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ORIGINAL RESEARCH

Association Of Hyponatremia And Short-term Outcome In Patients With Ischemic Stroke

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ABSTRACT

Background-We aimed to determine the prevalence of hyponatremia on admission in ischemic stroke patients and to compare morbidity as well as mortality in ischemic stroke patients presenting with and without hyponatremia.

Methodology-This study was conducted as a prospective cohort study on all patients with ischemic stroke admitted in People's Hospital Bhopal those fulfilling inclusion criteria. during the study period on admission serum sodium was assessed and severity of ischemic stroke was determined using Modified Rankin Scale. Follow-up of all patients was done at discharge or death and after 1 month of discharge.

Results-We reported hyponatremia in 37.3% cases with ischemic stroke, with mild, moderate and severe hyponatremia 31.4%, 2.9% and 2.9% cases respectively. Mortality was found in significantly higher proportions of cases with hyponatremia ($p<0.05$). Though we found no significant association of hyponatremia with mRS score at admission as well as at the time of discharge or death ($p>0.05$), hyponatremia was significantly associated with higher mortality rate after 1 month of discharge ($p<0.05$).

Conclusions-Severe hyponatremia at the time of admission in hospital carries higher mortality in patients with acute ischemic stroke. Our study highlights the multifaceted impact of hyponatremia on clinical outcomes, treatment strategies, and short-term functional recovery in patients with ischemic stroke. The evaluation of hyponatremia levels can help us in understanding the severity at which a patient can develop adverse outcomes in stroke, thereby helping us to review and revise their management in time to decrease the mortality rate.

Keywords- Hyponatremia, ischemic stroke, mortality, functional outcome, modified Rankin score

INTRODUCTION

Ischemic stroke is the most common type of stroke, attributing to approximately 85% of all the strokes, and rest are hemorrhagic strokes.[1]According to World Health Organization, stroke is the third leading cause of disability and second leading cause of death globally. Approximately 1 in 4 individuals during their lifetime are at risk of developing stroke, and approximately 70% of strokes are estimated to be occurring in low- and middle-income countries.[2]

Literature suggests that approximately half of the patients with acute ischemic stroke have sodium and water perturbations and electrolyte imbalance, particularly hyponatremia is common in such patients.[3]Hyponatremia is defined as serum sodium level below 135 mmol/L. Joint European guidelines classify hyponatremia as mild, moderate and severe as serum Sodium concentration of 130 to 134 mmol/L,125 to 129 mmol/L and <125 mmol/L respectively.[4] Even mild hyponatremia is associated with adverse outcome such as prolonged hospitalization and higher mortality rate in patients with stroke.[5-8]

Pathophysiological response to hyponatremia in ischemic stroke could be development of cerebral edema, raised intracranial pressure, worsening of sensorium, seizure and delayed cerebral infarction. hyponatremia alsocauses neurological symptoms such as nausea, headache, disorientation, lethargy etc. However, if plasma sodium concentration falls between 115 and 120 mmol/L, cerebral edema may lead to seizures/ convulsions, coma, permanent brain damage and in some cases even death.[9]Apart from this, syndrome of inappropriate antidiuretic hormone (SIADH), cerebral salt wasting syndrome (CSWS) and inappropriate fluid intake has been implicated as contributory factors for hyponatremia in patients with ischemic stroke.[10-12] In cases with ischemic stroke, hyponatremia can be an important cause of persistent altered sensorium. Hyponatremia could be

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precipitated by multiple factors such as dietary restriction of sodium, use of certain drugs (such as selective serotonin reuptake inhibitors, Angiotensin Converting Enzyme inhibitors, diuretics, angiotensin receptor blockersetc.[13]

As hyponatremia is associated with poor outcome in ischemic stroke patients. Hyponatremia (even mild) may lead to catastrophe, if not recognized and/or treated correctly. Thus, early detection of hyponatremia in ischemic stroke patient may have some benefit in improving the outcome if identified and managed timely. With the above background, the present study was conducted to determine the prevalence of hyponatremia on admission in ischemic stroke patients and to compare morbidity as well as mortality in ischemic stroke patients presenting with and without hyponatremia.

