Section: General Medicine

Original Research Article

SERUM ELECTROLYTES IN ACUTE STROKE AND THEIR CORRELATION WITH SEVERITY OF STROKE AS WELL AS SHORT TERM CLINICAL OUTCOMES - A THREE MONTH FOLLOW UP STUDY

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ABSTRACT

Background: Stroke, world's second-most common cause of morbidity, is a devastating illness in itself. When complicated metabolic issues, the outcomes in stroke begin to significantly differ. One such important metabolic derangement is electrolyte imbalance, an important coexisting finding seen in stroke patients. Our study focusses on serum electrolyte levels in acute stroke, and their correlation with stroke severity as well as clinical outcomes in acute stroke patients.

Materials and Methods: The present study was a hospital based prospective observational study and was carried out on 110 patients presenting with symptoms of Acute Stroke from March 2021- July 2022. The patients were followed up for a period of 3 months after getting discharged from the hospital; lost to follow up were contacted telephonically. Serum electrolyte levels were measured at the time of admission. Estimation of Severity of stroke was done using National Institute of Health Stroke Scale (NIHSS) and Clinical outcome of the study was analysed according to data collected.

Results: Hemorrhagic stroke was seen 31.8% and ischemic stroke was seen in 68.2%. 15 subjects (13.6%) showed hyponatremia while 34 subjects (30.9%) had hypernatremia and the remaining 61 subjects (58.5%) had normal sodium levels. Hypernatremia was more common in hemorrhagic stroke (37%) than in ischemic stroke (28%). 29 subjects (26.4%) showed hypokalaemia while 7 subjects (6.4%) had hyperkalaemia and the remaining 74 subjects (67.2%) had normal potassium levels. Hypokalemia was more common in hemorrhagic stroke (42.9%) than ischemic stroke (18.7%). 4 subjects (3.6%) showed hypochloraemia while 38 subjects (34.6%) had hyperchloremia and the remaining 68 subjects (61.8%) had normal chloride levels. Hyperchloremia was seen in both ischemic (25 subjects out of 75, 33.3%) and hemorrhagic stroke (13 subjects out of 35, 37.1%). Electrolyte imbalances overall were found to be unrelated to stroke severity or outcomes at 3 months and the difference was not statistically significant. A higher number of patients with sodium imbalance expired (7 out of 15 i.e 46.6% in the hyponatremia group, 13 out of 34 ie 38.2 % in hypernatremia group; compared to 16 out of 61 i.e 26.2 % in the normal sodium group); this difference though did not show a statistical significance.

Conclusion: Electrolyte disturbance is a frequently encountered problem in acute stroke patients, particularly those with a brain stem stroke. The incidence of electrolyte derangements in acute stroke patients appears to be high and, on the other hand, severe stroke cases are found to have the highest rates of dysnatremia, dyskalemia and dyschloremia. Presence of sodium imbalance was found to be related to a higher mortality in stroke patients, though this

difference failed to achieve a statistical significance. Moreover, the overall outcomes in the surviving patients were unchanged at three months. Hypernatremia and hypokalemia were more common in hemorrhagic stroke (37%, 42.9%) as compared to ischemic stroke (28%,18.7). The problem necessitates rapid detection of electrolyte imbalance and their careful monitoring, as it may closely affect the short-term prognosis and mortality.
Keywords: Acute stroke, hypernatremia, hyponatremia, hyperkalemia, hypokalemia.

INTRODUCTION

Stroke, world's second most common cause of morbidity, is a devastating illness in itself and when complicated with metabolic issues, the outcomes in stroke begin to significantly differ. Electrolyte imbalance is an important coexisting metabolic derangement in stroke.

