EVALUATION OF IMPACT OF HYPERGLYCEMIA AND HYPONATREMIA ON CLINICAL OUTCOME OF ACUTE STROKE

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ABSTRACT

Hyponatremia and hyperglycemia are common metabolic disorders which could worsen the outcome after a cerebrovascular accident (stroke). This study aimed to evaluate the impact of hyponatremia and hyperglycemia on stroke and its clinical outcome, including morbidity and mortality.

This prospective cohort study included 50 stroke patients admitted in tertiary care hospitals. Stroke severity, Glasgow coma scale (GCS), conscious level, gag reflex, clinical presentations, and outcomes were recorded. Following a stroke, patients were monitored for a period of six months, during which the patient's death was recorded on the event form. Linear logistic regression model was used to determine the stroke mortality. Hyponatremia and hyperglycaemia were associated with higher odds ratio of deaths, poor functional recovery, severe disability, low mean GCS score as compared to normonatremic and normoglycemic patients (odds ratio [OR] = 4.7; 95% CI= 0.929-43.782) and hyperglycaemia (OR= 2.74; 95% CI=0.577-13.03). Stroke patients admitted with hyperglycemia or hyponatremia were associated with greater morbidity and mortality and poor functional recovery.

Key Words: Stroke, hyperglycemia, hyponatremia, Morbidity, mortality

INTRODUCTION

Cerebrovascular accident or stroke is the disruption of blood supply to the brain, which occur due to the clot formation or a hemorrhage (1). A continuous supply of blood, oxygen and glucose is required by nerves in the brain to function properly. If this supply is interrupted, brain function stops temporarily and if the interruption remains for prolonged time, then it causes permanent brain damage. Human body is controlled by the brain, so stroke patient could have symptoms depending on the affected part of the brain(2).

Each year 130,000 Americans die due to stroke, making it fifth prominent cause of death (3). Ischemic stroke constitute about 87% of the total reported cases of stroke (4). The risk of stroke rises with advancing age, however there is no known \youngest age limit. About 34% of patients were younger than 65years who were admitted to hospital with stroke in 2009 (5). Stroke could be caused by blocked artery (ischemic stroke) or may be due to bursting of blood vessel (haemorrhagic stroke)(5).

Hyponatremia and hyperglycemia are considered to be poor predictive elements of stroke(6, 7). In many neurological disorder i.e. meningitis, stroke, subarachnoid haemorrhage (SAH) and cerebral bleed, hyponatremia is a common electrolyte disorder(8). Hyponatremia increases mortality in patients with stroke(9). Tzoulis studied stroke patients and found a 17.3% increase in in-patient mortality rate in hyponatremic patients (10). In the prospective study carried out by Huang et al on 925 stroke patients, it was found that hyponatremic group had poor survival as compared to their normonatremic counterparts(11).

Hyperglycemia is also a risk factor of stroke, as diabetic patients are more likely to suffer from cerebrovascular accidents as compared to non-diabetic population. It has negative impact on brain tissues and is linked with poor outcomes(12). A previously reported included 416 stroke patients and showed significantly higher mortality in patients who were hyperglycaemic(13). Williams et al found that 40% of 656 acute stroke patients were hyperglycemic and concluded that hyperglycemia was an important indicator in worsening the clinical outcomes after acute stroke attack(14). A number of cases are reported of cerebrovascular accidents every year in Pakistan, however, there is limited data available regarding hyponatremia and hyperglycemia in stroke. In addition most of the reported studies explored serum sodium or glycemic level separately. This study was aimed to find out the effect of hyponatremia and hyperglycemia on clinical outcome of acute stroke in terms of morbidity and mortality.

METHODS

In this prospective cohort study, patients with primary diagnosis of stroke in emergency department of multiple public sector tertiary care hospitals based in Karachi, Pakistan were studied. Patients were diagnosed with symptoms and neuroimaging and was established by Magnetic Resonance Imaging (MRI) or else computed tomography (CT Scan). Demographic characteristics of patients such as height, patient's economic status, age, body mass index (B.M.I), gender, and weight were recorded. Moreover, patient's Glasgow coma scale (GCS), gag re-flex, conscious level, comorbidities and patient medication history were recorded.

Patients included in the study distributed in different groups accord-ing to their blood glucose and sodium levels. Groups included, normonatremic subjects with serum Na level of 135-145meq/L, hyponatremic subjects with serum Na level less than 136 mEq/L, hypernatremia with Na level >145meq/L. Glycaemic groups were classified as normoglycemic with fasting blood glucose level (FBGL) ranging from 90 to 126 mg/dL and hyperglycemic with FBGL of more than 126 mg/dL.

