke risk factors and treatment<sup>5</sup>.

Stroke is classified into two main types - Ischemic Stroke and Hemorrhagic Stroke. Ischemic stroke accounts for about 83% of all cases and it occurs as a result of an obstruction within a blood vessel. Obstruction may be either by thrombus or an embolus<sup>6</sup>.

The markers of inflammation like C-reactive protein, intercellular adhesion molecule- I, lipoprotein associated phospholipase A2, elevated white blood cell count, interleukins, variant endothelial nitric oxide synthase, infectious agents like Chlamydia pneumonia, helicobacter pylori and cytomegalovirus, homocysteine, renin angiotensin system; tissue factor, fibrinogen, lipoprotein(a), cytokine transforming growth factor etc., have been proposed as new risk factors for stroke<sup>7</sup>. One more addition to the growing list is microalbuminuria<sup>8</sup>.

Microalbuminuria is considered as a marker of vascular endothelial damage, the latter being the underlying cause of vascular diseases<sup>9</sup>.

Microalbuminuria may be related to vascular damage by several biological pathways like renal dysfunction, transvascular escape of albumin, endothelial dysfunction or inflammation<sup>10</sup>.

Microalbuminuria is now considered to be an atherosclerotic risk factor, has been widely published in literature<sup>11</sup> and microalbuminuria has been

positively correlated with carotid intimal thickness, a well recognized marker of cerebrovascular atherosclerosis<sup>12</sup>.

However, there has been little information regarding microalbuminuria as a predictor of severity and prognosis in ischemic stroke. Hence this work was done to study the role of microalbuminuria as a potential predictor of severity and as a prognostic marker in acute ischemic stroke.

### **AIMS AND OBJECTIVES**

Microalbuminuria as to predict severity and prognosis of non-diabetic acute non-haemorrhagic stroke patients in first twenty eight days of admission using National institutes of Health Stroke Scale (NIHSS).

### **MATERIALS AND METHOD**

The present observational prospective study was conducted at SMS Medical College and Attached Hospitals, Jaipur during year 2017-18. Patients (Age>14 Years) with history of recent non-hemorrhagic stroke presenting within 7 days, confirmed by computed tomography/ MRI of brain, were included in the study.

The patients those with established kidney disease, diabetes mellitus, abnormal urine routine, any febrile patient, long standing hypertension or on NSAID's or other immunosuppressants and who did not give consent were excluded from the study. A total of 120 patients admitted with ischemic stroke were recruited for the study.

A detailed history and examination were done followed by relevant investigations which were sent at admission and 28 days follow up was done. Microalbuminuria was assessed and stroke severity assessed by NIH Stroke Severity Scale.

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**Statistical Analysis**

Data was summarised and classified in MS excel worksheet in the form of the master chart. Qualitative data was expressed in percentage and proportion, Quantitative data was expressed in Mean ± SD, Significance of difference in Proportion: - Chi-square test, Significance of difference in Mean± SD: student 'T' test and other appropriate statistical tests were used. P value less than 0.05 was considered as statistically significant.

**RESULTS**

In this study 66 patients (55%) were microalbuminuria positive while 54 patients (45%) were microalbuminuria negative.

The mean age of male and female patients were 57.84 ± 14.52 and 64.58 ± 14.69 years respectively. It was observed that mean age of female patients were found to be higher as compared to mean age of male

patients. The difference of mean age in male and female patients were statistically significant i.e. P <.05.

In our study, we used NIHSS to assess stroke severity. According to NIHSS, stroke falls in 4 categories, minor, moderate, moderate to severe and severe stroke. NIHSS was applied on admission (day 0) for assessment of severity of stroke.

Patient with MA positive have minor stroke in 3 (4.54%) cases, moderate stroke in 19 (28.79%) cases, moderate to severe stroke in 19 (28.79%) cases, severe stroke in 25 (37.88) cases and patient without microalbuminuria have minor stroke in 10 (18.52%) cases, moderate stroke in 27 (50.00%) cases, moderate to severe stroke in 12 (22.22%) cases, severe stroke in 5 (9.26%) cases. It is statistically significant (P<0.001) that patient with microalbuminuria present with more severe stroke than patient without microalbuminuria.

**Table 1: Stroke Severity at admission with microalbuminuria**

Stroke severity at admission	MA Positive		MA Negative		Total	
	No.	%	No.	%	No.	%
Minor stroke	3	4.54	10	18.52	13	10.83
Moderate stroke	19	28.79	27	50.00	46	38.33
Moderate to severe stroke	19	28.79	12	22.22	31	25.83
Severe stroke	25	37.88	5	9.26	30	25.00
<b>Total</b>	<b>66</b>	<b>100.00</b>	<b>54</b>	<b>100</b>	<b>120</b>	<b>100.00</b>

On admission NIHSS was applied, MA positive patients have NIHSS score 17.32 ± 7.20 and MA negative patients have NIHSS score 12.15 ± 6.56 with P<0.05, it is statistically significant that patient with microalbuminuria present with more severe stroke than patient without microalbuminuria.