WHO defines stroke as "rapidly developing clinical signs of focal disturbance of cerebral function; lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin".[1] In 2013 AHA/ASA Expert Consensus Document gave an updated definition of ischemic stroke.[2] According to this term, ischemic stroke should be used to include any infarct in brain/ spinal cord which is due to ischemia, based on pathology or radiological imaging, or any other objective evidence of cerebral or spinal cord ischemic injury in a defined vascular distribution; or clinical evidence of cerebral, spinal cord ischemic injury based on symptoms staying ≥24 hours or until death, and other causes excluded. Ischemic stroke being more common than the hemorrhagic stroke, accounts for 80-85% of all the stroke cases.

Stroke is a major burden of morbidity and mortality, being the third leading cause of mortality in developed countries after coronary heart disease and cancer.[3] It has been projected that by the year 2020, stroke will be the second leading cause of death and disability in developed regions of the world.[4] Stroke patients are at higher risk of death in first week after the event and between 20-50 percent die within first month, depending on the type, severity, age, comorbidity and effectiveness of the treatment and complications.

Patients of acute stroke frequently are found to have sodium and water disturbances, which affect 50% of cases.[5,6] These illnesses are linked to longer hospital stays, higher rates of morbidity and mortality, and a wide range of clinical signs and symptoms.[7,8] The pathophysiology is not clearly understood, and treating these people well is difficult and frequently not at their best. The methodological rigour of local guidance materials on the assessment and treatment varies at the moment because there are no agreed-upon standards. Furthermore, there is a lack of consistency in management recommendations, leading to a variety of institution-based rather than patient-specific, evidence-based approaches to the therapy of these illnesses.[9]

MATERIALS AND METHODS

Study Design

This was a prospective observational study. The study was conducted in a tertiary care hospital in rural India. 110 patients with newly diagnosed acute stroke admitted at Hospital were considered for study. The patients were briefed about the nature of study, and written informed consent was obtained from them.

Sample Size Calculation

Outcome parameter: Proportion of acute stroke patients with serum electrolyte disturbance

For estimation of sample size, the following formula has been used, n =[Zα 2 P Q]/d2

Where; Zα = Value of standard normal variate corresponding to α level of significance

P = Likely value of parameter, Q = 1 – P, d = Margin of errors which is a measure of precision

Assumptions:

P = Proportion of acute stroke patients with serum electrolyte disturbance = 33%

(Sodium disturbance = 37.0% & Potassium disturbance = 33.0%) 10

Zα = 1.96 (Corresponding to 95% confidence interval), Precision (d) = ± 10%

Under these assumptions the sample size works out as 84. Assuming the lost to follow-up up to 20%, a minimum sample size of 100 suggested.

Inclusion Criteria

1. Age > 18 years
2. Newly diagnosed cases of stroke (according to WHO definition) admitted within 72 hours of onset of symptoms.
3. Confirmed cases of acute stroke on clinical findings or radiologically, on CT head/MRI brain

Exclusion Criteria

1. TIA (Transient ischemic attacks)
2. Patients with previous stroke
3. Taking steroids / diuretics
4. Diarrhoea
5. Chronic kidney disease (CKD) / Renal Failure
6. RTA (Renal tubular acidosis)

Follow Up Period

The patients were followed up for a period of 3 months after getting discharged from the hospital, lost to follow up were contacted telephonically.

Stroke Severity Scale

National Institute of Health Stroke Scale (NIHSS),[11-13]

The NIHSS is a neurologic assessment stroke scale used to assess consciousness, visual-field loss, extraocular movement, language, neglect, sensory loss, motor strength, dysarthria, and ataxia following an acute cerebral infarction. The patent's capacity to answer questions and conduct activities is evaluated by a professional observer. Each item is rated on a 3- to 5-point scale, with 0 being the lowest score, and untestable objects are allowed. The scale runs from 0 to 42, with higher ratings indicating more seriousness. It takes less than 10 minutes to complete a single patient assessment. NIHSS is used to rate the severity of ischemic strokes. This score when assessed within first 48 hours following stroke, have been shown to correlate with clinical outcomes at the 3 month and 1-year mark. A high score signifies a worse clinical state.