After their initial stroke event, patients were subsequently monitored for a further period of six months. The consultant neurologist evaluated all subjects and related information such as con-scious level, gag reflex, GCS score, sodium and glucose blood levels were recorded. Stroke sever-ity was determined by GCS score. Death of the patient was duly recorded on the form. GCS score 13-15 was considered as mild, 9-12 as moderate and below 8 as severe (5). Hypertension was considered if the blood pressure was more than 140/90mmHg. White blood cell(WBC) count above 11,000/ mm(5) were considered as leucocytosis. Patients in whom the stroke was caused by tumour, trauma, and intraventricular haemorrhage were excluded from the study. Pregnant women and referred stroke patients were also excluded.

Statistical Methods

Statistical package for social sciences (SPSS version 20.0) was used for data analysis. T-test was used to link the mean and Standard Deviation (±SD) of continuous variables among groups. Stroke mortality

was assessed by using liner logistic regression test method. A p-value of less than 0.05 was considered significant for hypothesis testing

RESULTS

A total of 48 stroke patients were included in the study, where 47.9% were females, average age of subjects was 49±14year (the youngest patients was of 32years and the oldest was of 85years). Mean weight of the patients was 62±7 kg. 40 patients (83.3%) suffered from ischemic stroke. The mean random blood glucose level on admission was 162±48 (90-242). Out of total patients, 16 (33.3%) patients had hyperglycemia and 32 (66.7%) patients had normoglycemia. The mean ad-mission sodium level was 136±7 (range, 119-153). We found hyponatremia in 10 (20.8%) patients and 36 (75%) patients had nor-monatremia. Hypernatremia was observed in two (4.2%) stroke pa-tients.

Out of 48 patients, 10 patients (21.3%) died. An improvement was seen in 10 patients (27%), where-as 2 patients (5.4%) showed worsening in their symptoms. Hyponatremia and hyperglycaemia in-creased stroke mortality because deceased stroke patients showed low mean sodium levels (133±8) also high random serum blood glucose levels (190±39) as related to those acute stroke pa-tients who survived. Mean GCS score was lowered in deceased stroke patients as compared to survivors. (Table 1)

Table 1. Comparison of Patient Demographic Characteristics, Clinical Outcome and Risk Factors among Survivors and Deceased Acute Stroke Patients

	Full sample n=48	**Survivors n=38 (78.7%)**	**Deceased n=10 (21.3%)**
Age (Years)			
mean ± SD	49±14	46±10	59±20
Gender			
Female	23 (47.91%)	17 (44.70%)	6 (60%)
Male	25 (52.11%)	21 (55.3%)	4 (40%)
Economic Status			
Low	27(56%)	24 (63.1%)	4 (40%)
Middle	20(41.6%)	13 (34.2%)	6 (60%)
High	1(2%)	1 (2.6%)	0
Weight (kg)			
mean ± SD	62±7	62±6.5	61±9
Height (cm)			
mean ± SD	167±9	168±9	167±10
Stroke Sub-type			
Ischemic	40 (83.3%)	33 (86.8%)	7 (70%)
Haemorrhagic	8 (16.7%)	5 (13.2%)	3 (30%)
Co-morbidities			
Hypertension (HT)	30 (66.7%)	27 (71%)	4 (40%)
Diabetes (DM)	5 (11.1%)	5 (13.1%)	2 (20%)
HT and DM	8 (17.8%)	5 (13.1%)	3 (30%)
HT and CKD	2 (4.4%)	1 (2.6%)	1 (10%)
Blood Pressure (BP)			
***SBP (mm Hg)**	155±21	160±17	134.5±25
***DBP (mm Hg)**	91±10	93±9	82.5±9

Sodium levels mEq/L			
Mean ± SD	136±6.8	137±6.3	133±8
Hyponatremia	10 (20.8%)	5 (13.2%)	5 (50%)
Normonatremia	36 (75%)	33 (86.8%)	5 (50%)
Glucose Levels mg/dl			
***RBGL**	162±48	159±48	190±39
***FBGL**	106±25	102±15	109±29
Normoglycemia	32 (66.7%)	28 (73.6%)	4 (40%)
Hyperglycemia	16 (33.3%)	10 (26.4%)	6 (60%)
GCS			
Mean ± SD	12±2	13±2	10±3
Mild	28 (58.3%)	25 (65.7%)	3 (30%)
Moderate	18 (37.5%)	13 (34.3%)	5 (50%)
Severe	2 (4.2%)	-	2 (20%)
Conscious Level			
Oriented	26 (54.2%)	22 (57.8%)	4 (40%)
Altered	22 (45.8%)	16 (42.2%)	6 (60%)

