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Original Article

Frequency of hyponatremia and its outcome in critically ill patients

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Abstract:

Background: *Disorders of sodium (Na^+) and water homeostasis are common in hospitalized patients particularly in Intensive Care Unit (ICU). Irrespective of the etiology it is associated with worse outcome and increase length of ICU stay.*

Objectives: *Objective of the current study is to determine the frequency of hyponatremia and its association with the outcome of critically ill Patients admitted in the Department of Critical Care Medicine, BIRDEM General Hospital.*

Methods: *This prospective observational cross-sectional study was taken place in department of Critical Care Medicine for a period of one year from 1st July, 2017 to 30th June, 2018. Consecutive 296 critically ill patients during this time period were included in this study according to selection criteria. Data were collected in preformed data collection sheet and analyzed by the statistical packages for social science (SPSS) software (version 20.0)*

Results: *In this study total 296 patients after fulfilling the inclusion criteria were selected as study participants. The mean age of the patients was 62.21±12.974 years and there were61.5% male and 38.5% female. Among male patients 39.6% had hyponatremia and among female patients 44.9% (p=0.09). Overall frequency of hyponatremia was 41.2%. Majority of the patients presented with respiratory distress (61.5%), altered level of consciousness (33.4%), hypotension (30%) and fever (18.9%). DM (90.5%), HTN (75.5%) and CKD (50.5%) were the most frequent comorbidities present among the participants. Most of the hyponatremic patients were euvolemic (50.00%). Mean APACHE ll score among hyponatremic patients was significantly high (p= 0.001) moreover, hyponatremic patients required more mechanical support (p= 0.001).Duration of ICU stay was not related to severity of baseline hyponatremia during admission (p= 0.08)). In addition, outcome of the patients also depends on the overall incidence of hyponatremia and degree of hyponatremia (p<0.05 in both cases).*

Conclusion: *More than one-third of critically ill patients had hyponatremia and it was related to poor outcome of the critically ill patients.*

Key words: *hyponatremia, Acute Physiology and Chronic Health Evaluation ll Score (APACHE ll Score), Syndrome of Inappropriate Antidiuretic Hormone (SIADH), Arginine vasopressin (AVP), Cerebral salt wasting syndrome (CSWS).*

Introduction

Hyponatremia is a common electrolyte imbalance seen among the critically ill patients. It is defined as a decrease in the serum sodium concentration to a level below 135 mmol per liter[1,2]. Prevalence of hyponatremia in hospital admissions vary 3.4% to 39.4% and even higher in ICU setup[3]. Hyponatremia can occur with normal, low, or even high total body sodium[4]. Patients are usually asymptomatic in case of mild hyponatremia of any duration. With severe and rapidly developing hyponatremia convulsion, coma, permanent brain damage, respiratory arrest, brain stem herniation and death can occur[5]. If hyponatremia develops slowly, the process of adaptation by the brain results in asymptomatic or less severe symptoms even in severe hyponatremia. Associated other metabolic disturbance like acidosis, hypoxia, potassium deficiency and comorbidities like hepatic failure, malnutrition usually worsen the severity of symptoms of hyponatremia as well as accelerate the risk of its complications[6,7].

Hyponatremia due to syndrome of inappropriate antidiuretic hormone (SIADH) is common in hospitalized patients because arginine vasopressin (AVP) is released in response to hypoxia, pain, or stress. Patients at particularly high risk include postsurgical patients, elderly persons, persons admitted to the intensive care unit, and patients with central nervous system disorders. In addition to the general hospital population, recent studies have found that preoperative hyponatremia was an independent marker for multiple perioperative complications, including 30-day morbidity and mortality[8]. Another prospective study was done by Padhi et al. (2014) and found the frequency of hyponatremia on ICU admission was 34.3%, most were euvolumic,58.96%. The SIADH criteria were met in 36.25% patients and pneumonia being the leading cause of SIADH[9].

