

## A Prospective Observational Evaluation of the Renal Function and its Relationship with Mortality in Patients with Acute Stroke

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Received: 07-11-2023 Revised: 20-12-2023. Accepted: 28-01-2024

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Conflict of interest: Nil

### Abstract

**Aim:** The aim of the present study was to investigate the renal function in patients with acute stroke and its relationship with in-hospital mortality.

**Methods:** The present study was a prospective, observational study conducted at Department of General Medicine for the period of one year. 150 patients were considered for present study.

**Results:** Patients were divided into two groups as per eGFR. Group A with eGFR>60 and Group B with eGFR <60. 66.66% were from group A while 33.34% were from group B. Most patients were from >65 years age group, male, BMI<30. Hypertension, smoking, diabetes mellitus, cardiovascular disease, alcohol consumption, dyslipidemia, previous history of stroke/TIA were common risk factors in both groups. On admission most patients had GCS score 5-13. 97 patients had ischemic stroke, while 53 had hemorrhagic stroke. We noted mortality within 30 days in 31 patients. We distributed patients according to Serum Creatinine concentration at time of presentation, most patients had serum creatinine in the range of 98-118 (32%) followed by 82-97 (28%). Maximum mortality was noted in >119 (38.70%) followed by 98-118 (32.25%) serum creatinine group. We distributed patients according to blood urea concentration at time of presentation, most patients had blood urea in the range of 6.8-8.9 (40%) followed by 5.3-6.7 (26.66%). Maximum mortality was noted in >9 (41.93%) followed by 6.8-8.9 (29.03%) blood urea group. We noted that age > 65 years, at the time of admission, smoking, diabetes mellitus and aspiration pneumonitis were predictors of death in stroke patients.

**Conclusion:** The severity of impaired kidney function in patients hospitalized with acute stroke is associated with increased mortality independent of age, sex, and major comorbidities. Unrecognized renal insufficiency noted by low eGFR is common in patients with acute stroke and is associated with higher mortality adverse short-term outcomes.

**Keywords:** acute stroke, estimated glomerular filtration rate (eGFR), serum creatinine, blood urea

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### Introduction

Stroke is the leading cause of neurological disability and the second commonest cause of death in the world. [1] Chronic kidney disease (CKD) is frequently associated with cardiovascular diseases; it is considered a cardiovascular risk equivalent. Patients with CKD are more likely to die of cardiovascular diseases (CVD) than to eventually develop renal failure requiring renal replacement therapy. [2] Conversely, diagnosis of CKD is higher among patients with cardiovascular diseases than in the general population. [3] CKD is associated with a significantly increased risk of cerebrovascular disease. Even subtle kidney dysfunction, as suggested by albuminuria, increases stroke risk. Stage 3 CKD with microalbuminuria increased stroke risk 1.5 to 2 fold. [3] Dialysis patients have six times increased risk of stroke. Stroke accounts for 3% of deaths in end-stage renal disease (ESRD).

Stroke in CKD could be ischemic, hemorrhagic, or both; Infarction strokes are more prevalent than hemorrhages. Risk factor reduction (primary and secondary prevention therapies) is the mainstay of therapy. [3]

Acute renal failure is a frequent co-morbid state in the population with a variety of medical conditions such as cardiovascular disorders, DM, HT, cerebrovascular disease, and in-patient treatment in an ICU. Acute renal failure occurs after stroke as its complication. Older patients (>60 years) with cardiovascular comorbid are managed through multiple drugs mostly for underlying acute renal failure. [4]

Patients with stroke and AKI have many similar risk factors that cause morbidity as well as mortality. It is found that most of the vascular origin diseases like

stroke are associated with AKI. The severity of AKI or damaged renal vessels are strongly associated with stroke severity. [5] According to many studies, haemorrhagic stroke tends to cause more AKI in contrast to ischemic stroke. Though after controlling for other factors, serum creatinine was proved to be an independently associated indicator of death and prolonged hospitalization in stroke survivors. Even though AKI is widespread and has a high morbidity and death rate, it is preventable, promptly detectable, as well as treatable. [6]

The aim of the present study was to investigate the renal function in patients with acute stroke and its relationship with in-hospital mortality.

### Materials and Methods

The present study was a prospective, observational study conducted at Department of General Medicine, Rajeshwar Hospital, Patna, Bihar, India for the period of one year. 150 patients were considered for present study.

#### Inclusion Criteria:

Patients above 18 years of age, admitted to the hospital or reporting in OPD/Emergency, with clinical diagnosis of acute stroke, confirmed by CT scan / MRI, willing to participate in study and follow up

#### Exclusion Criteria:

patients with acute kidney injury (AKI), head injury, metastasis, bleeding disorder, primary SOL (space occupying lesion), on anticoagulation therapy.

