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Dr. Thabish Syed
Resident, Department of Medicine, National Institute of Medical Sciences (NIMS), Jaipur, Rajasthan-303121, India

Dr. Manju Pandey
Assistant Professor, Department of Medicine, National Institute of Medical Sciences (NIMS), Jaipur, Rajasthan-303121, India

Dr. J.P. Rishi
Professor and Head, Department of Medicine, National Institute of Medical Sciences (NIMS), Jaipur, Rajasthan-303121, India

Dr. *Dilip Ahir*
Resident, Department of Medicine, National Institute of Medical Sciences (NIMS), Jaipur, Rajasthan-303121, India

Correspondence:
Dr. Thabish Syed
Resident, Department of Medicine, National Institute of Medical Sciences (NIMS), Jaipur, Rajasthan-303121, India

Microalbuminuria- an emerging risk factor in acute ischemic stroke

Thabish Syed, Manju Pandey, J.P. Rishi, Dilip Ahir*

Abstract

Objective: To study the role of biomarkers like microalbuminuria in acute ischemic stroke. **Material and Methods:** A total of 70 cases admitted in wards and ICU under Department of Medicine, NIMS Medical College & Hospital Jaipur and 70 controls that were the normal age/sex matched during study period of 15 months i.e. July 2014 to September 2015 were taken into study based on inclusion and exclusion criteria. Urine for microalbumin is tested at the time of admission. Stroke severity and prognosis is assessed by NIHSS score on day 0, 3, 7 & 14. Tests of statistical significance were done using Chi-square Test, unpaired't' test and fisher test. **Results:** Out of 70 age and sex matched cases and controls, Microalbumiuria is seen in 51.43% of cases and 2.86% of controls, which is statistically significant (P <0.001). Mean urine albumin creatinine ratio (UACR) is 65.10 + 79.12 in cases where as it is 7.53 + 8.04 in controls which is also statiscally significant (p<0.001). Hence MA is considered as a risk factor in acute ischemic stroke. Among 70 acute ischemic stroke cases studied, MA was seen in 36 in whom 11 patients fell in severe NIHSS score and 16 very severe which is statistically significant (Chi-square = 27.605 with 3 degrees of freedom; P <0.001) * Mean NIHSS score for the patients with MA at the time of admission and discharge was 22.05 and 16.16 compared to 8.36 and 3.61 at the time of admission and discharge in patients without MA , most of our comatose patients had microalbuminuria 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, Ischemic stroke, Cerebrovascular disease, NIHSS.

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].

Cerebrovascular disease or stroke is one of the leading cause of death and disability throughout the world [2], leading to serious medical, socio economic and rehabilitation problems. Stroke is also called as "Brain Attack" because it involves an acute insult to the brain causing major disability many a times. Lack of proper prevention programmes, poor awareness about stroke risk factors and warning signals by the public and lack of proper emergency medical and surgical management are main reason for this. This is unfortunate because stroke is well suited for prevention since it has high prevalence, high burden of illness and economic cost, well defined modifiable risk factors and effective preventive measures [3].

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 [4].

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. [5], The realization that atherosclerosis is an inflammatory disease has lead to a search for new stroke risk factors and treatment [6].

The markers of inflammation like c-reactive protein, intercellular adhesion molecule-1, 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 [7]. One more addition to the growing list is microalbuminuria [8].

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 [9] or early morning urine albumin concentration of 20-200 mg/L [10].

Third National Nutrition Examination Survey (NHANES 3) in United States reported that microalbuminuria is very common in diabetic and hypertensive patients, although it is also seen in more than 5% of otherwise healthy subjects [11].

Microalbuminuria is considered as a marker of vascular endothelial damage, the latter being the underlying cause of vascular diseases [12]. Microalbuminuria may be related to vascular damage by several biological pathways like renal dysfunction, transvascular escape of albumin, endothelial dysfunction or inflammation [13].

Microalbuminuria as an independent risk factor for hemorrhagic stroke has been widely published in literature [14] and microalbuminuria has been positively correlated with carotid intimal thickness, a well recognized marker of cerebrovascular atherosclerosis [15].

However there has been little information regarding microalbuminuria as an independent risk factor for stroke or as a predictor of stroke outcome.

Hence this work is being planned to study the role of MA as an independent risk factor as well as a potential prognostic marker in acute ischemic stroke.

MATERIAL AND METHODS

- This study was carried out in the Department of Medicine, NIMS Medical College and Hospital, Shobha Nagar, Jaipur, Rajasthan from July 2014 to September 2015, over the period of 15 months.
- Study was done on both male and female acute ischemic stroke patients of age more than 30 years presented within 24 hrs, admitted in wards and ICU under the Department of Medicine, NIMS Hospital, Jaipur and normal healthy controls both male and female more than 30 years of age.
- Type of study **:** case control study with follow-up of cases
- Study design: longitudinal urine for microalbumin is tested at the time of admission. stroke severity and prognosis is assessed by NIHSS score on day 0 & day 7. Statistical tests like Chi- square test, unpaired‘t’ test, fisher exact test was applied. A p value <0.05 was considered statistically significant. Data obtained was analysed statistically by SPSS software.

