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SPOT URINE ALBUMIN CREATININE RATIO IN ACUTE ISCHEMIC STROKE: A CASE-CONTROL STUDY

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A B S T R A C T

Background and Aim: Microalbuminuria (MA) signifies abnormal vascular permeability and its presence may be considered as kidney's notice for markedly enhanced cerebrovascular risk. Urine albumin-to-creatinine ratio (UACR) is linked with the risk of stroke. This study aimed to determine the prevalence/frequency of MA or UACR in acute ischemic stroke patients. **Methodology:** This is a case-control study conducted with total of 140 patients from December 2023 to December 2024. 70 patients with no history of stroke and transient ischemic attack were enrolled in control group. Another 70 patients with symptoms suspicion stroke were enrolled in case group. The severity of stroke was assessed by National Institutes of Health Stroke Scale (NIHSS). **Results:** The mean age of study subjects in control and cases group was found to be 53.06 ± 14.97 and 54.57 ± 14.03 years. Male predominance was observed in both control (58.60%) and cases (67.10%) groups. Hypertension is the major comorbid condition observed in both control and cases group followed by diabetes mellitus. Majority of the study subjects enrolled in the study i.e., 35.7% were suffering from small vessel followed by cardioembolic (34.3%), and large vessel (30%). The mean UACR of study subjects in control and cases group was found to be 17.21 ± 7.27 and 497.83 ± 427.29 respectively with statistically significant difference ($p<0.0001$) between control and cases. Majority of the study subjects enrolled in the study i.e., 30% were suffering from moderate to severe stroke followed by minor & moderate stroke (24.28%), and severe stroke (21.42%). **Conclusion:** Microalbuminuria may be an important prognostic marker in acute ischemic stroke. Furthermore, it was inferred that that urine albumin excretion might be much more dependent on the severity of the stroke process than age. Higher the NIHSS score more the urine albumin excretion and *vice versa*

Keywords: Stroke severity, Microalbuminuria, Spot UACR, Hypertension, Diabetes mellitus.

INTRODUCTION

Worldwide, cerebrovascular accidents (stroke) are the second leading cause of death and the third leading cause of disability.[1] Stroke, the sudden death of some brain cells due to lack of oxygen when the blood flow to the brain is lost by blockage or rupture of an artery to the brain, is also a leading cause of dementia and depression.[2] Stroke is defined by the World Health Organization as a clinical syndrome consisting of rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin.[3]

Stroke is classified broadly into three categories; ischemic stroke, haemorrhagic stroke and subarachnoid haemorrhage. Ischemic stroke occurs due to blockage of blood vessel which limits the blood supply to the brain whereas haemorrhagic stroke occurs due to rupture of blood vessel leading spillage of blood in the intracranial cavity.[4] Depending on the site of blood spillage the haemorrhagic stroke could be classified as intracerebral haemorrhage or subarachnoid haemorrhage. Approximately 60–80% of all strokes is ischemic. Globally, 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years occur in low-and middle-income countries.[5]

Chronic kidney disease (CKD) is a considerable public health challenge worldwide. Growing evidence indicates that the presence of protein in the urine, which represents an early sign of kidney disease, may be related to the risk of stroke. There are different data regarding whether proteinuria, which is often measured via the urine albumin-to

creatinine ratio (UACR), could be a risk factor for stroke and its subtypes.[6] Moreover, over the last 4 decades, several prospective clinical studies have identified a series of independent risk factors for symptomatic vascular events, including stroke.[7,8] However, a better understanding of the multifactorial pathogenesis of atherosclerosis, the underlying entity behind most vascular events, and the fact that many of these events occur in persons who do not harbor conventional vascular risk factors has prompted a search for novel risk factors for prediction of cardiovascular disease. Nonetheless, the clinical value of many of these emerging risk factors remains uncertain largely due to inconsistency of data, paucity of studies, or lack of evidence that their predictive ability is independent of conventional risk factors.[9]

One such emerging vascular risk factor is microalbuminuria. Microalbuminuria (MA) is generally defined as a urinary albumin excretion rate (or albumin excretion rate) of 30 to 300 mg/day or spot urinary albumin : creatinine ratio (UACR) of 30 to 300 mg/mmol in men and 3.5 to 25 mg/mmol in women.[10] Few studies have been done in India which also show a similar correlation of MA in ischemic stroke.[11,12] However, there is a scarcity of studies in India, relating to UACR in acute ischemic stroke. Hence, the present study was designed with the main objectives to determine the prevalence/frequency of UACR in acute ischemic stroke patients.