A written informed consent was taken from relatives of stroke patient. Patient details were recorded (demographic data, medical history of diabetes, hypertension, alcohol consumption, smoking/nicotine use, drug use, trauma, past history

of TIA/stroke, cardiovascular disease or any other medical illness). At admission detailed clinical examination for vital parameters, neurological deficit and Glasgow coma scale scoring were done in all patients. Routine investigations (complete haemogram, ESR, BT, CT, PT, aPTT, platelet count, routine and microscopic examination of urine, RBS, blood urea, serum creatinine, eGFR, serum electrolytes, LFT, lipid profile), CT scan/MRI head, ECG, Chest X-Ray were done in all patients. Other investigations such as echocardiography, connective tissue workup, etc. were done whenever needed.

Glomerular filtration rate (eGFR) on admission was assessed using Modification Diet for Renal Disease (MDRD) formula :eGFR (in ml/min per 1.73m<sup>2</sup>) = 186.3 x P<sup>cr</sup> (e<sup>[-1.154]</sup>) x Age (e<sup>[-0.203]</sup>) × (0.742 if female) × (1.21).

Patients were divided into two groups on the basis of eGFR:

Group A -patients with eGFR>60 ml/min/1.73 m<sup>2</sup> of body surface area (BSA).

Group B -patients with eGFR <60 ml/min/1.73 m<sup>2</sup> of body surface area (BSA).

All patients received standard care. Outcome in stroke patients was assessed in terms of mortality at 30 days since stroke episode. Follow up was kept till 3 months. Data was collected prospectively in proforma and analyzed by means of appropriate statistical technique. Data was analysed using SPSS Statistics software (version 23). The qualitative data between two groups was compared using Chi Square test and for comparison of the continuous variable, student t-test was used. p<0.05 was considered statistically significant.

### Results

**Table 1: General characteristics**

Characteristics	Group A (eGFR>60 ml/min/1.73 m <sup>2</sup> )	Group B (eGFR<60 ml/min/1.73 m <sup>2</sup> )
Total patients	100	50
<b>Age (in years)</b>		
18-40	5 (5%)	2 (4%)
40-65	22 (22%)	15 (30%)
>65	73 (73%)	34 (68%)
<b>Sex</b>		
Male	68 (68%)	35 (70%)
Female	32 (32%)	15 (30%)
<b>BMI (kg/ m<sup>2</sup>)</b>		
<30	60 (60%)	36 (72%)
>30	40 (40%)	14 (28%)
<b>Risk Factors</b>		
Hypertension	57 (57%)	31 (62%)
Smoking	43 (43%)	24 (48%)
Diabetes Mellitus	40 (40%)	30 (60%)
Cardiovascular disease	39 (39%)	31 (62%)
Alcohol	36 (36%)	19 (38%)

Dyslipidemia	35 (35%)	19 (38%)
Previous history of stroke/TIA	18 (18%)	16 (32%)
<b>GCS score</b>		
3-4	22 (22%)	6 (12%)
5-8	29 (29%)	9 (18%)
9-13	38 (38%)	25 (50%)
>13	11 (11%)	10 (20%)
<b>Type of stroke</b>		
Ischaemic	66 (66%)	31 (62%)
Haemorrhagic	34 (34%)	19 (38%)
Mortality (within 30 days of presentation)	15 (15%)	16 (32%)

Patients were divided into two groups as per eGFR. Group A with eGFR>60 and Group B with eGFR <60. 66.66% were from group A while 33.34% were from group B. Most patients were from >65 years age group, male, BMI<30. Hypertension, smoking, diabetes mellitus, cardiovascular disease, alcohol

consumption, dyslipidemia, previous history of stroke/TIA were common risk factors in both groups. On admission most patients had GCS score 5-13. 97 patients had ischemic stroke, while 53 had hemorrhagic stroke. We noted mortality within 30 days in 31 patients.

**Table 2: Distribution of Patients according to Serum Creatinine concentration at time of presentation and Mortality within 30 days**

Serum Creatinine (umol/L)	No. of patients (n=150)	Outcome (Mortality within 30 days) (n=31)
30-81	25 (16.66%)	3 (9.67%)
82-97	42 (28%)	6 (19.35%)
98-118	48 (32%)	10 (32.25%)
>119	35 (23.34%)	12 (38.70%)

We distributed patients according to Serum Creatinine concentration at time of presentation, most patients had serum creatinine in the range of 98-118 (32%) followed by 82-97 (28%). Maximum mortality was noted in >119 (38.70%) followed by 98-118 (32.25%) serum creatinine group.