RESULTS

Incidence of microalbuminuria among study population

Table 1: Urine albumin creatinine ratio (UACR)- Quantitative

UACR	Case		Control		Total	
	No.	%	No.	%	No.	%
MA negative	34	48.57	68	97.14	102	72.86
MA Positive	36	51.43	2	2.86	38	27.14
Total	70	100.00	70	100.00	140	100.00

- Chi-square = 39.334 with 1 degree of freedom; P <0.001
- Microalbuminuria (qualitative) was found in 36(51.43%) patients with acute ischemic stroke compared to 2(2.86%) control. Thus MA is increased in patients of acute ischemic stroke as P<0.001 which is highly significant.

Table 2: Mean UACR value

UACR	Case	70	65.10	79.12	P<0.001
	Control	70	7.53	8.04	

Mean UACR is 65.10 $\pm$ 79.12 in cases compared to 7.53 $\pm$ 8.04 in controls. With P<0.001 it is highly significant.

Stroke Severity and MA (Pattern of NIHSS and MA)

In our study, we used NIHSS to assess stroke severity as well as stroke prognosis,

According to NIHSS, stroke falls in 4 categories, minor, moderate, severe and very severe. NIHSS is applied on admission (day 0), day 3, day 7, day 14.

On admission NIHSS is applied on all cases, patients with MA presented with high NIHSS score (increased stroke severity) compared to patients without MA. with P<0.001 it is statistically significant.

Table 3: Stroke Severity AND MA. (Pattern of NIHSS and MA)

NIHSS-DAY 0	MA Negative		MA Positive		Total	
	No.	%	No.	%	No.	%
Mild	11	32.35	1	2.78	12	17.14
Moderate	18	52.94	8	22.22	26	37.14
Severe	3	8.82	11	30.56	14	20.00
Very Severe	2	5.88	16	44.44	18	25.71
Total	34	100.00	36	100.00	70	100.00

Chi-square = 27.605 with 3 degrees of freedom; P <0.001

Table4: Association of mean NIHSS score and MA-Stroke prognosis

Mean NIHSS	MA Negative	MA Positive
0th day	8.36	22.05
3rd day	7.27	21.89
7th day	5	17.48
14th day	3.61	16.16

Mean NIHSS score is significantly increased with the presence of MA.

