



Original Research Article

Assessment and Prognostic significance of renal dysfunction in acute stroke patients

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ABSTRACT

Context: During hospitalization due to stroke, patients can have acute kidney injury (AKI) as a possible complication which is frequently overlooked and underestimated in clinical trials.

Aims: To assess the prevalence of renal dysfunction in acute stroke patients and to assess its prognostic significance

Design, Methods and Materials: A total of 100 patients were recruited for this study with diagnosis of stroke. Renal dysfunction was evaluated in the form of Acute kidney injury and unrecognized renal dysfunction (Baseline Normal serum Creatinine < 1.2 mg/dl with EGFR < 60 ml/min on admission). The primary functional outcome was measured using the modified Rankin Scale at the time of discharge, 1 month after stroke onset.

Statistical analysis: Analysis of data was done using SPSS-17. Independent t-test and chi-square test were used to calculate difference between two groups

Results: Our study shows prevalence of acute kidney injury in patients of stroke is 15%. Moreover, the study showed that AKI after stroke was associated with higher in-hospital mortality and poorer functional outcome at 1 month.

Conclusions: Acute kidney injury appears to be a common complication after stroke and is related to increased mortality and disability in stroke.

Key Messages: AKI is common complication after stroke and frequent cause of poor functional outcome.

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1. Introduction

Stroke is the second leading cause of death worldwide.¹ Stroke is classically defined as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin”.² Transient ischemic attacks are episodes of temporary and focal dysfunction of vascular origin, which are variable in duration, commonly lasting from 2 to 15 minutes, but occasionally lasting as long as a day (24 hours) with no persistent neurological deficit.³ The incidence of stroke ranged from 105 to 152/100,000 persons per year and the crude prevalence of stroke ranged from 44.29 to

559/100,000 persons in different parts of India during the past decade.⁴

Stroke is a major cause of long-term disability among patients and has enormous emotional and socio-economic consequences.⁵ The increasing economic burden that patients with stroke impose, as well as the significant loss of manpower, renders the study of prognostic factors that can affect short- and long-term mortality after stroke indispensable. Renal dysfunction is commonly seen in hospitalized stroke patients. Ischemic stroke is frequently associated with renal dysfunction and nearly a third of patients hospitalized with intracerebral haemorrhage (ICH) have chronic kidney disease (CKD) (estimated glomerular filtration rate [e-GFR] < 60 ml/minute per 1.73 m²).^{6,7} Occurrence of acute renal failure (ARF) is more common

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in patients with intracerebral haemorrhage (ICH) compared with those with other stroke subtypes.⁸

Impaired renal function is a significant predictor of both short and long term mortality in these patients.⁹ Patients with stroke are often at increased risk of dehydration as they have a reduced level of consciousness, are physically dependent, unable to communicate, have difficulties in swallowing and decreased oral intake.¹⁰

Elderly patients presenting with transient ischaemic attack or acute ischaemic stroke often demonstrate increased plasma osmolality that likely represents a fluid depleted state, and possibly contributes to cerebral ischaemia and worse neurological outcome in stroke patients.¹¹ The role of volume depletion or dehydration as a risk factor contributing to early neurological deterioration has been demonstrated. blood urea nitrogen/creatinine (BUN/Cr) ratio higher than 15 and urine specific gravity (USG) > 1.010 were more frequently seen in SIE (Stroke in Evolution) patients.^{12,13} Early identification of dehydration is essential for timely intervention to improve outcome. Unfortunately, the clinical assessment of dehydration by physicians is not always accurate especially in geriatric patients.

Hence, biochemical parameters like plasma osmolality, BUN/creatinine ratio and urine specific gravity have been used by various investigators for assessment of hydration status, but the results have been inconsistent.¹⁰ Additionally, severity of the renal impairment and the requirement of renal replacement therapy for stroke patients in the course of their treatment are important management issues not currently well addressed by the literature.

Hence proper and routine evaluation of renal function in hospitalized patients with cerebrovascular accident needs to be ensured to improve the outcome of these patients

The present study is aimed to assess the prevalence of renal dysfunction in acute stroke patients and to assess its prognostic significance.

2. Subjects and Methods

2.1. Aims & Objectives

1. To study the prevalence of renal dysfunction in patients with acute stroke, both AIS and ICH.
2. To evaluate the effect of renal dysfunction on stroke morbidity and mortality, both AIS and ICH.