METHODOLOGY

Study population

This is a case-control study conducted with total of 140 patients admitted at Department of General Medicine, J. J. M. Medical College, and Bapuji hospital, Davangere, Karnataka. The ethical committee approval was obtained before the conduct of study.

Inclusion criteria

Patients;

1. Aged between 40-65 years
2. Either gender
3. With symptoms suspicion stroke
4. Who are willing to give consent

Exclusion criteria

Patients with;

1. Renal diseases
2. Eclampsia and preeclampsia
3. Malignancy
4. Urinary infection
5. Rheumatic heart disease
6. Cardiomyopathy
7. Who are not willing to give consent

Study design

Seventy patients with no history of stroke and transient ischemic attack and fulfilling exclusion criteria were enrolled in control group. Another seventy patients with symptoms suspicion stroke fulfilling inclusion criteria were enrolled in case group.

Data collection and Assessment parameters

The demographic details, such as age, gender occupation, co-morbidities, socioeconomic status were noted. The cases were subjected to detailed history and physical examination, and laboratory investigations. Type of stroke was recorded.

The severity of stroke was assessed by National Institutes of Health Stroke Scale (NIHSS) (Table 2). The NIHSS is a 15-item neurologic examination stroke scale used to evaluate the effect of acute ischemic stroke on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss that provide a quantitative measure of stroke-related neurologic deficit.[13]

Table 1: National Institutes of Health Stroke Scale (NIHSS)

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

MA was detected by usingurine auto-analyzer which gives the outcome value of spot UACR as follows; (i) <30 mg/g – normal, (ii) 30–300 mg/g – abnormal, and (iii) >300 mg/g – high abnormal.

Statistical analysis

Data was entered in Microsoft Excel 2021 and analysis was done using Statistical Software for Social Sciences (SPSS) version 21. Categorical variables were represented in the form of percentages, and frequencies. Continuous variables were presented as descriptive statistics (Mean and Standard deviation).

RESULTS

The mean age of study subjects in control and cases group was found to be 53.06 ± 14.97 and 54.57 ± 14.03 years. Male predominance was observed in both control (58.60%) and cases (67.10%) groups. Hypertension is the major comorbid condition observed in both control and cases group followed by diabetes mellitus (Table 2).

Table 2. Distribution of study subjects based on demographic and baseline characteristics

Variables	**Control (n=70)**	**Cases (n=70)**
Age (years)	53.06 ± 14.97	54.57 ± 14.03
Gender		
Male, n (%)	41 (58.60)	47 (67.10)
Female, n (%)	29 (41.40)	23 (32.90)
Comorbidities		
Diabetes, n (%)	21 (30.00)	21 (30.00)
Hypertension, n (%)	34 (48.60)	36 (51.40)
Smoking, n (%)	7 (10.00)	6 (8.60)
Alcoholic, n (%)	6 (8.60)	5 (7.10)
Obesity, n (%)	2 (2.90)	2 (2.90)

Values are expressed as mean ± standard deviation (SD) unless otherwise stated

Majority of the study subjects enrolled in the study i.e., 36% were suffering from small vessel followed by cardioembolic (34%), and large vessel (30%) (Figure 1).