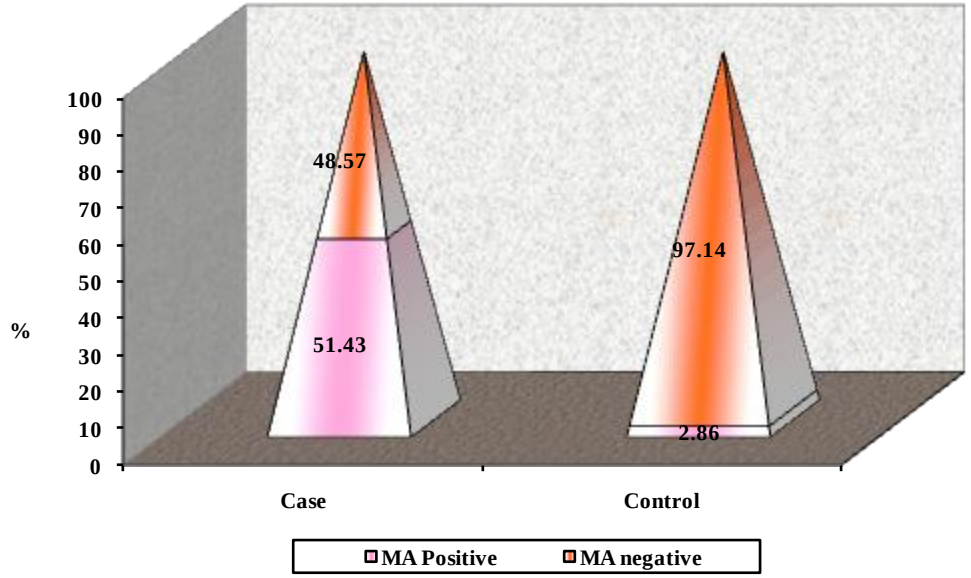

Figure 1: UACR in study

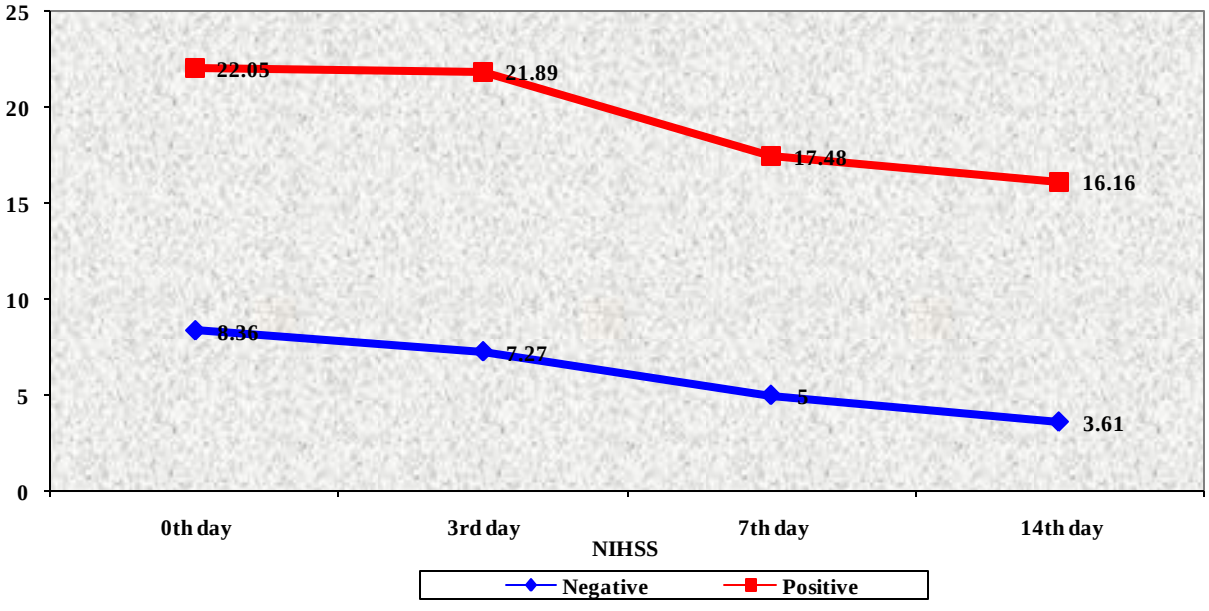

Figure 2: Mean NIHSS score day 0, 3, 7 and 14 in cases

DISCUSSION

Incidence of Microalbuminuria

According to our study among 70 age and sex matched cases and controls, Microalbumiuria is seen in 51.43% of cases and 2.86% of controls, which is statistically significant (P <0.001). Mean urine albumin creatinine ratio (UACR) is 65.10 ± 79.12 in cases where as it is 7.53 ± 8.04 in controls which is also statiscally significant (p<0.001).

This is in line with Nancy B.Beamer *et al*, [16] Turaj W *et al*, [17] C. Gumbinger *et al*, [18] Das S, Ghosh KC *et al* [19].

Table 5: Comparison with various previous studies

Study	Place &Year of study	MA in cases	MA in controls
Nancy B.Beamer *et al*	Portland- 1998	29%	10%
Turaj W *et al*	Poland- 2001	46.1%	13.5%
C. Gumbinger *et al*	Germany- 2010	43%	No controls
Das S, Ghosh KC *et al*	India- 2012	66%	8%
Present study	India- 2015	51.43%	2.86%

Above data showed 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 to lipid insudation [20], raised sialic acid [21] in vessel wall, impaired arterial dilatory capacity [22]and hyperhomocysteinemia [23] which are considered as causes of MA in atherosclerosis. In other words, MA may be a common marker in the urine for vascular pathologies like lipid insudation, raised sialic acid, impaired arterial dilatory capacity and hyperhomocysteinemia.

Among 70 acute ischemic stroke cases studied, MA was seen in 36 in whom 11 patients fell in severe NIHSS score and 16 very severe which is statistically significant (Chi-square = 27.605 with 3 degrees of freedom; P <0.001).

Mean NIHSS score for the patients with MA at the time of admission and discharge was 22.05 and 16.16 compared to 8.36 and 3.61 at the time of admission and discharge in patients without MA , most of our comatose patients had microalbuminuria thus predicting seriousness of stroke in patients with microalbuminuria. This is in line with Das S, Ghosh KC *et al* [19]and Meng Lee *et al*, [24].

Mean NIHSS score for the patients with MA at the time of admission (day 0) and at day 14 was 22.05 and 16.16 compared to 8.36 and 3.61 at day 0 and day 14 in patients without MA. This shows the seriousness as well as poor prognosis of stroke in patients with MA.

CONCLUSION

The present study found microalbuminuria in 51.43% (p<0.001) of ischemic stroke patients and is consistent with previous studies associating MA with cerebro-atherovascular disease. In the present study, we also found that stroke patients with Microalbuminuria presented with increased severity according to National Institutes of Health Stroke Scale (NIHSS) and also had poor prognosis. Hence, this study may contribute to testing MA even in patients without diabetes, hypertension, renal disease etc., to predict the pathogenicity of atherosclerosis in cerebral vasculature. However, longer studies may be required to establish whether it is optimum to regularly test for Microalbuminuria in asymptomatic patients after particular age and control of MA prevents incidence and seriousness of stroke.

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