METHODOLOGY

The present study was conducted as a prospective cohort study on all patients admitted with ischemic stroke under medicine department, PCMS & RC, People's Hospital, Bhopal during the study period from 1st November 2022 to 30th April 2024. All the patients presenting with ischemic stroke within 72 hours of onset, with or without co-morbidities such as hypertension and diabetes mellitus belonging to more than 18 years of age and willing to participate in the study were included whereas patients presenting with Hemorrhagic stroke, with comorbidities other than hypertension and diabetes, admitted after getting intravenous Saline from any other hospital, with known case of any bleeding or clotting disorder and patients who left against medical advice (LAMA) without proper treatment were excluded from the study.

After obtaining ethical clearance from Institutional Ethics Committee, all the patients fulfilling inclusion criteria were enrolled in the study. Detailed data regarding sociodemographic variables and clinical history was obtained and patients were subjected to clinical examination. Neurological examination included level of consciousness, power on both the side, speech, swallowing and convulsions. Modified Rankin Scale was used to assess the severity of ischemic stroke.[14]

Serum sodium was assessed at admission as well as near discharge. Serum sodium of less than 135 mmol/L was considered as hyponatremia. Apart from this, all patients were subjected to NCCT brain or MRI brain. All the patients were monitored during the hospital stay and their final outcome was assessed with respect to mortality and mRS score at the time of discharge and recorded in study proforma. Follow-up of all patients was done at 1 month of discharge either in medicine OPD or telephonically and mRS score were reassessed based on information provided by patients or their relatives. If any patient did not respond after 1 month on follow up /by telephonic conversation then such cases were also excluded from the study.

Statistical analysis-Data was transcribed into MS Excel and analyzed with the help of IBM SPSS software version 20 (IBM Corp. Illinois, Chicago). Categorical variables were expressed as frequency and proportion whereas continuous data was represented as mean and standard deviation. Based upon serum sodium levels, patients were categorized as hyponatremia and normonatremia, and patients with hyponatremia were further subdivided based on severity of hyponatremia. Morbidity at discharge and at 1 month follow up of ischemic stroke patients (by modified Rankin Scale) was compared using Chi square test between the groups. P value of less than 0.05 was considered statistically significant.

RESULTS

The present study was conducted on a total of 102 patients with ischemic stroke with mean age of 61.53±13.98 years. 66.7% cases were males. We reported hyponatremia in 37.3% cases with stroke, with mild, moderate and severe hyponatremia 31.4%, 2.9% and 2.9% cases respectively (Figure 1).

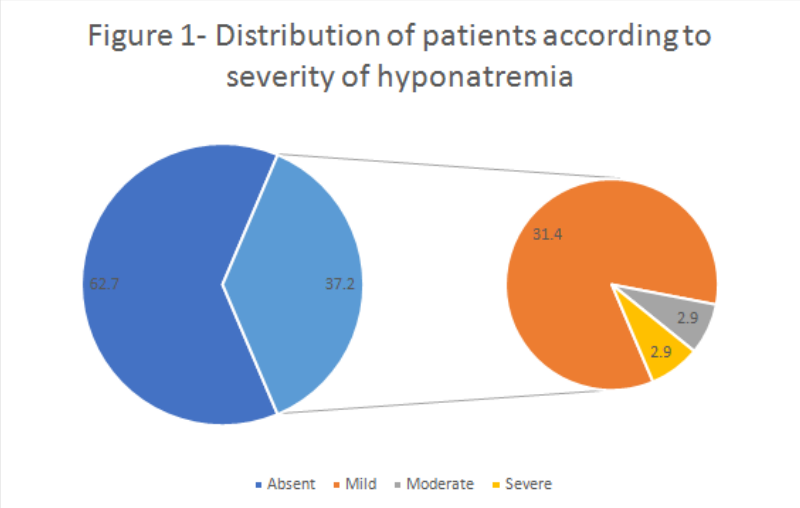

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Table. 1- Association of hyponatremia with morbidity and mortality variables in patients with ischemic stroke

