Original Article

Incidence of Acute Kidney Injury after Stroke and Its Association with 30-day Mortality of Stroke Patients

Amber Shahzadi,[1] Saima Ambreen,[2] Aimen Malik,[3] Mubariz Ahmed[4], Sidra Jahangir,[5] Basil Usman[6]

Abstract

Objective: To investigate the incidence of AKI in stroke patients and its association with 30-day mortality of stroke patients.

Method: This descriptive study was conducted in Medical Unit-I, Holy Family Hospital from June 2020 to January 2021. 130 patients with CT-confirmed stroke (both ischemic and hemorrhagic) with symptoms ranging from 1-24 hours were included in the study using consecutive (non-probability) sampling, after informed consent from the attendants. Patients with a history of recurrent stroke, renal dysfunction before stroke (urea > 52mg/dl and creatinine > 1.2mg/dl, eGFR < 90 ml/min, proteinuria, or patients on dialysis as per medical record), uncontrolled hypertension (BP ≥ 180/110 mmHg), alcohol use, intravenous drug abuse and diabetes (BSR > 200 mg/dl) were excluded from the study. Patients' baseline serum creatinine levels were recorded and were noted again after 72 hours. A > 0.3 mg/dl increase from the baseline was defined as acute kidney injury. Mortality was recorded in patients who died within 30 days of stroke.

Results: The mean age of the patients was 55.48 ± 10.85 years. 81 patients (62.3%) were male and 49 (37.7%) were female. 25 (19.2%) patients had acute kidney injury. 25 (19.2%) patients (amongst both with and without acute kidney injury) died within 30 days. There was a significant association between acute kidney injury and 30-day mortality of the stroke patients (p-value<0.001). This association was significant in all age groups, both genders, regardless of present or absent history of smoking and regardless of duration of symptoms prior to arrival (p value <0.001).

Conclusion: Acute kidney injury affects a proportion of patients of stroke. There is a significant association between AKI and 30-day mortality after stroke, suggesting there might be a link between them.

Keywords: stroke, mortality, acute kidney injury.

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Introduction

Globally, stroke is the second most common cause of death. It is also a major cause of neurological disability with great human and economic costs.[1] Epidemiological studies show that the incidence of stroke varies greatly between different populations and regions and has been on the decline in recent decades in high-income countries due to advances in prevention, early recognition and management of risk factors. Thus, currently low-and middle- income countries share the greatest burden of the disease.[2] In Pakistan, the estimated annual incidence of stroke is 250/100,000.[3]

Complications associated with stroke include post stroke depression (PSD), anxiety disorders, post-stroke fatigue, new onset dementia, falls and subsequent injuries and chronic pain among others.[4] One of the complications, which is sometimes under-recognized is Acute Kidney Injury (AKI).[5] Acute kidney injury (AKI), defined as

1-3. Department of Medicine, Holy Family Hospital, Rawalpindi.
4,5. Holy family Hospital, Rawalpindi
6. Rawalpindi Medical University.

Correspondence:
Dr. Aimen Malik, *Senior Registrar, Department of Medicine, Holy Family Hospital, Rawalpindi, Pakistan E-mail malikzone@gmail.com.*

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a measurable increase in the serum creatinine (Cr) concentration (usually relative increase of 50% or absolute increase by 44–88 μmol/L [0.5–1.0 mg/dL]).[6] Many studies have shown that AKI is a common complication after stroke.[5,7-11] Diabetes, ischemic heart disease, history of heart failure and greater age have all been associated with a higher risk of developing AKI after stroke.[9] Studies have also found association of AKI after stroke with increased mortality.[8,12]

AKI after stroke may develop due to physiological changes e.g., hormone levels, blood pressure and physical disability, and may also be due to the treatments provided to stroke patients[13]. Activation of sympathetic nervous system, HPA axis and RAAS induced by stroke may alter hormone and neurotransmitter release, which in turn may mediate kidney dysfunction.[14] In resource-limited countries like Pakistan, patients with AKI after stroke have a very poor prognosis. Knowledge about this complication and early detection can be helpful in preventing poorer outcomes and can also help in formulating preventative and management protocols. Local data in this regard is scarce; therefore we decided to conduct this study. The objective of this study is to determine the incidence of acute kidney injury after stroke and to find the association of AKI after stroke with 30-day mortality of the patients.

