

# Acute Kidney Injury in Acute Stroke in Relation to Immediate Outcome- A Hospital Based Study

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## ABSTRACT

### BACKGROUND

Acute stroke is the second leading cause of death. The association of renal function and stroke is poorly understood. The present study is focused at assessing renal functional status in acute stroke and its prognostic significance on final outcome.

### METHODS

Patients presenting with acute stroke numbering 200 were included for study duration of 1 year. Serum creatinine and 24-hour urine output were monitored after admission, at 24 and 48 hours and were evaluated during the in hospital stay. AKI has been defined according to KDIGO criteria.

### RESULTS

The mean age of study population was 60±8.5 years. The overall incidence of AKI in stroke was 17% and commoner in subjects with haemorrhagic stroke. Patients with AKI had longer hospital stay and were associated with higher risk of mortality as compared to those who did not develop AKI.

### CONCLUSIONS

Incidence of AKI complicating acute stroke is associated with increased mortality and adverse outcome. This highlights the need for early diagnosis, better risk stratification and preparedness for need for long-term care in this vulnerable population.

### KEYWORDS

Acute Stroke, Incidence, AKI, Haemorrhagic, Risk Stratification

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**BACKGROUND**

Acute stroke of whatever aetiology or pathology is ultimately a devastating condition and contributes to disability and poor quality of life.<sup>1</sup> Stroke is defined as an abrupt onset of a neurological deficit that is attributable to a focal vascular cause. Stroke is the second leading cause of mortality.<sup>2</sup> The prognosis and outcome of acute stroke are determined not only by the neurological deficits and age of the patient but also by the associated medical comorbidities such as cardiovascular disease, hypertension, diabetes, dyslipidaemia and renal dysfunction.<sup>3,4,5</sup>

Acute kidney injury (AKI) is relatively underdiagnosed and under cared feature which is however a common comorbid condition in the community and may be associated with cardiovascular disease, diabetes mellitus, hypertension and various cerebrovascular events. It complicates 5-7% of acute care hospitalization and around 30% of those in intensive care unit.<sup>6</sup> AKI is characterized by abrupt deterioration in renal function and has a deleterious prognosis in the final outcome of various medical conditions notably acute stroke. Henceforth, it shall not be improper to state that AKI is one of the important determinants defining the outcome in an acute cerebrovascular event.

Although, AKI is common and imposes a heavy burden of illness, it is amenable to prevention thus warrants prompt detection and effective management. In 2012, AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) (KDIGO AKI Work Group 2012) as any of the followings: increase in SCr by  $\geq 0.3$  mg/dl within 48 h; or increase in SCr to  $\geq 1.5$  times baseline, which is known or presumed to have occurred within the prior 7 days; or decrease in urine volume to  $< 0.5$  ml/kg/h for 6 h.<sup>7</sup>

We wanted to study the incidence of AKI in acute stroke in relation to immediate outcome.

**METHODS**

This was a hospital based prospective case control study which included 200 patients presenting with acute stroke conducted from 1<sup>st</sup> January 2018 to 31<sup>st</sup> May 2019. Patients admitted in the Department of Medicine, Silchar Medical College and Hospital (SMCH), Silchar with diagnosis of acute stroke were randomly selected and included in the study. Inclusion criteria for patients were: 1) patients with ischemic or haemorrhagic strokes, and 2) patients admitted to the hospital within 48 hours of the onset of stroke.

Serum creatinine and 24-hour urine output were meticulously monitored and repeated after 24 and 48 hours. Patients who developed AKI as defined by KDIGO criteria were documented and compared with age and sex matched controls (stroke patients with normal renal function) for 7 days for in-hospital morbidity and mortality. Informed consent to participate in the study were obtained from the patients or their relatives. Exclusion criteria for the study were: H/o glomerulonephritis, urinary tract obstruction, pre-existing chronic renal failure; exposure to radiocontrast

agents, nephrotoxic medications, drug overdose, etc. Statistical analysis and all the statistical graphs were been prepared using Microsoft Excel 2016 and SPSS version 21.0. p value  $< 0.05$  was considered statistically significant.