3. Materials and Methods

This study will be conducted in department of Neurology, GMC, Kota in the period for period of one year after getting clearance from ethical committee. Subjects will be included from adult subjects admitted in stroke unit, emergency. All patients will be included after written informed consent.

3.1. Study population

A total of 100 patients were recruited for this study with clinical features and imaging findings consistent with acute ischemic or hemorrhagic stroke.

On admission, patients were assessed by physical examination, neurological examination and scoring with the GCS and NIHSS scores. The severity of stroke was graded as mild (NIHSS ≤ 8), moderate (NIHSS 9–15) or severe (NIHSS ≥ 16). The severity of impaired level of consciousness if present was rated as mild (GCS 15), moderate (GCS 8–14), or severe (GCS ≤ 7). Immediately after assessment, patient was sent for imaging studies (CT/MRI Brain), ECG and routine blood investigations including Blood urea and Serum Creatinine, Blood urea nitrogen, Urine specific gravity.

Renal dysfunction was evaluated in the form of Acute kidney injury and unrecognized renal dysfunction. AKI was diagnosed by either an increase in serum creatinine by > 0.3 mg/dl (26.5 μ mol/l) within 48 hours; or increase in serum creatinine to >1.5 time's baseline, which was known to have occurred within the prior 7 days.¹⁴ Serum creatinine level at admission was taken as baseline serum creatinine. Assessment of blood urea, serum creatinine, blood urea nitrogen, was done on alternate day. Unrecognized renal dysfunction will be defined as Baseline Normal serum Creatinine < 1.2 mg/dl with EGFR < 60 ml/min.¹⁵

The primary functional outcome was measured using the modified Rankin Scale at the time of discharge, 1 month after stroke onset. An unfavorable functional outcome was defined as mRS of 3–6 points. Patients will be followed-up for a period of 1 months after stroke onset to confirm whether recurrent ischemic stroke had occurred or not.

3.2. Statistical analysis

Analysis of data was done using SPSS-17. For the categorical (qualitative) variables, frequency and percentage were calculated. Mean and standard deviation (SD) were calculated for numerical (quantitative) variables. $p < 0.05$ was taken as significant. Independent t-test and chi-square test were used to calculate difference between two groups.

3.3. Inclusion criteria

1. Patients 18 yrs. or older
2. Diagnosed with acute ischemic or haemorrhagic stroke based on the history, physical examination, computed tomography (CT) scan / diffusion-weighted magnetic resonance imaging scan
3. Patient with unrecognized renal dysfunction (Baseline Normal serum Creatinine < 1.2 mg/dl with EGFR < 60 ml/min on admission)
4. Willing to sign the informed consent form

3.4. Exclusion criteria

1. Those diagnosed with infection within 1 week before stroke onset or within 72 hours after admission
2. CT diagnosis of cerebral haemorrhage, subdural hematoma, intracerebral mass, or cerebrovascular damage secondary to trauma
3. Patients with pre-existing renal disorders having abnormal Blood Urea and Serum creatinine
4. Use of steroids or immunosuppressants
5. Past history of stroke

4. Results

In our study it was found that the Age profile in Stroke patients was 60.36 ± 10.7 . For Ischemic stroke it was 61.56 ± 11.3 and 58.39 ± 9.62 for Haemorrhagic stroke. Male and female ratio stood at 1.6:1 for stroke patients.

In the study it was observed that hypertension was the major risk factor in 88% for overall stroke patients. In Ischemic and haemorrhagic stroke it was 90% and 84.2% respectively. Other information regarding this is provided in the table above.

In the study it was found that the Prevalence of Unrecognised Renal dysfunction in stroke patients is 15.68%. For Ischemic stroke it was 16.12%, while for Hemorrhagic stroke it was 15.78%. (Table 1)

In the study it was found that the Prevalence of AKI in stroke patients was 15%. For Ischemic stroke it was 14.51% and for hemorrhagic stroke it was 15.78% respectively. (Table 2)

In the data observed it was found that the AKI in relation to location of bleed in Hemorrhagic stroke was highest in Putamen and Lobar at 33.33% while lowest in Brainstem and Thalamus at 16.67%. But P value for all was insignificant.

In our study it was found that mean hematoma volume in patients who had AKI was 29.16 ± 3.97 , while in patients who didn't have AKI, mean hematoma volume was 25.9 ± 8.23 . p value was non significant for the group.