Stroke severity is divided into five groups:[14]

No stroke symptom (0), Minor stroke (1-4), Moderate stroke (5-15)

Moderate -Severe stroke (16-20), Severe stroke (21-42)

The capacity of the observer to accurately and consistently assess the patient is critical in determining the severity of a stroke. NIHSS can also predict the outcome for patients with primary intracerebral hemorrahge. 15,16

Statistical Analysis

The analysis included profiling of patients on different demographic, clinical and laboratory, parameters. Descriptive analysis of quantitative parameters was expressed as means and standard deviation. Categorical data was expressed as absolute number and percentage. Independent Student t – test was used for testing of mean between independent groups whereas Paired Student t – test was used for paired observation. Cross tables were generated, and Chi square test was used for testing of associations. P-value < 0.05 was considered statistically significant. All analysis was done using SPSS software, version 24.0.

RESULTS

Majority of subjects (65.5%) were above 50 years of age. Both hemorrhagic and ischemic strokes were common in above 60 years of age and were more commonly seen in males as compared to females. M:F ratio was 1.75:1. Hypertension was seen in 90 subjects whereas diabetes mellitus was present in 36 subjects. History of alcohol use was seen in 41 subjects whereas smoking history was present in 30 subjects. Diabetes and smoking were more common in patients with ischemic stroke and this difference was statistically significant ($p<0.05$).

32 subjects required ventilator assistance. 16 subjects each from hemorrhagic and ischemic stroke had to be ventilated while 59 subjects of ischemic stroke and 19 subjects of hemorrhagic stroke did not require ventilatory support. This difference was statistically significant ($p<0.05$). Motor weakness was the most common presentation seen in 108 subjects followed by facial asymmetry (55 subjects), gaze palsy (25 subjects), ataxia (9 subjects) and bulbar weakness (7 subjects). Facial asymmetry and gaze palsy were more common in patients with ischemic stroke and both were statistically significant ($p<0.05$). [Table 1]

15 subjects showed hyponatremia while 34 subjects had hypernatremia and the remaining 61 subjects had normal sodium levels. Hypernatremia was more common in hemorrhagic stroke (37%) than in ischemic stroke (28%).

29 subjects showed hypokalaemia while 7 subjects had hyperkalaemia and the remaining 74 subjects had normal potassium levels. Hypokalemia was more common in hemorrhagic stroke (42.9%) than ischemic stroke (18.7%) and there was statistically significant difference seen between the groups ($p<0.05$).

4 subjects showed hypochloraemia while 38 subjects had hyperchloremia and the remaining 68 subjects had normal chloride levels. Hyperchloremia was seen in both ischemic (33.3%) and hemorrhagic stroke (37.1%). [Table 2]

The above table shows distribution of subjects based on stroke severity at admission with serum electrolyte levels. In 34 subjects with hypernatremia, 13 had severe stroke, 13 had moderate stroke, 7 had moderate – severe stroke and 1 had minor stroke. Out of 15 hyponatremia subjects, 6 had severe stroke, 3 had moderate – severe stroke, 5 had moderate stroke and 1 had minor stroke. In 29 subjects with hypokalemia, 12 had severe stroke, 12 had moderate stroke, 4 had moderate – severe stroke and 1 had minor stroke. In 38 subjects with hyperchloremia, 15 had severe stroke, 12 had moderate stroke, 9 had moderate – severe stroke and 2 had minor stroke. Patients with NIHSS score >16 (moderate- severe and severe stroke) had higher rate of hypernatremia, hypokalemia and hyperchloremia but ,there was no statistically significant difference between the groups. [Table 3]

