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ROLE OF MICROALBUMINURIA AS A SEVERITY AND PROGNOSTIC INDICATOR IN PATIENTS WITH ACUTE ISCHAEMIC STROKE

General Medicine

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ABSTRACT

Objective: To find association between microalbuminuria and stroke severity based on NIHSS and Modified Rankin Scale. **Material and Methods**: A total of 100 cases and 100 controls that were age/sex matched and admitted during March 2018 to October 2019 were taken into study based on inclusion and exclusion criteria. Urine for microalbumin is tested at the time of admission. Stroke severity was assessed by NIHSS score on admission and prognosis by mRS score at discharge /death**.**
Results: Microalbuminuria is seen in 65%of cases and 8% of controls, (P <0.001). Among100 stroke patients, 100% patients with very severe NIHSS score and 78.26% patients with severe NIHSS score were with microalbuminuria (P <0.001), thus predicting seriousness of stroke in patients with microalbuminuria.
Conclusion: We found that MA is an independent risk factor and potential prognostic marker in acute ischemic stroke.

KEYWORDS

microalbuminuria, NIHSS score, mRS score, ischemic stroke.

INTRODUCTION

Stroke is defined as "rapidly developing clinical signs due to focal disturbance of cerebral function; lasting more than 24 hrs or leading to death, with no apparent cause other than vascular origin." [1] Among stroke, ischemic strokes are the most common (≈85%), the rest being haemorrhagic that include cerebral and subarachnoid (≈15%).

The incidence of strokes occurring every year worldwide is about 17 million and it is the second leading cause of death after coronary artery disease and leading to serious medical, socio economic and rehabilitation problems. This is unfortunate because stroke is well suited for prevention since it has well defined modifiable risk factors and effective preventive measures.[2]The realization that atherosclerosis is an inflammatory disease has lead to a search for new stroke risk factors and treatment. One more addition to the growing list is microalbuminuria.

Microalbuminuria is defined as urinary albumin excretion of 30 to 300 mg/24 hr or urinary albumin to creatinine ratio in the first voided sample in the morning (clean, midstream) greater than 30-300mg/g[3] or early morning urine albumin concentration of 20-200 mg/L.

Microalbuminuria is considered as a marker of vascular endothelial damage. Microalbuminuria may be related to vascular damage by several biological pathways like renal dysfunction, transvascular escape of albumin, endothelial dysfunction or inflammation[4].

Therefore, microalbuminuria may be a useful marker for screening Ischemic stroke in health care system of India where higher imaging facilities are very scarcely distributed. So this study has been planned to observe the microalbuminuria as a severity and prognostic indicator in local population with acute Ischemic stroke.

AIMS AND OBJECTIVE

- To study the presence of microalbuminuria in acute ischemic stroke in comparison to normal healthy individuals.
- To correlate the level of microalbuminuria with the severity of stroke.
- To evaluate the prognostic significance of microalbuminuria in acute ischemic stroke patient.

MATERIAL AND METHODS

This was a case control study of patients with acute ischemic stroke who were consecutively admitted in JLN medical collage & hospitals Ajmer in the time period from March 2018 to October 2019. Patients included were those who had an acute ischemic stroke and confirmed by CT scan/MRI within 72 hours of onset. In this study 200 subjects were enrolled after inclusion and exclusion criteria. Out of these 100 subjects were acute ischemic stroke patients as cases and 100 subjects were controls. Inclusion criteria for controls was age and sex matched normal healthy individuals, with or without any past history of hypertension, diabetes, hepaticorrenal in sufficiency. We excluded: (1) Patients with hemorrhagic stroke, subarachnoid hemorrhage or cerebral venous thrombosis (2) Raised S. creatinine level (above upper limit of normal) (3) Congestive cardiac failure (4) Menstruating women (5) Patients with history of acute infections like UTI, Bacterial Meningitis (within 2 weeks) (6) Connective tissue disorders (7) Malignancy (8) Recent history of surgery or severe trauma Neurological evaluation was done with the help of National Institute of Health Stroke Scale (NIHSS) scores on admission. Computed Tomography (CT) head/MRI brain was done in all patients to confirm the diagnosis. The other investigations that were done for the patients were routine.

