SERUM CREATININE AS PREDICTOR OF OUTCOME IN HOSPITALIZED PATIENTS AFTER ACUTE STROKE

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Abstract

Background/Aims: *Acute stroke is one of the leading causes of mortality and morbidity worldwide. The adverse outcome following acute stroke depends not only on severity of the neurological defects but also on other co-morbidities. Associated renal impairment has been found to be a major predictor of different outcome following acute stroke in several studies. The aim of this study was to evaluate the impact of the serum creatinine on the outcome of hospitalized patients after acute stroke.*

Methods: *This was a Prospective cohort study conducted on 100 consecutive adult patients who were admitted in the Neurology department of Dhaka Medical College Hospital following acute stroke during January 2018 to December 2019.The patients were followed up for two weeks after the incident stroke.*

Results: *Among the 100 patients with acute stroke 57(57%) were ischaemic and 43(43%) were haemorrhagic stroke. Mean age(SD) was 60.4(10.6) years. Patients with ischaemic stroke were older compared to haemorrhagic stroke (61.1(9.6); 53.8(9.4) years respectively; p<0.05). The mean (SD) serum creatinine on admission in patients with both types of stroke, who deteriorated or died, were significantly higher than in those who survived. Others predictors of mortality and morbidity in both types of acute stroke were age, gender, hypertension, diabetes mellitus, ischemic heart disease, dyslipidaemia.*

Conclusions: *Patients with impaired renal function had worse outcome after hospitalization in both types of acute stroke. Haemorrhagic stroke, older age, high baseline serum creatinine, hypertension were significantly associated with increased mortality and morbidity following acute stroke. Appropriate measures should be taken to patients with impaired renal function to reduce the mortality and morbidity following acute stroke.*

Key words: *Acute stroke, Serum creatinine, Risk factors, Outcome*

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Introduction

Acute stroke is one of the leading causes of death and disability worldwide.[1,2] It causes serious disability which has a profound impact on long term survival of the patients. The early hours after an acute stroke are crucial, because it is the most useful time for effective intervention.[3] It is important to determine the prognostic factors as early as possible. There is growing evidence in medical literature regarding the role of cerebrovascular and cardiovascular disorders in renal impairment in view of the similarities between vascular beds of kidney, brain and heart.[15] Renal impairment may suggest a higher co-morbidity burden, especially of atherosclerotic risk factors and diseases.[18] Renal insufficiency is a common co-morbid condition in different medical conditions

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including cerebrovascular disease, cardiovascular disorders, diabetes mellitus and hypertension.[13] Following acute stroke renal impairment may develop as a possible complication. Various common risk factors between acute stroke and renal insufficiency lead to higher mortality and morbidity in patients with acute stroke.[4] Almost all types of vascular disease including stroke have been found to be associated with renal dysfunction and the severity of acute stroke may predict the degree of injury in small renal vessels.[8] Serum creatinine has been found to be an independent predictor of mortality and morbidity even after adjustment among stroke survivors.[6] Serum creatinine is a routine laboratory test which is of low cost, easily available & can predict the severity & outcome of many disease conditions with high accuracy.[9] In this study the mortality and neurological status within second week after onset of acute stroke will be compared between patients with their level of serum creatinine in predicting the outcome after acute stroke which will also help to manage these patients more appropriately keeping in mind this association.

