Original Article

A Study of Relationship of Hyponatremia with in Hospital Mortaliy in Acute Stroke

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ABSTRACT

Introduction : Stroke is a global health problem. It is the second commonest cause of death and fourth leading cause of disability worldwide. Hyponatremia is a common electrolyte disorder encountered in patients of stroke which is found to be an independent risk factor increasing mortality.

Objective : The aim of this study is to study the prevalence of hyponatremia in patients of stroke admitted in tertiary care hospital & to find out the association between hyponatremia and in-hospital mortality in patients of stroke.

Materials and Methods : This is an observational study conducted in a tertiary care hospital from October 2015-November 2017. A total of 200 patients of ischaemic as well as haemorrhagic stroke were included in the study. Patients underwent detailed clinical examination and laboratory assessment. Various parameters were compared between Patients of Stroke with hyponatremia and those with normal sodium levels.

Results : Total 200 patients of acute stroke were included in our study of the 200 patients, 55 (27.5%) patients were found to have hyponatremia, whereas 145 (72.5%) patients had normal sodium levels. When patients were divided according to the type of stroke hyponatremia was observed in 28.2% patients of ischemic stroke, 12% patients of haemorragic stroke and 3% patients of SAH (Subarachnoid haemorrhage). The mortality was found to be significantly higher in hyponatremic patients of ischemic and hemorrhagic stroke but not in patients of SAH.

Conclusion : Hyponatremia was seen to affect significantly the overall mortality of ischaemic and haemorrhagic stroke patients But the mortality did not differ significantly in patients of SAH.

Key words : Stroke, hyponatremia.

Introduction :

Stroke is a global health problem. It is the second commonest cause of death and fourth leading cause of disability worldwide.[1] Hyponatremia is a common electrolyte disorder encountered in patients with neurological disorders such as stroke, subarachnoid hemorrhage, and meningitis.[2] It is defined as a decrease in the serum sodium concentration to a level below 135 mmol per liter. However, patients in whom the serum sodium concentration is greater than 130 meq/L are usually asymptomatic.[3] Water intake and circulating Arginine Vasopressin (AVP) constitute the two key effectors in the defense of serum osmolality; defects in one or both of these defense mechanisms cause most cases of hyponatremia.[4] The cause of hyponatremia in acute stroke may be either due to Syndrome of inappropriate ADH secretion or due to Cerebral Salt Wasting Syndrome.[5] Hyponatremia in stroke is associated with poor outcome. Studies which are conducted in this regard shows that the mortality ranges from 14%-44 %.[2,5,6]

Aims and Objectives :

1. To study the prevalence of hyponatremia in patients of stroke admitted in tertiary care hospital.

2. To study the association between hyponatremia and in-hospital mortality in patients of stroke.

Materials and method : It was an observational study conducted at G.M.C, Nagpur. Patients admitted in medicine wards and intensive care unit were included. It was carried out from November 2015 to November 2017. 200 cases of acute stroke were included in this study.

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Inclusion Criteria :

1. All CT proven cases of acute stroke admitted in medicine wards and Medicine ICCU were included in this study.

Exclusion Criteria :

1. Renal impairment.
2. Hepatic impairment.
3. Patients on drugs causing hyponatremia.
4. Refusal to give consent.

All the patients were subjected to detailed clinical history and physical examination with special emphasis on neurological examination, including GCS score on admission. Data collected was noted in the predesigned proforma. The study was approved by ethical committee of the hospital. Informed consent was taken from all participants or from their close relatives.

All patients were subjected to a standard protocol of clinical and lab assessment as follows :

1. CT scan of head
2. Serum sodium levels
3. Random blood sugar
4. Renal function test
5. Liver function test
6. Lipid profile

Total 200 patients of stroke were included in our study. These were subjected to CT scan of the head. Cases of ischemic stroke, hemorrhagic stroke and subarachnoid hemorrhage were included in this study. All patients of stroke were evaluated for hyponatremia. Serum sodium was done at the time of hospitalization and was repeated every day for 7 days. Hyponatremia was considered when the serum sodium was < 130 meq/l. at any point of time within this period.

Results :

Total 200 patients of acute stroke were included in our study and were evaluated for hyponatremia. 55 (27.5%) patients were found to have hyponatremia whereas 145 (72.5%) patients had normal sodium levels.

Mean age of study population was 58.2 ± 10.46. Maximum number of patients were in the age group 51-60. There were total 127 males and 73 females. There was no significant statistical difference of age and sex between the three types of stroke.

There were 102 patients of ischemic stroke, 85 patients of hemorrhagic stroke and 13 patients of SAH (subarachnoid hemorrhage) in this study.

