JALALABAD MEDICAL JOURNAL

Original Article

Effect of Plasma Osmolarity on the Short Term Outcome of Acute Stroke

Mohammed Fazle Bari[1], Ismail Patwary[2], Md Matiur Rahman[3], Momtaz Begum[4]

[1]Assistant Professor, Department of Medicine, Jalalabad Ragib-Rabeya Medical College, Sylhet.
[2]Professor, Department of Medicine, Sylhet Women's Medical College, Sylhet.
[3]Chief Consultant, Department of Neurology, Mount Adora Hospital, Sylhet.
[4]Professor, Department of Medicine, Jalalabad Ragib-Rabeya Medical College, Sylhet.

ABSTRACT

After acute stroke, patients are at risk of development of dehydration which is usually hyperosmolar. This abnormal physiological environment may influence early neurological deterioration and unfavorable outcome after acute stroke. We evaluated the association of raised plasma osmolarity with acute stroke outcome at 28 days. We enrolled two independent groups of acute stroke patients. Fifty patients of acute stroke with high plasma osmlarity (Plasma osmolarity ≥296 mmol/L) were included in the hyperosmolar group and another 50 patients with normal osmolarity included in the normal osmolar group (Plasma osmolarity ≥280 to <296 mmol/L). We applied quota method of sampling to enroll the samples. Plasma osmolarity was calculated on admissions who were admitted within 24 hours after acute stroke. Chi square test and logistic regression test were done to evaluate the association of osmolarity and outcome (Death and functional status). Functional status was measured with Birthel Index score scale. Thirty four deaths were observed during the study period. Among the death cases, 21 acute stroke patients were hyperosmolar (Mean osmolarity 303.43 with SD±6.60) on admission and 13 acute stroke patients were normalosmolar on admission (Mean osmolarity 289.13 with SD±5.76). Statistical analysis showed admission hyperosmolarity was not associated with fatal acute stroke outcome crude OR 2.06 (p value 0.09) and adjusted OR 0.923 (95% CI 0.338 to 2.523, p value 0.87). Among the 66 survivor, 21 were towards dependent and 8 patients were towards independent after 28 days in hyperosmolar group. Logistic regression analysis showed hyperosmolarity was not associated with poor functional outcome of acute stroke than that of normal osmolarity group with adjusted OR 0.250 (95% CI 0.054 to 1.164). So raised plasma osmolarity was not associated with acute stroke mortality and poor functional outcome.

Keywords: *Hyperosmolarity, Birthel Index Score.*

[Jalalabad Med J 2020; 17(1): 10-16]

INTRODUCTION

Stroke is a global problem and is the 2nd most common cause of death in the world and top most cause of disability[1,2]. In Bangladesh stroke is the third leading cause of death and WHO ranks the mortality rate due to stroke in Bangladesh as number 84 in the world[3]. Recent studies showed that there is change in the stroke incidence among high-income and low to middle income countries over the past four decades, with a 42% decrease in stroke incidence in high-income countries and greater than 100% increase in low to middle income countries[4]. The incidence of stroke is predicted to rise because of the rapidly aging population, dietary and lifestyle behaviours. The

Address of Correspondence:
Dr. Mohammed Fazle Bari, Assistant Professor, Department of Medicine, Jalalabad Ragib-Rabeya Medical College, Sylhet. Mobile: +8801715642508, Email: bari.fazle@gmail.com

estimated economic loss in Bangladesh stands to 408 million US dollar per year due to stroke morbidity and mortality[5]. For the last few decades, considerable number of researches has been done with drug therapy and treatment strategy in respect to management of acute stroke. The development of stroke unit is the landmark in reducing mortality and morbidity of acute stroke patients[6]. There is evidence that organized management in stroke units improves survival and reduces dependency of acute stroke patients[7]. Monitoring and stabilizing the acute physiological parameters such as blood pressure, temperature, plasma glucose, oxygen saturation, hydration status, and electrolyte imbalance have become a part of standard stroke management[8].

