



Original Research Article

Microalbuminuria in patients of acute ischemic stroke

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ABSTRACT

Background: Microalbuminuria has evolved from being a feature of impaired renal function in diabetic nephropathy to an indicator of generalized endothelial dysfunction. It is gaining increasing recognition as a risk factor for cardiovascular and cerebrovascular diseases including ischemic stroke. This study aimed to determine the presence of microalbuminuria in patients of acute ischemic stroke and to determine the relationship between microalbuminuria and severity of stroke.

Materials and Methods: The study included 68 patients of acute ischemic stroke as cases and 68 age/sex matched healthy controls. Stroke severity was assessed using modified National Institute of Health Stroke Scale. Morning void urine sample was collected from cases and controls. Urinary albumin concentration was measured by immunofluorescence method.

Results: Microalbuminuria was present in 57.4% cases and 17.6% controls. Among cases, those with microalbuminuria had a mean severity score of 11.08 and those without microalbuminuria had a mean severity score of 7.83. A statistically significant association was found between microalbuminuria and acute ischemic stroke. Patients of acute ischemic stroke with microalbuminuria had more severe strokes than those without microalbuminuria.

Conclusion: Microalbuminuria has a role as a risk factor and as a predictor of stroke severity in acute ischemic stroke.

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1. Introduction

Microalbuminuria (MA) is the excretion of albumin in urine in minute quantity which is not detected with conventional dipstick method. It is quantitatively defined in several ways as urinary albumin excretion of 30 to 300 mg per 24 hours or urinary albumin-creatinine ratio of 30-300 mg/g in the first voided morning sample or urinary albumin concentration of 20-200 mg/L in the first voided morning sample.^{1,2} MA was initially recognized as a feature of diabetic nephropathy. Subsequently, Steno hypothesis postulated that albumin leakage in kidneys is an indicator of widespread vascular damage that results in renal and extra renal complications.³

Various studies conducted on association of MA with hypertension, ischemic heart disease, heart failure, acute respiratory distress syndrome, carotid atherosclerosis, rheumatoid arthritis and inflammatory bowel disease have changed the status of MA from a marker of impaired renal function to that of an indicator of generalized endothelial injury, with cardiovascular and cerebrovascular implications.^{2,4-9}

2. Materials and Methods

The study was conducted with objectives of determining the presence of MA in patients of acute ischemic stroke and determining the relationship between presence of MA and severity of stroke. It included 68 cases of acute ischemic

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stroke and 68 age/sex matched healthy controls. Patients of acute ischemic stroke (with confirmation by brain imaging) aged 18 years and above, belonging to both genders who agreed to give a written informed consent were included. Patients with hemorrhagic stroke, urinary tract infection, hematuria, fever, systemic infections, chronic kidney disease, heart failure and nephrotic syndrome and those who refused to give consent were excluded from the study. Severity of stroke was measured using modified National Institute of Health Stroke Scale (mNIHSS). It is a simplified version of National Institute Of Health Stroke Scale.¹⁰ For comparison purposes, cases were categorized as mild (mNIHSS score 0-7), moderate (mNIHSS score 7-14), severe (mNIHSS score 14-21) and very severe (mNIHSS score 21-31). MA can be detected either traditionally by using a timed sample of urine collected over 24 hours or on a spot urine sample which is less cumbersome and not prone to collection errors as can happen in the case of 24-hour collection method. In a spot urine sample, either albumin concentration or albumin: creatinine ratio can be measured. Both urine albumin concentration and urinary albumin to creatinine ratio are acceptable tests for population screening for albuminuria in Indo-Asians.¹¹ Morning urine sample was collected from cases and controls in a capped sterile 40 ml plastic container. Albumin concentration in urine does not change significantly if stored at temperature of 20 degree centigrade for upto one week.¹² Urinary albumin concentration was measured using standard F U-Albumin FIA test kits. The method is based on Immunofluorescence and utilizes standard F analyzer (SD BIOSENSOR 2400). Microalbuminuria was defined as a urinary albumin concentration of 20-200 mg/L.

2.1. Statistical methods

Continuous variables were expressed as Mean \pm standard deviation (SD) and categorical variables were expressed as frequencies and percentages. Student's independent t-test was employed for comparing continuous variables. Chi-square test was applied for comparison of categorical variables. Pearson coefficient was used to determine strength of correlation between MA and stroke severity (mNIHSS). A two tailed p value was used for calculating statistical significance; a value of < 0.05 was taken as significant.

3. Results

Mean age (\pm SD) in years was 61.84 ± 12.66 among cases and 59.19 ± 11.94 among controls (Table 1). Hence the two groups were matched with respect to age (p value 0.21). Among cases, 33 (48.5%) were males and 35 (51.5%) females (Table 1). Among controls, 32 (47.1%) were males and 36 (52.9%) females. Thus the two groups of study population were sex-matched (p value 0.086).

MA was present in 39 out of 68 (57.4%) cases and 12 out of 68 (17.6%) controls (Table 2). Hence patients with acute ischemic stroke were 3.26 times more likely to have MA and statistical analysis revealed a significant difference (p value < 0.05).

On analyzing the subset of non-diabetic cases and using appropriate subset of age and sex matched controls, MA was found to be present in 28 out of 45 cases (62.22%) and 6 out of 45 controls (13.33%), revealing a significant difference (p-value < 0.05) on statistical analysis.(Table 3)

Among cases, those with MA had a mean mNIHSS score of 11.08 and those without MA had a mean mNIHSS score of 7.83 (Table 4), showing a significant difference on statistical analysis (p value < 0.05).