Here we found that there was a non significant difference in patients who had mild and moderate NIHSS score in AKI and non-AKI patients (P-value > 0.05) at presentation. But, there was a significant difference in patients who presented with severe NIHSS score in AKI and Non-AKI patients (P-value = 0.0209). (Table 3)

In our study it was observed that the recovery in NIHSS in relation to Renal dysfunction stood at 12.06 ± 3.94 at admission and 11.30 ± 4.34 at discharge. For Non renal dysfunction 11 ± 5.56 at admission and 8.37 ± 5.53 at discharge.

In our study it was observed that the Recovery in mRS in relation to renal dysfunction stood at 3.37 ± 0.54 at admission and 3.51 ± 1.17 at 28 days and for Non renal dysfunction it stood at 3.23 ± 0.71 at admission and

2.52 ± 0.97 at 28 days. P value at admission is 0.11 which shows that the difference is non-significant. P value at 28 days is 0.0001 and shows significant difference. (Table 4)

In our study it was observed that in stroke patients there was significant difference in mortality in renal and non-renal dysfunction patients (P-value = 0.0002). Mortality in stroke patients in relation to renal dysfunction in Ischemic stroke was 18.7% while P value is 0.022. The result shows significant difference as the p value is < 0.05 and in Hemorrhagic stroke it was 27.3% with P value 0.10. The result is non-significant. 81.3% patients of renal dysfunction in ischemic group are discharged and 72.7% patients are discharged in haemorrhagic group. The p value for ischemic and haemorrhagic group is 0.6 which shows the difference is non-significant. (Table 5)

5. Discussion

Renal dysfunction is considered a valuable predictor of poor outcomes including mortality in patients with ischemic stroke.^{16,17} Very few studies have evaluated the role of renal dysfunction in short term mortality and morbidity in stroke patients.

In our study it was found that the Age profile in Stroke patients was 60.36 ± 10.7 . For Ischemic stroke it was 61.56 ± 11.3 and 58.39 ± 9.62 for Haemorrhagic stroke. Male and female ratio stood at 1.6:1 for stroke patients. Hamed et al¹⁶ included 80 patients with acute stroke (male = 44; female = 36), with mean age 62.5 ± 6.2 years. The majority of patients had ischemic stroke (72.5%) while 27.5% had hemorrhagic stroke. A similar study by Mahmoud M et al¹⁸ shows comparable results.

Our study shows that the prevalence of Unrecognised Renal dysfunction in stroke patients is 15.68%. In Ischemic stroke it was 16.12%, while in Hemorrhagic stroke it was 15.78% respectively. In a study by Pereg D et al,¹⁵ around 10.4% patients had unrecognized renal dysfunction similar to our study. Mahmood et al¹⁸ founded that 30.2% had renal dysfunction (eGFR < than 60 ml/min/1.73 m²) which was high. Presence of baseline renal dysfunction was recorded as an independent predictor of early mortality in the setting of acute ischemic stroke beside other well-known prognostic factors.

In the study it was found that the prevalence of AKI was around 14.70% in overall stroke patients. In Ischemic stroke is at 14.51% and hemorrhagic is at 15.7%. Khatri M et al¹⁹ founded that AKI was common and developed in 18% of the overall cohort, with significantly higher rates amongst Hemorrhagic stroke cases as compared to ischemic stroke (21% vs. 14%). Tasgalis G⁵ et al and Covic A²⁰ et al shown similar result with our study.

In our study it was seen that the AKI in relation to location of bleed in Hemorrhagic stroke was highest in Putamen and Lobar at 33.33% while lowest in Brainstem and Thalamus at 16.67%. P value for all was insignificant.

Table 1: Prevalance of unrecognized renal dysfunction in stroke patients

Prevalance	Stroke	Ischemic (%)	Hemorrhagic (%)
Unrecognized renal dysfunction	16(15.68%)	10(16.12%)	6(15.78%)

Table 2: Prevalance of aki in stroke patients

Prevalance	Stroke	Ischemic (%)	Hemorrhagic (%)
AKI	15(15%)	9(14.51%)	6(15.78%)

Table 3: Relation of AKI to NIHSS severity at admission (Ischemic stroke)

NIHSS	AKI		Non AKI		P Value
	No.	%	No.	%	
Mild(1-5)	0	0%	11	20.75	-
Moderate(6-16)	5	55.6%	29	54.7	0.9201
Severe(>16)	4	44.4%	13	24.6	0.0209
Total	9		53		

