Original Article

Renal Dysfunction Among Stroke Patients, Hospital Based Cross Sectional Study, Addis Ababa, Ethiopia, 2021

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Abstract

Background: - Stroke is the leading explanation for neurological disability and the second commonest cause of death in the world. Even though renal dysfunction is among commonly encountered comorbidity in acute stroke patients, there was no data on the prevalence and associated factors of renal dysfunction among acute stroke patients in Ethiopia.

Objective: This study aimed to determine the magnitude of renal dysfunction and factors associated with renal dysfunction among hospitalized acute stroke patients.

Method: Hospital based retrospective cross sectional study wasonducted among all acute stroke patients admitted to Saint Peter's specialized hospital from January to December 2021. The Data were collected from patient medical charts using a structured checklist. SPSS 23.0 was used to analysis the collected data. In order to evaluate the factors associated with renal dysfunction, statistical logistic regression with a level of α set at 0.05 was employeed. For variables with a $p<0.05$, statistical significance was considered.

Result: The study included 118 acute stroke patients, with a mean and standard deviation age of 60.1±14.9 years, and 63(53.4%) were males. 22 (18.6%) of the study, population had renal dysfunction. Males were more commonly 12(54.5%) affected than females. Diabetes mellitus had statistically significant association with renal dysfunction (p=0.031). Patients who had renal dysfunction had a higher mortality rate (31.8%) as compared with patients with normal renal function (21.9%).

Conclusion: Renal dysfunction is a frequent comorbidity in patients who are admitted with the diagnosis of acute stroke and had a higher mortality rate than stroke patients with normal renal function. [*Ethiop. J. Health Dev.* 2023; 37(1) 000-000]

Key words: Renal Dysfunction; Stroke; Mortality; Ethiopia

Introduction

Stroke is the leading cause of neurological disability and the second commonest cause of death in the world (1). Renal dysfunction is a frequent comorbidity in patients with the diagnosis of acute stroke and was associated with an increased risk of in-hospital mortality. Chronic kidney disease is frequently associated with cardiovascular disease (CVD); in fact, it can be considered a cardiovascular risk equivalent. CKD patients are more likely to die of CVD than to eventually develop renal failure requiring renal replacement therapy. Conversely, diagnosis of CKD is higher among patients with cardiovascular disease than the general population (2). CKD is associated with a significant increased risk of cerebrovascular disease. Even subtle kidney dysfunction, as suggested by albuminuria, increases stroke risk. Stage three CKD with microalbuminuria increased stroke risk 1.5 to 2 fold. Dialysis patients have six times increased risk of stroke. Stroke accounts for 3% of deaths in ESRD(3, 4).

The traditional risk factors for cerebro-renal link are shared with the general population but more prevalent in renal patients. These include hypertension, hypervolemia, dyslipidemia, sympathetic over activity and Hyperhomocytinemia. In addition, novel (CKD related) factors are also postulated to further increase the risk of stroke. These are generalized inflammation, anemia, hypophosphatemia, hyperparathyroidism, increased FGF-23 and sleep apnea (5) and cardio embolic stroke from atrial fibrillation is a common cause of stroke in CKD (6).

A meta-analysis of 21 articles showed that baseline GFR <60 ml/min/1.73 m^2 had 43% risk of future stroke (7). A cohort study conducted on patients with acute stroke in Israeli reported that 19.1% had recognized renal insufficiency and 10.4% had unrecognized renal insufficiency (8). A similar study conducted in Greece and Poland showed that the prevalence of decreased eGFR (<60 mL/min./1.73m2) among ischemic stroke patients were 28.1% and 18.6% respectively (9,10). Another prospective study also found that 48.1% of hospitalized acute stroke patients had renal dysfunction (11).

Acute kidney injury (AKI) complicating acute stroke is common with an estimated incidence of 8-21% (12). Largely, stroke patients with severe neurological deficits, cardiac abnormalities such as heart failure, atrial fibrillation and ischemic heart disease, hyperglycemia, hypertension, low estimated Glomerular Filtration Rate (eGFR), or advanced age were more susceptible to developing AKI [5,6,12,13]. Renal dysfunction in stroke patients was associated with female sex, diabetes mellitus and physical disability (10).

