

A Study to Investigate the Renal Function in Patients with Acute Stroke and its Relationship with in-Hospital Mortality

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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 in the Department of Medicine, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for the period of 1 year. 200 patients were considered for present study.

Results: 80% were from group A while 20% 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. 104 (65%) patients had ischemic stroke, while 48 (30%) had hemorrhagic stroke. We noted mortality within 30 days in 24 (15%) 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 (30%). Maximum mortality was noted in >119 (40%) followed by 98-118 (35%) 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 (25%). Maximum mortality was noted in >9 (45%) followed by 6.8-8.9 (30%) blood urea group.

We noted that age > 65 years, GCS score > 10 at the time of admission, smoking, diabetes mellitus and aspiration pneumonia 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

Chronic kidney disease stage 2 or higher is a major risk factor for cardiovascular diseases including stroke as shown on more than 15,000 participants in Atherosclerosis Risk in Communities (ARIC) study. [1] The Cardiovascular Health Study (CHS) has reported that patients aged 65 years or older with

elevated serum creatinine were associated with higher annual mortality (7.7% vs 2.9%) and higher mortality from cardiovascular disease (3.6% vs 1.3%) compared to patients with normal serum creatinine. [2] Analysis of Heart Outcomes Prevention Evaluation Study (HOPE) has shown

that mild degrees of renal dysfunction was associated with increased risk of incident ischemic stroke or TIA. [3] In addition, an independent association was observed between a reduced estimated glomerular filtration rate-eGFR and the risk of death and cardiovascular events. [4] However, in the recent study on Chinese population, proteinuria increased the risk of stroke, while eGFR was not associated with incident stroke after adjustment for established cardiovascular risk factors. [5] In many studies, reduced GFR and/or albuminuria were independently associated with cardiovascular risk factors, prevalent cardiovascular disease and all-cause mortality compared to patients without CKD. [6,7] In pooled analyses of 4 prospective community-based cohorts low eGFR was significantly associated with increased risk of ischaemic, but not haemorrhagic, stroke risk, while high albumin/creatinine ratio was associated with both stroke types. [8]

AKI is a common co-morbid condition in the community with different medical events which include cardiovascular disease, diabetes mellitus, hypertension and cerebrovascular stroke and hospitalisation in intensive care unit. In the immediate period following a stroke, acute kidney injury (AKI) may develop as a possible complication. AKI and its presence can be explained by the particular characteristics of the stroke-prone population: Elderly individuals (typically over 60 years), associated multiple cardiovascular co morbidities frequently treated with multiple drug associations, and usually underlying impaired renal function. [9] 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. [10,11]

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 in the Department of Medicine, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for the period of 1 year. 200 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 : $eGFR \text{ (in ml/min per } 1.73m^2) = 186.3 \times P \text{ cr (e} [-1.154] \text{) } \times \text{Age (e} [-0.203] \text{) } \times (0.742 \text{ if female) } \times (1.21 \text{ if black)}$.

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

Table 1: General characteristics

| Characteristics | Group A (eGFR>60 ml/min/1.73 m ²) | Group B (eGFR<60 ml/min/1.73 m ²) |
|--------------------------------------------|------------------------------------------------|------------------------------------------------|
| Total patients | 160 (80%) | 40 (20%) |
| Age (in years) | | |
| 18-40 | 8 (5%) | 2 (5%) |
| 40-65 | 40 (25%) | 12 (30%) |
| >65 | 112 (70%) | 26 (65%) |
| | Sex | |
| Male | 104 (65%) | 26 (65%) |
| Female | 56 (35%) | 14 (35%) |
| BMI (kg/ m ²) | | |
| <30 | 100 (62.5%) | 28 (70%) |
| >30 | 60 (37.5%) | 12 (30%) |
| | Risk Factors | |
| Hypertension | 88 (55%) | 26 (65%) |
| Smoking | 70 (43.75%) | 18 (45%) |
| Diabetes Mellitus | 64 (40%) | 24 (60%) |
| Cardiovascular disease | 56 (35%) | 26 (65%) |
| Alcohol | 58 (36.25%) | 16 (40%) |
| Dyslipidemia | 52 (32.5%) | 16 (40%) |
| Previous history of stroke/TIA | 28 (17.5%) | 14 (35%) |
| | GCS score | |
| 3-4 | 32 (20%) | 4 (10%) |
| 5-8 | 52 (32.5%) | 6 (15%) |
| 9-13 | 56 (35%) | 18 (45%) |
| >13 | 20 (12.5%) | 12 (30%) |
| | Type of stroke | |
| Ischaemic | 104 (65%) | 24 (60%) |
| Haemorrhagic | 48 (30%) | 16 (40%) |
| Mortality (within 30 days of presentation) | 24 (15%) | 14 (35%) |

80% were from group A while 20% 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. 104 (65%) patients had ischemic stroke, while 48 (30%) had hemorrhagic stroke. We noted mortality within 30 days in 24 (15%) patients.