**Table 3: Distribution of Patients according to Blood Urea concentration at time of presentation and mortality within 30 days**

Blood Urea (mmol/L)	No. of patients (n=150)	Outcome (Mortality within 30 days) (n=31)
1.8-5.2	14 (9.33%)	4 (12.90%)
5.3-6.7	40 (26.66%)	5 (16.12%)
6.8-8.9	60 (40%)	9 (29.03%)
>9	36 (24%)	13 (41.93%)

We distributed patients according to blood urea concentration at time of presentation, most patients had blood urea in the range of 6.8-8.9 (40%) followed by 5.3-6.7 (26.66%). Maximum mortality was noted in >9 (41.93%) followed by 6.8-8.9 (29.03%) blood urea group.

**Table 4: Predictors of death among stroke patients**

	Alive (n=119)	Died (n=31)	p value
Age (In years)	62.8 ± 12.3	68.2 ± 11.7	< .01
Hypertension	60	28	0.25
Smoking	45	22	0.028
Diabetes Mellitus	42	28	0.042
Cardiovascular disease	43	27	0.0726
<b>Type of stroke</b>			
Ischaemic	77	20	0.22
Haemorrhagic	40	13	0.1

We noted that age > 65 years, at the time of admission, smoking, diabetes mellitus and

aspiration pneumonitis were predictors of death in stroke patients.

## Discussion

Acute stroke is one frequent cause of emergency admission. Stroke being the disease of the elderly, has associated with high morbidity and mortality rate. Stroke is the second most common cause of mortality and third most common cause of disability worldwide. Globally, 68% of all strokes are ischemic and 32% are hemorrhagic. [7] In India prevalence of stroke 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. [8,9] In prospective studies, advanced age, hypertension, diabetes mellitus, smoking and atrial fibrillation have been found as risk factors for stroke and the relevant mortality. [10]

Patients were divided into two groups as per eGFR. Group A with eGFR>60 and Group B with eGFR <60. 66.66% were from group A while 33.34% were from group B. Most patients were from >65 years age group, male, BMI<30. Hypertension, smoking, diabetes mellitus, cardiovascular disease, alcohol consumption, dyslipidemia, previous history of stroke/TIA were common risk factors in both groups. On admission most patients had GCS score 5-13. 97 patients had ischemic stroke, while 53 had hemorrhagic stroke. Factors associated with impaired renal function that may contribute to the adverse outcome of patients with stroke include insulin resistance, oxidative stress, inflammation, endothelial dysfunction, vascular calcifications and increased plasma levels of fibrinogen and homocysteine. [11] Katarzyna Snarskaa et al [12] noted that 6% of patients with ischemic stroke and 4% of patients with stroke had a high proportion of elevated serum creatinine at admission. The mean serum creatinine at admission was significantly higher among patients who died in both types of stroke. Similar findings were noted in present study. The best indicator of renal function is estimated GFR rather than creatinine. [13] Individuals with a decreased eGFR have less effective cerebral autoregulation. A prospective study of patients after acute ischemic stroke found that poorer autoregulation was correlated with lower eGFR and associated with an increased risk of hemorrhagic transformation of ischemic stroke. Hemorrhagic transformation may result from breakthrough hyperperfusion and microvascular injury in the setting of impaired autoregulation. [14]

We noted mortality within 30 days in 31 patients. We distributed patients according to Serum Creatinine concentration at time of presentation, most patients had serum creatinine in the range of 98-118 (32%) followed by 82-97 (28%). Maximum mortality was noted in >119 (38.70%) followed by 98-118 (32.25%) serum creatinine group. We distributed patients according to blood urea concentration at time of presentation, most patients

had blood urea in the range of 6.8-8.9 (40%) followed by 5.3-6.7 (26.66%). Maximum mortality was noted in >9 (41.93%) followed by 6.8-8.9 (29.03%) blood urea group. We noted that age > 65 years, at the time of admission, smoking, diabetes mellitus and aspiration pneumonitis were predictors of death in stroke patients. A study on 821 consecutive patients with acute stroke (ischemic or hemorrhagic) demonstrated that chronic renal dysfunction defined as estimated glomerular filtration rate <60 mL/min/1.73 m<sup>2</sup>, was associated with increased mortality and adverse outcomes compared with patients with normal renal function. [15] Similarly, in a pooled analyses of 4 prospective community based cohorts low eGFR was significantly associated with increased risk of ischemic, but not haemorrhagic, stroke risk, while high albumin/creatinine ratio was associated with both stroke types. [16] Lee et al. in meta-analysis of 21 articles derived from 33 prospective studies, found that patients with a baseline eGFR of <60 ml/min/1.73 m<sup>2</sup> had a risk of future stroke that was 43% greater than those with a normal baseline eGFR. [17]

## Conclusion

The severity of impaired kidney function in patients hospitalized with acute stroke is associated with increased mortality independent of age, sex, and major comorbidities. Unrecognized renal insufficiency noted by low eGFR is common in patients with acute stroke and is associated with higher mortality adverse short-term outcomes.

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