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Prognostic significance of microalbuminuria in non-diabetic patients with acute ischemic stroke

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ABSTRACT

Microalbuminuria (MA) is nowadays recognized as an independent risk factor for ischemic stroke. In our study we investigate MA in acute ischemic stroke without diabetes and it's correlation with severity of stroke. This is a prospective observational study done on 50 patients with non diabetic ischemic stroke. All the patients were subjected to a detailed history, clinical examination, biochemical and radiological investigations and assessment of the National Institutes of Health Stroke Scale (NIHSS) for grading the severity of ischemic stroke with the measurement of microalbuminuria.

Cases with a mean NIHSS of 26 ± 11.418 were positive for MA, while cases with a mean NIHSS of 12.85 ± 9.06 were negative for MA, indicating that higher NIHSS were positive for MA. The relationship between MA and NIHSS was statistically significant (p <0.0001). At admission, the mean NIHSS Score for Minor stroke patients was 3.55556 ± 0.527, while 14.3125 ± 0.4787 for moderate stroke cases, 19.0769 ± 1.605 for moderate to severe stroke, and 38.4545 ± 0.478 for severe stroke patients. The correlation between microalbuminuria and NIHHS score is 0.650, with a significant p-value of 0.0001. MA was associated with the severity of cerebral infarction at admission and clinical outcomes 1 month after onset, and it could be used as a potential indicator of poor prognosis in patients with ischemic stroke.

Keywords: microalbuminuria, NIHSS, ischemic stroke

INTRODUCTION

A stroke is also referred to as a brain attack. Stroke is defined as a clinical syndrome of rapid onset cerebral deficit lasting on 24 hours or leading to death with no apparent cause other than vascular one. Put simply, it means quick loss of the function of the brain because something went wrong with the blood supply to that particular area in your head. It occurs around 800,000 times each year or once every 40 seconds making it the second most common cause of death globally [1]. In India, its prevalence rate stands at about 1.54 per thousand people [2]. There are three main types: ischemic strokes, hemorrhagic strokes and transient ischemic attacks (TIA).

Ischemic stroke occurs in approximately 80-85% of cases due to extracranial or intracranial thrombosis or cardioemboli. In India, large vessel atherosclerosis is the most common cause of acute ischemic stroke. Stroke can be prevented by controlling its risk factors. Antiplatelet drugs, intravenous thrombolysis, endarterectomy and intracranial artery stenting are some of the treatment options for strokes along with hypertension management and monitoring of intracranial pressure. There are many factors that predict post-stroke mortality and morbidity such as severity of stroke, type of stroke, age (older), sex (male), vascular risk factors and level of consciousness at onset. Interest in finding unifying mechanisms in ischemic stroke pathogenesis has increased over time. C reactive protein, lipoprotein A, lipoprotein phosphatase A2, increased leukocyte count (pro inflammatory interleukins), endothelial nitricoxide, tissue factors, intracellular adhesion molecules homocystine plasma fibrinogen were identified as cerebrovascular ischemic stroke risk factors. The realization that atherosclerosis being an inflammatory disease has fueled new search for risk factors including microalbuminuria [3] among others which can be used to treat strokes like it's done elsewhere around the world where this condition is rampant too but not limited only there since they have similar climates among other things relat-

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ed to health care provision thus making them comparable even though different regions might have varying degrees depending on their specific localities within each country involved here.

Microalbuminuria (MA) is defined as a urinary albumin excretion rate of 30 to 300 mg/day [4]. Several studies showed that MA in diabetic patients may predicts diabetic nephropathy [5]. Epidemiological studies found that MA can be a predictor of ischemic stroke in diabetic and non-diabetic subjects [6,7]. Mykkanen et al. noted that the thickness of the intima-media complex in carotid arteries that results the progression of atherosclerosis in these vessels and correlates well with the presence of MA [8]. Recently, Beamer et al. showed that the prevalence of microalbuminuria is three-fold greater in patients with recent stroke when compared to controls with the same profile of cardiovascular risk factors [9]. Hence, the aim of the study was to evaluate the prognostic significance of MA in non- -diabetic acute stroke patients.

MATERIALS AND METHODS

A prospective observational study was conducted in the departments of General Medicine and Neurology at Narayana Medical College & Hospital, Nellore, Andhra Pradesh. The study was approved by the Institutional Ethical Committee, and informed consent was obtained from all participants. The study included non-diabetic patients presenting with acute ischemic stroke, who met the inclusion and exclusion criteria. Recruitment occurred in the outpatient department and inpatient wards of the aforementioned departments. The study duration was 18 months, from January 2021 to June 2022. The sample size for this study was set at 50 patients.

Inclusion criteria

Patients eligible for inclusion were those with a clinical diagnosis of acute ischemic stroke, confirmed by non-contrast CT scan or MRI of the brain, who provided informed consent.