Patients presenting with acute ischemic stroke are predominantly either euvolaemic or hypovolaemic. Hypovolaemia predispose to hypoperfusion and exacerbate the ischaemic brain injury, cause renal impairment and potentiate thrombosis[9]. On the other hand there is a decreased sensation of thirst and often dehydration present among the elderly population and elderly patients presenting with acute ischaemic stroke. They have high plasma osmolality levels which are possibly a contributing factor to cerebral ischaemia[10]. Initial dehydration is frequently hyperosmolar, caused by an inadequate intake of water due to drowsiness, dysphagia and reduction of thirst or presence of infection[11]. Dehydration, which is very common among acute stroke patients, increases blood viscosity by affecting plasma osmolality, thus affects cerebral haemodynamic and alters cerebral blood flow[12,13]. Rowat et al. found that, out of 2591 patient 36% patients were dehydrated on the day of admission and 62% were dehydrated at some point during their admission period[14]. Though hyperglycaemia, hypertension, smoking increase mortality and associated with poor outcome in acute stroke[15,16,17], some studies also showed that raised plasma osmolality independently related to mortality and is associated with severe stroke and poor outcomes at hospital discharge[7,8,14].

There is no gold standard biomarker for detection of dehydration. Plasma osmolality and urea creatinine ratio is commonly used for the assessment of dehydration. We used calculated plasma osmolarity as the biomarker for detection of dehydration. Plasma osmolarity is interchangeable with plasma osmolality (Measured) in clinical ground and plasma osmolality is not available in clinical setting readily. On the other hand it is not feasible to perform plasma osmolality frequently since in acute condition dehydration may need to assess for several times. Therefore, we have used calculated plasma osmolarity, which is more convenient and available. So far, there is no evidence regarding the effect of raised plasma osmolarity on the outcome of acute stroke in Bangladesh. Such data are desirable considering the potentially adverse but presumably modifiable nature of hyperosmolarity in acute stroke. In this study, raised plasma osmolarity in acute stroke and its association with short term outcome (Such as death and dependency within 28 days since acute stroke) is evaluated.

MATERIALS AND METHODS

This cross sectional comparative study was done in the department of medicine and the department of neurology, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet from 1st January 2013 to 31st December 2014. Consecutive 50 hyperosmolar and 50 normalosmolar acute stroke patients were included in the study by quota sampling method who presented with acute stroke and confirmed by computed tomography (CT) or magnetic resonance imaging (MRI). Age <18 year and patient with significant co-morbidity were excluded from the study. Socio-demographic characteristics age, sex, clinical state at the time of admission to hospital and co-morbidities (A history of hypertension, myocardial infarction, diabetes mellitus, atrial fibrillation, and previous cerebro-vascular disease) were identified through medical history. After written consent blood samples were taken within 24 hours of stroke onset (Admission) and biochemical parameters like sodium, potassium, plasma glucose, urea were done. Calculated plasma osmolarity was estimated by using the equation (All in mmol/L): 2 x (Na^++K^+) + Plasma Glucose + Blood Urea. Patients were assessed at day 28th after stroke if alive and death cases were also recorded. All patients were managed according to acute stroke management protocol of the hospital. Outcome assessment included death and dependency at 28 days by the Barthel Index Score. In special situations 28 days functional outcome data for the Barthel Index score were collected over cell phone. Data were collected by a preformed questionnaire. Collected data were edited manually and analyzed with the help of computer program statistical package for social science (SPSS) 17. Data were expressed in mean, standard deviation and percentage. Test of significance were done where necessary. For all tests, a p value <0.05 was considered statistically significant. In the bivariate analysis, chi-squared tests were performed to identify the association between functional outcomes and selected categorical variables, while a t-test was used to measure this for continuous covariate age. In the multivariate setup, logistic regression was fitted to model the functional outcome as a function of several covariates. Statistical significance of the parameters involved in the logistic regression model was carried out by Wald test.

RESULTS

In our study, age of acute stroke patients was ranging from 40 years to 95 years, with the mean age of 62.57±9.92 years (Mean±standard deviation). The majority of the sample were males (79%) and most of the patients were in the age of 50 to 79 years (Table-I). Their mean plasma osmolarity in the hyperosmolar group and normalosmolar group was 303.43 (±6.60) mmol/L and 289.76 (±5.76) mmol/L respectively. Total 16 patients died before completion of day 7 and 18 patients died after day 7 within the period of follow up. Forty two patients in the hyperosmolar group and 37 patients in the normal osmolar group had severe stroke NIHSS (15). Hyperglycaemia present on admission in 29 patients in the hyperosmolar group and 16 patients in the normal osmolar group (Table-II).