Out of 61 subjects with normal serum sodium levels – 33 (54.1%) patients clinically improved,16 (26.2%) expired, 4 (6.6%) worsened and 1 (1.6%) remained constant. Whereas in 34 hypernatremia subjects – 15 (44.1%) subjects improved clinically, 13 (38.2%) expired and out of 15 hyponatremia subjects 6 (40%) improved clinically,7 (46.6%) expired, 1 (6.7%) worsened and 1 (6.7%) remained constant. In74 subjects with normal serum potassium levels - 37 (50%) improved clinically, 26 (35.1%) expired and 2 (2.7%) worsened. Whereas in 29 hypokalemic subjects -13 (44.8%) improved, 9 (31%) expired, 3 (10.3%) worsened and 1 (3.4%) remained constant and in 7 hyperkalemic subjects - 4 (57.1%) improved and 1 (14.3%) expired &1 (14.3%) remained constant. In 68 subjects with normal serum chloride levels - 33 (48.5%) improved clinically, 19 (27.9%) expired, 5 (7.4%) worsened, 1 (1.5%) remained constant. Whereas in 38

hyperchloremic subjects - 18 (47.4%) improved clinically, 16 (42.4%) expired and 1 (2.6%) remained constant and in 4 hypochloremic subjects 3 (75%) improved clinically and 1 (25%) expired. There was no statistically significant difference between the groups. [Table 4]

Table 1: Demographic and Clinical Characteristics of study participants

Characteristics	Hemorrhagic stroke (n=35)	Ischemic stroke (n=75)	Total (n=110)	p-value
Age (in years)				
< 40	6	5	11	0.397
41-50	8	19	27	
51-60	8	21	29	
> 60	13	30	43	
Gender				
Female	12	28	40	0.464
Male	23	47	70	
Personal History				
Hypertension	31	59	90	0.162
Diabetes Mellitus	5	31	36	0.004
Alcohol Association	9	32	41	0.065
Smoker	3	27	30	0.002
VENTILATOR				
NO	19	59	78	0.008
YES	16	16	32	
Clinical Signs				
Motor Weakness	35	73	108	0.463
Facial Asymmetry	13	42	55	0.05
Bulbar Weakness	0	7	7	0.062
Gaze Palsy	1	24	25	<0.001
Ataxia	1	8	9	0.154

Table 2: Electrolyte levels of study participants

Electrolyte (mEq/L)	Hemorrhagic stroke (n=35)	Ischemic stroke (n=75)	Total (n=110)	p-value
Na Level				
Hyponatremia (<135)	6	9	15	0.37
Normal (135-145)	16	45	61	
Hypernatremia (>145)	13	21	34	
K levels				
Hypokalemia (<3.5)	15	14	29	0.023
Normal (3.5-5.5)	19	55	74	
Hyperkalemia (>5.5)	1	6	7	
Cl levels				
Hypochloremia (<96)	1	3	4	0.899
Normal (96-106)	21	47	68	
Hyperchloremia(>106)	13	25	38	

Table 3: Distribution of study participants according to Stroke Severity - Admission (NIHSS) with serum electrolyte levels

Stroke Severity - Admission (NIHSS)	Na levels			p-value	K levels			p-value	Cl levels			p-value
	Hypo	Normal	Hyper		Hypo	Normal	Hyper		Hypo	Normal	Hyper	
MINOR (5)	1	3	1	0.724	1	3	1	0.289	1	2	2	0.205
MODERATE (47)	5	29	13		12	32	3		2	33	12	
MODERATE-SEVERE (25)	3	15	7		4	18	3		0	16	9	
SEVERE (33)	6	14	13		12	21	0		1	17	15	
Total	**15**	**61**	**34**		**29**	**74**	**7**		**4**	**68**	**38**	

Table 4: Distribution of study participants according to Clinical Outcome at 3 months with electrolyte levels

Clinical Outcome	Na levels			p-value	K levels			p-value	Cl levels			p-value
	Hypo	Normal	Hyper		Hypo	Normal	Hyper		Hypo	Normal	Hyper	
CONSTANT (2)	1	1	0	0.245	1	0	1	0.153	0	1	1	0.544
EXPIRED (36)	7	16	13		9	26	1		1	19	16	
IMPROVED (54)	6	33	15		13	37	4		3	33	18	
LOST TO FOLLOW UP (13)	0	7	6		3	9	1		0	10	3	

WORSENED (5)	1	4	0		3	2	0		0	5	0	
Total	15	61	34		29	74	7		4	68	38	

DISCUSSION

The present study was a hospital based prospective observational study and was carried out on 110 patients presenting with symptoms of Acute Stroke.