**Demographic and Clinical Characteristics**

Baseline medical and neurological assessments were done in all patients. Demographic data included: age, sex, and history of vascular risk factors, relevant drug history etc. Laboratory investigations and imaging studies were done as needed. A non-contrast CT brain scan examination was done in all patients to diagnose stroke while MRI-brain was done in selected patients.

**Laboratory Measurements**

Laboratory measurements included: serum creatinine (SCR), electrolytes, complete blood count and differential leucocyte count, blood sugar, liver function test, fasting lipid profile, and routine examination of urine. CrCl (ml/min) was calculated using the Cockcroft and Gault (1976) formula:  $CrCl = (140 - age) \times weight (kg) / (serum creatinine \times 72 (\times 0.85 \text{ for women}))$ . The test results were compared with the reference values of central composite laboratory, SMCH.

**RESULTS**

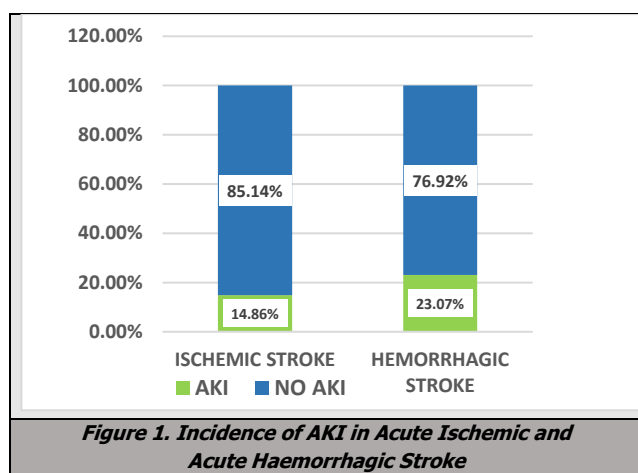
This study included 200 patients with acute stroke (male = 136; female = 64), with mean age  $60 \pm 8.5$  years. The majority of patients had acute ischemic stroke (148/200). Among 148 patients with acute ischemic stroke, 106 (71.62%) were male and 42 (28.38%) were female whereas out of 52 patients with acute hemorrhagic stroke, 30 (57.69%) were male and 22 (42.31%) were female. Most of the study population (38%) were aged 60-69 years. Total number of subjects in age group  $\geq 70$  years, 50-59 years, 40-49 years and  $< 40$  years are 62, 40, 16 and 6 respectively (Table 1).

Incidence of Stroke	Ischemic Stroke	Haemorrhagic Stroke
	148 (74%)	52 (26%)
<b>Sex Distribution</b>		
Gender	Ischemic Stroke	Haemorrhagic Stroke
Male	106 (71.62%)	30 (57.69%)
Female	42 (28.38%)	22 (42.31%)
<b>Age Distribution</b>		
Age in Years	Ischemic Stroke	Haemorrhagic Stroke
< 40	4 (2.70%)	2 (3.85%)
40- 49	8 (5.41%)	8 (15.38%)
50- 59	26 (17.57%)	14 (26.92%)
60- 69	66 (44.59%)	10 (19.23%)
$\geq 70$	44 (29.73%)	18 (34.62%)

**Table 1. Demographic Characteristics of Study Subjects**

According to KDIGO criteria, AKI complicated 14.86% (22/148) of acute ischemic stroke and 23.07% (12/52) of acute haemorrhagic stroke (Figure 1). Out of 148 patients with acute ischemic stroke, 17.57% had embolic stroke and 67.57% and 14.86% had small vessel and large vessel stroke respectively. The incidence of AKI among subjects with embolic stroke, small vessel and large vessel stroke accounted for 17.57%, 67.57% and 14.86% respectively. Out of 52 patients with acute haemorrhagic stroke, 42.31% had intracerebral haemorrhage (ICH), 50% had