Table 4: Recovery in mRS in relation to Renal dysfunction

Mean + SD (Mrs)	Renal dysfunction (N=27)	Non Renal dysfunction (N=73)	P value
mRS at admission	3.37±0.54	3.23±0.71	0.1181
mRS at 28 days	3.51±1.17	2.52±0.97	0.0001

Table 5: Mortality in stroke patients in relation to renal dysfunction

Mortality	Ischemic			Hemorrhagic			P-value (I-H)	Stroke		
	Renal dysfunction	Non-Renal dysfunction	P-value	Renal dysfunction	Non-Renal dysfunction	P-value		Renal dysfunction	Non-Renal dysfunction	P-value
Death	3 (18.7%)	1(2.2%)	0.0226	3 (27.3%)	2 (7.4%)	0.1	0.6042	6 (22.2%)	3 (4.1%)	0.0002
Discharge	13 (81.3%)	45(97.8%)		8 (72.7%)	25 (92.6%)			21 (77.8%)	70 (95.9%)	
Total	16	46		11	27			27	73	

In our study it was found that mean hematoma volume in patients who had AKI was 29.16±3.97, while in patients who didn't have AKI, mean hematoma volume was 25.9±8.23. p value was non significant for the group. A study conducted by Shrestha et al⁹ found that the the location of the intracerebral bleed in the haemorrhagic stroke group did not predispose the patient to renal impairment. In the haemorrhagic stroke group, the mean volume of hematoma in the patients that developed renal impairment(29.23 ± 24.23 mL) and in the patients that did not develop renal impairment(28.61± 42.24 mL) was also not statistically significant (p=0.966). Hence, the volume of bleed did not influence the patient developing renal impairment.

We found that there was a non significant difference in patients presenting with mild and moderate NIHSS score in AKI and non-AKI patents (P-value>0.05). But, there was a significant difference in severe NIHSS score in AKI and Non-AKI patients (P-value=0.0209). Mahmud et al¹⁸ showed that the stroke severity (NIHSS) was

higher in those with impaired than those with normal renal function (13.4±1.42, 8.98±2.75 respectively. Patients with severe stroke at presentation are often at increased risk of dehydration as they have a reduced level of consciousness, are physically dependent, unable to communicate, have difficulties in swallowing and decreased oral intake which may predispose them to acute kidney injury.

In our study it was observed that the recovery in mRS in relation to renal dysfunction was 3.37±0.54 at admission and 3.51±1.17 at 28 days and for Non renal dysfunction it stood at 3.23±0.71 at admission and 2.52±0.97 at 28 days. P value at admission is 0.11 which shows that the difference is non-significant. P value at 28 days is 0.0001 and shows significant difference. In a study by Saeed et al^{8,17} Patients of hemorrhagic stroke with ARF had higher incidence of moderate to severe disability (41.3% versus 30%; P<0.0001). In a similar study patients of ischemic stroke with ARF had higher proportion of moderate-to-severe disability (49.5% versus 44.2%; P, .0001)

In our study it was observed that there was significant difference in stroke mortality in patients with renal dysfunction (22.2%) vs Non renal dysfunction (4.1%). And p value was significant. (P-value= 0.0002). Pereg et al found that Mortality rates were highest in patients with recognized renal insufficiency, followed by patients with unrecognized renal insufficiency, and were lowest in patients with normal renal function (9.9%, 9.1%, and 4.4%, respectively, $P < .0001$). Higher mortality rate in our study may be because of small sample size. The association between reduced renal function and adverse outcomes in patients with acute stroke is not completely understood and seems to be multifactorial. 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.¹⁵

6. Limitations

Our study has few limitations. Main limitation was the absence of long term follow up at 3 months. Long term follow up would have given us better picture of post stroke disability in patients with and without renal dysfunction. Other main limitation in our study was small sample size.

7. Conclusion

The prevalence of renal dysfunction is common in stroke patients, both ischemic and hemorrhagic stroke. Our study shows patients who have acute kidney injury following stroke or those patients who have unrecognized renal dysfunction (Egfr<60ml/min with Normal Serum creatinine) have significant mortality as well as poor functional recovery at 1 month. Furthermore, appropriate approach to deal with patients with renal dysfunction (i.e. adequate hydration, avoidance of nephrotoxic drugs, drug dose adjustment etc) should be considered as preventive and therapeutic strategies of acute stroke which can influence overall mortality and morbidity.

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No financial support was received for the work within this manuscript.

9. Conflict of Interest

The authors declare they have no conflict of interest.

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