In our study, 65.5% of subjects were above 50 years of age. Majority of subjects (63.6%) were male while 26.4% were females with M:F ratio was 1.75:1.There was no statistically significant difference for age and gender. Wissam et al. (2018) 17 studied 50 stroke patients in which 30% were females and 70% males similar to our study and age ranged from 40 to 80 years of age as in our study. Mansoor et al (2021),[18] Saha et al. (2021),[19] Mohan Kumar et al. (2020),[20] Kabir et al (2022),[21] also had similar age and gender distribution as in our study.

In our study hemorrhagic stroke was seen in 35 subjects (31.8%) and ischemic stroke was seen in 75 subjects (68.2%). In a study by Wissam et al. (2018),[17] 20% of the patients experienced hemorrhagic stroke, while 80% of the patients had ischemic stroke. Mansoor et al (2021),[18] in his study on 300 patients with stroke reported 46.3% subjects with ischemic stroke and 53.7% subjects with hemorrhagic stroke.

In our study, 15 subjects (13.6%) (6 hemorrhagic, 9 ischemic) showed hyponatremia while 34 subjects (30.9%) (13 hemorrhagic, 21 ischemic) had hypernatremia and the remaining 61 subjects (58.5%) (16 hemorrhagic, 45 ischemic) had normal sodium levels. Hypernatremia was more common in hemorrhagic stroke (37%) than in ischemic stroke (28%).[29] subjects (26.4%) (15 hemorrhagic, 14 ischemic) showed hypokalaemia while 7 subjects (6.4%) (1 hemorrhagic, 6 ischemic) had hyperkalaemia and the remaining 74 subjects (67.2%) (19 hemorrhagic, 55 ischemic) had normal potassium levels. Hypokalemia was more common in hemorrhagic stroke (42.9%) than ischemic stroke (18.7%) and there was statistically significant difference seen between the groups ($p<0.05$). 4 subjects (3.6%) (1 hemorrhagic, 3 ischemic) showed hypochloraemia while 38 subjects (34.6%) (13 hemorrhagic, 25 ischemic) had hyperchloremia and the remaining 68 subjects (61.8%) (21 hemorrhagic, 47 ischemic) had normal chloride levels. Wissam et al. (2018),[17] showed that electrolyte disturbances were quite common after acute stroke; hyponatraemia and hypokalaemia being the most common abnormalities in both ischaemic and haemorrhagic stroke patients. Ahmed et al (2020),[22] reported hypokalemia more common in brain infarction as compared to the hemorrhagic stroke. Setyawati et al (2020),[23] however concluded that hypokalemia was higher in hemorrhagic stroke. In another study of 50 patients by Mohan Kumar et al (2020),[20] including 64% (32) men, and 36% (18) women, the majority (52% of 26) of the strokes were ischemic, followed by intracerebral hemorrhagic stroke (46% of 26) and subarachnoid hemorrhagic stroke (2% of 1) in that order. Among patients with hemorrhagic stroke 66.6% (16) had dyselectrolytemia and 33.4% (8) had normal electrolytes and among patients with ischemic stroke 46.2% (12) had dyselectrolytemia and 53.8% (14) had normal electrolytes. So, the most frequent electrolyte imbalances in both ischemic and hemorrhagic stroke are hyponatremia and hypokalemia.