Variables			Hyponatremia				Total (n=102)		P value
			Present (n=38)		Absent (n=64)				
			n	%	n	%	N	%	
Clinical findings	Speech difficulty	No	13	34.2	26	40.6	39	38.2	0.519
		Yes	25	65.8	38	59.4	63	61.8	
	Dysphagia	No	13	34.2	26	40.6	39	38.2	0.519
		Yes	25	65.8	38	59.4	63	61.8	
	Convulsions	No	33	86.8	56	87.5	89	87.3	0.923
		Yes	5	13.2	8	12.5	13	12.7	
	Level of consciousness	Conscious	26	68.4	55	85.9	81	79.4	0.15
		Drowsy	9	23.7	7	10.9	16	15.7	
		Stupor	2	5.3	2	3.1	4	3.9	
		Unconscious	1	2.6	0	0	1	1	
Length of stay		Mean ±SD	8.34±5.16		7.72±4.21		7.95±4.57		0.51
Condition at discharge		Improved	7	18.4	10	15.6	17	16.7	0.793
		DOR	29	76.3	52	81.2	81	79.4	
		Death	2	5.3	2	3.1	4	3.9	
Outcome		Alive	31	81.6	62	96.9	93	91.2	0.012*
		Death	7	18.4	2	3.1	9	8.8	

As observed from table 1, though we found no significant association of hyponatremia with clinical findings, length of hospital stay and condition at discharge ($p>0.05$), we reported mortality in significantly higherproportions of cases of ischemic stroke with hyponatremia (18.4%) as compared topatients with normonatremia (3.1%) ($p<0.05$). All the cases (n=3; 100%) with severe hyponatremia succumbed to death whereas mortality was documented in 4 out of 32 (12.5%) cases with mild hyponatremia and none in moderate hyponatremia. Thus, mortality was found in significantly higher proportions of cases with severe hyponatremia ($p<0.05$).

Table.2- Association of hyponatremia with functional outcome (mRS score) in patients with ischemic stroke

mRS score			Hyponatremia				Total (n=102)		P value
			Present (n=38)		Absent (n=64)				
			N	%	n	%	n	%	
Admission (n=102)	0	No symptoms	0	0	0	0	0	0	0.095
	1	No significant disability	2	5.3	2	3.1	4	3.9	
	2	Slight disability	5	13.2	1	1.6	6	5.9	
	3	Moderate disability	5	13.2	17	26.6	22	21.6	
	4	Moderately severe disability	15	39.5	23	35.9	38	37.3	
	5	Severe disability	11	28.9	21	32.8	32	31.4	
	6	Death	0	0	0	0	0	0	
Discharge/ death (n=102)	0	No symptoms	0	0	0	0	0	0	0.786
	1	No significant disability	4	10.5	3	4.7	7	6.9	
	2	Slight disability	3	7.9	3	4.7	6	5.9	
	3	Moderate disability	6	15.8	14	21.9	20	19.6	
	4	Moderately severe disability	14	36.8	25	39.1	39	38.2	
	5	Severe disability	9	23.7	17	26.6	26	25.5	
	6	Death	2	5.3	2	3.1	4	3.9	
1 month after discharge (n=98)	0	No symptoms	1	2.8	0	0	1	1	0.002*
	1	No significant disability	3	8.3	6	9.7	9	9.2	
	2	Slight disability	3	8.3	4	6.5	7	7.1	

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	3	Moderate disability	1	2.8	19	30.6	20	20.4	
	4	Moderately severe disability	11	30.6	20	32.3	31	31.6	
	5	Severe disability	12	33.3	13	21	25	25.5	
	6	Death	5	13.9	0	0	5	5.1	

Though we found no significant association of hyponatremia with mRS score at admission as well as at the time of discharge or death ($p>0.05$), hyponatremia was significantly associated with higher mortality rate after 1 month of discharge ($p<0.05$) (Table 2).