AKI is associated with increased adverse stroke outcomes and mortality, with increased severity of AKI paralleling death risk. Therefore, acute management of kidney dysfunction after stroke may be important to improve post stroke outcome and decrease mortality rates [5,6,12,13]. Intracranial hemorrhage patients with acute renal failure (ARF) had higher rates of in-

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hospital mortality (28.7% versus 22.4%; P < .0001) compared with those without ARF (14).

The prevalence of renal dysfunction in patients with stroke in Ethiopia is unknown. As a result, this study will provide information on the magnitude of renal dysfunction in acute stroke patients and factors associated with renal dysfunction as well as the effect of renal dysfunction on stroke patients' in-hospital outcomes. In addition, the result will be important as a source of information for concerned stakeholders and policymakers. The finding will also helpful to healthcare workers as an input in improving stroke outcomes of patients with renal dysfunction by taking appropriate measures and it will pave the way for future research.

Materials and Methodology

Study area and period

This study was conducted at Saint Peter's Specialized Hospital, Addis Ababa, Ethiopia from January to December 2021. Saint Peter's Specialized Hospital is one of the hospitals managed at the federal level, which offers routine medical services to Addis Ababa and accepts referrals from other regional states in Ethiopia. It is the country's largest tuberculosis (TB) referral facility and has a long history of TB management, having been the first hospital in the country to implement TB case management in June 1961. It now has about 12 departments and 400 beds. It provides a comprehensive range of acute care services, including an Emergency Room.

Study design: Hospital based retrospective cross sectional record review study was employed

Source population: The source population comprises all acute stroke patients admitted to St. Peter's specialized hospital.

Study population: All acute stroke patients admitted to St. Peter's specialized hospital during the study period.

Inclusion and Exclusion criteria: All acute stroke patients admitted to adult medical ward and ICU during the study period were included as study participants and patients who had no documented serum creatinine level within 24 hours of admission had excluded from the study.

Table 1: Eligible patients with acute stroke at St. Peter specialized hospital, Addis Ababa, Ethiopia, 2021

Patients with acute stroke (n)	Included (n)	Excluded (n)	Excluded %
131	118	13	9.9

Data collection tools: Structured checklists from earlier, comparable studies that had been published in the English language were used to collect data after being pretested and modified to fit the local conditions (8, 9). The checklist had five parts. The first contains information about the demographic characteristics of the patient. The second contains the clinical profiles of the patient at admission. The third part assesses cardiovascular risk factors. The fourth contains laboratory profiles, and the last part assesses in-hospital outcome of the patient.

Data collection procedures: The medical record numbers of patients presented with acute stroke at adult medical emergency from January 01/2021 to December 31/2021 were listed from the registration book and all patient charts were collected from the chart store by two public health officers under the supervision of one medical doctor (general practitioner). Then cross-checked with the registration book and only cases eligible for the inclusion criteria were selected.

Operational Definitions

Stroke:- An abrupt onset of a neurologic deficit that is attributable to a focal vascular cause and the neurologic signs and symptoms last for >24 hours. Neuro-imaging, brain CT/MRI was used to classify stroke as ischemic or hemorrhagic.

Transient ischemic attack: Is defined when a subject had a TIA diagnosed by a neurologist as a temporary, focal neurological deficit presumably related to ischemia and lasting < 24 hours.

Renal dysfunction:- Recognized renal dysfunction is defined as serum creatinine level >1.2 mg/dl (8). GFR is preferable to determine renal dysfunction than serum creatinine alone but GFR is used to determine whether a patient has CKD or not. To confirm that a patient has CKD, we should wait for at least three months after the baseline measurement. However, in this study, we took a single measurement of serum creatinine on the arrival of a patient at emergency department. From here, if a patient has serum creatinine derangement, we can surely say the patient has renal dysfunction. Nevertheless, cannot say a patient has CKD by calculating a single measurement of GFR. In addition, for GFR to be applied the serum creatinine should be in a steady state which is very unlikely in a patient with acute medical conditions like stroke. Therefore, it was preferable to use serum creatinine than GFR to determine renal dysfunction for this particular study.