subarachnoid haemorrhage (SAH) and 7.69% had both ICH and SAH. Incidence of AKI in patients with ICH and SAH was 36.36% and 15.38% respectively (Table 2). In comparison to subjects with acute haemorrhagic stroke, the prevalence of atrial fibrillation (AF), hypertension (HTN), diabetes mellitus (DM), dyslipidaemia, smoking history and coronary artery disease (CAD) were higher in subjects with acute ischemic stroke. Among patients with acute ischemic stroke, the prevalence of AF, HF, HTN, CAD, dyslipidaemia, history of smoking, DM and TIA are 25%, 12.50%, 75%, 37.50%, 37.50%, 25% and 37.50% respectively in subjects with AKI and 16%, 2%, 68%, 22%, 40%, 30%, 26% and 6% respectively in subjects without AKI. Among patients with acute haemorrhagic stroke, the prevalence of AF, HF, HTN, CAD, dyslipidaemia, history of smoking, DM and TIA are 22.22%, 11.11%, 66.67%, 22.22%, 22.22%, 22.22%, 33.33% respectively among subjects with AKI and 15.15%, 6.06%, 63.63%, 15.15%, 21.21%, 18.18%, 18.18% and 6.06% respectively in subjects without AKI (Figure 2 and 3).



Ischemic Stroke (148)		
Stroke Subtypes	Incidence	Incidence of AKI (22)
Embolic	26 (17.57%)	14 (53.85%)
Small vessel	100 (67.57%)	2 (2%)
Large vessel	22 (14.86%)	6 (27.27%)
Haemorrhagic Stroke (52)		
STROKE SUBTYPES	INCIDENCE	INCIDENCE OF AKI
ICH	22 (42.31%)	8 (36.36%)
SAH	26 (50%)	4 (15.38%)
ICH + SAH	4 (7.69%)	

Table 2. Stroke Subtypes and Incidence of AKI

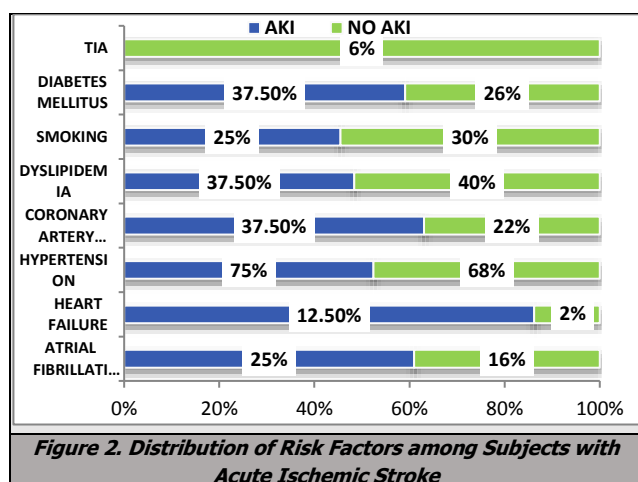


Figure 2. Distribution of Risk Factors among Subjects with Acute Ischemic Stroke

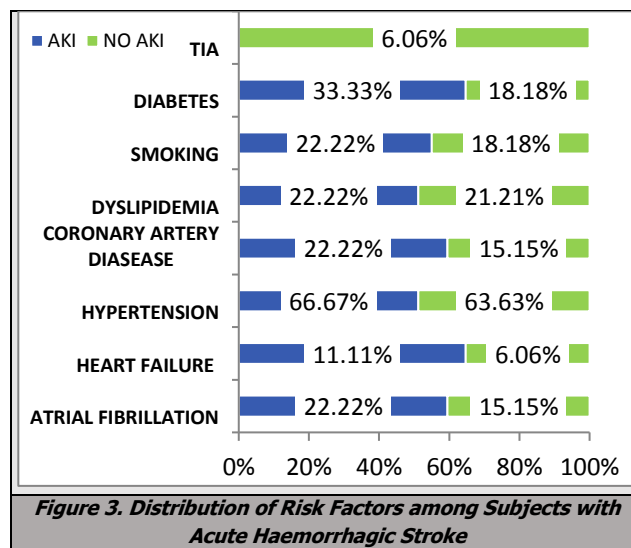


Figure 3. Distribution of Risk Factors among Subjects with Acute Haemorrhagic Stroke

