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Short-Term Hospital Outcome in Patients with Spontaneous Intracerebral Hemorrhage Based on Admission Hyponatremia

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Abstract **Original Research Article**

Background: Spontaneous intracerebral haemorrhage (S-ICH) is a life-threatening neurological emergency with high morbidity and mortality. Admission hyponatremia, commonly resulting from syndrome of inappropriate antidiuretic hormone secretion (SIADH), is frequently observed in S-ICH patients and may negatively impact outcomes. ***Aim of the Study*:** The aim of this study was to predict the short-term hospital outcome in patients with spontaneous intracerebral haemorrhage on the basis of admission hyponatremia. ***Methods:*** This hospital based observational study was conducted in Department of Neurology, Dhaka Medical College Hospital, Dhaka, Bangladesh from January, 2015 to December, 2016. Total 100 patients with spontaneous intracerebral haemorrhage were included in this study. ***Result:*** Most of the patients were over 60 years old (75%), with majority (57%) being male. Hypertension was common (68%) and smoking was a major risk factor among males (64.9%). Headache (82%) and hemiparesis or hemiplegia (73%) were the most frequent presenting features, followed by vomiting (62%) and altered consciousness (30%). Convulsions were rare (9%). At two weeks, 62% of patients had disability (mRS >2), and 18% had died. Patients with serum sodium <135 mmol/L had higher rates of low GCS, larger hematoma volume and infratentorial bleed, though not statistically significant. However, they showed significantly higher disability (85%) and mortality (40%) compared to those with normal sodium, with relative risks of 1.51 and 3.20, respectively. ***Conclusion:*** The current study concludes that admission hyponatremia is associated with higher proportion of disability (mRS>2) at the end of second week after onset and higher mortality within this period in patients with spontaneous intracerebral haemorrhage.

Keywords: Short-term Hospital Outcome, Spontaneous Intracerebral Hemorrhage and Admission Hyponatremia.

INTRODUCTION

Stroke is a huge burden on society [1]. It is a major cause of mortality and morbidity around the world. It is the third most common cause of death in developed countries after coronary heart disease and cancer [2]. At least half of the patients with a neurologic disorder attending general hospitals suffer from stroke [3]. The high number of disability-adjusted life-years lost due to stroke (485 per 10000 people) shows that stroke severely impacts the economy of Bangladesh [4]. Stroke is broadly classified as ischaemic and haemorrhagic which constitute approximately 80 and 20 percent of total stroke patients respectively [5]. Haemorrhagic stroke is further divided into intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH), accounting for 80 and 20 percent of cases respectively. In Bangladesh, a study conducted among 1020 patients registered during the period of August 1996 to April 2000, 590 (57.84 %) patients had ischemic and 430 (42.16 %) had haemorrhagic stroke [6]. Spontaneous intracerebral haemorrhage (S-ICH) is defined as neurological deficit documented by a brain CT indicating the presence of haemorrhage in brain parenchyma in absence of trauma [7]. Spontaneous intracerebral haemorrhage accounts for approximately 10 to 15 percent of all strokes [8]. Prevalence of stroke in Bangladesh is approximately 3 per 1000 person-years overall and 10 per 1000 person-years in people aged 70 years or more [9]. Spontaneous ICH comprised 31 and 28 percent of all stroke patients in studies conducted in Bangladesh and Pakistan