SBP= Systolic blood pressure, DBP= Diastolic blood pressure, RBGL= Random blood glucose level, FBGL= Fasting blood glucose level

In this study, normonatremia was observed in 86% stroke survivor patients and in 50% who died, whereas 73.6% patients were normoglycemic who survived acute stroke attack whereas 60% de-ceased subjects were normoglycemic. Amongst 38 survivor's patient, we have found hyponatremia in 5 patients (13.2%), hyperglycaemia in 10 (26.4%) and hypernatremia in 2 (5.4%) patients. In 10 deceased patients, hyponatremia was seen in 5 (50%) patients and hyperglycaemia in 6 (60%) patients. A summary of the data is presented in Table 2.

Table 2. Occurrence of Blood Glucose and Sodium Concentrations in Survivors and Deceased Stroke Patients

	Hyponatremia (n) (%)	**Normonatremia (n) (%)**	**Hypernatremia (n) (%)**	**Total (n) (%)**
		Survivors		
Normoglycemia	2 (5.40%)	24 (62.10%)	2 (5.40%)	28 (73.6%)
Hyperglycemia	3 (8.11%)	7 (18.92%)	-	10 (27.1%)
Total	5 (13.5%)	31 (81%)	2 (5.4%)	38 (100%)
		Deceased		
Normoglycemia	2 (20%)	2 (20%)	-	4 (40%)
Hyperglycemia	3 (30%)	3 (30%)	-	6 (60%)
Total	5 (50%)	5 (50%)	-	10 (100%)

DISCUSSION

Stroke causes long-term debility and important reason of death in humans(15). Many studies have reported the relation of hyponatremia and hyperglycemia on stroke morbidity and mortality, but all included only single variable, which is either hyperglycemia or hyponatremia. The present study is distinctive in this regard, as it encompassed both hyperglycemia and hyponatremia in the same situation and finding out their influence on stroke morbidity and mortality. Linear logistic regression test is used to determine the morbidity and mortality in stroke patients. Hyponatremia and hyperglycemia are metabolic abnormalities that have negative impact in stroke patients (16) and both are considered as a threat reason of stroke(17). Kostulas et al and Rodrigues et al found that hyponatremia and hyperglycemia is related to increased stroke morality and deaths(13, 16). Various researches have shown that hyponatremia has adverse outcomes(18). In neurological patients, sodium imbalance are reported to be more common(19).

Hyperglycemia is also considered as a risk factor of stroke. It has been learnt from a 15year cohort study that those patients who has diabetes, they have increased chances of ischemic stroke attack as compared to those patients who did not have diabetes(20). The patients whose blood glucose levels were more then 6.1-7.0 mm/L on admission were associated with poor functional outcomes and increased risk of 30 days mortality(21). Apoptotic ability was lower in hyperglycaemic patients as compared to normoglycemic patients. Neutrophil accumulation result due to lower apoptotic ability and increased cell proliferation. Free radical, proteolytic enzyme and other harmful substances released due to the neutrophil accumulation. This damages the blood vessels and increases cellular permeability. Damage to the blood brain barrier could also occur due to which cerebral oedema can occur(22). Patients who were hyponatremic and hyperglycemic showed lower survival. There is increased morbidity and mortality in patients who had hyponatremia and hyperglycemia when they were admitted(23). Patients who were hyponatremic or hyperglycaemic have poor gag reflex, low mean GCS score, altered conscious level and poor functional recovery as compared to normonatremic and hyperglycaemic patients. Haemorrhagic stroke was more prevalent in patients who has hyperglycaemia on admission. Higher odd of death occurred to the patients who has hyponatremia or hyperglycaemia. The limitation of the study is small sample size. The true impact of hyponatremia or hyperglycaemia on patient mortality can be determine by large sample.

CONCLUSION

Stroke patients who were admitted with hyponatremia or hyperglycaemia, had poor clinical out-comes and were associated with increased morbidity and mortality. Improving blood glucose and sodium levels have positive outcomes in stroke patients GCS score, gag reflex and symptoms improve after correcting the glucose and sodium levels. Further large scale studies are required on the subject.

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