Chronic kidney disease: With abnormal kidney function; Impaired kidney function or raised proteinuria that is confirmed on two or more occasions at least 3 months apart. Functional Criteria are defined as GFR < 60ml/min/1.73m^3 for >3 months and structural criteria is defined as Kidney damage for >3 months.

Acute kidney injury:- Absolute or relative change in creatinine (absolute increase in serum creatinine ≥ 0.3mg/dl or a percentage increase of >50%).

Hypertension: Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or both, diagnosed at least twice before the stroke or treatment of hypertension has been implemented.

History of Diabetes mellitus:-The use of a blood-sugar-lowering drug before the occurrence of the stroke or if the fasting blood glucose level exceeded 126

mg/dl known before the stroke or if documented in the medical records by the treating physician.

***Admission*:** Starting from the arrival of the patient at the emergency department

Data quality assurance

To assure data quality, the checklist had been pretested and training was given to the two data collectors and one supervisor for half a day to familiarize them with the research goal, methodology and each of the items included in the study tools. On a weekly basis, the principal investigator rigorously monitored the performance of the data collectors in the hospital. The filled checklists were checked for completeness, accuracy, and consistency by the supervisor during data collection and at the end of each day, and remedial steps were performed.

Data analysis and processing

The coded data was encoded to SPSS version 23.0 statistical software. Prior to analysis, data cleaning and management were completed. Descriptive statistics included mean with SD for continuous variables, and frequency and percentage tables were used for categorical data. Bivariate and multivariate analyses were used to see the effect of independent variable on outcome variable. Variables, which are significant on bivariate analysis at p value less than 0.25, was taken to multivariate analysis. In multivariate analysis P value of less than 0.05 was used as a cut-point for presence of association. Strength of association was measured by 95% confidence interval and odd ratio.

Ethical consideration

All participants' document and record privacy, and autonomy were respected. The name of the study subject were not listed on the questionnaire rather codes were used and more personal secrets were kept closed. The study received ethical approval from institutional review board of St. Peter's specialized hospital with Protocol/Version number of V353/26/8/2021.

Results

One hundred thirty -one patients with the diagnosis of acute stroke were admitted during the study period and thirteen were excluded. The age of study population was between 19 and 95 with the mean and SD of 60.1±14.9 years. Forty one (34.7%) of the study population was ≥70 years. The aata for this study were collected from 63(53.4%) men and 55(46.6%) women stroke patients. Patients who had ischemic stroke were 38(54.3%) men and 32(45.7%) women, and who had hemorrhagic stroke were 25(52.1%) men and 23(47.9%) women *(Table 2).*

Table 2: Sociodemographic characteristics of stroke patients with renal dysfunction and normal renal function at St. Peter specialized hospital, Addis Ababa, Ethiopia, 2021

		Renal Dysfunction (n = 22)		Normal Renal Function (n = 96)	
Sociodemographic variables		**n**	**%**	**n**	**%**
Age (years)	≥70	10	45.4	31	32.3
	<70	12	54.6	65	67.7
Sex	Male	12	54.6	51	53.1
	Female	10	45.4	45	46.9

The minimum and maximum serum creatinine value of the study population on admission was in between 0.3mg/dl and 4.6mg/dl with the mean and SD of 0.9±0.6 mg/dl. Among the 118 stroke patients, 22 (18.4%) had renal dysfunction and 54.5% were males.

The finding of this study shows that , 79 (67.0%) of the study participants had a history of cardiovascular risk factors of which the most commonly reported risk factor was hypertension 59 (74.7%), from which 38 (48.1%) has only history of Hypertension, followed by history of previous TIA/stroke 13 (16.5%). Among stroke patients with renal dysfunction, 10 (45.5%), five (22.7%) and two (9.1%) had history of hypertension, Diabetes Mellitus and previous TIA/Stroke respectively. Among all the study populations; more than half 70 (59.3%) had a high blood pressure of ≥160/100 mmHg, more than two-third 83 (70.3%) had normal pulse rate (60-99 beats per minute) and 2 (1.7%) have a pulse rate of ≥120 beats per minute on admission at emergency room. Majority 66 (55.9%) of patients had decreased mentation, of which 49 (41.5%) and 17 (14.4%) patients presented with GCS of 9-14 and coma (GCS of 3-8) respectively. Half of patients with renal dysfunction presented with decreased mentation and more than half 12(54.5%) presented with high blood pressure (BP) ≥160/100 mmHg. Even though Ischemic stroke was by far the most common presentation of patients in both groups of renal function, it is more common in patients with renal dysfunction than patients with normal renal function did (*Table 3*).