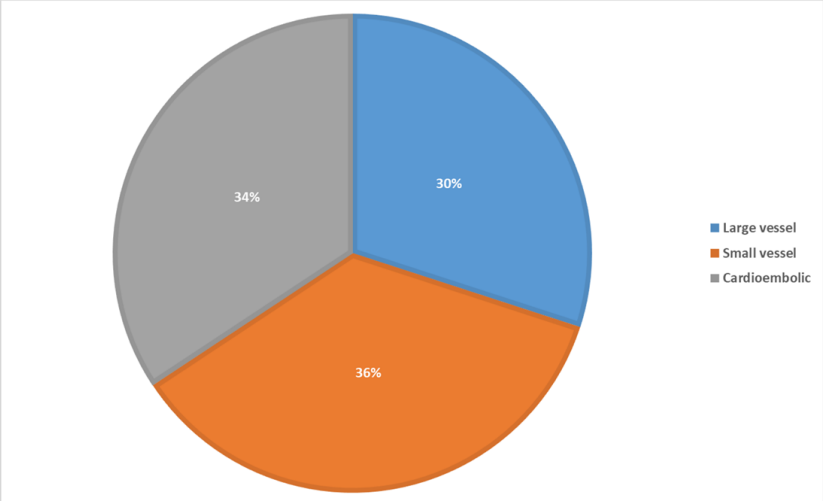

Figure 1. Distribution of study subjects based on type of stroke

The mean UACR of study subjects in control and cases group was found to be 17.21 ± 7.27 and 497.83 ± 427.29 respectively with statistically significant difference ($p<0.0001$) between control and cases (Table 2).

Table 2. Comparision of mean UACR between control and case groups

Variable	Control (n=70)	Cases (n=70)	p-value
UACR	17.21 ± 7.27	497.83 ± 427.29	<0.0001

Values are expressed as mean ± SD

Majority of the study subjects enrolled in the study i.e., 30% were suffering from moderate to severe stroke followed by minor & moderate stroke (24.28%), and severe stroke (21.42%) (Figure 2).

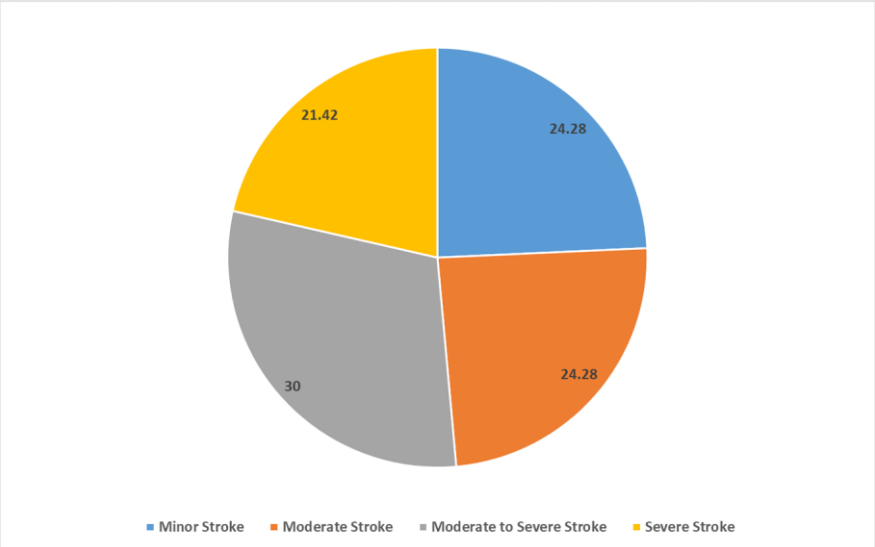

Figure 2. Distribution of study subjects based on severity of acute ischemic stroke

DISCUSSION

Microalbuminuria signifies abnormal vascular permeability and its presence may be considered as kidney's notice for markedly enhanced cerebrovascular risk.[14] The importance of microalbuminurea was first appreciated in the early 1980s when two landmark studies in London and Denmark independently reported that it was predictive of development of overt diabetic nephropathy and progressive renal failure. Although microalbuminurea is associated with clinical risk factors for stroke including diabetes, hypertension, aging, history of myocardial infarction and left ventricular hypertrophy there was little information regarding microalbuminurea as being an independent risk factor for stroke or as predictor of stroke outcome.[15] With this context in the present case-control study we aimed to determine the prevalence/frequency of UACR in acute ischemic stroke patients.

