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Study Of Hyponatremia In Intensive Care Unit Patients

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Abstract

Hyponatremia is the most common electrolyte disorder among hospitalized patients and has been associated with increased mortality. The aims of the study are to study the incidence, clinical manifestations and symptomatology and clinical conditions which are associated with hyponatremia and analyse clinically possible cause of hyponatremia. This was a study of 100 patients admitted in the ICU of tertiary care hospital with serum sodium levels <135 mEq/L and age >15 years over a period from November 2019 to April 2021. Descriptive statistical analysis has been carried out in the present study. Among the 100 patients studied, 62% were males and 38% were females. The conscious patients have mild hyponatremia while moderate to severe hyponatremic patients came with altered sensorium. 44% patients were having renal causes while 21% patients had cardiac condition. The mortality was 14% in this study. Critically-ill patients suffer from hyponatremia due to various causes, including kidney disease, diuretics, heart failure, cirrhosis of the liver as well as infections. It presents with various symptoms and is linked to high morbidity and mortality in patients. Therefore, physicians must find signs and symptoms of patients in order to reduce mortality and morbidity and provide better care to the patients.

Key words: Renal, Hyponatremia, Diuretics, Seizure, Hypervolemia

Introduction

Hyponatremia is common in both inpatients and outpatients (Yeates et al., 2004). It is the most common electrolyte disorder among hospitalized patients (Gone NE et al., 2005; Bhananker SM et al., 2004; Coenraad MJ et al., 2003) and has been associated with increased mortality (Douglas I et al., 2006) ranging from 5% to 50%, depending on severity and acuity of onset (Beri T, 1990). Various studies have indicated that elderly patients showed a higher predisposition to develop hyponatremia (Driniger MN and Zazulia AR, 2006; Miller M, 1998). Various studies have emphasized the susceptibilities of hospitalized elderly patients to hyponatremia (Fegan G, 2009; Kugaler JP and Husted T, 2000). Studies have shown that elderly patients are more prone to hyponatremia as a result of conditions such as cardiac, renal and hepatic failure (Fegan G, 2009 and Schrier RW, 1990), physiological changes such as a decrease in glomerular filtration rate (Young A, 1997; Beck LH, 2000), altered water metabolism (Fulop T et al., 1985) and polypharmacy (Allison SP and Lobo DN, 2004). Hyponatremia in elderly in-patients is common during in-hospital stay is strongly associated with increased length of stay and loss of independence (Melvin C et al., 2007). The treatment of hyponatremia depends on the duration of hyponatremia and volume status of the patients. There is serious neurologic sequel if hyponatremia is inappropriately treated. Limited data is available on whether the presence of hyponatremia on intensive care unit (ICU) admission is independently associated with excess mortality. Therefore, we investigated incidence, clinical manifestations and symptomatology and clinical conditions which are associated with hyponatremia. We also investigated cause and its impact on patient outcomes in medical ICU.

Materials and Methods

The present study was conducted in patients admitted in the ICU of our hospital over a period of one and a half year. We have studied 100 cases of hyponatremia according to selection criteria.

Selection Criteria

Inclusion criteria

- Patients admitted to the hospital in ICU wards with serum sodium levels <135 mEq/L.
- Age of patients >15 years.

Exclusion criteria

- Patients admitted to the hospital in ICU wards with serum sodium levels ≥ 135 mEq/L.

- Age of patients ≤ 15 years.
- Postoperative patients.
- Patients with pseudohyponatremia (Defined by hyponatremia in the absence of any obvious etiology and presence of hyperproteinemia,hyperlipidemia,hyperglycemia).

Study Protocol

Over a period of one and a half year from 01/11/2019 to 30/04/2021, data on patients admitted to this hospital in the medical ICU with hyponatremia were collected. Patients admitted to the hospital suspected to have metabolic derangement were evaluated for biochemical abnormalities. 100 patients with serum sodium < 135 mEq/L were selected for the study according to selection criteria. A detailed history was delineated with special thrust to the events occurred prior to admission and the symptomatology whichever these patients manifested at the time of admission were recorded. The information thus obtained was recorded in the proforma. These patients were then evaluated clinically to assess their fluid status.

Based on fluid status, they were further divided as hypervolemic, hypovolemic and euvolemic. The routine investigations done in these patients were haemoglobin, total blood count, differential count, erythrocyte sedimentation rate, electrocardiogram, chest x ray, 24 hour urine sample for urinary sodium, urine urea and urine glucose, blood sugar, urea and creatinine, serum lipid. Patients suspected with other causes were investigated accordingly.