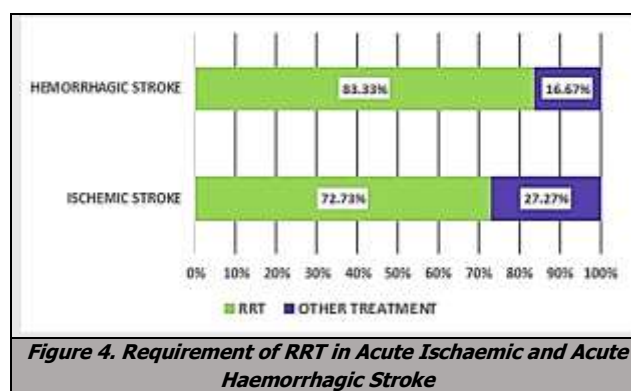


Figure 4. Requirement of RRT in Acute Ischaemic and Acute Haemorrhagic Stroke

	Survivors with AKI	Survivors without AKI	p value
Mean duration of Hospital stay (in days)	8	2.9	0.0001

Table 3. Comparison of Mean Duration of Hospital Stay among Survivors

Mortality among Subjects with AKI and with Normal Renal Function			
	Patients Expired	Patients Survived	p value
Patients with AKI	22 (64.71%)	12 (35.29%)	0.000006
Patients without AKI	20 (12.05%)	146 (87.95%)	
Mortality among Subjects with AKI in Ischemic and Haemorrhagic Stroke			
	Patients Expired	Patients Survived	p value
Ischaemic stroke with AKI, n= 22	12 (54.55%)	10 (45.45%)	0.192530
Haemorrhagic stroke with AKI, n= 12	10 (83.33%)	2 (16.67%)	

Table 4. Comparison of Mortality

Out of 22 patients with AKI in acute ischemic stroke subjects, 16 patients required RRT in the form of hemodialysis (HD) whereas among subjects with acute haemorrhagic stroke, RRT was needed for 10 subjects. Although the need for RRT was higher in subjects with acute haemorrhagic stroke the result was insignificant at p value 0.784. The mean duration of hospital stay among the survivors with AKI was 8 day and was significantly more in comparison to patients with normal renal function (Figure 4 and Table 3). In this series, overall mortality was higher in patients with acute haemorrhagic stroke, 22/52 (42.31%), as compared to acute ischemic stroke, 20/148 (13.51%). Mortality was also higher in patients who developed AKI as compared to those with normal renal function. Among acute ischemic stroke patients who developed AKI, 54.55% of the

patients expired and among patients with acute haemorrhagic stroke, AKI contributed to 83.33% of mortality (Table 4).

## DISCUSSION

This study included 200 patients with acute stroke (male = 136; female = 64). A total of 76% of study subjects had acute ischemic stroke (106 (71.62%) male and 42 (28.38%) female) and 26% had acute haemorrhagic stroke (30 (57.69%) male and 22 (42.31%) female). Mean age of the study population was  $60 \pm 8.5$  years. These results were comparable to the study done by Fahmi Yousef Khan ET al<sup>8</sup> who evaluated 270 patients with acute stroke with 198 (73%) male and 72 (27%) female. A total of 217 (80.4%) patients had acute ischemic stroke (male 157 and female 60) whereas 88.7% (47 patients) had intracerebral haemorrhage (35 males and 12 females), and subarachnoid haemorrhage occurred in 11.3% (6 patients; 5 males and 1 female). The mean age was  $57.1 \pm 13.3$  years. However, the observed incidence of stroke in the present study varied as compared to study by Maitreyee Bandyopadhyay et al<sup>9</sup> who observed the incidence of acute ischemic stroke, ICH and SAH to be 53%, 45% and 2% respectively.