Table 3: **Clinical profiles of stroke patients at admission based on their renal function group at St. Peter specialized hospital, Addis Ababa, Ethiopia, 2021**

Clinical profiles		Renal dysfunction (n = 22)		Normal renal function (n = 96)	
		n	**%**	**n**	**%**
History of HTN	Yes	10	45.4	49	51.0
	No	12	54.6	47	49.0

History of DM	Yes	5	22.7	6	6.2
	No	17	77.3	90	93.8
History of previous	Yes	2	9.1	11	11.5
TIA/Stroke	No	20	90.9	85	88.5
History of Cardiac disease	Yes	0	0.0	9	9.4
	No	22	100.0	87	90.6
BP in mmHg	≥160/100	12	54.6	58	60.4
	<160/100	10	45.4	38	39.6
PR in beats per minute	≥100	7	31.8	25	26.0
	<100	15	68.2	71	74.0
GCS	<15	11	50.0	55	57.3
	15	11	50.0	41	42.7
Types of stroke	Ischemic	15	68.2	55	57.3
	Hemorrhagic	7	31.8	41	42.7

GCS – Glasgow coma scale, TIA – Transient ischemic stroke, mmHg –millimeter mercury, HTN – Hypertension, DM – diabetes mellitus

Among stroke patients who had history of higher random blood sugar level (≥200mg/dl) and total cholesterol ((≥200mg/dl), six (40%) and one third respectively had developed renal dysfunction (Table 4).

Table 4: Laboratory test profiles of stroke patients at admission based on their renal function group at St. Peter specialized hospital, Addis Ababa, Ethiopia, 2021

Laboratory test profiles		**Renal dysfunction**		**Normal renal**	
		n	**%**	**n**	**%**
RBS in mg/dl	≥200	6	27.3	9	9.4
	<200	16	72.7	87	90.6
Urine dipstick	≥+2	3	17.6	9	12.3
	<+2	14	82.4	64	87.7
Total cholesterol	≥200	5	31.2	10	15.9
	<200	11	68.8	53	84.1
HDL	<35	4	28.6	14	29.8
	≥35	10	71.4	33	70.2
LDL	≥130	4	28.6	7	14.9
	<130	10	71.4	40	85.1
Triglyceride	≥200	0	0.0	10	16.9
	<200	14	100.0	49	83.1
Sodium (Na)	<135	5	22.7	23	25.3
	≥135	17	77.3	68	74.7
Potassium (K)	< 3.3	2	9.1	6	6.6
	≥3.3	20	90.9	85	93.4
Chloride (Cl)	< 98	5	23.8	16	20.2
	≥98	16	76.2	63	79.8

RBS – Random blood sugar, HDL – High-density lipoprotein, LDL – Low-density lipoprotein

In full model of multivariate regression analysis, the following parameters were included: age, gender, History of HTN, history of DM, previous TIA/stroke, cardiac disease, blood pressure, GCS, type of stroke, glucose, creatinine, urine dipstick, total cholesterol, HDL, LDL and triglycerides. Stepwise logistic regression analysis was performed by including only variables with p<0.25 in the full model. The results of a multivariate analysis revealed that a person's history of diabetes mellitus was the sole independent predictor of renal failure in stroke patients. When compared to stroke patients without DM, people with both DM and stroke had seven times the risk of developing renal dysfunction (p = 0.031; AOR = 7.1 (1.2,42.6)) (*Table 5*).