Table 3- Comparison of functional outcome by mRS score among ischemic stroke patients with normonatremia and hyponatremia at admission, discharge and follow up.

mRS			Admission (n=102)		Discharge (n=102)		1 month after discharge (n=98)		P value
			n	%	n	%	n	%	
Normonatremia	0	No symptoms	0	0	0	0	0	0	0.001 *
	1	No significant disability	2	3.1	3	4.7	6	9.7	
	2	Slight disability	1	1.6	3	4.7	4	6.5	
	3	Moderate disability	17	26.6	14	21.9	19	30.6	
	4	Moderately severe disability	23	35.9	25	39.1	20	32.3	
	5	Severe disability	21	32.8	17	26.6	13	21	
	6	Death	0	0	2	3.1	0	0	
Hyponatremia	0	No symptoms	0	0	0	0	1	2.8	0.001 *77+
	1	No significant disability	2	5.3	4	10.5	3	8.3	
	2	Slight disability	5	13.2	3	7.9	3	8.3	
	3	Moderate disability	5	13.2	6	15.8	1	2.8	
	4	Moderately severe disability	15	39.5	14	36.8	11	30.6	
	5	Severe disability	11	28.9	9	23.7	12	33.3	
	6	Death	0	0	2	5.3	5	13.9	

Table 3 shows that the improvement in condition of patients based on mRS score was found to be statistically significant ($p<0.05$) in patients with normonatremia over the period of follow up. We observed a significant decline in condition of patients with hyponatremia at discharge and at follow up visit. Severe disability in hyponatremic patients at time of discharge was observed in 28.9%, whereas at discharge and at 1 month after discharge, 23.7% and 33.3% cases had severe disability. However, mortality was observed in 5.3% cases at discharge and 13.9% cases after 1 month of follow up ($p<0.05$).

DISCUSSIONS

We aimed to compare the short-termoutcome of ischemic stroke patients presenting with and without hyponatremia and comparing mortality duringadmission and within 1 month after discharge in patients with and withouthyponatremia. In present study, hyponatremia was documented in 38 cases, of them, majority had mild hyponatremia (84.2%), moderate hyponatremia and severe hyponatremia in 7.9%cases. These findings underscore the prevalence of mild hyponatremia among ischemic stroke patients, with fewer patients experiencing more severe forms of hyponatremia. This distribution is consistent with prior research indicating that mild hyponatremia is more common in clinical settings, while moderate to severe hyponatremia is less frequent but often associated with worse outcomes. For instance, in research by Kidwai et al, mean serum sodium level was 128.4±6.07.Mild, moderate and severe hyponatremia was found in 60%, 29.1%and 10.9% patients respectively.[15] Similarly, Mahesar et al reported that the majority of the patients (25%) had mild hyponatremia (130-134mMol/L), only a few (9.8%) had moderate (125-129 mMol/L) or severe(<125mMol/L)hyponatremia(3.8%).[16]Further more, in a study by Potasso et al 5.6% patients had sodium level below125mmol/L, 16.7% had 125-129mmol/L and majority of them i.e., 77.8% had sodium level between 130-134mmol/L.[17]

Hyponatremia can influence neurological function, potentially exacerbating symptoms such as speech difficulty, dysphagia, and convulsions. We found no significant association of hyponatremia with clinical findings ($p>0.05$). However, the lack of statistical significance in our study suggests that while these symptoms are more prevalent in severe hyponatremia cases, other factors related to stroke severity and location may play a more critical role. This aligns with findings by Brink Koetter et al, who reported that hyponatremia can aggravate neurological symptoms like dysphagia (14%), dementia (40.7%) and delirium in 14.7% cases but is not the sole determinant.[18] Similarly, Babaliche et al found that confusion was

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significantly high in patients with severe hyponatremia as compared to patients with moderate hyponatremia (22 vs. 4, P < 0.001).[19]

At the time of admission, mRS score was suggestive of moderate to severe disability in majority of patients with hyponatremia 39.5%. At the time of death or discharge,36.8% cases with hyponatremia had moderate to severe disability. Death was documented in 5.3% cases with hyponatremia. Similarly,ElHabr et alreported that among all patients, 43.6% were discharged home, 41.4%were sent to inpatient rehab facility, and 15.0% to skilled nursing facility. On discharge the mRS score of 22.9% patient was zero, 4 for 21.8%, 1 for 20.4%, 5for 5.4% and 3 for 16.8% patients.[20]However, at 1 month follow up, death was documented in 13.9% cases with hyponatremia. Study by ElHabr et al documented that the 30-day mRSscore was zero for 22.9%, 1 for 20.4%, 4 for 20.7% 5 for 5.4% and 6 for 1.4%patients.[20] Similarly in a study by Wang et al documented poor functional outcome (mRSscore 3–6) in 14.34% patients and mRS score 2–6 occurred in 27.06% patients at 3months, while at 1-year follow-up, 13.55% patients had mRS score 3–6, 24.30% patients had mRS score 2–6.[21]In another study by Saha et al, themean mRS at the time of admission and discharge was4.16±1.03 and 3.56±1.21 respectively in hyponatremia patients.[9]