In the present study, total number of subjects in age group,  $\geq 70$  years, 60-69 years, 50-59 years, 40-49 years and  $< 40$  years were 31%, 38%, 20%, 8% and 3% respectively. However, Mahdi Habibi- Koolae et al<sup>10</sup> observed that most of the study subjects were aged more than 70 years and comprised of 43% of the study population. Population aged  $< 40$  years, 40-49 years, 50-59 years and 60-69 years comprised of 3.2%, 8.8%, 19.7% and 25.3% respectively. The incidence of AKI in acute stroke patients was 17% in the present study and it was low as compared to study by George Tsagalis et al<sup>11</sup> where 26.7% of acute stroke patients developed AKI. In the present series, AKI was more common among subjects with acute haemorrhagic stroke (14.86% for acute ischemic stroke and 23.07% for acute haemorrhagic stroke). Similarly, Minesh Khatri et al<sup>12</sup> also observed the incidence of AKI in acute ischemic stroke and acute haemorrhagic stroke to be 14% and 21% respectively. In the present series, incidence of AKI among subjects with embolic stroke, small vessel and large vessel stroke were 17.57%, 67.57% and 14.86% respectively whereas in subjects with ICH and SAH it was 36.36% and 15.38% respectively. Min Young Kim et al<sup>13</sup> have found the incidence of AKI in intracerebral haemorrhage, subarachnoid haemorrhage, ICH + SAH and SDH/EDH to be 37.5%, 25%, 12.5% and 37.5% respectively and was comparable to the observations made in the present series.

In the present series, among patients with acute ischemic stroke, the prevalence of AF, HF, HTN, CAD, dyslipidaemia, history of smoking, DM and TIA were 25%, 12.50%, 75%, 37.50%, 37.50%, 25% and 37.50% respectively in subjects with AKI and 16%, 2%, 68%, 22%, 40%, 30%, 26% and 6% respectively in subjects without AKI. Among patients with acute haemorrhagic stroke, the

prevalence of AF, HF, HTN, CAD, dyslipidaemia, history of smoking, DM and TIA were 22.22%, 11.11%, 66.67%, 22.22%, 22.22%, 22.22%, 33.33% respectively among subjects with AKI and 15.15%, 6.06%, 63.63%, 15.15%, 21.21%, 18.18%, 18.18% and 6.06% respectively in subjects without AKI.

Minesh katri et al<sup>12</sup> in their study found that among patients with ischemic stroke, the prevalence of AF, HF, HTN, CAD, hyperlipidaemia, DM, previous TIA and previous stroke were 25%, 7%, 72%, 31%, 31%, 28%, 7% and 32% respectively among subjects those who developed AKI and 17%, 2%, 68%, 22%, 39%, 27%, 7% and 32% respectively among those who didn't develop AKI. Also, among patients with haemorrhagic stroke, the prevalence of AF, HF, HTN, CAD, hyperlipidaemia, DM, previous TIA and previous stroke were 16%, 1%, 64%, 16%, 19%, 25%, 4% and 12% respectively among subjects those who developed AKI and 16%, 2%, 64%, 16%, 21%, 18%, 6% and 19% respectively among those who didn't develop AKI. In the present study the requirement of HD was more among subjects with AKI in acute haemorrhagic stroke as compared to that of acute ischemic stroke group though the result was not statistically significant ( $p > 0.05$ ). The mean duration of hospital stay among the survivors with AKI was 8 day and significantly more in comparison to patients with normal renal function.

In this study, overall mortality was higher in patients with acute haemorrhagic stroke, 22/52 (42.31%), as compared to acute ischemic stroke, 20/148 (13.51%). Mortality was also higher in patients who developed AKI as compared to those who did not develop AKI. Among acute ischemic stroke patients who developed AKI, 54.55% of the patients expired. Also, among patients with acute haemorrhagic stroke, AKI contributed to 83.33% of mortality. In a study done by Florica Gadalean ET al<sup>14</sup> on 45 patients with stroke with median follow up of 12 days, 50% of patients who developed AKI expired and among subjects who did not develop AKI only 3.44% expired.

## CONCLUSIONS

AKI is not only a common and important complication of stroke contributing to longer hospital stay but the most important determinant of the final outcome with regard mortality and morbidity in acute stroke. Management of blood pressure and diabetes mellitus, and avoidance of potential nephrotoxic insults could potentially prevent the development of AKI. Maintenance of adequate hydration, monitoring of urine output and avoiding over zealous use of mannitol are also important to prevent the development of AKI. The use of angiotensin-converting enzyme inhibitors in high cardiovascular-risk patients to lower blood pressure is important in secondary prevention.

### Limitations

In the present study renal function was only assessed during hospitalization and patients were not followed up in the long term.

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