Original Research Article

# Study of renal function in patients of acute stroke and its relationship with in-hospital mortality

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## Abstract

**Background:** Stroke being the disease of the elderly, has associated with high morbidity and mortality rate. It is increasingly apparent that individuals with chronic renal disease are more likely to die from cardio-cerebrovascular diseases. Stroke is an emergency disease and shares the same atherosclerotic risk factors with ischemic heart disease but the association of renal function and stroke is poorly investigated. In this study, we aimed to investigate the renal function in patients with acute stroke and its relationship with in-hospital mortality. **Material and Methods:**The present study was a prospective, observational study conducted in patients admitted to Basaveshwar Teaching and General hospital attached to M R Medical College reporting in OPD/Emergency, with clinical diagnosis of acute stroke, confirmed by CT scan / MRI. Glomerular filtration rate (eGFR) on admission was assessed using MDRD formula. Outcome in stroke patients was assessed in terms of mortality at 30 days since stroke episode. **Results:** 132 patients were considered for present study. Patients were divided into two groups as per eGFR. Group A with eGFR>60 and Group B with eGFR <60. 74% were from group A while 26% 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. Maximum mortality was noted in >119 umol/L (41%) followed by 98-118 mmol (33%) serum creatinine group. While in blood urea group , maximum mortality was noted in >9 mmol/L (44%) followed by 6.8-8.9 mmol/L (30%). We noted that age > 65 years, GCS score > 10 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.

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

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## INTRODUCTION

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.[1] In India prevalence of stroke was 147/100,000 and the annual incidence rate was 36/100,000. Overall prevalence of stroke ranges from

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147–922/100,000 in various studies.[2,3]In prospective studies, advanced age, hypertension, diabetes mellitus, smoking and atrial fibrillation have been found as risk factors for stroke and the relevant mortality.[4] Various common risk factors between stroke and kidney dysfunction lead to a higher morbidity and mortality in patients of stroke. Almost all types of vascular disease including stroke have been found to be associated with renal function impairment and severity of stroke could reflect the degree of injury in small renal vessels.[5]Reduced renal function may reflect both the duration and severity of different cardiovascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia, and it is often linked with the development of other less established vascular risk factors such as anemia, oxidative stress, electrolyte imbalance, and hyperhomocysteinemia.[6] It is increasingly apparent that individuals with chronic renal disease are more likely to die from cardio-cerebrovascular diseases.[7]Stroke is an emergency disease and shares the same atherosclerotic risk factors with ischemic heart disease but the association of renal function and stroke is poorly investigated. Stroke is a vascular disease, and it is important for the development of both preventive and therapeutic strategies to identify the role of renal function on global cardiovascular risk after an acute stroke.In this study, we aimed to investigate the renal function in patients with acute stroke and its relationship with in-hospital mortality.

## MATERIAL AND METHODS

The present study was a prospective, observational study conducted at Basaveshwar Teaching and General Hospital attached to M R Medical College during Nov 2018 to Oct- 2019 (1 year). Institutional ethical committee approval was taken prior to start of 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. 73m2) = 186.3 x P cr (e [−1. 154] ) x Age (e[-0. 203]) × (0.742 if female) × (1.21 if black).

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

**Group A -**patients with eGFR>60 ml/min/1.73 m2 of body surface area (BSA).

**Group B -**patients with eGFR <60 ml/min/1.73 m2 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

132 patients were considered for present study. Patients were divided into two groups as per eGFR. Group A with eGFR>60 and Group B with eGFR <60. 74% were from group A while 26% 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. 85 (64%) patients had ischemic stroke, while 47(36%) had hemorrhagic stroke. We noted mortality within 30 days in 27 (20%) patients.

**Table 1:** General characteristics

| Characteristics | Group A ( eGFR>60 ml/min/1.73 m2 ) | Group B ( eGFR<60 ml/min/1.73 m2 ) |
|---|---|---|
| Total patients | 98 (74%) | 34 (26%) |
| Age (in years) | | |
| 18-40 | 4 (4%) | 1 (3%) |
| 40-65 | 23 (23%) | 10 (29%) |
| >65 | 71 (72%) | 23 (68%) |
| | Sex | |
| Male | 65 (66%) | 23 (68%) |
| Female | 33 (34%) | 11 (32%) |
| BMI (kg/ m2) | | |
| <30 | 59 (60%) | 24 (71%) |
| >30 | 39 (40%) | 10 (29%) |
| | Risk Factors | |
| Hypertension | 55 (56%) | 21 (62%) |
| Smoking | 41 (42%) | 16 (47%) |
| Diabetes Mellitus | 39 (40%) | 20 (59%) |
| Cardiovascular disease | 37 (38%) | 21 (62%) |
| Alcohol | 35 (36%) | 13 (38%) |
| Dyslipidemia | 34 (35%) | 13 (38%) |
| Previous history of stroke/TIA | 18 (18%) | 11 (32%) |
| | GCS score | |
| 3-4 | 21 (21%) | 4 (12%) |
| 5-8 | 29 (30%) | 6 (18%) |
| 9-13 | 37 (38%) | 17 (50%) |
| >13 | 11 (11%) | 7 (21%) |
| | Type of stroke | |
| Ischaemic | 64 (65%) | 21 (62%) |
| Haemorrhagic | 34 (35%) | 13 (38%) |
| Mortality (within 30 days of presentation) | 16 (16%) | 11 (32%) |

We distributed patients according to Serum Creatinine concentration at time of presentation, most patients had serum creatinine in the range of 98-118 (33%) followed by 82-97 (27%). Maximum mortality was noted in >119 (41%) followed by 98-118 (33%) serum creatinine group.