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In another study, Bissram et al. (2007) found that symptomatic hyponatraemia was mostly associated with volume depletion (32.6% cases) and other causes were congestive heart failure, SIADH, use of drugs like thiazide diuretic, SSRI and in 21.3% of cases, the cause of hyponatremia was multifactorial (congestive heart failure, SIADH or medication use with volume depletion)[10]. Two important causes are SIADH or Cerebral salt wasting syndrome (CSWS), where the treatment option is fluid restriction for SIADH and replacement of salt and fluid is for CSWS. So, it is very much important to evaluate the causes for hyponatremia for the better treatment and prognosis of the patients.

Not only does hyponatremia represent a heavy threat for patients however its management additionally represents a good challenge for clinicians. Failure to correct acute hyponatremic patients timely & properly can develops metabolic encephalopathy, convulsion and even brain herniation. Again, very rapid correction of hyponatremia can lead to central pontine myelinolysis[11]. This is due to the osmotic gradient across cell membranes which dictates the distribution of water between the intracellular and extracellular compartments.

In another study, Shakhe et al. (2013) found an increased requirement of ventilator days along with increase length of ICU stay among the patients who had hyponatremia during ICU admission[12]. Pillai et al. (2018) in a tertiary care hospital found significant increase in duration of stay in ICU in patients with hyponatremia (p=0.003)[3]. They found most common cause of hyponatremia was SIADH. Another prospective study was done by Padhi et al. (2014) and found the patients with hyponatremia had longer ICU stay (P = 0.02) and required longer mechanical ventilator days (P < 0.05)[9]. In virtually every disease state examined to date, the presence of hyponatremia has been found to be an independent risk factor for increased mortality[13].

The hyponatremia patients have significantly higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score when compared to those of the normal serum sodium levels[14]. Funk et al. (2010) demonstrated that all types and grades of dysnatremia were associated with increased mortality[15]. Limited data is available on whether the presence of hyponatremia on intensive care unit (ICU) admission is independently associated with excess mortality[14]. However, no data exist about the frequency of hyponatremia and its consequences among the ICU patients in our country. So, the current study was designed to look at usefulness of hyponatremia to predict and the outcome of critically ill patients in Bangladesh. Obtained data from this study would be helpful for the intensivists as well as policy maker to emphasize on serum sodium levels for the better outcome of critically ill patients.

Materials and methods:

This Prospective observational cross-sectional study was carried out in the Department of Critical Care Medicine, BIRDEM General Hospital aiming at finding out the frequency of hyponatremia and its association with the outcome in critically ill patients. This study period was last for one year extending from 1st July, 2017 to 30th June, 2018. All consecutive critically ill patients were selected for the purpose of the study after applying the inclusion and exclusion criteria.

- **Inclusion criteria**: All patients admitted to ICU with age ≥18 years.
- **Exclusion criteria:** Age <18 years**,** patient having blood glucose level >13mmol/L**,** patients getting mannitol**,** patients with prior diagnosis with paraproteinemia and patients who took discharge on risk bond (DORB) during the study period.

Clinical history and detailed examination were done in all the patients at the time of ICU admission. Parameters like age, gender, ICU stay in days, variables useful to calculate APACHE II were recorded and relevant investigations were done. The study population were divided into euvolemic, hypervolemic and hypovolemic status depending on the clinical parameters: pitting edema (pedal or sacral), jugular venous pressure, skin turgor and capillary refill time. The patients were divided into two groups: patients with hyponatremia (serum sodium level less than 135 mmol/L) and patients with eunatremia (135-145 mmol/L).

21 days were taken as follow up period for all patients in this study. Outcome was measured by mortality. Those who were discharged or transferred categorized as survivors and who died during hospital stay categorized as non survivors.

Statistical analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc Chicago Illinois USA) and Microsoft Excel were utilized for data management and analysis. Exploratory data analysis was carried out to describe the study population where categorical variables were summarized using frequency tables and continuous variables were summarized using measures of central tendency and dispersion such as mean, median, percentiles and standard deviation. To determine association chi squared tests was used. Means and proportions were compared with Chi-square (χ^2) and t-Test. A p-value of less than 0.05 was considered statistically significant.

Result:

Total 296 admitted patients who had fulfilled the inclusion criteria were selected as study population. The findings of the study obtained from data analysis are presented below.