Table 5: Subgroup analysis of factors associated with the primary outcome of renal dysfunction among stroke patients at St. Peter specialized hospital, Addis Ababa, Ethiopia, 2021

Category	**Variables**	**RD %**	**Normal RF %**	**COR (95%, CI)**	**AOR (95%, CI)**	**P-value**
Age in years	≥70	24.4	75.6	1.7 (0.7,4.5)	2.2 (0.6,7.8)	0.212
History of DM	Yes	45.5	54.5	4.4 (1.2,16.1)	7.1 (1.2,42.6)	0.031
RBS in mg/dl	≥200	40	60	3.6 (1.1,11.6)	2.9 (0.6,14.1)	0.193
Total cholesterol	≥200	33.3	66.7	2.4 (0.7,8.4)	2.8 (0.7,11.5)	0.163

RD = Renal dysfunction; RF = Renal function; TIA =Transient ischemic attack. RBS – Random blood sugar, DM – Diabetes mellitus

Eighty-seven (73.7%) of the study participants were discharged home and three (2.6%) went against medical advice. Twenty-eight (23.7%) of the study participants were dead, with one quarter of them having had renal dysfunction. The proportions of mortality were significantly different between the two groups, with disproportionately higher rate 31.8% in patients with renal dysfunction and 21.9% in patients with normal renal function.

Discussion

According to our findings, the magnitude of renal dysfunction among hospitalized acute stroke patients was 18.6%, which is consistent with the study done in Israeli on recognized renal insufficiency based on the prospective National Acute Stroke Israeli (NASIS) registry in 2016 of 19.1% (8) and 18.6% of a study conducted in Poland among surviving 352 stroke patients(10). According to a cohort study of 1350 hospitalized first-ever stroke patients conducted in Athens, Greece over a 10-year period, 28.1% of acute stroke patients had moderate or severe renal impairment [9], which is higher than our finding. Small sample size and included only patients with recognized renal dysfunction could have underestimated the magnitude of renal dysfunction in this study. A prospective cohort study conducted on 52 patients admitted to intensive care unit in Nepal from 2014 to 2015 showed that 48.1% had renal impairment (11). This outlier discrepancy could be due to significant overestimation of GFR, because direct measurement of creatinine clearance to determine renal function is imprecise in critically ill patients due to the increased secretion of creatinine in the renal tubules. This study also showed that more than half of stroke patients with renal dysfunction were males, which is similar to a study report of Israeli 56.9% (8) and a Greece study reported that, male gender had a statistically significant association with renal impairment (p=0.000) (9).

History of DM, previous TIA and ischemic type stroke was more common in patients with renal dysfunction as compared with normal renal function. The result of a study conducted in 2016 on the prevalence and impact of undiagnosed renal impairment in patients with stroke in Israeli and a study conducted in Greece on Renal dysfunction in acute stroke patients were congruent with these findings (8,9). A multivariate analysis also showed that, diabetes mellitus was a statistically significant predictor of renal dysfunction among acute stroke patients with renal dysfunction (AOR = 7.1, 95% CI: 1.2, 42.6, p=0.031)

Patients who had renal dysfunction had higher mortality rate as compared with patients with normal renal function. 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 calcification, and increased plasma levels of fibrinogen and homocysteine (8). Other studies also showed that serum creatinine >1.3mg/dL was associated with an increased risk of cardiovascular mortality (15). Sweileh et al., identified in stroke patients, three predictors of in hospital mortality: creatinine clearance (p = 0.004), number of post-stroke complications (p = 0.001), and type of stroke (p = 0.034), (16).

This study had several limitations: Creatinine is an unreliable proxy that is impacted by a variety of characteristics such as age, gender, race, and lean body weight. As a result, even if serum creatinine is normal, there may be unrecognized renal dysfunction (eGFR <60 ml/min/1.73m^2), which may lead us to underestimate the magnitude of renal dysfunction. In addition to this, the small sample size, being cross sectional retrospective study and unable to determine eGFR, since the patient is in acute medical condition were the major limitations of the study.

Conclusion and Recommendations

The magnitude of renal dysfunction among hospitalized patients with acute stroke is high and DM is a scientifically significant predictor. Patients with renal dysfunction had higher rate of mortality as compared with normal renal function. We recommend feature researchers to have baseline creatinine and to determine renal dysfunction using eGFR as well as to do a cohort study to know short and long-term impact of renal dysfunction.

Conflict of interest: the authors declare no competing interests

Contribution of authors

All the authors have equally participated in every aspect of the study including conceptualization, designing and methodology, fund acquisition, data collection, data entry and cleaning, data analysis, drafting the manuscript, reviewing the manuscript and approval of the final manuscript.

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