Based on serum sodium level, they were divided into Mild hyponatremia with(121-134 mEq/L), Moderate hyponatremia(111-120 mEq/L) and Severe hyponatremia(≤ 110 mEq/L).

Based on severity of symptoms they were divided into Mild, Moderate and Severe hyponatremia. Nausea,Vomiting, Headache, Giddiness, Diarrhoea were considered here as Mild symptoms, Fatigue, Irritability and Cramps as Moderate symptoms and Seizures, Drowsiness and Unconsciousness as severe symptoms.

Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean $\pm$ SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

Suggestive significance (p value: $0.05 < p < 0.10$)

Moderately significant (p value: $0.01 < p \leq 0.05$)

Strongly significant (p value: $p \leq 0.01$)

Results

135 patients had hyponatremia out of 804 patients admitted in ICU during period of one and a half year giving the incidence rate of hyponatremia in ICU patients was 16.79%. For this study 100 patients were selected according to selection criteria from the patients with serum sodium < 135 mEq/L. Among the 100 patients studied, 62(62%) were males and 38(38%) were females. The male to female ratio was 1.63:1. The mean age of patients was 50.50 ± 20.00 . The age varied from 16 to 75 years in males and 16 to 85 years in females (Table 1).

Table 1: Age and Gender wise distribution

Age (years)	Male	Female	Total
16-25	4	1	5
26-35	3	2	5
36-45	11	5	16
46-55	14	8	22
56-65	16	7	23
66-75	14	9	23
76-85	0	6	6
Total	62	38	100

Among these, 26 patients were ≤ 45 years and 74 patients were > 45 years (Table 2).

Table 2: Age and Gender wise distribution

Age in years	Male	Female	Total
≤ 45 years	18	8	26
> 45 years	44	30	74
Total	62	38	100

36(36%) patients had mild hyponatremia with serum sodium 121-134 mEq/L, 40(40%) patients had moderate hyponatremia with serum sodium level 111-120 mEq/L and 24(24%) patients had severe hyponatremia with serum sodium ≤ 110 mEq/L.

Based on Table 3, patients above the age of 45 years were found to be more in moderate to severe hyponatremia. In patients below age of 45 years were found to be more in mild hyponatremia. The p-value is 0.00627928. This result is significant at $p < 0.05$.

Table 3: Age and Severity wise distribution

Age	Hyponatremia	Hyponatremia	Hyponatremia	Total
	Mild	Moderate	Severe	
≤45 yr	16	7	3	26
>45 yr	20	33	21	74
Total	36	40	24	100

The symptoms of this patients varied from gastrointestinal to neurological symptoms. The gastrointestinal symptoms were predominantly nausea, vomiting, diarrhoea. The neurological symptoms were headache, giddiness, fatigue, cramps, irritability, seizures, drowsiness. There is overlapping of symptoms in between them (Table 4).

Table 4: Symptoms and Severity wise distribution

Symptoms	Hyponatremia	Hyponatremia	Hyponatremia	Total
	Mild	Moderate	Severe	
Nausea	32	13	15	60
Vomiting	20	15	10	45
Headache	23	11	19	53
Giddiness	16	10	8	34
Fatigue	6	11	13	30
Irritability	3	9	15	27
Seizures	0	14	10	24
Cramps	0	13	13	26
Drowsiness	0	16	10	26

The conscious patients have mild hyponatremia while moderate to severe hyponatremic patients came with altered sensorium. 56% patients came with consciousness while 26% patients came drowsy. 18% patients came with unconsciousness (Table 5).

Table 5: Association of Sensorium with Severity of Hyponatremia

Sensorium	Hyponatremia	Hyponatremia	Hyponatremia	Total
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	Mild	Moderate	Severe	
Conscious	36	14	6	56
Drowsiness	0	16	10	26
Unconscious	0	10	8	18
Total	36	40	24	100

The p-value is 0. This result is not significant at $p < 0.05$.

Hydration status of the patients is determined by clinical examination. The signs of hypovolemia included tachycardia, orthostatic falls in blood pressure, decrease skin turgor, dry mucous membrane and decreased peripheral perfusion with a delayed capillary refill more than 3 seconds. Hypervolemic state was defined by the presence of anasarca, ascites, symmetrical and pitting pedal edema and raised jugular venous pressure(JVP).