Materials and Methods

This descriptive study was conducted in Medical Unit-I, Holy Family Hospital from June 2020 to January 2021, after ethical approval from Institutional Research Forum of Rawalpindi Medical University (Reference number 11/MU-1/HFH/RWP). 130 Male and female patients aged 35 to 85 with stroke were chosen using consecutive (non-probability) sampling. Stroke was diagnosed based on clinical features and the diagnosis was supported by positive CT scan findings i.e., presence of hypodense area on CT scan in case of ischemic stroke and hyperdense area in case of hemorrhagic stroke. Patients who had a history of recurrent stroke (on medical record), renal dysfunction before stroke (urea>52mg/dl & creatinine >1.2mg/dl, eGFR <90ml/min, proteinuria, or patients on dialysis as per medical record), uncontrolled hypertension (BP ≥ 180/110mmHg), alcohol use, intravenous drug abuse and diabetes (BSR>200mg/dl) were excluded from the study. Informed consent was obtained from the attendants. Demographic information including name, age, gender, duration of symptoms and history smoking were noted.

Blood samples were obtained through a disposable syringe under aseptic measures and were sent to the hospital laboratory for routine tests. Serum creatinine levels which were subsequently recorded. The patients were admitted and managed. After 72 hours, blood samples were again sent to the hospital laboratory for determining new creatinine levels. An increase of >0.3 mg/dl from the baseline was considered as acute kidney injury. If the patient died within his or her hospital stay, then in-hospital mortality was recorded. Otherwise, they were discharged and followed-up on an out-patient basis for 30 days. If the patient died within 30 days, then mortality was noted. The data was analyzed using SPSS version 20. Quantitative variables like age, duration of symptoms and creatinine levels were presented as mean and standard deviation. Qualitative variables like gender, history of smoking, acute kidney injury and mortality were presented as frequency and percentage. The Chi-square test was applied to compare the mortality between patients with acute kidney injury and those without. P-value ≤ 0.05 was considered as significant. Data was stratified for age, gender, duration of symptoms and history of smoking. Post-stratification, Chi-square test was applied to compare mortality in patients with or without acute kidney injury for each stratum. P-value ≤ 0.05 was considered as significant.

Results

The mean age of the patients was 55.48 ± 10.85 years, with the minimum being 35 years and maximum being 82 years. Out of 130, 81(62.3%) of the patients were male and 49 (37.7%) were female. 37 (28.5%) had a history of smoking and 93 (71.5%) had none. The mean duration of symptoms prior to hospital arrival was 13.51 ± 5.04 hours. The minimum duration of symptoms was 1 hour, and maximum was 24 hours. The mean creatinine level at baseline was 0.55 ± 0.26 mg/dL and after 72 hours it was 0.92 ± 0.71 mg/dL. A total of 25 (19.2%) patients out of 130 had acute kidney injury. A total of 25 (19.2%) patients with stroke died within 30 days. Among them 16 were male and 9 were female. There was a significant association between acute kidney injury in stroke patients and 30-day mortality (p-value <0.001) (Table-1). This significant association was reflected in all age groups i.e., 35-50 years, 51-65 years and more than 65 years (p-values: <0.001, <0.001 and <0.001) (Table-2). In addition, the significant association between acute kidney injury after stroke and mortality was present among both males and females (p-values:

<0.001 and <0.001). In 16 males with 30-day mortality, 15 (93.75%) had acute kidney injury. In 9 females with 30-day mortality, all had acute kidney injury. Mortality could have been caused by other factors such as degree of disability, aspiration pneumonia, urinary tract infections or seizures but we did not inquire about these variables. The association between acute kidney injury and mortality was significant regardless of presence or absence of history of smoking i.e., it was significant in both groups (table 3) (p-value<0.001). A total of 64 patients presented with symptom duration of 1-12 hours and 66 patients presented with symptom duration of 13-24 hours. 7 patients had 30-day mortality in the 1-12 hours group, out of which 6 (85.7%) had acute kidney injury. In the 13-24 hours group, 18 patients had 30-day mortality, and all had acute kidney injury. In both the groups there was significant association between acute kidney injury and mortality (p value <0.001).