The assessment of microalbuminuria was based on random morning spot urine done on the first morning after admission. Urine albumin was measured using immunoturbidimetry method and urine creatinine by Jaffe's method. Urine albumin excretion was estimated as the Urine Albumin Creatinine Ratio (UACR) in mg albumin/ creatinine. The patient's clinical status was evaluated again on the day of discharge with Modified Rankin Score (MRS).

STATISTICAL ANALYSIS

In this study statistical analysis was done using unpaired t-test for quantitative and continuous variables to compare UACR, NIHSS, MRS in terms of case and control, gender, age etc. For categorical variables, Chi square or Fisher's exact test is appropriated for analysis purpose. All the tests are two sided, with a p value of 0.05 or less considering statistically significant.

OBSERVATIONS AND RESULTS

Hence cases and controls were age and sex matched.

TABLE: 1 Urine albumin creatinine ratio (UACR) Qualitatively

UACR	Case		Control		Total		p-value
	No	%	No	%	No.	%	(x^2 test)
MA (-ve)	35	35	92	92	127	63.5	<0.001(S)
MA(+ve)	65	65	8	8	73	36.5	
Total	100	50	100	50	200	100	

As per table 1, 65 (65%) cases and 8 (8%) controls were present with microalbuminuria while 35 (35%) cases and 92 (92%) controls were without microalbuminuria (p <0.001). Among cases mean UACR was 50.56 ± 34.07 while among controls it was 17.5 ± 9.04 (p <0.001).

Table: 2 Association Of Age With The Presence Of Microal buminuria (MA) In Cases.

MA	N	Mean age	'p' Value
Positive	65	63.58±13.46	0.0212
Negative	35	57.26±12.22	

Table: 3 UACR in patients older than 60 years and younger than 60 years in patients with and without microalbuminuria (MA)

	Patient with MA		Patient without MA	
Age Group	≤60yr	>60yr	≤60yr	>60yr
MEAN UACR	73.28	65.78	16.48	17.83
SD	29.97	27.93	6.11	6.18
p-value	0.3093 (NS)		0.539 (NS)	

As per table 2, mean age of patients with microalbuminuria was 63.58±13.46 years compared to 57.26 ± 12.22 years in patients without microalbuminuria, which is statistically significant (P=0.0212) and **as per table 3,**on intra group analysis mean UACR in patients with microalbuminuria (MA) was 73.28 ± 29.97 in ≤60 year of age group and 65.78 ± 27.93 in >60 year of age group (p=0.3093) while mean UACR in patients without microalbuminuria (MA) was 16.48 ± 6.11 in ≤60 year of age group and 17.83 ± 6.18 in >60 year of age group (p=0.539).

Out of 100 acute ischemic stroke patients 18 (36.37%) males and 17 (33.33%) females were without microalbuminuria whereas 31 (63.27%) males and 34 (66.67%) females were with microalbuminuria, which is statistically not significant (p =0.8833). Mean age of patients without microalbuminuria was 52.83 ± 9.89 years in males, 61.94 ± 12.87 years in females and 57.25 years combinedly. While mean age of patients with microalbuminuria (MA) was 60.45 ± 12.97 years in males, 66.59 ± 13.41 years in females and 63.58 years combinedly. Hence in our study female patients was older then male patients. Mean UACR of patients with microalbuminuria (MA) was 63.32 ± 24.06 in males and 73.53 ± 32.00 in females (p=0.154). While mean UACR of patients without microalbuminuria (MA) was 16.11 ± 5.49 in males and 17.82 ± 6.70 in females (p=0.412). Hence mean UACR was higher in female patients.

In our study 21 (34.43%) non-smokers and 14 (35.90%) smokers were without microalbuminuria whereas 40 (65.57%) non-smokers and 25 (64.10%) smokers were with microalbuminuria, and there was no statistically significant difference (p =0.999).

Table: 4 Association of Co-morbidity (Diabetes, HTN) with the presence of Microalbuminuria.

Comorbidity	MA(–ve)	MA(+ve)	Total	p-value
No	17 (44.74%)	21 (55.26%)	38(38%)	0.11 (NS)
Yes	18 (29.03%)	44 (79.97%)	62(62%)	
Total	35 (35%)	65(65%)	100(100%)	

As per table 4, 17 (44.74%) patients without co-morbidity and 18 (29.03%) patients with co-morbidity were without microalbuminuria whereas 21 (55.26%) patients without co-morbidity and 44 (70.97%) patients with co-morbidity were with microalbuminuria, and we didn't found any difference in the distribution of these stroke risk factors (co-morbidity) among the two group (with or without microalbuminuria) (p=0.11).

