HYPONATREMIA IN STROKE PATIENTS AND ITS ASSOCIATION WITH EARLY MORTALITY

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ABSTRACT: BACKGROUND: Hyponatremia is an important cause of mortality and morbidity in cerebrovascular accident (CVA). Timely treatment is very effective and can decrease mortality significantly. However, studies showing the extent of dyselectrolytaemia in CVA patients are rare from India. **MATERIALS AND METHODS:** We studied the serum sodium levels in CVA patients, after proper exclusion of confounding factors like renal failure and infection. The measurements were done on days 1 of admission. The data was then analysed for any correlation with mortality. Logistic regression analysis was also performed with mortality as dependent variable. **RESULTS:** We had 224 patients in our study, with 65% having cerebral infarction. Maximum number of patients was in the 51–70 year age group. We found hyponatremia in 54% of cases at presentation. Hyponatremia was significantly linked to mortality by regression analysis. There was no statistical difference between haemorrhage and infarct cases in terms of dyselectrolytaemia. **DISCUSSION AND CONCLUSION:** This observational study found hyponatraemia as a significant factor in CVA mortality. Treatment of this hyponatremia is essential to prevent further complications. Further randomised trials are needed to delineate the cause, treatment and prognosis of electrolyte disturbances in CVA patients.

KEYWORDS: Cerebrovascular accident, Hyponatremia, Serum sodium.

INTRODUCTION: Cerebrovascular accident (CVA) or 'Stroke' is the third leading cause of death and a major cause of disability. World Health Organization [WHO] defines Stroke as a clinical syndrome consisting of 'rapidly developing clinical signs of focal (at times global) disturbances of cerebral function, lasting more than 24hrs or leading to death with no apparent cause other than that of vascular origin'.¹

Stroke is the third leading cause of death and a major cause of disability in the United States. Cerebral infarction is the most common type of stroke in developed countries, making up more than 70% of cases. Intracerebral haemorrhages account for approximately 10% to 15% of strokes, and SAHs make up less than 5%, while the remainder are of undetermined etiology.²

Approximately 1.44-1.64 million new cases of strokes are reported every year in india.³ CVA or strokes are capable of causing crippling morbidity in young as well as elderly individuals. It also has marked social, psychological and economic implications. 6,398,000 DALYs are lost due to stroke in India.³ Due to its wide prevalence and its high cost in economic terms as well as human disability, cerebrovascular accidents have evoked much interest in medical fraternity.

Sodium is the chief cat ion of the extracellular fluid. About 50% of body sodium is present in the bones, 40% in the extracellular fluid and the remaining (10%) in the soft tissue.⁴ Sodium in association with chloride and bicarbonate, regulates the body's acid-base balance, maintains osmotic pressure and fluid balance. It is necessary for the normal muscle irritability and cell permeability and is involved in the intestinal absorption of glucose, galactose and amino acids. Its deficiency state is known as hyponatremia where its serum concentration falls below 135mEq/L.

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In general, there are no large prospective randomized controlled trials investigating the clinical impact of hyponatremia in stroke. For neurointensive care patients, only few studies are available focussing on postoperative neurosurgical patients, traumatic brain injury, and subarachnoid haemorrhage supporting the associations of hyponatremia with increased mortality, longer hospital stay, and raised complications.⁵⁻⁷

For ischemic or hemorrhagic stroke (Intracerebral hemorrhage, ICH), there is very scarce data available in literature. This study is the first to investigate the relative incidence of hyponatremia in ischemic and hemorrhagic stroke patients and to find its association with early (30 day) mortality.

AIMS AND OBJECTIVES:

1. To find out the incidence of hyponatremia in stroke patients.
2. Relative incidence of hyponatremia in ischemic and hemorrhagic stroke patients.
3. Association of hyponatremia with early mortality (30 days) in stroke patients.

MATERIALS AND METHODS: The study is designed to determine the incidence of hyponatremia in stroke patients (both in ischemic and hemorrhagic stroke patients) and to find out its association with early (30 days) mortality.

Method of Sample Collection: 224 patients admitted in Department of General Medicine Hamidia Hospital Bhopal, who fulfilled the inclusion/exclusion criteria, were enrolled in this study.

Inclusion Criteria:

1. Ischemic and hemorrhagic stroke diagnosed on clinical/radiological basis.
2. Patients directly reporting to Hamidia Hospital Bhopal.

Exclusion Criteria:

1. Previous stroke/ uncertain stroke patients.
2. Patients referred from primary/secondary health centers following first aid.
3. Patients reporting after 3 days of onset of symptoms
4. Patients with serious co-morbidities such as pulmonary or endocrine disease, hepatic failure, renal failure with dialysis.
5. Patients who use diuretics before the stroke attack.
6. Patients with uncertain clinical diagnosis and non-reassuring imaging.
7. Transient ischemic attack patients.
8. Patients having random blood sugar more than 300 mg%.
9. Patients with serum triglycerides more than 300 mg%.