Improvement is considered as satisfactory if NIHSS score improved from day 0 to day 28 (e.g. Severe became moderately severe, moderately severe

became moderate, moderate became minor etc.). Out of 66 microalbuminuria positive patients, 35 (53.03%) patients had satisfactory outcome and 28 (42.42%) patients had nonsatisfactory outcome and 3 patients died. Out of 54 microalbuminuria negative patients, 41 (75.93%) patients have satisfactory outcome and 13 (24.07%) had non-satisfactory outcome. With P<.01, it is statistically significant that prognosis is poor in microalbuminuria positive patients.

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**Table 2: Mean change± SD of NIHSS score from at the time of admission to at 28<sup>th</sup> day**

	<b>MA Positive</b>	<b>MA Negative</b>	<b>P value</b>	<b>Significance</b>
Mean Change ± SD of NIHSS Score	4.54 ± 2.14	5.72 ± 2.27	< .05	Sig

Change in NIHSS score from admission (day 0) to day 28, in MA positive patients was 4.54 ± 2.14 while in MA negative was 5.72 ± 2.27. With P<0.05, it is statistically significant that prognosis in patients with MA is poor compared to patients without MA.

**DISCUSSION**

After analysis of 120 patients with reference to inclusion and exclusion criteria microalbuminuria was present in 66 of 120 subjects, 54 patients were microalbuminuria negative.

It was observed that mean age of female patients were found to be higher as compared to mean age of male patients. The difference of mean age in male and female patients was statistically significant i.e. P < .05. This was consistent with Xio-yingyanlin et al<sup>13</sup> study. In this study total number of ischemic stroke patient were 1027, out of them 621 were male and 406 were female patients. Female patients were much older than male patients (71.1 versus 65.0 years, p<0.001) when experiencing their first ischemic stroke attack.

Patient with MA positive have minor stroke in 3 (4.54%) cases, moderate stroke in 19 (28.79%) cases, moderate to severe stroke in 19 (28.79%) cases, severe stroke in 25 (37.88%) cases.

Patient with MA negative have minor stroke in 10 (18.52%) cases, moderate stroke in 27 (50.00%) cases, moderate to severe stroke in 12 (22.22%) cases, severe stroke in 5 (9.26%) cases. With p<0.001, patient with MA positive present with more severe stroke than patient with MA negative.

Mean NIHSS score for the patients with MA positive at the time of admission was 17.32 ± 7.20 and MA negative was 12.15 ± 6.56. With (P<0.05), patients with MA positive presented with high NIHSS score (increased stroke severity) compared to MA negative patients.

It was statistically significant that patient with microalbuminuria presented with more stroke severity than patient without microalbuminuria.

This was in line with Vadher AB. et al<sup>14</sup>. Vadher AB et al<sup>14</sup> revealed out of 46 ischemic stroke patients, 34 (73.9%) had microalbuminuria. Patients with microalbuminuria had higher NIHSS score on admission; p value<0.05 (significant), and thus correlating with increased severity.

In our study, we used NIHSS to assess stroke prognosis, out of 66 microalbuminuria positive patients, 35 (53.03%) patients had satisfactory outcome and 28 (42.42%) had nonsatisfactory outcome and 3 patients died. Out of 54 microalbuminuria negative patients, 41 (75.93%) patients had satisfactory outcome and 13 (24.07%) have nonsatisfactory outcome. With P<0.05, it is statistically significant that patient with microalbuminuria have poor prognosis than patient without microalbuminuria.

Change in NIHSS score (from admission day 0 to follow up on day 28) in MA positive patients was 4.54 ± 2.14 while in MA negative was 5.72± 2.27. With P<0.05, It was statistically significant that patient with microalbuminuria have poor prognosis than patient without microalbuminuria.

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This was in accordance with Das Set al.<sup>5</sup> According to Das S, Ghosh KC et al 01, out of 50 ischaemic stroke patients 33 (66%) had microalbuminuria. Among 11 patients who died, 10 (90.9%) had microalbuminuria and NIHSS score was 33.64 and 25.0 on day 1 and day 7. Among 39 patients who were discharged, 23 patients (58.97%) were MA positive and NIHSS score was much less than death group i.e., 23.38 and 16.38 on day 1 and day 7 respectively. So this study revealed micro-albuminuria, itself results in higher risk for ischaemic stroke compared to control group and it shows good predictive value for early assessment of clinical severity and subsequent fatal outcome.

### CONCLUSION

In the present study, we found that non-diabetic acute nonhemorrhagic stroke patients with Microalbuminuria presented with increased severity according to National Institutes of Health Stroke Scale (NIHSS) and also had poor prognosis and this is well supported by various previous studies, thus opening a window of opportunity to predict the cerebro-atherovascular disease by regularly screening the urine for microalbumin.

Hence, this study may contribute to testing microalbuminuria even in patients without diabetes, hypertension, renal disease etc., to predict severity and prognosis in ischemic stroke.

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