**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=132) | Outcome (Mortality within 30 days) (n=27) |
|---|---|---|
| 30-81 | 21 (16%) | 2 (7%) |
| 82-97 | 36 (27%) | 5 (19%) |
| 98-118 | 44 (33%) | 9 (33%) |
| >119 | 31 (23%) | 11 (41%) |

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 (39%) followed by 5.3-6.7 (27%). Maximum mortality was noted in >9 (44%) followed by 6.8-8.9 (30%) blood urea 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=132) | Outcome (Mortality within 30 days) (n=27) |
|---|---|---|
| 1.8-5.2 | 11 (8%) | 3 (11%) |
| 5.3-6.7 | 36 (27%) | 4 (15%) |
| 6.8-8.9 | 52 (39%) | 8 (30%) |
| >9 | 33 (25%) | 12 (44%) |

We noted that age > 65 years, GCS score > 10 at the time of admission, smoking, diabetes mellitus and aspiration pneumonitis were predictors of death in stroke patients.

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

| | Alive (n=105) | Died (n=27) | p value |
|---|---|---|---|
| Age (In years) | 61.9 ± 11.2 | 67.1 ± 10.6 | < .01* |
| GCS score > 10 | 50 (48%) | 22 (81%) | < .01* |
| Hypertension | 55 (52%) | 21 (78%) | 0.21 |
| Smoking | 38 (36%) | 19 (70%) | 0.023* |
| Diabetes Mellitus | 37 (35%) | 22 (81%) | 0.038* |
| Cardiovascular disease | 42 (40%) | 16 (59%) | 0.072 |
| Type of stroke | | | |
| Ischaemic | 67 (64%) | 18 (67%) | 0.19 |
| Haemorrhagic | 38 (36%) | 9 (33%) | 0.1 |
| Aspiration pneumonitis | 25 (24%) | 21 (78%) | < .01* |

(*- p value < 0.05 considered statistically significant)

## DISCUSSION

Various risk factors for stroke include non-modifiable factors, such as male gender, age, non-Caucasian ethnicity, prior stroke, transient ischemic attack, heart attack and positive family history. Modifiable risk factors include high blood pressure, smoking, diet, obesity, sedimentary lifestyle and atrial fibrillation.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.[8]Katarzyna Snarskaa *et al..*,[9] noted that 18,6% of patients with ischemic stroke and 9,4% 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.[10] 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 hyper-perfusion and microvascular injury in the setting of impaired autoregulation.[11]Analysis of Heart Outcomes Prevention Evaluation Study (HOPE) has shown that mild degrees of renal dysfunction were associated with increased risk of incident ischemic stroke or TIA.[12] Ischemic stroke is frequently associated with renal dysfunction and nearly a third of patients hospitalized with intracerebral haemorrhage (ICH) have chronic kidney disease.[13] This explains relation of low eGFR and stroke. Multivariate analysis in a study, noted that independent predictors of mortality in patients with ischemic stroke were: ischemic heart disease or myocardial infarction in the past, diabetes, glucose at admission, and eGFR on admission, while in patients with haemorrhagic stroke were: age and glucose at admission.[9] In present study we noted that eGFR<60, age > 65 years, GCS score > 10 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 m2, was associated with increased mortality and adverse outcomes compared with patients with normal renal function.[14] 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.[15] 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 m2 had a risk of future stroke that was 43% greater than those with a normal baseline eGFR.[16]There is an ∼7% increased relative risk of stroke for every 10 mL/min per 1.73 m2 decrease in glomerular filtration rate, and the finding is consistent across major stroke subtypes.[17] A retrospective cohort including more than 500,000 participants identified a stepwise association between eGFR and ICH, where the risk of hemorrhage decreased by 9% (95% CI 8–11%) for each 10 mL/min/1.73 m2 increase in eGFR, including after adjustment for medical comorbidities, albuminuria, antiplatelet therapy, and use of anticoagulants.[18]The heightened risk of stroke in patients with low eGFR represents the interplay of the vascular co-morbidities that occur with renal impairment.[19] Early detection of deranged renal function could stimulate its treatment geared toward reducing the deterioration of renal function and preventing future risk of cardiovascular and cerebrovascular complications.[20] In patients with high risk factors for stroke, regular evaluation of renal function could reduce risk of stroke as well as complication and mortality after stroke. The specific causes for the adverse outcome and whether a

more aggressive therapeutic approach can improve the prognosis of these patients should be assessed by future studies.

## 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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