Among the study participants, hyponatremia was found in 41.20% (n=122). Mean age was 62.21±12.974 years, ranging from 23 to 96 years and there were 61.5% male and 38.5% female. Among the hyponatremic patients majority of the study population (n=112, 37.8%) were aged 61-70 years. Among male patients 39.6% (n=72) had hyponatremia, and among female 43.9% (n=50) had hyponatremia (p= 0.09). Table 1 shows distribution of hyponatremia in critically ill patients according to gender (n=296)

Table 1:

Sex	Hyponatremia		Total
	Present N (%)	Absent N (%)	
Male	72(39.6%)	110(60.4%)	182(100%)
Female	50(43.9%)	64(56.1%)	114(100%)
Total	122(41.2%)	174(58.8%)	296(100%)

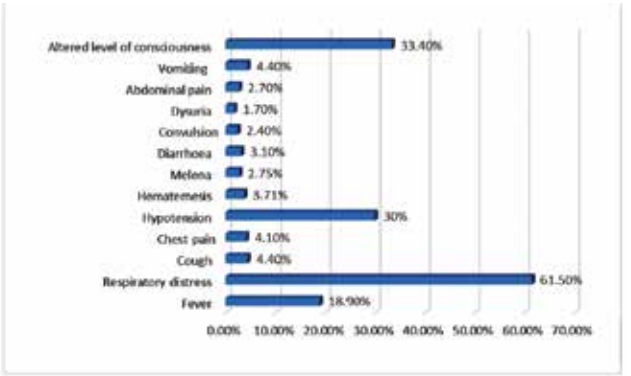

Figure 1: Clinical presentations (n=296)

Figure 2 shows commonest co-morbidities among the study subjects were DM (90.5%), followed by HTN (75.5%), CKD (50.5%), IHD (38%).Table 2 shows disease association among the study population (n=296).

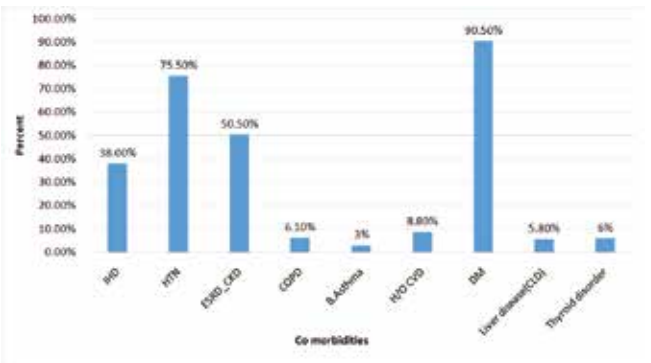

Figure2

Table 2

Diagnosis(n=296)	Frequency	Percentage %)
Pneumonia	128	43.24
Renal Failure (AKI/ AKI on CKD)	85	28.71
Stroke	37	12.5
NSTEMI	24	8.1
GBS	2	0.7
Acute pulmonary edema	55	18.58
Meningoencephalitis	29	9.8
UTI	90	30.41
Hepatic failure	10	3.4
Acute gastroenteritis	7	2.4
Sepsis/Septic shock	74	25
Acute exacerbation of COPD	9	3.0
Acute severe Asthma	4	1.4
Acute Pancreatitis	7	2.4
Viral fever with complication (Dengue, Chikungunya fever)	14	4.8

Table 3 shows volume status according to clinical criteria among study subjects (n=296). Mean APACHE ll score among the study population was 19.27±7.54 ranging from 4 to 42 (n=296). Table 4 shows relation between hyponatremia and APACHE ll score (n=296).