respectively [10, 11]. Hypertension is responsible for 70 to 80 percent of S-ICH [12]. Spontaneous ICH associated with hypertension and amyloid angiopathy is grouped as primary intracerebral haemorrhage [13]. Other causes of S-ICH are vascular malformations, vasculitic disorders, moyamoya disease, tumour haemorrhages, haemorrhagic infarcts, haemorrhagic diathesis and those associated with use of anticoagulant or fibrinolytic drugs [14]. Hyponatremia is the most frequent electrolyte abnormality in hospitalized patients, especially those with neurologic injury, and is associated with increased morbidity and mortality [15]. It is associated with a worse outcome in traumatic brain injury, postoperative neurosurgical patients and subarachnoid haemorrhage [16-18]. Early identification and correction of hyponatremia is essential in these patients in order to prevent additional complications or worsening outcomes [19]. While hyponatremia has been widely described after traumatic brain injury, SAH and neurosurgical intervention, there is limited information describing the incidence, etiology and outcomes of hyponatremia in patients with S-ICH. Recently, a strict association between the presence of hyponatremia at hospital admission and poor outcome in spontaneous ICH has been reported [20]. Immediate prognosis for S-ICH is grave; 30 to 35 percent die within 30 days [3]. Metabolic disturbances, especially hyponatremia and hyperglycaemia are associated with worse outcome [20, 21]. An observational study done by Kuramatsu *et al*., [20], showed that S-ICH patients with hyponatremia had an increased risk of mortality of 2.0 fold compared to patients with normal Sodium. So far, the knowledge goes, this might be the first ever study in Bangladesh. The aim of the study is to predict the short term hospital outcome in patients with spontaneous ICH on the basis of admission hyponatremia.

Objectives

To predict the short term hospital outcome in patients with spontaneous intracerebral haemorrhage on the basis of admission hyponatremia.

METHODOLOGY & MATERIALS

This hospital based observational study was conducted in Department of Neurology, Dhaka Medical College Hospital, Dhaka, Bangladesh from January, 2015 to December, 2016. Total 100 patients with spontaneous intracerebral haemorrhage were included in this study. Study population were divided into two groups, Group-I: Patients with normal serum sodium (Sodium 135-145mmol/L) and Group-II: Patients with low serum sodium (Sodium <135 mmol/L). All patients received standard medical management for spontaneous ICH per AHA/ASA guidelines (Morgenstern, 2010), including correction of hyponatremia where applicable. Clinical follow-up continued daily for two weeks post-symptom onset, with monitoring of vital signs and neurological status. Disability was assessed using the modified Rankin Scale (mRS) at two weeks and any deaths during this period were recorded. Poor outcomes were defined as mRS >2 or mortality within two weeks. Outcomes were then compared between the two sodium-level groups. Approval from the ethical review committee of Dhaka Medical College was obtained prior to the commencement of this study. The aims and objectives of the study were explained to the patients in easily understandable local language and then informed consent was taken from each patient. It was assured that all information and records would be kept confidential and the study would be helpful for both the physician and the patients in making rational approach of the case management. The data analysis was done manually using standard statistical procedures. Statistical Products and Service Solutions (SPSS) version 20 was used whenever required and also to crosscheck the results. Qualitative and quantitative data were analyzed with Chi-square or Fisher's exact test and Anova test respectively. Associations were expressed in terms of relative risk and considered statistically significant if p-value was < 0.05.

Inclusion Criteria

- Age: ≥ 18 years, both sexes.
- Patients with first ever spontaneous intracerebral haemorrhage.
- Hospital admission within 24 hours of symptom onset.
- Patients or attendants willing to give consent.

Exclusion Criteria

- Head injuries.
- ICH related to tumors, arteriovenous malformations, anticoagulation, thrombolysis or coagulopathy (excluded clinically and by CT head findings).
- Serious co-morbidity like chronic kidney disease, heart failure, decompensated chronic liver disease, respiratory failure (excluded clinically).
- Infections-Aspiration pneumonia.
- Patients with high serum Sodium level (Sodium >145 mmol/L.)
- Patients undergoing neurosurgical procedure.