Patients who did not have signs of hypovolemia or hypervolemia are considered as euvolemic.

According to that the patients were divided into hypovolemic, hypervolemic and euvolemic(Table 6).

Table 6: Hydration and Level of Hyponatremia

Hydration Status	Hyponatremia	Hyponatremia	Hyponatremia	Total
	Mild	Moderate	Severe	
Hypovolemia	8	8	6	22
Hypervolemia	12	22	14	48
Euvolemia	16	10	4	30
Total	36	40	24	100

The p-value is 0.13657681. This result is not significant at $p < 0.05$.

Hyponatremia is frequently multifactorial, particularly when severe. Clinical examination, oral intake, detail drug history, watch for signs of septicemia like high temperature, leucocytosis, pulse rate, routine and radiological investigation done whenever needed and according to that probable underlying etiology were found below(Table 7).

Table 7: Etiology

Causes	Number of patients having hyponatremia
Renal cause	44

(Chronic renal failure + Acute kidney injury)	
Cardiac cause (Congestive Cardiac Failure)	21
Gastrointestinal cause (Cirrhosis + Hepatic Encephalopathy + Acute Gastro Enteritis)	7
Endocrinal cause (Hypothyroidism)	11
Neurological cause (CVA + Meningitis)	11
Respiratory cause (Pneumonia + COPD + Pulmonary TB)	6
Patients having Diuretics (thiazide + loop diuretics + spironolactone)	40
Patients having septicemia	28
Patients having decreased intake	2

Underlying clinical condition is associated with severity of hyponatremia(Table 8). We found that hyponatremia is more severe in patients with renal and cardiac causes.

Table 8: Severity in various clinical condition

Clinical condition		Hyponatremia severity		Total
Etiology	Mild	Moderate	Severe	Total
Renal	12	19	13	44
Cardiac	6	8	7	21
GI cause	3	3	1	7
Endocrinal	5	6	0	11
Neurological	5	3	3	11
Respiratory	5	1	0	6
Total	36	40	24	100

The p-value is 0.20506921. This result is not significant at $p < 0.05$.

Patients having underlying renal and cardiac conditions are mostly hypervolemic while patients having underlying neurological, gastrointestinal or respiratory condition were euvoletic, hypovolemic and hypervolemic (Table 9).

Table 9: Hydration and Etiology

Clinical condition		Hydration status		Total
Etiology	Hypovolemia	Hypervolemia	Euvoletic	Total
Renal	8	30	6	44
Cardiac	4	12	5	21
GI	3	2	2	7
Endocrinal	2	1	8	11
Neurological	4	2	5	11
Respiratory	1	1	4	6
Total	22	48	30	100

The p-value is 0.00135039. This result is significant at $p < 0.05$.

In present study, we found that diuretics is one of the underlying cause of hyponatremia, among that thiazide diuretics are a major cause of hyponatremia. Out of 40 patients on diuretics, 26(65%) patients on thiazide and 14(35%) patients on loop diuretics and spironolactone.

40 patients were on diuretic. Among that 20(50%) had mild, 16(40%) had moderate and 4(10%) patients having severe hyponatremia.

40 patients were on diuretic. Among that 18(45%) were hypovolemic, 4(10%) were hypervolemic and 18(45%) were euvoletic.

In present study, only 2 patients had decreased intake due to old age and having equal distribution of mild and moderate hyponatremia (Table 10).

Table 10: Intake and Severity

Patients having decreased intake		Severity		Total
	Mild	Moderate	Severe	
2	1(50%)	1(50%)	0	2(100%)

In present study, only 2 patients had decreased intake due to old age and having euvolemic hyponatremia.

Septicemia associated with hyponatremia is known to have increased morbidity and mortality. The cause of this phenomenon is unknown but may be related to dilution of extracellular space with retained exogenous fluid.

Clinically septicemia is defined by high temperature, rapid pulse, malaise, hypotension and associated with marked leucocytosis.

In present study, 28 patients were having signs of septicemia. 3(11%), 13(46%) and 12(43%) had mild, moderate and severe hyponatremia respectively. Out of 28 patients having septicemia, 15(53%) were hypervolemic, 8(29%) were hypovolemic and 5(18%) were euvolemic.

In this study, 86 patients were improved. Among them 35% had mild, 30% had moderate and 21% patients had severe hyponatremia. Outcome with severity wise distribution is as below (Table 11).