Table 3

Volume status	Hyponatremia n(%)	Eunatremia n(%)
Euvolemic	61(50.0%)	112(64.4%)
Hypervolemic	28(23.0%)	39(22.41%)
Hypovolemic	33(27.0%)	23(13.22%)

Table 4

	APACHE-ll Score 20 or less	APACHE-ll Score 21-25	APACHE-ll Score >25	Total	p value
Hyponatremia Absent n(%)	104 (59.77)	61(35.06)	09(5.17)	174	
Hyponatremia Mild>125 n(%)	36(50.70)	16(22.54)	19(26.76)	71	
Moderate (124-120) n(%)	08(33.33)	09(37.50)	07(29.17)	24	0.001
Severe <120) n (%)	05(18.52)	06(22.22)	16(59.26)	27	
Total	153	92	51	296	

Table 5 shows Use of mechanical ventilation (MV) among study population (n=296).

Table 5

Use of MV	Hyponatremia n(%)	Eunatremia n(%)	P value
Yes	66(54.10)	62(35.63)	
No	56(45.90)	112(64.37)	0.001
Total	122(100)	174(100)	

Table 6 shows Hyponatremia and its relation with duration of ICU stay (n=296)

Table 6

Hyponatremia	ICU STAY DURATION						
	0-7days	8-14 days	>14 days	Total	Mean	SD	P value
Present n(%)	84	35	3	122			
	(68.9%)	(28.7%)	(2.5%)	(100%)	6.5	±3.93	
Absent n(%)	127	28	19	174			
	(73%)	(16.1%)	(10.9%)	(100%)			0.08
Total n(%)	211	63	22	296			
	(71.3%)	(21.3%)	(7.4%)	(100%)			

Table 7 shows Hyponatremia and its outcome among the critically ill patients (n=296).

Table 7

Hyponatremia	Survivors	Non survivors	Total	p value
Present n(%)	86(70.49)	36(29.51)	122(100)	
Absent n(%)	145(83.33)	29(16.67)	174(100)	0.009
Total n(%)	231(74.04)	65(21.96)	296(100)	

Table 8 shows severity of outcome in relation to severity of hyponatremia (n= 122)

Table 8

Hyponatremia	Survivors	Non survivors	Total	p value
Mild(125 - 134) n (%)	55(77.46)	16(22.54)	71(100)	
Moderate(124-120) n (%)	15(62.50)	09(37.50)	24(100)	0.02
Severe(<120) n (%)	16(59.26)	11 (40.74)	27(100)	
Total	86(70.49)	36(29.51)	122(100)	

DISCUSSION

Hyponatremia is a common electrolyte abnormality seen in hospitalized critically ill patients. It is important to recognize because of its potential morbidity, mortality and economic impact on the patient and health care. In this study a total 296 of critically ill patients were included in the final analysis.

Mean age was 62.21±12.974 years, ranging from 23 to 96 years. Majority patients 112(37.8%) were aged 61-70 years. Among male patients 39.6% had hyponatremia and among female patients 44.9% (p=0.09). Hawkins (2003) found increasing age is a strong independent risk factor for hyponatremia[16]. It may be due to aging is associated with a decreased capacity to cope with environmental as well as disease related stresses in sodium and water balance. Upadhyay et al. (2006) stated in their epidemiologic study on hyponatremia that demographic characteristics of hyponatremia were highly variable[13].

In a prospective observational study on ICU patients over a period of 12 months reported 34.3% patients had hyponatremia[9]. In our study out of 296 patients 122(41.2%) patients had hyponatremia. Cumming et al. (2014), in their study on hyponatremia found 26.0% of patients had hyponatremia[17]. Difference between these findings may be due to different patient population and different base line characteristics. As 90.5% of our study population had DM, it may be also a contributory factor for high frequency of hyponatremia among ICU patients. Further controlled trial may be recommended to establish the issue. In an observational study the most common co-morbidities among patients with hyponatremia in ICU setting were hypertension (82%), DM (55%), ischemic heart disease (28%), and renal failure (16%)[18]. Our study was done in the largest diabetic hospital of the country so the most common co-morbidities were DM (90.5%), HTN (75%), CKD (50.5%), IHD (38%). This can be attributed to frequency, morbidity and mortality related to hyponatremia.