RESULT

Table I and figure 1 shows the baseline characteristics and sex distribution of the patients. Majority of cases aged more than 60 years (75%), in both sexes (71.9% and 79% among males and females respectively). Majority (93%) of the participants were married. Hypertension was found in 68% of patients. Smoking was a major risk factor in males (64.91%). History of DM, family history of stroke and IHD were found in both sexes. Fifty seven (57%) were males and forty three (43%) were females. Table II shows the presenting features of the patients with spontaneous intracerebral haemorrhage. Headache was the most frequent complaint, present in eighty two percent (82%) of patients. Hemiparesis/hemiplegia was the next

common presenting feature and most frequent (73%) focal neurological deficit. Vomiting was also common, present in sixty two percent (60%) of patients. Thirty percent (30%) patient presented with deterioration of consciousness. Convulsion was not a common presenting feature, found in only nine percent (9%) of patients. Table III shows the overall outcome of spontaneous ICH patients in this study. Disability (mRS>2) at the end of second week was found in sixty two percent (62%) of patients. Overall mortality within that period was found eighteen percent (18%) of patients. Table IV shows that percentages of patients with initial GCS <9, haematoma volume ≥ 30 cc and infratentorial location were higher in the low serum Sodium group (< 135 mmol/L) compared to the normal Sodium group (135-145 mmol/L), although the differences were not statistically significant (p=0.084, p= 0.136, p=0.81 respectively). Table V shows the association between admission serum Sodium of the patient and their in-hospital outcome. The data shows that proportion of disability (mRS>2) and mortality increases significantly in the low serum Sodium group (85% and 40% respectively,) compared to normal Sodium group (56.25% and 12.5% respectively), which are statistically significant (p= 0.03 and p= 0.011 respectively). Table VI compares the disability (mRS >2) at day 14 and mortality within that period between patients with and without hyponatremia. Serum Sodium < 135 mmol/L was associated with higher proportion of disability (mRS>2) at day 14 with relative risk 1.51 which was statistically significant (95 percent CI 1.15 – 1.97, p-value 0.02). A significantly higher mortality was observed too in these patients (relative risk 3.20, 95 percent CI 1.45 – 7.05, p-value 0.011).

Table I: Baseline characteristics of the study people (N=100)

Characteristics	Frequency	Percentage
Age		
≤ 30	2	2%
31 – 40	2	2%
41 – 50	4	4%
51 – 60	17	17%
61 – 70	36	36%
71 – 80	26	26%
>80	13	13%
Marital status		
Married	93	93%
Unmarried	7	7%
Risk factors and co-morbidities		
Hypertension	68	68%
Smoking	39	39%
Family history of stroke	16	16%
History of DM	19	19%
History of IHD	13	13%
Alcoholism	5	5%

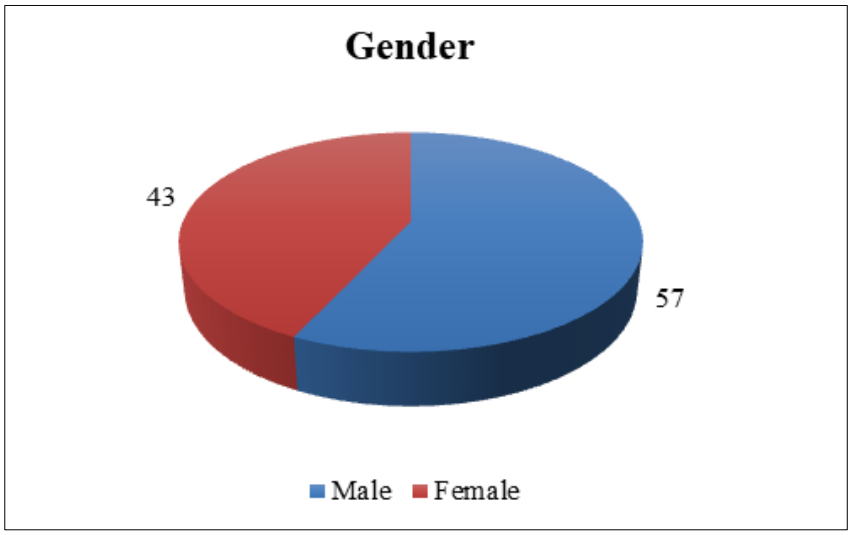

Figure 1: Gender distribution of the study people (N=100)

Table II: Presenting features (N= 100)