In present study, though we found no significant association of hyponatremia withmRS score at admission as well as at the time of discharge or death (p>0.05), hyponatremia was significantly associated with higher mortality rate after 1month of discharge (p<0.05).The lack of significant association between hyponatremia and initial mRS scores may suggest that sodium levels do not directly impact the initial severity of stroke-related disability. However, the significant association observed at one-month post-discharge highlights the long-term impact of hyponatremia on functional recovery and mortality in ischemic stroke patients. This finding aligns with study by Pelouto et al. which emphasize that Hyponatremia was associated with a worse mRS score at3 months adverse outcomes.[22] Similarly Potasso et al reported that patients with hyponatremia both on admission and at discharge (in-hospital persistent hyponatremia) had a higher mRS at 3 months (odds ratio 2.46; 95% CI, 1.20-5.03, fora shift to higher mRS).[17]

The lack of a significant association between hyponatremia and length of hospital stay in our study suggests that while hyponatremia may contribute to specific symptoms and complications, it does not independently prolong hospitalization in ischemic stroke patients. One possible reason for no significant difference in length of hospital stay among hyponatremia and norm natremia may be due to large number of patients were discharge on request in our study. Whereas Shima et al reported that stroke patients with hyponatremia had significantly longer length of hospital stay than patients without hyponatremia and higher 90-day mortality (OR, 1.73; 95% confidence interval (CI), 1.24-2.42.[23]Similarly, Kidwai et al documented that mean duration of hospital stay was 4.7 ± 2.06 days in their patients.[15]

We reported mortality in significantly higher proportions of cases of ischemic stroke with hyponatremia (18.4%) as compared to patients with normonatremia (3.1%) (p<0.05).Also, mortality was found in significantly higher proportions of cases with severe hyponatremia (p<0.05).This significant association underscores the critical impact of severe hyponatremia on patient outcomes. Hyponatremia can lead to cerebral edema and increased intracranial pressure, which can be fatal in the context of an ischemic stroke. Similarly, Saleem et al reported significantly higher mortality in patients with hyponatremia (156 out of 353) as compared to patients with normonatremia (94 out of 647) (p<0.05).[14]Corona et al in their meta-analysis showed that moderate hyponatremia increased the risk of death from any cause (RR (relative risk)= 2.60; 95% CI: 2.13–2.93).[24] Furthermore, Zhenget al. showed that patients with moderate or profound hyponatremia were characterized by a higher risk of death compared to those with mild hyponatremia.[25]

Our study highlights that hyponatremia is associated with specific clinical findings and higher mortality rates in ischemic stroke patients. Severe hyponatremia significantly affects patient outcomes, emphasizing the need for careful management of sodium levels in stroke patients to improve survival rates.

Our study had certain limitations, smaller sample size may limit the generalizability of the findings to other settings and populations. The follow-up period of 1 month is too short to fully capture the long-term outcomes in terms of morbidity and mortality and potential complications associated with hyponatremia in ischemic stroke patients. Follow up assessment of functional outcome of patients after 1 month of discharge was done in majority of patients by telephonic consultation with the patients/ their relatives rather than direct assessment.

CONCLUSIONS

Severe hyponatremia at the time of admission in hospital carries higher mortality in patients with acute ischemic stroke. Our study highlights the multifaceted impact of hyponatremia on clinical outcomes, treatment strategies, and short-term functional recovery in patients with ischemic stroke. Close monitoring of serum sodium levels helped us in finding the exact decrement level in patients of all ages and both genders and it was established that most of the cases only developed mild hyponatremia, if they developed any. The evaluation of hyponatremia levels can help us in understanding the severity at which a patient can develop adverse outcomes in stroke, thereby helping us to review and revise their management in time to decrease the mortality rate.

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