Materials and Methods

We collected demographic and clinical data from 100 consecutive adult patients with acute stroke (57 patients with ischaemic and 43 patients with haemorrhagic stroke) who admitted in the department of Neurology, Dhaka Medical College Hospital during January 2018 to December 2019. Patients aged ≥18 years who presented within 72 hours of onset of stroke symptoms were included in the study. It was a Prospective Observational study and the sampling method was Consecutive sampling. Stroke was diagnosed based on history, clinical examination and computed tomography scan (CT scan) of head and or Magnetic Resonance Imaging (MRI) of the brain. Patients with subarachnoid haemorrhage, transient ischaemic attack (TIA), head trauma and patients with incomplete data were excluded. Patients with pre-existing renal disease, acute myocardial diseases, heart failure, glomerulonephritis from any causes and urinary tract obstruction were also excluded from the study. After obtaining clearance from Ethical Review Committee of Dhaka Medical College, Dhaka and due consideration of inclusion and exclusion criteria, written consent was taken from patient and or attendant for the study. A detailed history and clinical examination was done in all patients who were included into the study. Serum creatinine along with other biochemical parameters were measured on admission. The patients were followed up daily till two weeks after onset of acute stroke with special attention to mortality and neurological deterioration. Neurological status was defined by Modified Rankin scale (MRS) score. All the data were collected in a preformed schedule. Subjects with incomplete data or inadequate follow up were excluded before final analysis. Equal number of new cases, as before, were recruited to replace them.

All laboratory parameters: blood sugar, serum creatinine, blood urea, serum electrolyte, lipid profile (total cholesterol, HDL cholesterol, Triglycerides, LDL cholesterol) were assessed using standard methods in Biochemistry department of Dhaka Medical College Hospital . Serum creatinine was measured using a Jaffe method, alkaline picrate kinetic (Architect, Abbott, IL, USA). The method for creatinine measurement was IDMS traceable.

Statistical analyses

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation and categorical variables as frequencies and percentage. The differences between the groups were analyzed by student t- test or chi-square test and shown with cross tabulation. Data evaluated by ANOVA test. Significance was defined by p value<0.05.

Table I

Demographic and clinical characteristics of the studied population(N=100)

	Stroke		Ischaemic		Haemorrhagic		P
	N	M±SD%	N	M±SD%.	N	M±SD	
Age (Years)	100	60.40± 10.66	57	61.12±9.64	43	53.82±9.37	>0.05
Female	49	49%	31	54.39%	18	41.87%	>0.05
Male	51	51%	26	45.61%	25	58.13%	>0.05
Hypertension	69	69%	41	61.2%	28	84.8%	<0.05
Diabetes	67	67%	43	64.2%	24	72.7%	>0.05
Ischaemic heart disease	29	29%	19	28.4%	10	30.3%	>0.05
Dyslipidaemia	38	38%	23	34.3%	15	45.5%	>0.05

Results

Characteristics of the study population

We collected data from 100 patients(Male 51 and Female 49) with acute stroke. Among them 57 patients were with Ischaemic stroke [Male 26(45.61%), Female 31 (54.39%)]and 43 patients were with haemorrhagic stroke [Male 25(58.13%) and Female 18(41.87%)]. The age of study population was18 years and above (mean age 60.40±10.66 years). Patients with ischaemic stroke were significantly older compared to haemorrhagic stroke (61.12±9.64 and 53.82±9.37 years respectively); p<0.05).A total of 65(65%) patients were discharged at home, 25(25%) patients were transferred to other health care facilities and 10(10%) patients died. Among ischaemic stroke 40(70.17%) patients were discharged at home, 13(22.81%) patients were transferred to other health care facilities, 4(7.02%) patients died. On the other hand 20(46.51%) patients with haemorrhagic stroke were discharged at home,17(39.53%) patients were transferred to other health care facilities and 6(13.95%) patients died.

Demographic and clinical characteristic of the studied population is displayed in the Table 1

Renal function assessment

On admission the mean serum creatinine of study population was 1.21±0.06 mg/dl. Among 44(68.75%) patients with ischaemic stroke and 20(31.25%) patients with haemorrhagic stroke had normal levels of serum creatinine (Female <1.2mg/dl and Male <1.4mg/dl- according to WHO). The mean serum creatinine was significantly higher among patients with haemorrhagic stroke compared to patients with ischaemic stroke(1.71±0.08 vs 1.15±0.06 mg/dl respectively) (p<0.05).