Table: 5 Microalbuminuria with NIHSS score

NIHSS	MA(-ve)	MA(+ve)	Total	p-value
Mild(<5)	16 (69.57%)	7 (30.43%)	23 (23%)	<0.001 (S)
Moderate (5-15)	14 (51.85%)	13 (48.15%)	27 (27%)	
Severe (16-20)	5 (21.74%)	18 (78.26%)	23 (23%)	
Very severe (>20)	0	27 (100%)	27 (27%)	
Total	35 (100%)	65 (100%)	100 (100%)	

Table: 6 Microalbuminuria (MA) with MRS score

MRS	MA(-ve)	MA(+ve)	Total	p-value
≤3	25 (51.02%)	24 (48.98%)	49 (49%)	0.002 (S)
>3	10 (19.61%)	41 (80.39%)	51 (51%)	
Total	35(100%)	65 (100%)	100 (100%)	

As per table 5, 16 patients have mild, 14 have moderate, and 5 have severe, and no one have very severe NIHSS score and all were without microalbuminuria while 7 patients have mild, 13 have moderate, 18 have severe, 27 have very severe NIHSS score and all were with microalbuminuria. Patients without microalbuminuria mean NIHSS score was 8.17 ± 5.52 while in patients with microalbuminuria mean NIHSS score was 17.09 ± 7.33.

As per table 6, 25 (62.86%) patients of MRS score ≤3 and only 10 (19.61%) patients of MRS score >3 were without microalbuminuria while 24 (48.98%) patients of MRS score ≤3 and 41 (80.39%) patients of MRS score >3 were with microalbuminuria. Mean MRS score was 2.66 ± 1.41 in patients without microalbuminuria while in patients with microalbuminuria mean MRS score was 3.45 ± 1.42.

On study without comorbidity acute ischemic stroke patients, 8 patients have mild, 7 have moderate, and 2 have severe, and no one have very severe NIHSS score and all were without microalbuminuria whereas 2 patients have mild, 4 have moderate, 6 have severe, 9 have very severe NIHSS score and all were with microalbuminuria, (p=0.00045)and in these without comorbidity acute ischemic stroke patients with respect to MRS score, 15 (71.43%) patients of MRS score ≤3 and only 2 (11.76%) patients of MRS score >3 were without microalbuminuria while 6 (28.57%) patients of MRS score ≤3 and 15 (88.23%) patients of MRS score >3 were with microalbuminuria, (p=0.00024).

DISCUSSION

The present study was conducted in Department of Medicine, JLN Medical College and Hospital, Ajmer, Rajasthan during March 2018 to October 2019 in which 100 cases of acute ischemic stroke and 100 age/sex matched normal controls were enrolled after inclusion and exclusion criteria.

In our study the mean age was higher in female patients as compared to male patients. Hence in our study female patients were older as compared to male patients. **In** our study among patients of acute ischemic stroke mean age was higher in patients with microalbuminuria (63.58±13.46) compared to patients without microalbuminuria (57.26 ± 12.22). It was statistically significant (P=0.0212). This is in line with Nany B Beamer et al[5] and Turaj W et al[6], Muralidhara N et[11]. However anupathampy et al[9], J Chowdhury et al[10] and PattanaikS. et al[13]as well did not found any significance.

In our study there was no statistical significance found between gender and Microalbuminuria (P=0.8833). Which means there is no impact of gender on patients with or without microalbuminuria.This is in line with C.Gumbinger et al[7] (P=0.149), Turaj W et al[6], anupathampy et al[9] and J Chowdhury et al[10] as well.

In our study microalbuminuria was found in higher number (qualitatively) among patients with acute ischemic stroke (65%) as compared to controls (8%), (p <0.001). This was in line with the past studies in acute cerebrovascular accidents, conducted by Gumbinger C et al[7], W. Turaj et al[6], AnupaThampy et al[9] and Vadher, Abhishek et al.[12] However Toth et al.[16] did not confirm that immunoreactive (immunologically intact) albumin, which is typically measured as a marker MA serves as an independent risk factor for stroke severity.