Table 1 : **Prevalence of Hyponatremia in Different Types of Stroke**

Type of Stroke	No. of Patients	Hyponatremia	Normal Sodium Levels	Prevalence of Hyponatremia
Ischemic	102 (51%)	25 (12.5%)	77 (38.5%)	24.5%
Haemorrhagic	85 (42.5%)	24 (12%)	61 (30.5%)	28.2%
SAH	13 (6.5)	6 (3%)	7 (3.5)	46.1%
Total	200 (100)	55 (27.5%)	145 (72.5)	27.5%

Of 102 patients of ischemic stroke, 25 (28.2%) patients had hyponatremia and in 77 patients' sodium levels were normal. Out of 85 patients of hemorrhagic stroke, 24 (12%) had hyponatremia and 61 (30.5%) patients had normal sodium levels. Out of 13 patients of subarachnoid hemorrhage 6 (3%) patients had hyponatremia & 7 (3.5%) had normal sodium levels.

Table 2 : **Correlation of sodium levels with mortality**

Acute stroke	Hyponatremia		Normal Sodium Levels		p-value
	Survived	Non survived	Survived	Non survived	
Ischemic (n-102)	10	20	50	22	0.001, HS
Haemorrhagic (n-85)	4	14	50	17	<0.001, HS
SAH (n-13)	3	4	5	1	0.266, NS
Total	17	38	105	40	<0.001, HS

When mortality was compared in patients of stroke with hyponatremia and patients with normal sodium levels it was found that out of 200 patients, 55 (27.5%) had hyponatremia and out of these 55 patients 38 patients expired. But out of 145 patients with normal sodium levels 40 patients expired.

Table 3 : **Relationship of Hospital stay and outcome of patients.**

Hospital Stay (in days)	Survived	Not Survived
1-4	95	58
5-10	25	17
>10	2	3
Mean	3.84 2.12	3.17 2.74
p-value	0.7155, NS	

The length of hospital stay was correlated with the outcome of patients. Statistical analysis does not show any difference in the outcome.

Table 4 : **Relationship of Glasgow coma scale with the severity of hyponatremia.**

GCS	<120	121-<130	>130	P-value
3-5	7	20	32	Chi sq =
6-10	0	27	72	34.1286
11-15	0	1	41	p-value =
Mean	3.57 ± 0.53	6.18 ± 2.14	8.36 ± 3.32	0.001 HS

Mean GCS in patients having sodium values < 120 was 3.57 ± 0.53, mean GCS in patients with sodium values between 121- $\leq$ 130 was 6.18 ± 2.14 and with normal sodium levels was 8.36 ± 3.32. The statistical difference was significant; it means the low sodium levels lower the GCS.

Table 6 : **Multiple Logistic Regression Analysis for independent predictors of acute stroke affecting mortality.**

Variable	Adj Odd Ratio	95% Confidence Interval	p-value
Age > 60	2.08	1.13 - 3.84	0.018, S
Hypertension	2.41	1.00 5.77	0.048, S
Fever	1.87	1.02 3.44	0.043, S
h/o old CVE	2.12	1.08 4.13	0.027, S

Table 5 : **Association of various factors with mortality in patients of stroke**

Variable			Mortality	Survived	OR	95% C.I.	P-value
Old age (>60)	Yes		46	46	2.37	1.27- 4.43	0.0032, HS
	No		32	76			
Hypertension	Yes		70	87	3.52	1.47 - 9.30	0.0020, HS
	No		8	35			
Hperglycemia	Yes		53	66	1.92	1.02 - 3.64	0.0284, S
	No		25	60			
Fever	Yes		42	45	1.99	1.07 - 3.70	0.0183, S
	No		36	77			
Hypertension	Yes		59	70	2.30	1.18 - 4.59	0.0085, HS
	No		19	52			
Diabetes	Yes		38	40	1.94	1.04 - 3.63	0.0243, S
	No		40	82			
Previous history of stroke	Yes		30	24	2.55	1.28-5.08	0.0035, HS
	No		48	98			
Addiction	Yes		31	37	1.51	0.79-2.86	0.1704, NS
	No		47	85			
Deranged lipid	Yes		32	30	2.13	1.10-4.11	0.0142, S

When MLR analysis was done the factors which were found to be independent predictors of mortality of stroke were old age (> 60 yrs), raised BP > 140 systolic or > 90 diastolic, temperature more > 36.6 degrees Celsius and past history of stroke.

Discussion :

Stroke is a global health problem. Many factors affect the outcome of stroke, hyponatremia is one of them. Hyponatremia and stroke are associated with poor outcome. Hence this study was carried out to know the association of stroke with hyponatremia.