Table 1: *Frequency of mortality in patients with and without Acute Kidney Injury.*

Mortality	Kidney Injury		Total
	Yes	No	
Yes	24(96%)	1(1%)	**25**
No	1(4%)	104(99%)	**105**
Total	**25**	**105**	**130**
p-value		**<0.001**	

Table 2: *Frequency of mortality in patients with and without Acute Kidney Injury stratified for Age.*

		Kidney Injury		p-value
		Yes	No	
35-50	**Yes**	3(75%)	0(0%)	**<0.001**
	No	1(25%)	47(100%)	
51-65	**Yes**	11(100%)	1(2.2%)	**<0.001**
	No	0(0%)	44(97.8)	
>65	**Yes**	10(100%)	0(0%)	**<0.001**
	No	0(0%)	13(100%)	

Table 3: *Frequency of mortality in patients with and without Acute Kidney Injury stratified for History of Smoking.*

Smoking	Mortality	Kidney Injury		p-value
		Yes	No	
Yes	Yes	13(100%)	1(4.2%)	**<0.001**
	No	0(0%)	23(95.8%)	
No	Yes	11(91.7%)	0(0%)	**<0.001**
	No	1(8.3%)	81(100%)	

Discussion

Our results showed that 19.2 % of the patients had acute kidney injury after stroke and there was a significant association between acute kidney injury in stroke patients and mortality within 30 days. Compared to this, Tsagalis et al reported a 14.5% incidence of AKI that was associated with an increased 30-day mortality.[5] A meta-analysis study conducted in the USA taking into account 12 studies containing more than 5 million stroke patients, found that AKI prevalence in stroke patients was 11.6% (95% CI: 10.6-12.7%).1[5] Another meta-analysis described an overall incidence of AKI to be 12%.[16] The study also concluded that AKI after stroke was associated with higher 1-month mortality, a finding similar to ours. One of the main causes for the different reported rates might be the various different diagnostic criteria used in labelling AKI. Therefore, in our opinion, a single standard for determining AKI should be applied in evaluating the frequency of AKI following stroke.

According to Lima et al 2019, the presence of acute kidney injury is an important complication after ischemic stroke and a predictor of mortality within 30 days when severity of stroke is not considered.[7] Another study demonstrated that AKI frequently follows stroke and has association with greater hospital mortality.[8] Covic et al., found the 30-day mortality rate following AKI after stroke to be as high as 17.2%.[9] Our results that AKI is significantly associated with 30-day mortality in stroke patients support all this previous literature.

Several studies reported that older patients with AKI associated with stroke are a predictor of higher 30-day mortality.[5,17] Older people might be more likely to have a worse prognosis after a stroke. This may be due to previous disease and a higher severity of stroke compared to the young[18]. In contrast, our results showed significant association between acute kidney injury and mortality among all the age groups i.e., 35-50 years, 51-65 and above 65 years. Perhaps a larger sample size could have better elucidated this relationship.

It is important to note that our results don't address whether there is causal association between AKI and mortality even though we adjusted for a few possible risk factors, such as history of smoking and the time passed since symptoms started prior to arrival. Factors such as hemodynamic abnormalities, dehydration due to poor nutritional intake, and myocardial infarction could all cause AKI and lead to higher mortality. Evidence suggests that there is increased insulin resistance in patients with AKI, which potentially might cause hyperglycemia.[19] Hyperglycemia can worsen outcomes in both ischemic and hemorrhagic stroke.[20,21] AKI can also cause other physiologic derangements e.g., greater inflammation and oxidative stress, which might hypothetically worsen outcomes in patients suffering from stroke.[22,23] Our study had certain limitations. Firstly, we did not consider stroke severity (e.g., that categorized by NIHSS score) while determining the incidence of AKI and its effect on 30-day mortality. Secondly, we did not conduct stratification by type of stroke i.e., ischemic or hemorrhagic. In addition, there was no stratification by types of ischemic stroke. Thirdly, we did not explore the impact of period of hospital stay and in-hospital abnormalities such infections etc., on outcomes. We propose further studies on this topic, preferably with a larger sample size, so robust data relevant to our part of the world becomes available which would further shed light on incidence of AKI in stroke patients and its association with 30-day mortality. This could then be used as a basis to formulate better preventative and management protocols especially relevant to resource-limited settings.

Conclusion

Acute kidney injury is a complication that affects a proportion of patients of stroke. There is a significant association between AKI and 30-day mortality after stroke. This association is significant in all age groups after 35 and in both males and females. It is also significant regardless of a positive history of smoking and regardless of duration of stroke symptoms prior to arrival.

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Authors Contribution

AS: Conceptualization of Project
AS, SA, AM: Data Collection
AS, SA, SJ: Literature Search
AM, MA: Statistical Analysis
AS, SA, AM, SJ: Drafting, Revision
AM, MA, BU: Writing of Manuscript