Patients with cerebrovascular accidents (CVA) often have increased renal excretion of various cations which contribute to serum electrolyte imbalance. 24 The other postulated mechanism for sodium imbalances in stroke include area postrema syndrome and vomiting as well as poor oral intake as a part of the stroke syndrome. Are postrema is a circumventricular organ in dorsal medulla, which is characterized by capillary meshwork with no blood brain barrier. It contains CTZ receptors which trigger vomiting when activated. Patients with area postrema syndrome (APS) due to ischemic stroke present with intractable nausea, vomiting and hiccups. Due to continuous vomiting, there is loss of water and electrolyte imbalance leading to hypokalemia and hyponatremia. Apart from this, hyponatraemia resulting from inappropriate secretion of antidiuretic hormone (ADH), increase in Brain Natriuretic-peptide (BNP), Atrial Natriuretic peptide and inappropriate fluid intake and loss - all can lead to severe electrolyte imbalance, and to dreadful complications like seizures and may contribute to mortality unless corrected urgently.[25,26]

Our study showed that stroke and hyponatremia coexist, occurring in 13.6% of stroke patients. In the study by Gray et al (2014),[27] 24% of patients with stroke experienced hyponatraemia during their hospital stay, whereas in the study by Kuramatsu et al (2014),[28] 15.3% of patients had both stroke and concurrent hyponatraemia. Shima et al. (2020),[8] in his meta-analysis reported hyponatremia prevalence in stroke patients from 7.0 to 59.2%. Kabir et al (2022),[21] reported hyponatremia in 25% of study subjects out of 80 study subjects while hyponatremia was detected in 34.2% of patients by Ehtesham et al (2019).[6] Mahesar et al (2019),[29] in his study on 132 patients showed that the majority of the patients (25%) had mild hyponatremia (130-134 mMol/L), only a few (9.8%) had moderate (125-129 mMol/L) or profound (<125) hyponatremia (3.8%).

A study by Wafaa MA et al (2018) 30 found that the incidence of dysnatremia, dyskalemia, and dysmagnesemia were highest in patients with severe CVS (NIHSS >15), and there was a significant correlation between dysnatremia and the severity of the stroke ($p=0.006$), similary in our study patients

with NIHSS > 16 (moderate – severe and severe stroke) had the highest rate of hypernatremia, hypokalemia, hyperchloremia but this difference was not statistically significant.

In order to evaluate the short term hospital prognosis of ischemic stroke patients presenting with hyponatremia, Saha et al (2021),[19] undertook an observational prospective analysis. Patients with hyponatremia had mean mRS scores that were substantially higher than those with normonatremia at both the time of admission (4.16 vs. 3.74) and the time of discharge (3.56 vs. 3.04). The disability rate between the hyponatremia group and the normonatremia group (81.8% vs. 72.9%) did not differ significantly. Despite the fact that the mortality rate in the hyponatremia group was higher (12.0%) than in the normonatremia group (4%) ($p>0.05$), the difference was not statistically significant, similarly in our study electrolyte imbalances overall were found to be unrelated to stroke severity or outcomes at 3 months, except that a higher number of patients with sodium imbalance expired (7 out of 15 i.e. 46.6% in the hyponatremia group, 13 out of 34 i.e. 38.2 % in hypernatremia group ; compared to 16 out of 61 i.e. 26.2 % in the normal sodium group). However, this difference in clinical outcomes in dyselectrolytic patients again did not show any statistical significance.

In various other studies, a significant increase in mortality was seen in the stroke population among patients who had hyponatremia upon hospital admission as opposed to those who had normonatremia.[31–33]

In addition, according to a research by Soiza et al,[31] patients hospitalised owing to ischemic or haemorrhagic stroke, hyponatremia in acute stroke admissions is independently related to greater mortality in patients under 75 years of age; thus confounding factors above 75 years age notwithstanding.

CONCLUSION

Electrolyte imbalances are common in acute stroke. This study show that hypernatremia is more common than hyponatremia. The mortality was observed to be higher in hypernatremia group than normonatremia group of stroke patients. Hypokalemia was more common than hyperkalemia but there was no difference in 3 months outcome. Further study with larger group of cohort is required to find out whether correlation of electrolyte imbalance improves the outcome in stroke patients.

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