Informed consent was taken from attendants of all the patients. Patients fulfilling inclusion criteria were subjected to history, clinical examination, biochemical investigations, ECG and chest X-ray.

Venous blood sample for serum sodium were obtained at the time of admission along with which blood sample was taken for other biochemical investigations. Serum sodium was estimated with fully automated analysers using ion specific electrode method. Hyponatremia was defined as serum sodium below 135mEq/L. The stroke severity was determined using NIHSS scale.

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Patients were then followed up for a period of 30 days, either personally or through telephone and their mortality data were recorded.

STATISTICAL ANALYSIS: Continuous variables are presented as mean (SD) and categorical variables as numbers and percentages. The baseline characteristics of the groups were compared using analysis of variance for continuous variables and chi square for categorical variants. To determine the independent impact of hyponatremia on early mortality regression analysis was done.

Variants considered for analysis included age, gender, history of smoking, hypertension, diabetes mellitus. For the association with all-cause mortality, hyponatremia was defined as serum sodium below 135 mEq/L and its impact was tested using regression analysis.

STATISTICAL SOFTWARE: The Statistical software SPSS II.0 and Systat 8.0 were used for analysis of data and Microsoft excel and Word were used to generate tables, graphs, data entry etc. differences were considered statistically significant at the 2- sided $P < 0.05$ level.

RESULTS: This study was conducted over a period of 14 months and included 224 eligible patients with stroke. The main aim of the study was to find incidence of hyponatremia in stroke patients and to find its correlation with early 30 days mortality. Various other parameters were also studied in this study.

The average age of population was 59.49yrs. Majority ($n = 119$) belonged to age group 50-70 yrs. The mean age for males ($n=142$) was 59.48yrs and for females ($n=82$) was 59.53yrs.

In our study it was seen that the patients presenting to Hamidia hospital with stroke were predominantly male. Out of 224 patients 142 (63.4%) patients were male patients and 82 (36.6%) were female patients.

Most of the patients of study population were non-diabetic (65.2%). Rest of the patients was diabetic (34.8%).

Among our study population 65% of the patients had ischemic infarct whereas 35% patients had hemorrhagic stroke (Table-1).

	Frequency	Percent
Haemorrhage	79	35.3
Infract	145	64.7
Total	224	100

Table 1

Type of Strokes in Study Population: Incidence of hyponatremia in our study population was 54.0%. Incidence of hyponatremia in infarct patients was 52.4% whereas among hemorrhagic stroke patients this was 56.9%.

Hyponatremia was increased with age in both male and female patients. Maximum numbers of hyponatremia patients are seen in old ages (Above 50yrs of age). Hyponatremia was noticed in 53% of female patients whereas in male stroke patients this was found to be 54.22%; as is seen there is very little difference between these two value (p value = 0.975).

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Incidence of hyponatremia in hemorrhagic stroke patients were found to be higher than in infarct patients, in hemorrhagic patients the proportion of patients having hyponatremia were 56% whereas in infarct patients percentage of patients having hyponatremia were 52%(Table- 2).

	STROKE			Total
		Haemorrhage	Infraction	
HYPONATREMIA	No	34	69	103
	Yes	45	76	121
Total		79	145	224

Table 2

HYPONATREMIA IN STROKE: Overall mortality in the study group was found to be 35.26%, mortality was higher among the hemorrhagic stroke patients (46.8%) whereas in the infarct patients the mortality was significantly low (28.96%) (Table-3).

	OUTCOME		Total
	Alive	Dead	
Haemorrhage	42	37	79
Stroke			
Infarct	103	42	145
Total	145	79	224

Table 3

COMPARISON OF STROKE OUTCOME AFTER 30 DAYS: Overall incidence of death after 30 days in study population was 35.26%. Among the group of patients who had hyponatremia, mortality was 51% whereas the mortality among patients who were not having hyponatremia was calculated to be 16.5% (Table-4).

		OUTCOME		Total
		Alive	Dead	
HYPONATREMIA	No	86	17	103
	Yes	59	62	121
Total		145	79	224

Table 4

MORTALITY AFTER 30 DAYS IN HYPONATREMIC AND EUNATREMIC PATIENTS:

SEVERITY OF HYPOATREMIA AND MORTALITY: Higher mortality is seen among the patients having higher degree of hyponatremia, and mortality was decreasing as serum sodium level was increased. It suggests that there is a correlation between degree of hyponatremia and mortality (Table- 5).