We observed total 34 deaths during our study period. Among them 21 death occurred in high plasma osmolarity group and 13 death in the normal osmolarity group. The effect of osmolarity was not statistically significant (p value 0.09), the calculated crude odds ratio (OR) was found to be 2.06 and adjusted OR was obtained as 0.923 (95% CI 0.338 to 2.523, p value 0.87). Since p-value was large, there was not enough

Table-I: *Distribution of patients by age and sex (n=100).*

Study Subjects	Number	Range in Years	Age in Years Mean±SD
Total	100	40-95	62.57±9.92
Male	79	40-95	62.27±10.44
Female	21	45-75	63.66±7.73

Table-II: *Distribution of demographic and baseline characteristics among the hyperosmolar and normal osmolar patients (n=100).*

Characteristics	Hyperosmolarity (mean±SD mmol/L) (303.43±6.60 mmol/L)		Normal Osmolarity (mean±SD mmol/L) (289.76±5.76 mmol/L)	
	Dead	Alive	Dead	Alive
Gender				
Male	17	24	11	27
Female	4	5	2	10
Stroke severity				
Severe	21	21	10	27
Moderate	0	8	3	10
Hyperglycaemia				
Present	18	11	7	9
Absent	3	18	6	28
Hypertension				
Present	15	21	9	15
Absent	6	8	4	22
Smoking				
Present	15	18	8	22
Absent	6	11	5	15
Stroke type				
Ischaemic	9	18	5	25
Haemorrhagic	12	11	8	12
Death				
Within 7 days	12	-	4	-
After 7days during study period	9	-	9	-

evidence to conclude that, osmolarity level affected stroke outcome death. Among the 66 survivor 21 were towards dependent and 8 patients were towards independent after 28 days in hyper osmolar group. Logistic regression analysis showed hyperosmolarity was not associated with poor functional outcome than that of normal osmolarity group with adjusted OR 0.250 (95% CI 0.054 to 1.164, p value 0.077). The effect of age on functional outcome was highly significant (p value 0.001) but death was not significantly associated with age. Person with higher age is more likely to become dependent after stroke. We found severe stroke (Score ≥15) in 31 patient and moderate stroke (Score 6-14) in 3 patient out of 34 death, statistical analysis showed stroke severity strongly associated with case fatality in acute stroke adjusted OR-4.153 (95% CI 0.0963 to 17.924, p value 0.05). On the other hand out of 66 survived patients from acute stroke 37 were towards dependent and 12 patients were towards independent in severe stroke group and 7 patients and 10 patients were towards dependent and towards independent respectively in moderate stroke group. Statistical analysis revealed, severe stroke associated with poor functional outcome in acute stroke adjusted OR 4.326 (95% CI 0.991 to 18.895, p value 0.05). Sixty patients out of 100 acute stroke patients presented with systemic hypertension in the study. Out of 34 deaths, 24 were hypertensive and 10 acute stroke patients were non hypertensive on admission. Logistic regression analysis failed to demonstrate significant association between death and hypertension adjusted OR 1.409 (95% CI 0.480 to 4.133, p value 0.53). Also there was no significant difference in functional outcome between hypertensive and non hypertensive acute stroke patients adjusted OR 1.701 (95% CI 0.405 to 7.140, p value 0.46). Hyperglycaemia was found in 25 patients out of 34 deaths which is significantly associated with death OR 5.944 (95% CI 2.174 to 16.240, p value .001). Among the survivors with hyperglycaemia, 13 patients had functional activity score towards dependent and 8 patients towards independent. Statistical analysis revealed hyperglycaemia not significantly influence the functional outcome adjusted OR 0.458 (95% CI 0.122 to 1.867, p value 0.276. Which indicate hyperglycaemia of acute stroke patients strongly influences death but not functional outcome. Our statistical analysis revealed that there is not enough evidence that smoking affects acute stroke outcome; the adjusted OR 0.898 (95% CI 0.306 to 2.633) and 1.620 (95% CI 0.317 to 8.271) (Table-III, Table-IV, Table-V and Table-VI).

Table-III: *Association with different confounding variable with fatal outcome of acute stroke patients at day 28 (n=100).*

Characteristics	Survival Status		OR	Adjusted OR (95% CI)
	Alive Number (%)	Dead Number (%)		
Age				1.025 (0.975 to 1.076)
Gender				
Male	51 (64.6)	28 (35.4)	1.37	–
Female	15 (71.4)	6 (28.6)		
Smoking status				
Smoker	47 (67.1)	23 (32.9)	0.85	0.898 (0.306 to 2.633)
Non-smoker	19 (63.3)	11 (36.7)		
Hypertension				
Present	36 (60)	24 (40)	2	1.409 (0.480 to 4.133)
Absent	30 (75)	10 (25)		
Hyperglycaemia*△				
Present	21 (45.7)	25 (54.3)	5.95	5.944 (2.174 to 16.24)
Absent	45 (83.3)	9 (16.7)		
Stroke severity*△				
Severe	49 (61.2)	31 (38.8)	3.59	4.153 (0.963 to 17.924)
Moderate	17 (85)	3 (15)		
Osmolarity				
Hyper	29 (58)	21 (42)	2.06	0.923 (0.338 to 2.523)
Normal	37 (74)	13 (26)		