Feature	Frequency	Percentage
Headache	82	82%
Hemiplegia/paresis	73	73%
Vomiting	60	60%
Deterioration of consciousness	30	30%
Dysphasia/ aphasia	18	18%
Dysphagia	15	15%
Dysarthria	13	13%
Behavioural abnormalities	12	12%
Vertigo	11	11%
Convulsion	9	09%
Monoparesis	4	04%
Hemisensory loss	3	03%

Table III: Overall outcome of the study people (N = 100)

Admission serum Sodium (mmol/L)	Total	Disability (mRS >2, at the end of second week)	Mortality (during first two weeks)
135-145	80	45	10
<135	20	17	8
Total	**100 (100%)**	**62 (62%)**	**18 (18%)**

Table IV: Admission serum Sodium level in patients with initial GCS <9, haematoma volume ≥ 30 cc and location of haematoma

GCS & CT scan features of interest		Serum Sodium (mmol/L)		P value
		135-145	<135	
		(n= 80)	(n =20)	
GCS <9	Yes (n=23)	15 (18.75%)	8 (40%)	0.084*
	No(n=77)	65(81.25%)	12(60%)	
ICH vol ≥ 30 cc	Yes(n=29)	20(25%)	9(45%)	0.136*
	No(n=71)	60(75%)	11(55%)	
Location of haematoma: Infratentorial	Yes (n =11)	8(10%)	3(15%)	0.81*
	No(n=89)	72(90%)	17(85%)	

(Figures within parentheses indicating percentage)
*Chi-square test

Table V: Serum Sodium level with outcome (N= 100)

Outcome		Serum Sodium (mmol/L)		p-value
		135-145	<135	
		(n= 80)	(n =20)	
Disability (mRS >2) at the end of second week	Yes (n=62)	45 (56.25%)	17 (85%)	0.03*
	No (n=38)	35 (43.75%)	3 (15%)	
Mortality within first two weeks	Dead (n=18)	10 (12.5%)	08 (40%)	0.011*
	Alive (n=82)	70 (87.5%)	12 (60%)	

(Figures within parentheses indicating percentage)
*Chi-square test

Table VI: Association of hyponatremia with outcome (N = 100)

Outcome		Admission serum Sodium mmol/L		Relative risk	95 percent CI	p-value
		135-145	<135			
		(n=80)	(n=20)			
Disability(mRS>2) at the end of second week	Yes (n=62)	45 (56.25%)	17 (85%)	1.51	1.15 to 1.97	0.02**
	No (n=38)	35 (43.75%)	3 (15%)			
Mortality within first two weeks	Dead (n=18)	10 (12.5%)	8 (40%)	3.2	1.45 – 7.05	0.011*
	Alive (n=82)	70 (87.5%)	12 (60%)			

(Figures within parentheses indicating percentage)
*Chi-square test
**Fisher Exact test