In our study, 50.0% patients with hyponatremia were euvolemic, 23.0% were hypervolemic and 27.0% were hypovolemic. In a retrospective study over a period of 5 years among ICU patient by Bennani et al. (2003) it was found that among eunatremia group 25.7% patients were hypovolemic, 23.7% patients were hypervolemic and 50.7% patients were normovolemic[19]. In another hospital based prospective study in Intensive Care Unit in Mumbai, reported 55% patients were euvolemic, 25% patients were hypervolemic and 20% patients were hypovolemic among hyponatremic patients[18]. All these studies suggest euvolemic hyponatremia is common in ICU patients. Volume status can guide us to evaluate the cause and proper management but one of the limitations of the study was not to evaluate the cause of hyponatremia according to volume status of the patients.

In our study mean APACHE II score among 296 patients was 19.27±7.54. The mean score among hyponatremic patients were 31.17±6.3. The APACHE II score also proportionately increase with severity of hyponatremia (p= 0.001). Padhi et al. (2014) reported mean APACHE II score among patients with hyponatremia group was 31+8.98[9]. Another study found significantly high APACHE ll score in ICU patients with hyponatremia during ICU admission (p=<0.01)[14]. All these study findings are similar regarding APACHE ll score and suggest predicted mortality is high in patients with hyponatremia.

In our study mechanical ventilation was required in 128 patients out of 296 patients. Among them 54.10% (n=66) was hyponatremic patients and 35.63% (n= 62) was eunatremic patients (p= 0.001). Padhi et al. (2014) reported among hyponatremic group 37.45% patients required mechanical ventilation (OR=0.99)[9]. In an observational multicenter cohort study in patients admitted between 2005 and 2012 to French ICUs, 38.4% of the patients with hyponatremia required mechanical ventilation support (p=<0.001). The findings of these studies are not similar. The explanation of these different observations may be due to most of the patients in this study presented to ICU with respiratory distress (61.50%). Pneumonia (43.24%) and acute pulmonary oedema (18.58%) were the predominant causes for respiratory distress in this study which were responsible for requirement of mechanical ventilation support.

Friedman and Cirulli (2013) found in a study done in USA, duration of ICU stay was significantly associated with hyponatremia (p <0.001)[20]. In this study the length of ICU stay is not statistically significant between the patients with hyponatremia and eunatremia (p=0.08). Rather the duration of ICU stay was less among the patients with severe hyponatremia. These differences in findings might be due to severity of the disease condition as evident by high APACHE ll score among hyponatremia patients and ultimately mortality was high in this group of patients.

It was observed in our study that non survivors among patients with hyponatremia during admission were 29.51% (n= 36) in compare with 16.67% (n= 29) in patients with eunatremia (p=0.009). Again, the number of non-survivor patients were increased with severity of hyponatremia (p=0.02). Pillai et al. (2018) found lower serum sodium concentration during admission was linked with a lower survival (p= 0.041)[3]. Funk et al. (2010) reported observed mortality among severe hyponatremia to be 33.6%. In mild hyponatremia it was 32.9% and in borderline hyponatremia it was 21.2%[15]. From these studies it can be concluded that all grades of hyponatremia were associated with higher mortality. However, taking into account all co-morbidities and relative severity of illness mortality comparison would require a large-scale regression analysis and sub group analysis as per volume status for a definitive comment on prognosis.

LIMITATION

Like any other scientific study, the present study is not without limitations. The following limitations deserve mentioning:

1. As the sample size was collected from a single study place, therefore, the study findings derived from this study cannot be generalized to reference population.
2. This study was carried out in an adult intensive care unit (ICU). So, age bellow 18 years population was not included in this study.
3. The overall mortality could not be attributed to hyponatremia as because patients with hyponatremia had other confounding factors for outcome.
4. 90.5% of our study populations are diabetic, so the obtained data could not be applicable for overall critically ill patients.

CONCLUSION

This study concludes that more than one-third of critically ill patients had hyponatremia during ICU admission. DM was the most frequent co-morbid condition present among the participants. Most of the hyponatremic patients were euvolemic. Mean APACHE ll score among hyponatremic patients was significantly high. Hyponatremic patients required more mechanical ventilation support but duration of ICU stay was not related to severity of baseline hyponatremia

during admission. Additionally, it was also found that mortality was dependent on degree of hyponatremia.