In our study the mean age of study subjects in control and cases group was found to be 53.06 years and 54.57 years respectively with no significant differences. These findings were comparable with the findings of previous studies reported in the literature. In the Indian subcontinent, stroke happens nearly a decade earlier than West and young strokes constitute about 20% of stroke population in India.[16,17] The incidence of stroke increases with age.[1] Furthermore, Behera et al., reported the incidence of stroke is maximum in 51-70 years of age group which comprises of 59.46% of total patients.[1] In a study done by Banerjee et al. in 2001 crude prevalence rate of stroke in India was 147/100,000 and the annual incidence rate was 36/100,000. Overall prevalence of stroke ranges from 147–922/100,000 in various studies.[18]

In our study, in control and case group, male predominance i.e., 58.6% and 67.1% respectively was observed as compared to females. In concurrence to our study findings Behera et al., reported the male to female ratio was 1.48:1 and researchers concluded that incidence of stroke is more common in male sex.[1] The gender difference observed in the current study possibly resulted from inherent social bias in which female patients are less likely to be admitted to hospital compared to male patients. In the present study, higher male predominance among the acute ischemic stroke in young adults was observed which may be attributed to a socio-cultural bias in India and also males are more exposed to tobacco chewing/smoking and alcohol since in our study majority of the study subjects i.e., 48.6% were having hypertension as comorbidity followed by diabetes mellitus (30%), smoking (8.6%), alcohol abuse (7.1%), and 2.9% of study subjects having obesity as comorbidity in case group. Furthermore, our study findings were comparable to other Indian studies on stroke patients where greater preponderance was seen among males.[16,19] However, few literature reports evidenced that women had substantially higher age-adjusted prevalence rate (564/100,000 for women vs 196/100,000 for men) and incidence rate (204/100,000 for women vs 36/100,000 for men).[20,21]

Literature reports evidenced that proportion of ischemic stroke of 68% from community-based studies to 80% from hospital-based study.[20,22] In concurrence with literature findings in our study subject's majority of the acute ischemic stroke patients enrolled in the study i.e., 35.7% were suffering from small vessel followed by cardioembolic (34.3%), and large vessel (30%). In our study hypertension was the most common risk factor of acute ischemic stroke in adults. Similar finding had been observed in the studies by a group of Indian authors.[23,24] Hypertension is the dominant predisposing factor for stroke and is strongly related to atherothrombotic brain infarction as well as intracranial hemorrhage. Epidemiologic studies have reported that hypertension is associated with an increased likelihood of subclinical or silent stroke, which in turn has been linked with increased risk of recurrent stroke.[25]

Smoking is a known risk factor for ischemic stroke.[1] The prevalence of smoking in the present study was 8.6% in case which was comparable to the previous studies.[24,26] Alcohol is another important contributing risk factor in the development of ischemic stroke.[1] The current study had 7.1% patients with a history of excess alcohol intake in the case group which was higher compared to the previous studies.[24,26]

In the present study, the correlation of microalbuminuria with stroke severity was assessed using NIHSSS score. Majority of the study subjects enrolled in our study i.e., 30% were suffering from moderate to severe stroke followed by minor & moderate stroke (24.28%), and severe stroke (21.42%) based on NIHSS score. Results of mean UACR of study subjects between control and cases revealed that the mean UACR of study subjects in control and cases group was found to be 17.21 and 497.83 respectively with the mean difference of 480.62 and which was statistically significant ($p<0.0001$). The findings delineated that higher the NIHSS score, more the urine albumin excretion and *vice versa*. Hence microalbuminuria may be an important prognostic marker in acute ischemic stroke. Furthermore, it was inferred that that urine albumin excretion might be much more dependent on the severity of the stroke process than age as evidenced by its significant correlation with NIHSS in acute stroke victims.[27]

Previous study conducted by Beamer et al. reported microalbuminuria in 97 acute ischemic stroke patients with 51 controls, prevalence was 29% with significant p-value <0.001.[28] In another study conducted in acute cerebrovascular accidents, by Keen and Chlouverakis, where 52 patients with 37 subjects in control group where the prevalence was 46% with p-value of <0.05.[29] In India, study conducted by Mathur et al. showed that, advanced age in microalbuminurics with stroke than normoalbuminurics ($p<0.05$).[11]

CONCLUSION

In conclusion, microalbuminuria may be an important prognostic marker in acute ischemic stroke. Furthermore, it was inferred that that urine albumin excretion might be much more dependent on the severity of the stroke process than age. Higher the NIHSS score more the urine albumin excretion and *vice versa*.

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