Table 11: Outcome and Severity

Hyponatremia	Outcome	Outcome	Outcome
	Improved	Death	Total
Mild	35(35%)	1(1%)	36(36%)
Moderate	30(30%)	10(10%)	40(40%)
Severe	21(21%)	3(3%)	24(24%)
Total	86(86%)	14(14%)	100(100%)

The p-value is 0.01994055. This result is significant at $p < 0.05$.

The mortality was 14% in this study. Among this 2% patients were having hypovolemic, 10% patients were having hypervolemic and 2% patients were from euvolemic group. Outcome and hydration wise distribution is as below (Table 12).

Table 12: Hydration and Outcome

Hydration status	Outcome	Outcome	Total
	Discharge	Death	
Hypovolemic	20(20%)	2(2%)	22(22%)
Hypervolemic	38(38%)	10(10%)	48(48%)
Euvolemic	28(28%)	2(2%)	30(30%)
Total	86(86%)	14(14%)	100(100%)

Discussion

Hyponatremia is common electrolyte disturbance seen in hospital practice. The incidence of hyponatremia was 16.79% in one and a half year retrospective study in ICU patients. The incidence was 6.9% in the study done by Hochman et al(1989). Bennani et al(2003) found the incidence of hyponatremia to be 14% in ICU while Devita et al(1990) found the incidence of hyponatremia in ICU to be 29.6%. Study done by Nandini Chatterjee(2012) found 12% incidence. The incidence of hyponatremia (16.79%) in present study correlates well with most of the other studies and estimates the high incidence of hyponatremia medical wards. A number of studies have evaluated the incidence and etiology of hyponatremia in general, but there are very few relevant studies related to hyponatremia in inpatients in medical ICU. Delineating the cause of hyponatremia is important in order to impart specific treatment tailored to the etiology.

The present study included patients with serum sodium <135 mEq/L. There were 62 males and 38 females with ratio of 1.63:1. In general, in our hospital population, there were more males than females. Hence, this slight increase in males was not very significant. But in age group above 75 years comprised of only females. No conclusion was made on this difference in incidence.

In the present study, hyponatremia was seen more commonly in patients above 45 years than in younger patients. The ratio between numbers of patients > 45 years in comparison of ≤ 45 years 2.84:1. Similar trend was also observed by Hochman et al(1989) and Vurgese et al(2006). In their study, elderly patients were more prone for hyponatremia. The mean age in the present study was 50.50 ± 20.00 which is comparable to studies done by Anderson et al(1985) where the mean age was 58 years and study done by Vurgese et al(2006) where the mean age was $57.05 \pm 2SD$. The various factors responsible for hyponatremia in elderly are decreased glomerular filtration rate, impaired ability of kidney to conserve sodium, increased release of arginine vasopressin to a given osmotic stimulus, various drugs taken by them, decreasing appetite and concomitant illnesses.

Table 13: Comparison of Gender and Age

	Present study	Vurgese
Study Population		
Male	62%	56%
Female	38%	44%

Mean age	50.50±20.00	57.95±2SD
≥45 year aged pts with hyponatremia	74%	72.8%

There were 36(36%) patients with mild hyponatremia. There were 64 (64%) patients having moderate and severe hyponatremia. In study by Hochman et al(1989), there were 39% patients with mild hyponatremia and rest 61% had moderate to severe hyponatremia which is comparable to present study. The degree of hyponatremia could more or less predict the symptoms of hyponatremia. Some patients with serum sodium greater than 120 mEq/L had neurological symptoms like drowsiness. But patients with serum sodium less than or equal to 110 mEq/L showed severe neurological symptoms like seizures and unconsciousness. The presence or absence of symptoms and severity was more related to rapidity of fall of serum sodium rather than the amount of fall. The elderly patients with chronic hyponatremia can tolerate lower levels of hyponatremia without any symptoms. Hence, we conclude the more severe the hyponatremia and rapid fall of sodium, more severe the symptoms.

Table 14: Comparison of Hydration

Hyponatremia	Hochman (%)	Anderson (%)	Present study (%)
Hypovolemia	50	34	22
Hypervolemia	30.5	35	48
Euvolemia	19.5	31	30

The percentage of patients in various groups in the present study varies markedly with the above study. The reason for this variation was probably due to the limited number of patients and selection criteria in the present study.