* Obtained from chi-square test of association p value <0.05

△ Obtained from logistic regression p value <0.05

Table-IV: *The effects of multiple explanatory variables on functional outcome of acute stroke patients at day 28 (n=66).*

Characteristics	Functional Outcome		OR	Adjusted OR (95% CI)
	Independent Number (%)	Dependent Number (%)		
Age				1.190 (1.066 to1.328)
Gender			–	
Male	17 (33.3)	234 (66.7)	1	–
Female	5 (33.3)	10 (66.7)		
Smoking status				
Smoker	17 (36.2)	30 (63.8)	0.630	1.620 (0.317 to 8.271)
Non-smoker	5(26.3)	14(73.7)		
Hypertension				
Present	9(25)	27(75)	2.294	1.701 (0.405 to 7.140)
Absent	13(43.3)	17(56.7)		
Hyperglycaemia				
Present	9(42.9)	12(57.1)	0.541	0.458 (0.112 to 1.867)
Absent	13(28.9)	32(71.1)		
Stroke severity*				
Severe	12(24.5)	37(75.5)	4.404	4.326 (0.991 to 18.895)
Moderate	10(58.8)	7(41.2)		
Osmolarity				
Hyper	7(24.1)	22(75.9)	0.466	0.250 (0.054 to1.164)
Normal	15(40.5)	22(59.5)		

* $p \leq 0.05$ Obtained from logistic regression
n = Patient number

Table-V: *Association between age and survival status in the acute stroke patients at day 28 (n=100).*

Characteristics	Survival Status		t-statistic value	p value*
	Dead Mean±SD	Alive Mean±SD		
Age	64.44±8.88	61.61±10.35	1.36	0.18

* t-test for equality of two means was performed to obtain p value
p value<0.05 was taken as level of significance

Table-VI: *Association of age with the functional outcome of the acute stroke patients (n=66).*

Characteristics	Functional Outcome		t-statistic value	p value*
	Dependent (n=44) Mean±SD	Independent (n=22) Mean±SD		
Age	65.02±9.16	54.77±9.29	4.265	0.001

t-test for equality of two means was performed to obtain p value
p value <0.05 was taken as level of significance

DISCUSSION

Stroke is one of the most common causes of death and disability. Clinicians are often asked to predict outcome after stroke by the patient, family, other healthcare workers, and insurance providers. A wide variety of factors influence stroke outcome and dehydration is a common phenomenon after stroke, particularly in the elderly. With this background we evaluate the association between the presence of hyperosmolarity and outcome of acute stroke patients. In our study, age of the acute stroke patients was ranging from 40 years to 95 years, with the mean age of 62.57±9.92 years (Mean±standard deviation). The majority of the samples were males (79%) and most of the patients were in the age of 50 to 79 years. This result was supported by the study of Uddin MJ et al. where the mean age of ischemic stroke was 63.58±10.22 years and majority (80%) of the patients belonged to the age group 50 to 79 years and frequency of male and female was 72% and 28% respectively[18].

We observed total 34 deaths during our study period. Among them 21 death occurred in high plasma osmolarity group and 13 death in the normal osmolarity group. The effect of osmolarity on fatal outcome is not statistically significant, crude OR 2.06 (p value 0.09). This insignificant effect may be due to presence of confounding factors, such as stroke severity or hyperglycaemia. But osmolarity shows some evidence to be associated with survival status; this association is statistically significant at 10% level of significance. But in the logistic regression model, high plasma osmolarity failed to show any association with survival status of the acute stroke patients with adjusted OR 0.923 (95% CI 0.338 to 2.523, p value 0.87).

Bhalla et al. in his study worked with both calculated plasma osmolarity and measured osmolality, In their study, it was found that calculated osmolarity is not significantly associated with stroke mortality at 3 months, but measured high osmolality was significantly associated with fatal acute stroke outcome at 3 months. In another study O'Neill et al. found no significant differences in plasma osmolality between survivors and dead stroke patients, which support our study[7]. But our result was not supported by the study of Bhalla et al. and two other study Nag et al. and Rowat et al. They found that high plasma osmolality and dehydration associated with poor short term fatal outcome among the acute stroke patients[7,8,14]. It was difficult to say whether admission plasma osmolarity levels were a true indicator of hydration status on admission. As we used at least 4 variables (Sodium, potassium, urea, and glucose) to estimate plasma osmolarity, each with its own measurement error might contribute to the overall measurement error of the calculated plasma osmolarity.