In this study mean age of patients was 58.2 ± 10.46; with a mean age of males was 57.94 ± 10.91 and females were 58.64 ± 9.68. Maximum number (82) of patients were in the age group 51-60. **Kallol Bhattacharjee, Dwijen Das** *et al*[7] also got the similar findings.

Out of total 200 patients of the stroke there were 127 (63.5%) males and 73 (36.5%) females. This was comparable to studies done by **Kallol Bhattacharjee, Dwijen Das** *et al*[7] **and Hasan MK** *et al*[9]**.**

Out of total 200 cases of stroke, there were about 102 (51 %) cases of ischemic stroke, 85 (42.5 %) cases of hemorrhagic stroke and 13 (6.5 %) cases of SAH. Ischemic stroke was most prevalent in the study population. The distribution was comparable to study carried by **Kumar Natarajan** *et al*[8] who had the majority of the patients of ischemic stroke around 80%, Hemorrhagic stroke was seen in 16% and 4% had sub-arachnoid hemorrhage.

Out of total 200 cases of stroke, hyponatremia was seen in about 55 (27.5%) patients and 145 (72.5%) had normal sodium levels. So the overall prevalence of hyponatremia in acute stroke was found to be 27.5%. This was comparable to the study carried out by **Kumar Natarajan** *et al*[8] and by **Hasan MK** *et al*[9] who have found out 20% and 30% prevalence of hyponatremia respectively in patients of stroke.

After statistical analysis hyponatremia was found to significantly increase the length of hospital stay in stroke patients. This is comparable with **Kumar Natarajan** *et al*[8] who in their study found out that the mean duration of hospital stay was significantly higher in patients with hyponatremia as compared to patients with normal sodium levels. A poorer discharge disposition was also seen in the hyponatremia group in the study by **Rodrigues**[10] (p<0.004). This suggests hyponatremia significantly increases the hospital stay of patients but the increased duration of hospital stay was not significantly found to affect the outcome of patients.

Severe hyponatremia was more commonly seen to be associated in patients with lower GCS values. The statistical difference was found to be significant (p = 0.001) which suggested that fall in GCS is proportionate to the degree of severity of hyponatremia.

In this study, it was observed that out of 55 patients with hyponatremia in acute stroke, 38 patients (69.1%) died whereas in normonatremic group of 145 patients, 40 patients (27.6%) expired. After statistical analysis, the p-value was found to be < 0.001; which suggested that there was a strong significant association between hyponatremia withthe outcome of stroke. The outcome was similar to the studies carried out by **Kallol Bhattacharjee, Dwijen Das** *et al*[7]

In this study in case of ischemic stroke out of 30 hyponatremic patients, 20 (66.7%) died while among 72 patients with normal sodium levels, 22 patients (30.5%) died whereas in 18 hyponatremic patients of hemorrhage stroke, 14 patients (77.7%) died and 17 (24.5%) out of 67 patients with normal sodium levels died. After applying chi-square test, the p-value was 0.001 in ischemic stroke and 0.001 in the hemorrhagic stroke which suggested that hyponatremia was significantly associated with increased mortality in patients of ischemic and hemorrhagic stroke. Mortality was found similar to study carried out by **Kallol Bhattacharjee, Dwijen Das** *et al*[7] who found out 41.42% mortality in hyponatremic haemorrhagic stroke patients; versus 20.54% with haemorrhagic stroke patients having normal sodium levels with statistical significant p-value (p=0.048) and 24% mortality in hyponatremic ischemic stroke patients compared to 6% mortality in patients of ischemic stroke with normal sodium levels with a significant p-value = 0.029.

However, in case of SAH out of 6 hyponatremic patients, 4 (66.6%) died while among 7 non hyponatremic patients, 1 patients (14.28%) died. After statistical analysis, p value was found to be 0.135; which shows there is no significant association between hyponatremia with the outcome of stroke in SAH similar to **Kallol Bhattacharjee, Dwijen Das** *et al*[7] study they found out that in case of SAH out of 11 hyponatremic patients, 5 (45.45%) died while among 8 non hyponatremic patients, 3 patients (37.5%) died with no significant association of hyponatremia with outcome of SAH.

Age > 60 yrs., hypertension, hyperglycemia, fever during a hospital stay, or having deranged lipid profile were having significant impact on mortality. Hypertension, diabetes or patients having previous history of stroke also were seen to affect mortality of patients.

Conclusion :

- Hyponatremia of different magnitude has been associated with different types of acute stroke like Ischemic stroke, hemorrhagic and SAH.

- Prevalence of hyponatremia in all cases of acute stroke was found to be around 27.5%

- Hyponatremia was more frequent in SAH than ischemic and hemorrhagic strokes.

- Hyponatremia was seen to significantly affect the overall mortality of in ischemic and hemorrhagic stroke but mortality was not significant in SAH.

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