The mean serum creatinine among male with haemorrhagic stroke was significantly higher compared to male with ischaemic stroke (1.91±0.16 vs 1.12±0.06 mg/dl respectively) (p<0.05). The mean serum creatinine among female with haemorrhagic stroke was also significantly higher compared to female with ischaemic stroke (1.51±0.18 vs 1.02±0.04 mg/dl mg/dl respectively), (p<0.05).

Among patients aged less than 65 years, the mean serum creatinine was significantly higher in haemorrhagic stroke patients compared to patients with ischaemic stroke (1.68±0.12 mg/ dl vs 1.06 ±0.02 mg/dl) (p<0.05). Among patients aged 65 years or more, the mean serum creatinine was also significantly higher in haemorrhagic stroke patients compared to patients with ischaemic stroke (1.74±0.16 mg/ dl vs 1.12 ±0.12 mg/dl), (p<0.05).

Table-II

The mean serum creatinine level and type of stroke(N=100)

		Stroke		Type of stroke		P
				Ischaemic	Haemorrhagic	
Serum creatinine at admission	Within normal ranges Female <1.2 (mg/dl)	N	64	44	20	
	Male <1.4 (mg/dl)	%		68.75	31.25	< 0.05
	Elevated Female ≥1.2 (ml/dl)					
	Male ≥1.4 (mg/dl)	N	36	13	23	
		%		36.11	63.89	
Total		N	100	57	43	
		%		100.0	100.0	

Renal function and outcome

The mean serum creatinine in patients with ischaemic stroke who died was significantly higher than in those who survived (1.65±0.12 mg/dl vs 1.12±0.06 mg/dl, respectively); (p<0.05). Similarly the mean serum creatinine in patients with hemorrhagic stroke who died was significantly higher than in those who survived (2.75±0.21 mg/dl *vs* 1.55±0.32 mg/dl respectively) (p<0.05) (Table III).

Following acute stroke improvement was higher in ischaemic stroke whereas deteriorated and death patients were higher in haemorrhagic stroke and the difference was statistically significant p<0.05. The mean serum creatinine was found 1.005±0.05 mg/dl in improved group, 1.14±0.06 mg/dl in remained static group, 1.96±0.08 mg/dl in deteriorated group and 2.31±0.08 mg/dl in death group. Serum creatinine level was significantly (p<0.05) higher in deteriorated and death patients (Table IV).

Table-III

Renal function in patients with haemorrhagic and ischaemic stroke with regard to outcome(N=100)

	End of treatment	Ischaemic stroke			Haemorrhagic stroke		
		N	Mean± SD	P	N	Mean±SD	P
Creatinine at admission (mg/dl)	Stroke– Total	57	1.15±0.06		43	1.71±0.08	
	Survived	53	1.12±0.06	<0.0	37	1.55±0.32	<0.05
	Dead	04	1.65±0.12	5	06	2.75±0.21	

Table-IV

Comparison between Serum creatinine level after admission and outcome (N=100)

S. creatinine on admission mg/dl	Survived (N=90)	Improved (N=39)		Remained static (N=26)		Deteriorated (N=25)		Dead (N=10)		P Value
		N	%	N	%	N	%	N	%	
Normal (Male <1.4mg/dl Female <1.2 mg/dl)		29	74.35	20	76.92	6	24.00	3	30.00	
Elevated (Male ≥1.4 mg/dl Female 1.2 mg/dl)		10	25.65	6	23.08	19	76.00	7	70.00	<0.05
Mean SD (S. creatinine)		1.005±0. 05		1.14±0. 06		1.96±0. 08		2.31±0.08		

Table V

Distribution of acute stroke patients by Neurological status on admission by MRS. (N=100)

Neurological status on admission	Ischaemic N=57		Haemorrhagic N=43		P value
Modified Rankin Scale (MRS)	N	%	N	%	> 0.05
2	5	8.77	4	9.30	
3	30	52.63	18	41.86	
4	16	28.08	16	37.21	
5	6	10.52	5	11.62	