Among the 66 survivor 21 were towards dependent and 8 patients were towards independent after 28 days in hyper osmolar group. Logistic regression analysis showed hyperosmolarity was not associated with poor functional outcome than that of normal osmolarity group. Bhalla et al. in his study found that admission plasma osmolality was significantly higher in patients who were dependent after their stroke and Rowat et al. found that dehydrated on admission with acute stroke were less likely to be independent in daily activities at 6 months than those who were not dehydrated which not supported by our study[7,14] short study period might be a cause of such outcome. Power of our study was less with small non randomized sample size and also direct measurement of plasma osmolality and urine osmolality were not done.

CONCLUSIONS

In this study we observed that raised plasma osmolarity has no influence on mortality and functional outcome of acute stroke. The study did not reject the null hypothesis, that raised plasma osmolarity had no significant effect on stroke outcome. But admission hyperglycaemia and stroke severity were significantly associated with poor outcome at 28 days in acute stroke patients. So randomized controlled study involving multicentre, large scale and long follow up period should be conducted in future for the prediction of short term as well as long term outcome of acute stroke.

REFERENCES

1. World Health Organization. The top 10 causes of death WHO, Fact sheet N°310. Geneva: World Health Organization; 2013.
2. 1st Global Conference on Healthy Lifestyles and Non-communicable Diseases Control. Moscow; 2011.
3. Islam MN, Moniruzzaman M, Khalil MI, Basri R, Alam MK, Loo KW, et al. Burden of stroke in Bangladesh. Int J Stroke 2013; 8(3): 211-3.
4. Feigin VL, Lawes CMM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 2009; 8(4): 355-69.
5. Directorate General of Health Services. Stroke Management Guideline. Dhaka: Directorate General 0f Health Services; 2008.

6. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane Database Syst Rev 2007; 17(4): CD000197.
7. Bhalla A, Sankaralingam S, Dundas R, Swaminathan R, Wolfe CD, Rudd AG. Influence of raised plasma osmolality on clinical outcome after acute stroke. Stroke 2000; 31(9): 2043-8.
8. Nag C, Das K, Ghosh M, Khandakar MR. Plasma osmolality in acute spontanious intra-cerebral hemorrhage: Does it influence hematoma volume and clinical outcome? J Res Med Sci 2012; 17(6): 548-51.
9. Jauch EC, Saver JL, Adams HP (Jr), Bruno A, Connors JJB, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013; 44(3): 870-947.
10. Rodriguez GJ, Cordina SM, Vazquez G, Suri MFK, Kirmani JF, Ezzeddine MA, et al. The hydration influence on the risk of stroke (THIRST) study. Neurocrit Care 2009; 10(2): 187-94.
11. Bhalla A, Wolfe CDA, Rudd AG. Management of acute physiological parameters after stroke. Q J Med 2001; 94(3): 167-72.
12. Allport LE, Parsons MW, Butcher KS, MacGregor L, Desmond PM, Tress BM, et al. Elevated hematocrit is associated with reduced reperfusion and tissue survival in acute stroke. Neurology 2005; 65(9): 1382-7.
13. Stookey JD. High prevalence of plasma hypertonicity among community-dwelling older adults: results from NHANES III. J Am Diet Assoc 2005; 105(8): 1231-9.
14. Rowat A, Graham C, Dennis M. Dehydration in hospital-admitted stroke patients: detection, frequency, and association. Stroke 2012; 43(3): 857-9.
15. Sarah EC, Dereck H, Klas M, Parbeen P, Hertzel CG. Stress, Hyperglycemia and Prognosis of Stroke in Nondiabetic and Diabetic Patients: A Systematic Overview. Stroke 2001; 32(10): 2426-32.
16. Willmot M, Leonardi-Bee J, Bath PMW. High blood pressure in acute stroke and subsequent outcome: a systematic review. Hypertension 2004; 43(1): 18-24.
17. Ovbiagele B, Weir CJ, Saver JL, Muir KW, Lees KR. Effect of smoking status on outcome after acute ischemic stroke. Cerebrovasc Dis 2006; 21(4): 260-5.
18. Uddin MJ , Mondol BA, Ahmed S, Ullah AKMA, Jabbar MA, Mohammad QD. Smoking and Ischemic Stroke. Bangladesh J Neurosci 2008; 24(1): 50-4.