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Sodium Level	No. of Patients	Dead (%)	Alive (%)
95-104	6	6(100%)	0(0%)
105-114	4	4(100%)	0(0%)
115-124	20	13(65%)	7(35%)
125-134	91	39(42.85%)	52(57.15%)
135-144	84	13(15.47%)	71(84.53%)
145-154	19	4(21%)	15(79%)

Table 5

SEVERITY OF HYPONATREMIA AND MORTALITY:

DISCUSSION: In our study out of 224 patients 142 (63.4%) patients were male patients and 82 (36.6%) were female patients. This was in concordance with the other Indian study by Keshab Sinha Roy et al⁸ where the proportion of male patients were 65% and female patients were 35% of all.

Hyponatremia in hemorrhagic stroke patients were found to be in 56% whereas in infarct patients percentage of patients having hyponatremia were 52%.

Though there was a difference of 4% between incidence of hyponatremia in hemorrhagic and ischemic stroke patients, this difference was found to be insignificant (p value=0.514).

Overall mortality in the study group was found to be 35.26%, mortality was higher among the hemorrhagic stroke patients (46.8%) whereas in the infarct patients the mortality was significantly low (28.96%). This difference in mortality was statistically significant among these two groups (p value < 0.05).

This finding from analysis suggests that mortality among haemorrhage patients is significantly higher than infarct patients. It is similar to the findings of several other studies which have proven this fact beyond doubt.

Incidence of death in study population was 35.26%. Among the group of patients who had hyponatremia, mortality was 51% whereas the mortality among patients who were not having hyponatremia was calculated to be 16.5%. There were significant difference between these two groups, which was further supported by a p value < 0.001, which suggest very high significance of correlation between hyponatremia and mortality. This result from our study is similar to various other studies.

HYPONATREMIA AS INDEPENDENT PREDICTOR OF MORTALITY IN STROKE PATIENTS: There is a strong correlation between hyponatremia and early mortality (30 days) in stroke patients which is further supported by similar results from other studies. Yet in this study there were other variables which can affect the outcome adversely in stroke patients (e.g. age of the patients, hypertension, diabetes, stroke severity, RBS, Serum Triglyceride, and TLC).

To overcome this problem, logistic regression analysis of the data was performed which showed that hyponatremia was independently associated with mortality (OR, 7.282; 95% CI, 3.211–16.513; P<0.001) controlling for age, hypertension, diabetes, NIHSS and other nondependent variables (Table-6). This result is similar to the result of study done by kuramastu JB et al⁹ where he suggested hyponatremia as independent predictor of increased in-hospital and short term mortality.

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Wen-Yi Huang et al⁽¹⁰⁾ study from 925 first ever ischemic stroke patients concluded that hyponatremia in the stroke stage is a predictor of 3-year mortality in patients with first-ever ischemic stroke that is independent of other clinical predictors of adverse outcome.

	B	S.E.	Wald	Df	Sig.	Exp(B)	95% C.I.for	
							EXP(B)	
							Lower	Upper
AGE	.025	.013	3.641	1	.056	1.026	.999	1.053
DM	.136	.398	.116	1	.733	1.145	.525	2.498
HTN	.027	.405	.005	1	.946	1.028	.465	2.272
SMOKING	.070	.391	.032	1	.858	1.073	.498	2.310
STROKE	.324	.409	.628	1	.428	1.383	.620	3.081
HYPONATREMIA	1.985	.418	22.592	1	.000	7.282	3.211	16.513
K	-.024	.219	.012	1	.914	.977	.636	1.500
Ca	-.187	.113	2.735	1	.098	.829	.664	1.035
RBS	-.002	.003	.309	1	.578	.998	.992	1.005
S.Tri glyceride	.003	.003	.679	1	.410	1.003	.996	1.009
TLC	.000	.000	.089	1	.765	1.000	1.000	1.000
NIHSS	.292	.052	30.999	1	.000	1.339	1.208	1.484
Constant	-5.425	1.986	7.465	1	.006	.004		

Table 6

VARIABLES IN THE EQUATION: In our study we have compared hyponatremic and normo-natremic patients with all possible risk factors that can affect short term mortality like diabetes mellitus, hypertension, type of stroke etc.

In all comparisons, hyponatremic patients were found to have significantly increased mortality rates when compared to normonatremic patients.

Hence it is evident that hyponatremia per se significantly affects short term mortality in patients with stroke irrespective of multiple other risk factors that affect short term mortality.

Based on our study, hyponatremia can be considered as independent risk factor for early (30 days) mortality in patients with stroke.

We have certain limitations in our study as our study is limited by the small number of patients (n =224) and short follow-up (30 days). Also, the cause of hyponatremia was not determined in the study. Our study was also observational and the effect of various interventions like fluid restriction on the final outcome was not checked.

CONCLUSIONS: Incidence of hyponatremia in stroke patients is high in our study it was found to be 54%. Based on data the difference in incidence of hyponatremia among ischemic and hemorrhagic stroke patients is statistically insignificant, and thus we conclude from our study that hyponatremia is strongly associated with increased early mortality in stroke patients.

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