Exclusion criteria

The following patients were excluded from the study:

- Those with known diabetes and hypertension
- Those with intracranial hemorrhage
- Those with chronic kidney disease (CKD) or acute kidney injury (AKI)
- Those with urinary tract infection (UTI)
- Those with neoplasms
- Those with coronary artery disease

Data collection

Within 24 hours of admission, urine samples from acute ischemic stroke patients were tested for microalbuminuria. Stroke severity was evaluated using the NIH Stroke Scale (NIHSS) at admission and reassessed after one month.

NIHSS stroke severity scale

NIHSS score	Stroke severity
0	No stroke symptoms
1-4	Minor stroke
5-15	Moderate stroke
16-20	Moderate to severe stroke
21-42	Severe stroke

Statistical analysis

Statistical analysis was carried out using appropriate statistical software (SPSS). Baseline characteristics of the study population were summarized with descriptive statistics. Categorical variables are expressed as frequencies and percentages, while continuous variables are expressed as means and standard deviations. The relationship between microalbuminuria and stroke severity was assessed using chi-square tests for categorical variables and t-tests for continuous variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

TABLE 1. Association between stroke size and spot microalbuminuria

Stroke size	Spot microalbuminuria (-Ve)	Spot microalbuminuria (+Ve)	Total	p-value
SI	Frequency (n) = 22	Frequency (n) = 7	29	
	% within Spot microalbuminuria = 78.57%	% within Spot microalbuminuria = 31.81%	58%	0.0014
LI	Frequency (n) = 6	Frequency (n) = 15	21	
	% within Spot microalbuminuria = 21.42%	% within Spot microalbuminuria = 68.18%	42%	
Total	Frequency (n) = 28	Frequency (n) = 22	50	

Table 1 presents the association between stroke size and the presence of spot microalbuminuria in patients. The study categorized stroke size into small infarcts (SI) and large infarcts (LI). Spot microalbuminuria was measured and the results were grouped as either negative (-Ve) or positive (+Ve).

- Among patients with small infarcts (SI), 22 tested negative for spot microalbuminuria, while 7 tested positive. This translates to 78.57% of the SI patients being negative for microalbuminuria and 31.81% being positive.
- Conversely, among patients with large infarcts (LI), 6 tested negative and 15 tested positive for spot microalbuminuria. This means that 21.42% of the LI patients were negative for microalbuminuria, whereas 68.18% were positive.

The total number of patients included in the study was 50, with 28 testing negative and 22 testing positive for spot microalbuminuria. The statistical analysis indicated a significant association between stroke size and the presence of spot microalbuminuria, with a p-value of 0.0014. This suggests that larger infarcts are more likely to be associated with positive spot microalbuminuria.

Table 2 compares clinical parameters between stroke patients with and without spot microalbuminuria (MA). The study included 22 patients with MA and 28 without MA. There were no significant differences in systolic blood pressure (SBP), diastolic blood pressure (DBP), Barthel index (BI), total cholesterol (T Chol), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TGL), age, urea, creatinine, or random blood sugar (RBS) levels between the two groups. However, the NIH Stroke Scale (NIHSS) score was significantly higher in patients with MA (26 ± 11.42) compared to those without MA (12.57 ± 9.12), indicating more severe strokes in patients with microalbuminuria (p <0.0001).

Table 3 illustrates the correlation between spot microalbuminuria and the NIHSS stroke scale at admission among stroke patients. The NIHSS scale categorizes stroke severity into no stroke, minor stroke, moderate stroke, moderate to severe stroke, and severe stroke. The table compares the frequency and percentage of patients with positive (+ve) and negative (-ve) spot microalbuminuria across these categories.

For the no stroke category, only 1 patient (3.57%) without microalbuminuria fell into this category. In the minor stroke category, 9 patients (32.14%) without microalbuminuria were classified as having a minor stroke, with no patients with microalbuminuria in this category. For moderate strokes, 16 patients were identified, with 6 (27.27%) testing positive for microalbuminuria, and 10 (35.71%) testing negative. Among the 13 patients with moderate to severe strokes, 7 (31.8%) had microalbuminuria, while 6 (21.42%) did not. Of the 11 patients classified as having severe strokes, 9 (40.90%) tested positive for microalbuminuria, and 2 (7.14%) tested negative.

TABLE 2. Basic characteristics of stroke patients

Variable	Spot microalbuminuria (-Ve)	Spot microalbuminuria (+Ve)	N	Mean ± SD	p-value
SBP (mmHg)	117.64 ± 10.11	117.68 ± 11.33	22	117.68 ± 11.33	0.9898
DBP (mmHg)	74.21 ± 5.20	75.91 ± 5.36	22	75.91 ± 5.36	0.2648
BI (Barthel Index)	63.46 ± 12.73	61.59 ± 5.65	22	61.59 ± 5.65	0.5242
T Chol (mg/dL)	172.61 ± 39.18	180.86 ± 45.96	22	180.86 ± 45.96	0.4964
HDL (mg/dL)	36.25 ± 5.41	36 ± 4.38	22	36 ± 4.38	0.8609
LDL (mg/dL)	108 ± 46.68	111.18 ± 49.06	22	111.18 ± 49.06	0.8160
TGL	138.25 ± 37.54	162.45 ± 68.28	22	162.45 ± 68.28	0.1170
Age	49.89 ± 8.27	49.95 ± 8.49	22	49.95 ± 8.49	0.9795
Urea	31.25 ± 9.22	32.36 ± 7.52	22	32.36 ± 7.52	0.6486
Creatinine	1.12 ± 0.25	1.25 ± 0.25	22	1.25 ± 0.25	0.0902
RBS	104.5 ± 10.12	107.5 ± 11.56	22	107.5 ± 11.56	0.3333
NIHSS	12.57 ± 9.12	26 ± 11.42	22	26 ± 11.42	<0.0001