When cases were classified on the basis of stroke severity (Table 5), MA was seen to be present in 52% of mild cases, 50% of moderate cases, 75% of severe cases and 80% of very severe cases, thus indicating that prevalence of MA is more among cases with more severe strokes. Statistical analysis of quantitative values of MA in 39 cases, and their respective mNIHSS scores revealed a Pearson coefficient of 0.1826, which indicated that these two have a positive (> 0) albeit weak correlation.

4. Discussion

The realization that atherosclerosis is an inflammatory disease and the fact that conventional risk factors do not always explain all of the cerebrovascular disease risk have led to an interest in search for novel stroke risk factors.¹³ MA interacts with several conventional vascular risk factors and is an independent marker of endothelial dysfunction.¹⁴ MA is now gaining increasing recognition as an independent risk factor for ischemic Stroke.¹⁵ A meta-analysis conducted to study the impact of MA on incident stroke revealed that it is strongly and independently associated with incident stroke risk.¹⁶ MA has also been studied as a prognostic marker for acute ischemic stroke and its presence has been found to be associated with more severe neurological deficits on admission, more severe functional impairment on discharge and a poor outcome.¹⁷

This study, which included a total of 136 subjects comprising of 68 cases and an equal number of controls, was an observational study conducted to look for presence of MA in patients of acute ischemic stroke and to elucidate its relationship with severity of stroke. MA was seen in 39 out of 68 (57.4%) cases and 12 out of 68 (17.6%) controls (p-value < 0.05). Similar results were obtained by Gaurav et al. who observed that MA was present in 48.57 % of cases and 18 % of controls.¹⁸ The results were also comparable with those of Solanke et al. (MA seen in 45.19% of cases).¹⁹ Present study reinforces these and various other studies that have evaluated the role of MA as a risk factor of ischemic stroke. On considering only non-diabetic cases, microalbuminuria was seen in 22 out of 45 (62.22 %) cases

Table 1: Age distribution of study population

Age in years	Cases (% age)	Controls (% age)	Remarks
30-40	3 (4.4 %)	5 (7.4 %)	
40-50	6 (8.8 %)	9 (13.2%)	
50-60	14 (20.6%)	17 (25%)	
60-70	20 (29.4%)	23 (33.8%)	
70-80	19 (27.9%)	11 (16.2%)	
80-90	6 (8.8%)	3 (4.4%)	
Total	68 (100%)	68(100%)	
Mean \pm SD	61.84 \pm 12.66	59.19 \pm 11.94	t-statistic: -1.256 p-value: 0.21
Gender distribution of study population			
Sex	Cases (% age)	Controls (% age)	Remarks
Male	33 (48.5%)	32 (47.1%)	chi-square statistic: 0.0295 p-value: 0.86
Female	35 (51.5%)	36 (52.9%)	
Total	68 (100%)	68 (100%)	

Table 2: Microalbuminuria in study population

Microalbuminuria	Cases (% age)	Controls (% age)	Total	p-value
Present	39 (57.4%)	12 (17.6%)	51 (37.5%)	chi-square statistic 22.870 p-value < 0.05
Absent	29 (42.6%)	56 (82.4%)	85 (62.5%)	
Total	68 (100%)	68 (100%)	136 (100%)	

Table 3: Microalbuminuria in non-diabetic cases

Microalbuminuria	Cases (%age)	Controls (%age)	Total	Remarks
Present	28 (62.22%)	06 (13.33%)	34 (37.77%)	chi-square statistic 22.878 p-value < 0.05
Absent	17 (37.78%)	39 (86.67%)	56 (62.23%)	
Total	45 (100%)	45 (100%)	90 (100%)	

Table 4: Stroke severity and microalbuminuria among cases

Microalbuminuria	Mean mNIHSS score	Standard deviation	Remarks
Present	11.08	6.515	t-statistic: -2.123 p-value < 0.05
Absent	7.83	5.856	

Table 5: Stroke severity (mNIHSS) and microalbuminuria

Stroke severity	Microalbuminuria		Total
	Present (% age)	Absent (% age)	
Mild (mNIHSS Score 0-7)	13 (52%)	12 (48%)	25
Moderate (mNIHSS Score 7-14)	13 (50%)	13 (50%)	26
Severe (mNIHSS Score 14-21)	9 (75%)	3 (25%)	12
Very Severe (mNIHSS Score 21-31)	4 (80%)	1 (20%)	05
Total	29	29	68

and 6 out of 45 (13.33 %) controls (p-value <0.05). This finding is in agreement with other studies.²⁰ Thus even among patients who did not have underlying diabetes, which is a known cause of MA, the study revealed a significant association between acute ischemic stroke and presence of MA. Presence of microalbuminuria in cases was associated with a higher mean mNIHSS score of 11.08; cases without microalbuminuria had a lower mean mNIHSS score of 7.83 (p-value <0.05). Somewhat similar results were obtained by F Li et al. who found that mean NIHSS score was 17.07 in cases with MA and 7.62 in cases without MA and by

Gaurav et al. who found that mean NIHSS score was 17.71 in cases with MA and 13.03 in cases without MA.^{18,20} The higher stroke severity scores among cases in these studies is likely related to the use of different severity scale in these studies. Microalbuminuria was seen to be present in 52% of mild cases of ischemic stroke, 50% of moderate cases, 75% of severe cases and 80% of very severe cases. In 39 cases with MA, when their quantitative values of MA were compared with their corresponding mNIHSS scores, a Pearson coefficient of 0.1826 was calculated, implying that there is a positive correlation between presence of MA and

severity of stroke.

5. Conclusion

We conclude that all these findings of our present study demonstrate the role of MA as a marker of stroke severity and add to the findings of several other studies that have ascertained the relation between MA and stroke severity.

6. Ethical Clearance

The study was approved by Institutional Ethics Committee (IEC research protocol number RP-21/2021).

7. Conflict of Interest

The authors declare no conflict of interest


8. Source of Funding


None.


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