Mean UACR value was higher (quantitatively) among patients with acute ischemic stroke (50.56 ± 34.07) as compared to controls (17.5 ± 9.04), which was also statistically significant (p<0.001).This in line with past studies conducted by W. Turaj et al[6]. Above data shows that microalbuminuria (MA) is an independent risk factor in acute ischemic stroke, in other words those in whom albumin concentration in urine is increased are at greater risk of cerebro-atherovascular disease. This may be due to lipid insulation, raised sialic acid in vessel wall, impaired arterial dilatory capacity and hyper-homocysteinemia which are considered as causes of microalbuminuria (MA) in atherosclerosis. **In** our study shows that patients with microalbuminuria were older than patients without microalbuminuria (P value <0.05) but **on** intra-group analysis for graded correlation (i.e. by grouping the patients less than 60 years and more than 60 years) shows that urine albumin excretion and age defied a significant graded correlation. This in line with study conducted by PC Mathur et al[14]. So we infer that microalbuminuria might be much more dependent on the severity of the stroke process than age as evidenced by its significant correlation with NIHSS Score in acute stroke patients with microalbuminuria.

Mean UACR was higher in female patients as compared to male patients. This in line with Muralidhara N et al[11], which may be due to higher age of female patients in our study.

In our study there was no association found between smoking and Microalbuminuria (p =0.999). However Hiltege HL et al, Hisher D et al show significant association between smoking and Microalbuminuria.

In our study, the correlation of microalbuminuria with stroke severity

was assessed using NIHSS score. Based on NIHSS Score, cases were sub-grouped into 4 categories. Those with score <5 mild neuro-deficit, 5-15 into moderate neuro-deficit, 16-20 into severe neuro-deficit and >20 into very severe neuro-deficit.

In our study patients with acute ischemic stroke, NIHSS score was higher in patients with microalbuminuria (17.09 ± 7.33) compared to patients without microalbuminuria (8.17 ± 5.52) ($p<0.001$) and most of our comatose and died patients had microalbuminuria thus predicting seriousness of stroke in patients with microalbuminuria. So in the present study, we found that higher the NIHSS score, more the urine albumin excretion and vice versa. This is in line with Gumbinger C et al[7], Das S et al[8] and, Muralidhara N et al[11] and Shrestha S et al as well.

In our study, the correlation of microalbuminuria with stroke prognosis was assessed using MRS score. Based on MRS score, cases were sub divided into two groups, MRS score >3 are associated with poor prognosis and outcome and MRS score ≤3 are associated with relatively good prognosis and outcome. In our study patients with microalbuminuria (MA) show higher MRS score and poor prognosis as compared to patients without microalbuminuria (MA). This is in line with C Gumbinger et al[7], J chowdary et al[10], Vadher, Abhishek et al[12], Geert sulter et al[15] as well.

In our study patients with acute stroke, the high prevalence of microalbuminuria (MA) could be related to the very common presence of diabetes or hypertension. Diabetes and hypertension both were important risk factors for microalbuminuria and lead to cerebral-atherosclerosis and stroke. So in patients without diabetes and hypertension to predict the pathogenicity of atherosclerosis in cerebral vasculature and severity and prognosis of stroke, we also study microalbuminuria in patients without co-morbidity (diabetes and hypertension). When we compare patients with and without microalbuminuria (MA) we didn't found any differences in the distribution of these stroke risk factors (co-morbidity) among the two groups (with or without microalbuminuria) ($p=0.11$). We found that in acute ischemic stroke patient without co-morbidity, incidence of microalbuminuria was 55.26%. This in line with Muralidhara N et al[11], PattanaikS. et al[13].

Our study on without co-morbidity acute ischemic stroke patients also shows that patients with microalbuminuria have higher NIHSS score and more severe stroke as compared to patients without microalbuminuria, ($p=0.00045$). This in line with Vadher, Abhishek et al[12], Muralidhara N et al[11], and patients with microalbuminuria also have higher MRS score and poor prognosis as compared to patients without microalbuminuria, ($p=0.0045$). This is in line with Vadher, Abhishek et al[12], Geert sulter et al[15].

CONCLUSION

In the present study we found microalbuminuria in 65% of acute ischemic stroke patients($p<0.001$). We also found that acute ischemic stroke patients with microalbuminuria presented with increased severity according to National Institutes of Health Stroke Scale (NIHSS) and also had poor prognosis according to MRS score. So microalbuminuria may be an important marker to assess severity and prognosis in acute ischemic stroke patients. Therefore measurement of microalbuminuria may help to assess those who are at increased risk and to triage those who may need a more aggressive management protocol.

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