Table VI

Distribution of acute stroke patients by Neurological status on 14th day (or before in case of death of the patients) after admission.(N=100)

Neurological status on 14th day (or before in case death of the patient) after admission (On the basis of Modified Rankin Scale) (MRS)	Ischaemic N=57		Haemorrhagic N=43		P Value < 0.05
	N	%	N	%	
2	16	28.07	6	13.95	
3	26	45.61	12	27.91	
4	9	15.78	5	11.63	
5	2	3.51	14	32.55	
6	4	7.01	6	13.95	

Assessment of neurological status of acute stroke patients on the basis of Modified Rankin Scale (MRS)

On admission Modified Rankin Scale (MRS) was almost similar between two groups. On 14th day MRS score 3 was significantly ($p<0.05$) higher in ischaemic stroke patients, whereas score 5 was significantly ($p<0.05$) higher in haemorrhagic stroke patients. (Table V and VI)

Discussion

The short term outcome following acute stroke can be determined by acute renal impairment which is frequently overlooked and underestimated in different clinical research. In this study we demonstrated that the occurrence of acute renal impairment is frequently found following acute stroke and with severity of renal impairment it predict the adverse outcome of the acute stroke patients.

This Prospective Observational study was carried out in the Neurology department of Dhaka Medical College Hospital (DMCH), Dhaka, during the period of January 2018 to December 2019, with an aim to detect the outcome of acute stroke patients with the severity of renal impairment. A total 100 patients with acute stroke fulfilling the exclusion and inclusion criteria were included in this study. Serum creatinine level along with other biochemical parameters were measured following admission. Neurological status on admission & on 14th day after admission were detected on the basis of Modified Rankin Scale (MRC).

The following observations and results were obtained in this study:

On admission the mean serum creatinine of study population was 1.21±0.06mg/dl. Among 44(68.75%) patients with ischaemic stroke and 20(31.25%) patients with haemorrhagic stroke had normal levels of serum creatinine (Female <1.2mg/dl and Male <1.4 mg/dl- according to WHO). The mean serum creatinine was significantly higher among patients with haemorrhagic stroke compared to patients with

ischaemic stroke(1.71±0.08 vs 1.15±0.06 mg/dl respectively) ($p<0.05$). Fried et al.[19] confirmed that an elevated serum creatinine level was associated with increased risk of stroke compared to patients with normal level of creatinine (21.1% vs 11.9%). Shlipak et al.[23] identified that serum creatinine >1.4mg/dl was associated with increased risk of cardiovascular mortality. The Rotterdam study found that increased serum creatinine is a strong risk factor for haemorrhagic, but not ischaemic stroke. Similarly, in the Cardiovascular Heart Study (CHS), the Multi-Ethnic Study of Atherosclerosis (MESA) found that increased serum creatinine level was significantly associated with increased risk of haemorrhagic stroke.

In this study data was collected from 100 patients (51 male and 49 female) with acute stroke. Among them 57 patients were with Ischaemic stroke [Male 26(45.61%), Female 31 (54.39%)] and 43 patients were with haemorrhagic stroke [Male 25(58.13%) and Female 18(41.87%)]. The mean serum creatinine among male with haemorrhagic stroke was significantly higher compared to male with ischaemic stroke (1.91±0.16 vs 1.12±0.06 mg/dl respectively) ($p<0.05$). The mean serum creatinine among female with haemorrhagic stroke was also significantly higher compared to female with ischaemic stroke (1.51±0.18 vs 1.02±0.04 mg/dl mg/dl respectively), ($p<0.05$). Khatri et al also reported higher incidence of acute renal impairment (18%) in their study, with significantly higher rates among haemorrhagic stroke compared to ischaemic stroke (21% vs 14%).[13]