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

| Serum Creatinine (umol/L) | No. of patients (n=200) | Outcome (Mortality within 30 days) (n=40) |
|---------------------------------|-------------------------|-------------------------------------------|
| 30-81 | 32 (16%) | 2 (5%) |
| 82-97 | 60 (30%) | 8 (20%) |
| 98-118 | 64 (32%) | 14 (35%) |
| >119 | 44 (22%) | 16 (40%) |
| Blood Urea concentration | | |
| 1.8-5.2 | 20 (10%) | 4 (10%) |
| 5.3-6.7 | 50 (25%) | 6 (15%) |
| 6.8-8.9 | 80 (40%) | 12 (30%) |
| >9 | 50 (25%) | 18 (45%) |

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 (30%). Maximum mortality was noted in >119 (40%) followed by 98-118 (35%) 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 (25%). Maximum mortality was noted in >9 (45%) followed by 6.8-8.9 (30%) blood urea group.

Table 3: Predictors of death among stroke patients

| | Alive | Dead | P Value |
|------------------------|-------------|-------------|---------|
| Age (In years) | 62.8 ± 12.3 | 65.5 ± 10.8 | < .01 |
| GCS score > 10 | 78 (48.75%) | 32 (80%) | < .01 |
| Hypertension | 82 (52.5%) | 30 (75%) | 0.23 |
| Smoking | 58 (36.25%) | 28 (70%) | 0.024 |
| Diabetes Mellitus | 54 (33.75%) | 32 (80%) | 0.036 |
| Cardiovascular disease | 64 (40%) | 24 (60%) | 0.075 |
| Type of stroke | | | |
| Ischaemic | 104 (65%) | 28 (70%) | 0.18 |
| Haemorrhagic | 58 (36.25%) | 12 (30%) | 0.1 |
| Aspiration pneumonitis | 40 (25%) | 30 (75%) | < .01 |

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.

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. [12] 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. [13,14] In prospective studies, advanced age, hypertension, diabetes mellitus, smoking and atrial fibrillation have been found as risk factors for stroke and the relevant mortality. [15] 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. [16]

There is growing evidence in medical literature of the kidney's role in the development of cardiovascular disease, including stroke. Although the majority of stroke patients had mild AKI that in most cases were "clinically" reversible, it should be emphasized that in the tissue level, this does not always hold true. Endothelial damage, tubular inflammation, and activation of intrarenal fibrotic pathways during kidney repair may gradually damage kidney structure, leading to proteinuria, hypertension, and progressive decline in renal function. Renal dysfunction may indicate a higher comorbidity burden, especially in atherosclerotic risk factors and diseases. It seems that the degree of renal dysfunction present in stroke patients may simply be a marker of end organ damage from long standing arterial stiffness of small and large arteries due to atherosclerosis and its associated vascular risk factors. Hemorrhagic transformation may result

from breakthrough hyper-perfusion and microvascular injury in the setting of impaired autoregulation. [17] 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. [18] Ischemic stroke is frequently associated with renal dysfunction and nearly a third of patients hospitalized with intracerebral haemorrhage (ICH) have chronic kidney disease. [19]

80% were from group A while 20% 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. 104 (65%) patients had ischemic stroke, while 48 (30%) had hemorrhagic stroke. We noted mortality within 30 days in 24 (15%) 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 (30%). Maximum mortality was noted in >119 (40%) followed by 98-118 (35%) serum creatinine group. 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. [20] Maximum mortality was noted in >9 (45%) followed by 6.8-8.9 (30%) blood urea 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 (25%). Maximum mortality was noted in >9 (45%) followed by 6.8-8.9 (30%) blood urea group. 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. 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. [21] The heightened risk of stroke in patients with low eGFR represents the interplay of the vascular co-morbidities that occur with renal impairment. [22] 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. [23] 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.

Conclusion

The mortality rate of individuals hospitalised with acute stroke is higher in those with poor kidney function, regardless of their age, sex, and other comorbidities. Renal insufficiency, which is rarely recognised, is often seen in patients with acute stroke. This condition is characterised by a low estimated glomerular filtration rate (eGFR) and is linked to increased mortality and negative short-term outcomes.

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