TABLE 3. Correlation between spot microalbuminuria and NIHSS stroke scale

NIHSS Scale at admission	Microalbuminuria (+ve)	Microalbuminuria (-ve)	Total	p-value
No stroke	Frequency (n) = 0	Frequency (n) = 1	1	0.65576
	% within Spot microalbuminuria = 0%	% within Spot microalbuminuria = 3.57%		
Minor stroke	Frequency (n) = 0	Frequency (n) = 9	9	
	% within Spot microalbuminuria = 0%	% within Spot microalbuminuria = 32.14%		
Moderate stroke	Frequency (n) = 6	Frequency (n) = 10	16	
	% within Spot microalbuminuria = 27.27%	% within Spot microalbuminuria = 35.71%		
Moderate to severe	Frequency (n) = 7	Frequency (n) = 6	13	
	% within Spot Microalbuminuria = 31.8%	% within Spot microalbuminuria = 21.42%		
Severe	Frequency (n) = 9	Frequency (n) = 2	11	
	% within Spot microalbuminuria = 40.90%	% within Spot Microalbuminuria = 7.14%		
Total	**22 (44%)**	**28 (56%)**	50	

The total number of patients in the study was 50, with 22 (44%) having positive microalbuminuria and 28 (56%) having negative microalbuminuria. The p-value of 0.65576 suggested no statistically significant correlation between spot microalbuminuria and stroke severity as measured by the NIHSS scale.

DISCUSSION

Microalbuminuria has been used to monitor diabetes mellitus for a long time. In non-diabetic patients with acute stroke, we investigated the prognostic importance of MA. Microalbuminuria is associated with risk factors for stroke such as diabetes, hypertension, aging, myocardial infarction history, obesity, smoking and left ventricular hypertrophy.

A study conducted by Nancy B. Beamer et al. found that MA was present in 29% of recent stroke patients compared to 10% of those with clinical risk factors for stroke and was absent in healthy individuals [9]. In another study done by Yuyun MF et al. on a population-based prospective cohort involving 246 British stroke patients it was concluded that microalbuminuria independently increases the risk of general population strokes by approximately 50% [10].

Turaj W et al. studied 52 stroke victims in the Neurological Department at Jagiellonian University Cracow Poland within 24 hours after onset and reported significant correlation between micro albuminuria and severity of the disease [11]. According to our research patients who tested positive for MA had an average NIHSS score of 26 ± 11.418 while those who tested negative had an average NIHSS score of only 12.85 ± 9.06 showing higher levels were always associated with being positive for M A. The correlation between MA and NIHSS scores was statistically significant p <0.0001.

Gumbinger et al. included patients suffering from acute ischemic strokes admitted into their unit during this period where they used NIHSS upon admission together with modified Rankin scale (mRS) upon discharge assessment on how severe it was or what its outcome would be like thereafter which showed that acute ischemic stroke patients had micro albuminuria associated with severe neurological deficits on admission and severe functional impairment upon discharge moreover MA was shown to be an independent predictor of poor outcome during the acute phase [12].

Similarly Słowik et al. carried out research involving individuals brought within twenty-four hours after their first ischemic stroke whereby they used Scandinavian stroke scale (SSS) for assessment of neuro deficit and urinary albumin excretion measurement found that microalbuminuria occurred among 46.7% of patients with acute strokes, 16% in those who had previous strokes, while 16.7% were found among controls. Furthermore it was observed that on admission patients were more severely neurologically deficient if they also tested positive for MA.

In our study, the mean NIHSS score for minor stroke patients was 3.5 ± 0.5, while 14.31 ± 0.47 for moderate stroke cases, 19.07 ± 1.6 for moderate to severe stroke, and 38.4 ± 0.4 for severe stroke patients. The correlation between microalbuminuria and NIHHS score was 0.650, with a significant p-value of 0.0001. MA was associated with the severity of cerebral infarction at admission and clinical outcomes 1 month after onset, and it could be used as a potential indicator of poor prognosis in patients with ischemic stroke.

CONCLUSION

The higher the microalbuminuria level, the higher the NIHSS score and the poorer the outcome. We demonstrated that measuring microalbuminuria after a non diabetic ischemic stroke was a reliable predictor of stroke outcome. We concluded that microalbuminuria was found to be an independent marker of acute ischemic stroke. MA was also associated with the clinical severity of a stroke. Microalbuminuria measurement helps in identifying the patients at increased risk and aid in providing more aggressive management protocol.

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