References:

1. Fried LF, Palevsky PM. Hyponatremia and hypernatremia. *The Medical clinics of North America*. 1997;81(3):585–609.
2. Baylis PH. The syndrome of inappropriate antidiuretic hormone secretion. *The International Journal of Biochemistry & Cell Biology*. 2003; 35(11):1495–1499.
3. Pillai KS, Trivede TH, Mozlick ND. Hyponatremia in ICU. *The Journal of the Association of Physicians of India*. 2018;66(5):48–56.
4. Waikar SS, Mount DB, Curhan GC. Mortality after hospitalization with mild, moderate, and severe hyponatremia. *The American journal of medicine*. 2009;122(9): 857-865. doi:10.1016/j.amjmed.2009.01.027.
5. Adrogué HJ, Madias NE. Hyponatremia. *The New England journal of medicine*. 2000;342(21):1581–9.
6. WindpesslM, Schwarz C, Wallner. Bowel prep hyponatremia –a state of acute water intoxication facilitated by low dietary solute intake: case report and literature review. *BMC Nephrology*. 2017;18(1):54-56.
7. Filippatos TD, LiamisG, Elisaf MS. Ten pitfalls in the proper management of patients with hyponatremia. *Postgraduate medicine*. 2016;128(5):516-522.
8. LeungAA, McAlister FA, Rogers SO, Pazzo V, Wright A, Bates DW. Preoperative hyponatremia and perioperative complications. *Archives of Internal Medicine. 2012;*172(19):1474–1481.
9. PadhiR, Panda BN, Jagati S, Patra SC. Hyponatremia in critically ill patients. *Indian Journal of Critical Care Medicine*. 2014;18(2):83-87.
10. Bissram M, Scott FD, Liu L, Rosner MH. Risk factors for symptomatic hyponatraemia: the role of pre-existing asymptomatic hyponatraemia. *Internal medicine journal*. 2007;37(3):149-155.
11. RafatC, Flamant M, Gaudry S, Vidal-Petiot E, Ricard J, Dreyfuss D. Hyponatremia in the intensive care unit: How to avoid a Zugzwang situation?. *Annals of Intensive Care*. 2015;5(1):1–27.
12. Shakher J, GandhiN, Raghuraman G. Impact of hyponatraemia in critically ill patients. *Endocr Abstr*. 2013;31:55 doi:10.1530/endoabs.31.
13. Upadhyay A, JaberBL, Madias NE. Incidence and prevalence of hyponatremia. *American Journal of Medicine*. 2006;119(7A):30–35.
14. PashaSA, Pasha SA, Prabodh VS, Vidya SD, Suhasini T. Frequency of hyponatremia in critically ill patients. *Indian Journal of Applied Research*. 2016;6(6):43-45.
15. Funk GC, Lindner G, Drumi W, Metnitz B, Schwarz C, Bauer P *et al.* Incidence and prognosis of dysnatremias present on ICU admission. *Intensive care medicine*. 2010;36(2):304–11.
16. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clinica Chimica Acta. 2003; 337(1–2):169–172.
17. Cumming K, Hoyle GE, Hutchison JD, Soiza RL. Prevalence, incidence and etiology of hyponatremia in elderly patients with fragility fractures. *PLOS One*. 2014;9(2):pe88272.
18. PathanB, NagpalRR, Rai DS. Hyponatremia in critically ill patients : Assessment f incidence, etiology, clinical manifestations and outcomes in ICU setting. *Journal of Medical Science and Clinical Research*. 2018;06(03):591–598.
19. Bennani SL, Abouqal R, Zeggwagh AA, Mandani N, Abidi K, Zekaoui A *et al.* Incidence, causes and prognostic factors of hyponatremia in an intensive care unit. *La revue de medicine. 2003;*24(4):224–229.
20. FriedmanB, Cirulli J. Hyponatremia in critical care patients: Frequency, outcome, characteristics, and treatment with the vasopressin V2-receptor antagonist tolvaptan. *Journal of Critical Care*. Elsevier Inc. 2013;28(2):219.e1-219.e12.