Renal failure was the most common cause of hyponatremia in the present study representing 44% of cases while SIADH was the most common cause in study of Vurgese et al(2006). In patients with hypervolemic hyponatremia, 44 patients satisfied the criteria to diagnose Renal failure. They had low serum osmolality and high urinary sodium and altered renal function tests.

Diuretics (thiazide + loop diuretics + spironolactone) use was the 2nd most common underlying cause for hyponatremia in present study. 40 patients were on diuretics among that 26(65%) were

on thiazide diuretics and 14(35%) patients were on loop diuretics and spironolactone diuretics. Saeed et al(2002) studied hyponatremia in hospitalized patients in 19(33.3%) out of 57. In study by Huda et al(2006) 14 (63%) out of 22 patients of hyponatremia were taking diuretics. This warrants judicious and clinically monitored use of diuretics by clinicians particularly in elderly patients with chronic renal, cardiac and hepatic disease.

Septicemia is also a precipitating factor for hyponatremia. In present study, we found 28 (28%) patients had signs of septicemia. Study done by Padhi BN(2014) found 21.54% of patients with septicemia. Nandini Chatterji(2012) found 18% of patients with septicemia.

SIADH

SIADH was clinically suspected with most cases of euvolemic hyponatremia. The diagnostic criteria needed are low serum osmolality, high urine osmolality, high urine sodium and normal adrenal, thyroid, renal and liver functions. Common underlying causes of SIADH are pulmonary (pneumonia, lung abscess, bronchiectasis, tuberculosis), neurological (vascular diseases and infections), drugs (TCA, carbamazepine, SSRI), pain, psychosis, stress and idiopathic SIADH of elderly. Study done by Nandini Chatterjee(2012), 32.8% of patients having hyponatremia, had laboratory confirmation of SIADH. Most of the patients having underlying respiratory and neurological condition. In other study done by Hochman et al(1989) SIADH represented 28.3% of cases and 34% of patients in study of Anderson et al(1985). In present study, we found 30 (30%) patients were clinically euvolemic. Among them 13 patients had renal, cardiac and gastrointestinal condition, 17 patients had underlying respiratory disease, neurological disease and septicemia.

Monitoring of sodium was done on a 6 hourly to 12 hourly basis in most of the patients with moderate and severe hyponatremia. Fluid correction depended on the type, cause and presentation of symptoms. The mean rate of correction was adequate and comparable with most of the international studies. Normal saline alone, 3% saline, fluid restriction, extra salt diet, diuretics, dialysis, Vaptans were used to treat hyponatremia. The mortality in this study (death) is around 14% . The mortality depended on severity of the underlying illness rather than serum sodium or the rate of correction.

Table 15: Comparison of Mortality

Study	Present study	Nandini Chatterji et al	Nzerue et al
Mortality(%)	14%	13.5%	20.2%

Conclusion

Hyponatremia is common electrolyte abnormality in ICU patients. The incidence of hyponatremia in the present study was 16.79% of ICU patients. Hyponatremia is more common in elderly. The symptoms of hyponatremia vary from individual to individual. The symptoms increase with the severity of hyponatremia and the sensorium deteriorates at the lower levels. Majority of patients in present study were noticed to have underlying Renal, Cardiac, Gastrointestinal and Neurological diseases. Among Neurological diseases, Meningitis and Cerebrovascular Accidents were the commonest. Among Respiratory diseases, infections like Pneumonia were the commonest and in Cardiac diseases Congestive Cardiac Failure under treatment was commonest. Most of the patients in present study were found to have hypervolemic hyponatremia(48% of cases). Renal failure is the most common precipitating factor of hyponatremia. Diuretics are the 2nd common underlying factor found in hyponatremia patients. Septicemia was common finding among hyponatremia patients. The mortality associated with hyponatremia in the present study was 14%. Further evaluation appears essential to exclude SIADH in patients having euvolemic hyponatremia. Most of this appeared to be due to the underlying disease the patient had at the time of admission. Therefore, it is important to urgently identify the cause and treat the patient accordingly to reduce the morbidity and mortality.

Abbreviations

CCF :Congestive cardiac failure

COPD : Chronic obstructive pulmonary disease

CVA : Cerebrovascular accident

PTB : pulmonary tuberculosis

SIADH : Syndrome of inappropriate anti diuretic hormone

SD : Standard deviation

SSRI : Selective serotonin reuptake inhibitors

TCA : Tricyclic antidepressant

% : Percentage

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