e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(11); 699-703

Original Research Article

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

Rajnish Kumar[1], Siddharth Singh[2]

[1]Senior Resident, Department of Medicine, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, India

[2]Assistant Professor, Department of Emergency Medicine, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, India

Received: 10-09-2023 Revised: 15-10-2023 / Accepted: 26-11-2023
Corresponding Author: Dr. Siddharth Singh
Conflict of interest: Nil

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 at department of Medicine for the period of 2 years. 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 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.

Keywords: acute stroke, estimated glomerular filtration rate (eGFR), serum creatinine, blood urea

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 at department of Medicine, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, India for the period of 2 years. 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 (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

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/ m2)		
<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 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.

References

1. Jurkovitz CT, Abramson JL, Vaccarino LV, Weintraub WS, McClellan WM. Association of high serum creatinine and anemia increases the risk of coronary events: results from the prospective community-based atherosclerosis risk in communities (ARIC) study. Journal of the American Society of Nephrology. 2003 Nov 1;14(11):2919-25.
2. Fried LP, Kronmal RA, Newman AB, Bild DE, Mittelmark MB, Polak JF, Robbins JA, Gardin

JM, Cardiovascular Health Study Collaborative Research Group, Cardiovascular Health Study Collaborative Research Group. Risk factors for 5-year mortality in older adults: the Cardiovascular Health Study. Jama. 1998 Feb 25;279(8):585-92.
3. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitali zation. New England Journal of Medicine. 20 04 Sep 23;351(13):1296-305.
4. Koren-Morag N, Goldbourt U, Tanne D. Renal dysfunction and risk of ischemic stroke or TIA in patients with cardiovascular disease. Neurology. 2006 Jul 25;67(2):224-8.
5. Li Z, Wang A, Cai J, Gao X, Zhou Y, Luo Y, Wu S, Zhao X. Impact of proteinuria and glomerular filtration rate on risk of ischaemic and intracerebral hemorrhagic stroke: a result from the K ailuan study. European journal of neurology. 2015 Feb;22(2):355-60.
6. Shlipak MG, Fried LF, Crump C, Bleyer AJ, Manolio TA, Tracy RP, Furberg CD, Psaty BM. Cardiovascular disease risk status in elderly persons with renal insufficiency. Kidney international. 2002 Sep 1;62(3):997-10 04.
7. Yuyun MF, Khaw KT, Luben R, Welch A, Bingham S, Day NE, Wareham NJ. Microalbuminuria and stroke in a British population: the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. Journal of internal medicine. 2004 Feb;255(2):247-56.
8. Mahmoodi BK, Yatsuya H, Matsushita K, Sang Y, Gottesman RF, Astor BC, Woodward M, Longstreth Jr WT, Psaty BM, Shlipak MG, Folsom AR. Association of kidney disease measures with ischemic versus hemorrhagic strokes: pooled analyses of 4 prospective community-based cohorts. Stroke. 2014 Jul; 45 (7):1925-31.
9. Kannel WB. Left ventricular hypertrophy as a risk factor in arterial hypertension. European heart journal. 1992 Sep 1;13(suppl_D):82-8.
10. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemi-ology and Prevention. Circulation. 2003 Oct 2 8;108(17):2154-69.
11. Kobayashi M, Hirawa N, Morita S, Yatsu K, Kobayashi Y, Yamamoto Y, Saka S, Toya Y, Yasuda G, Umemura S. Silent brain infarction and rapid decline of kidney function in patients with CKD: a prospective cohort study. American journal of kidney diseases. 2010 Sep 1;56(3):468-76.
12. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al.. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380:2095.
13. Pandian JD, Sudhan P. Stroke Epidemiology and Stroke Care Services in India. Journal of Stroke. 2013;15(3):128-134.
14. Prasad K, Vibha D, Meenakshi. Cerebro-vascular disease in South Asia - Part I: A burning problem. JRSM Cardiovasc Dis. 2012 ;1:20.
15. Carter AM, Catto AJ, Mansfield MW, Bamford JM, Grant PJ. Predictive variables for mortality after acute ischemic stroke. Stroke 2007;38(6):1873-80.
16. Kobayashi M, Hirawa N, Morita S et al.. Silent brain infarction and rapid decline of kidney function in patients with CKD: a prospective cohort study. Am J Kidney Dis 2010; 56: 468-76.
17. Castro P, Azevedo E, Rocha I, Sorond F, Serrador JM. Chronic kidney disease and poor outcomes in ischemic stroke: is impaired cerebral autoregulation the missing link? BMC Neurol. 2018 Mar; 18(1): 21.
18. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and risk of death, cardiovascular events and hospital-lization. N Engl J Med 2004;351:1296- 1305.
19. Ovbiagele B, Schwamm LH, Smith EE, et al..: Hospitalized hemorrhagic stroke patients with renal insufficiency: clinical characteristics, care patterns, and outcomes. J Stroke Cerebrovasc Dis. 2014; 23(9): 2265– 73.
20. Yahalom G, Schwartz R, Schwammenthal Y, Merzeliak O, Toashi M, Orion D, Sela BA, Tanne D. Chronic kidney disease and clinical outcome in patients with acute stroke. Stroke. 2009 Apr 1;40(4):1296-303.
21. Molnar AO, Bota SE, Garg AX, Harel Z, Lam N, McArthur E, Nesrallah G, Perl J, Sood MM. The risk of major hemorrhage with CKD. Journal of the American Society of Nephrology: JASN. 2016 Sep;27(9):2825.
22. Nayak-Rao S, Shenoy MP. Stroke in Patients with Chronic Kidney Disease…: How do we Approach and Manage it? Indian J Nephrol. 2017 May-Jun; 27(3): 167– 71.
23. Baumelou A, Bruckert E, Bagnis C, Deray G. Renal disease in cardiovascular disorders. An underrecognized problem. Am J Nephrol. 200 5;25(2):95-105.