DISCUSSION

This observational study was carried out in the Department of Neurology, Dhaka Medical College, Hospital, Dhaka. In this study, short term hospital outcome in patients with spontaneous intracerebral haemorrhage was assessed. Admission serum Sodium in all S-ICH patients were measured assuming that hyponatremia may act as a poor prognostic factor for short term outcome in S-ICH. Detail information regarding S-ICH was collected by a data collection sheet and blood was collected to measure serum Sodium. It was a little endeavour to find out the prediction of short term hospital outcome in patients with S-ICH on the basis of admission hyponatremia in our country. One hundred patients of spontaneous intracerebral haemorrhage were included in this study. Most (75%) of the patients were of 60 years or more age. Mean age was 66.9 ± 11.9 years. The age distribution was similar to that of most of the previous studies conducted in Bangladesh and India [5-23]. The youngest and oldest patients were of 22 and 90 years respectively. Number of males (57%) was more than that of females (43%). Similar sex distribution was found in the study on spontaneous ICH patients in Heerlen, Netherlands [24]. Majority of the cases were hypertensive intracerebral haemorrhages (68%). This finding is consistent with that of Kase [25] and Ropper [3]. The cause could not be revealed in the rest of the patients as the study was done within the first two weeks of stroke and the more extensive investigations were deferred during that period. However, exclusion of tumour haemorrhages, haemorrhages in bleeding disorders, anticoagulant and fibrinolytic therapy, and haemorrhagic infarcts, was rationally suggestive of amyloid angiopathy and vascular malformations as the cause in non-hypertensive patients. Both age and sex were almost identically distributed among the groups of admission serum Sodium. The groups were almost homogenous in terms of IHD, H/O DM, and smoking habit. Headache was the most frequent presenting feature (82%) followed by hemiparesis/hemiplegia (73%), vomiting (60%) and deteriorated consciousness (30%). Convulsion was not a common presenting feature, found in 9% of patients. Siddique *et al*., [5], and Al-Dahhan [26], found similar results in spontaneous intracerebral haemorrhage. Nine percent patients presented with infratentorial haemorrhage. It was almost same as in a study in France, but was lower than that found in a study in Finland [27, 28]. Only three patients, both were hypertensive, had thalamic haemorrhage. No case of caudate haemorrhage was found. Spontaneous ICH in these locations are infrequent [12]. A relatively small sample size (100) might be the reason behind their low frequency in this study. Initial GCS <9 was found in 23% patients. The percentage of patients those having hamatoma volume ≥ 30 cc were 29 , similar to the study by Flemming *et al*., [29], and Chiewvit *et al*., [30]. In this study, it was found that location of haematoma (supratentorial versus infratentorial) did not show any statistically significant association with various levels of admission serum Sodium. Regarding outcome, disability (mRS >2) at the end of second week was sixty two (62%). Overall mortality within this period was eighteen (18%) which is lower than that found in a similar study done by Kuramatsu *et al*., [20], where overall mortality was 24.17%. This difference may be due to small sample size of this study. The focus of this study, admission serum Sodium level 135-145 mmol/L, and < 135 mmol/L were found in 80% and 20% patients respectively, which was almost consistent with most other studies [20-31]. An observational study done by Kuramatsu *et al*., [20], showed incidence of admission hyponatremia 15.6%, whereas study conducted by Gray *et al*., [31], showed incidence of 24%. In this research, it was found that patients with hyponatremia (< 135 mmol/L) had increased mortality of 3.2 times (95% CI 1.45-7.05, p= 0.011) and disability (mRS>2) of 1.5 times (95% CI 1.15-1.97, p= 0.02) than the patients with serum Sodium level 135-145 mmol/L. In terms of outcome , a similar study conducted by Kuramatsu *et al*., [20], in Germany, showed in-hospital mortality was roughly doubled in patients with hyponatremia compared to patients with normal serum Sodium (40.9%; n=27 versus 21.1%; n=75), translating into a 2.5-fold increased odds ratio (p= <0.001). Multivariable analyses of their study also identified hyponatremia as an independent predictor of in-hospital mortality (odds ratio, 2.2; 95% confidence interval, 1.05–4.62; p=0.037).

Limitations of the Study

The sample size was small as well as sample was collected by convenience sampling. Confounders like intraventricular extension, admission hyperglycaemia those had the potential to influence the clinical outcome, were not matched in this study. Outcome was assessed within the first two weeks of onset. Assessment would have been better if it were done over a month or more.

CONCLUSION AND RECOMMENDATIONS

The current study concludes that admission hyponatremia is associated with higher proportions of disability (mRS>2) at the end of second week after onset and higher mortality within this period in patients with spontaneous intracerebral haemorrhage. So, admission hyponatremia can be used as a reliable predictor of short-term disability and mortality in patients with spontaneous intracerebral haemorrhage. Admission hyponatremia can be used as a reliable predictor of short-term hospital outcome in patients with spontaneous intracerebral haemorrhage. Further research on this topic with a larger sample size collected by random sampling is recommended.

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