Among patients aged less than 65 years, the mean serum creatinine was significantly higher in haemorrhagic stroke patients compared to patients with ischaemic stroke (1.68±0.12 mg/dl vs 1.06 ±0.02 mg/dl) ($p<0.05$). Among patients aged 65 years or more, the mean serum creatinine was also significantly higher in haemorrhagic stroke patients compared to patients with ischaemic stroke (1.74±0.16 mg/dl vs 1.12 ±0.12 mg/dl), ($p<0.05$). Sarnak et al also reported higher incidence of acute renal impairment (14%) in their study, with significantly higher rates among haemorrhagic stroke compared to ischaemic stroke (25% vs 16%) regardless of the age.[3]

Majority of the patients who improved or remained static had normal Serum creatinine level and majority of the patients who deteriorated or died had high Serum creatinine level (Table 6) and the difference was statistically significant ($p<0.05$). Serum creatinine level was significantly ($p<0.05$) higher in deteriorated and death patients. In a study by Covic et al on patients with acute stroke, the overall incidence of acute renal impairment was 14.5% with unadjusted 30 day mortality rate of 43.1% compared to 12.8% for subjects without acute renal impairment.[14]

On admission Modified Rankin Scale (MRS) was almost similar between two groups. On 14th day MRS score 3 was significantly ($p<0.05$) higher in ischaemic stroke patients, whereas score 5 was significantly ($p<0.05$) higher in haemorrhagic stroke patients. Spratt et al reported the same outcome in their study.[15] Saeed et al showed that the risk of acute complications and poor functional outcome was significantly higher in patients with increased serum creatinine level.[6] Mahmoodi et al.[25] reported that after acute stroke, patients with increased serum creatinine level had a higher mortality and morbidity risk, similar to the study of Lin et al.[9]

Rapid and correct diagnosis of acute stroke and access to a high quality stroke unit is effective in reducing in-hospital fatality rate and the length of hospital stay. The length of hospitalization and in-hospital mortality was significantly higher in patients with haemorrhagic stroke than patients with ischaemic stroke. The recent study of Mohamed et al.[7] showed that the presence of renal impairment was associated with longer length of stay, which is the most predictive factor in determining in-hospital costs. Spratt et al reported disability at discharge from the hospital (MRC score>2), age>65 years, Diabetes mellitus and infection- a significant risk factor for prolonged hospital stay.[15] Shrestha et al reported higher mean hospital stay in patients with haemorrhagic stroke (14.58±7.19 days) compared to ischaemic stroke (9.86±5.12 days).[12]

This study showed that the independent predictor of mortality and morbidity in both types of acute stroke were Age, Hypertension, Diabetes mellitus, Ischaemic heart disease, Dyslipidaemia.

The strength of the study is the fairly large population of patients with both types of acute stroke and prospective collection of data. As serum creatinine is not routinely measured following hospitalization in acute stroke patients, we underwent this study to assess the role of renal insufficiency in stroke outcome. Higher occurrence of acute renal impairment in haemorrhagic stroke may contribute to worse outcome. It's established that renal function assessment is of paramount importance for the management of acute stroke patients.

The limitation of this study was a single center with short follow-up. It's acknowledged our results, although of clear and statistical significance, will need to be validated on a larger population.

Conclusion

Patients with impaired renal function has worse outcome following acute stroke. Patients with haemorrhagic stroke experienced worsening of renal function during hospitalization and had significantly worse outcomes than patients with ischaemic stroke. Haemorrhagic stroke, older age, high baseline serum creatinine level, hypertension are significantly associated with adverse outcome following acute stroke. The assessment of kidney function is prerequisite to employ the necessary measures to decrease the risk of in-hospital mortality among patients with acute stroke. Assessment of serum creatinine level can be considered as predictors of outcome in hospitalized patients after acute stroke.

Disclosure Statement

The authors clearly declare that they have no competing interests.

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