Section: General Medicine

Original Research Article

STUDY OF CLINICAL PROFILE AND OUTCOME OF HYPONATREMIA IN HOSPITALIZED PATIENTS

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Abstract

Background: Hyponatremia is the most common electrolyte imbalance, accounting for around 22% of all cases. It is the major cause of morbidity and mortality in Indian intensive care settings, but data is limited. The aim of the present research was to evaluate the etiological profile of admitted patients with symptomatic hyponatremia and their eventual in-hospital outcome. **Materials and Methods:** A prospective observational study was conducted on 100 patients meeting eligibility criteria. Patients' biochemical parameters, such as serum sodium, serum osmolality, urine sodium, and urine osmolality, were recorded. On the basis of serum sodium levels, patients were classified as mild, moderate, or severe. The incidence and clinical profile of hyponatremia in hospitalised patients were studied, and the clinical features were correlated with the biochemical profiles of the patients. Also, the patient's outcome of hyponatremia with various aetiologies and types was observed and recorded. **Result:** The symptoms of the patients varied from neurological to gastrointestinal to asymptomatic in this study, where the commonest symptom was revealed to be lethargy, followed by postural dizziness and nausea or vomiting. The most common cause of hyponatremia was revealed to be SIADH. Furthermore, 51% had euvolemic hyponatremia, 18% had hypervolemic hyponatremia, and 31% had hypovolemic hyponatremia. A total of 13% of the subjects died, whereas the rest (87%) recovered. More deaths were seen in females than in males. The highest incidence was recorded in age limit of 41-50 years aged individual. The majority of patients were asymptomatic, and the most common symptoms in severe cases were abnormal behaviour and coma. Also, the GCS score was inversely proportional to the incidence of hyponatremia. Good outcome of patients after treatment was observed in mild to moderate hyponatremia. **Conclusion:** Severe hyponatremia was more associated with mortality due to other primary causes.

INTRODUCTION

Hyponatremia is a frequent electrolyte disease that causes emergency hospitalization and considerable mortality and morbidity. A body status with a serum sodium content of less than 135 mmol/L is considered hyponatremia. It is classified into three categories: mild hyponatremia (130–134 mmol/L), moderate hyponatremia (120–129 mmol/L), and severe hyponatremia (120 mmol/L).[1-3] Up to 15% of hospitalized patients or institutionalized elderly suffer from mild hyponatremia.[4,5]

In the clinical setting, hyponatremia is frequently undetected when illness is either moderate or progresses slowly. On the other hand, severe hyponatremia (serum sodium 120 mmol/L), especially with fast onset, is linked to considerable morbidity and can be fatal. There is a high risk of morbidity and death in patients with moderate to severe hyponatremia.[6,7] The elderly aged people are particularly susceptible to this condition because of their compromised ability to maintain a healthy water and electrolyte balance in response to changes in their food, medication, and lifestyle. Although hyponatremia alone is not a disease, it can be a symptom of a number of potentially fatal disorders. Various disorders can cause hyponatremia, and their prevalence varies from one demographic to the other. The signs and symptoms of hyponatremia can vary with both the onset and severity of the condition. Hyponatremia is often asymptomatic in the chronic stage. Sodium depletion can cause mild symptoms whereas rapid depletion can show severe symptoms.[8] An acute form of hyponatremia is one

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in which symptoms appear within 48 hours. Cerebral oedema, caused by fluid shifts in the brain, contributes to the neurologic symptoms experienced by patients with acute hyponatremia. It is possible to have seizures, mental decline, coma, and even death as a result of the same. Patients with hyponatremia have a greater death rate compared to those who do not have the condition.[9] Published death rates, however, show a wide range, from a 1.5 to 60 fold increase compared to non-hyponatremic individuals.[10] In light of the variability in the increased risk that has been seen, it is probable that variables other than changes in sodium levels are at play here. Most studies lack methodologic robustness, which results in substantial discrepancies between univariate and multivariable analyses, as well as differences in clinical context and hyponatremia characterization.[11].Therefore, it is still unclear whether hyponatremia is a cause of higher mortality or simply a proxy for the severity of the underlying illness.[12] Therefore, it is possible that the increased risk of death observed in multiple observational studies results from a complex interplay of various patient- and setting-related variables.[13] Recognizing hyponatremia early on can help save lives. Without careful treatment, hyponatremia can have devastating long-term effects on prognosis.[14] The purpose of the current study was to evaluate the etiological profile of admitted patients with symptomatic hyponatremia and their eventual in-hospital outcome.

MATERIALS AND METHODS

Study Design

The current prospective observational study was conducted at Department of General Medicine, Medical College, Hospital and Research Centre, D.Y. Patil Deemed to be University Navi Mumbai. Approval of Institutional Ethics Committee was obtained before the commencement of the study (IEC Ref No: DYP/IECBH/2020/41; Dated 10/07/2020). Also, a well-informed written consent (in English, Hindi or Marathi) was taken prior to enrolling the subject in the study. The study was conducted from July 2019- July 2020.

Eligibility Criteria

IPD patients with age more than 18 years and plasma sodium more than 135 mmol/L were included in the study whereas pregnant women or patients under treatment for chronic hyponatremia were excluded.

Study procedure, Sample Size and Method

A total of 100 patients were included in the study using convenient sampling method. Patient's demographic data was recorded along with their biochemical parameters such as serum sodium, serum osmolality, urine sodium and urine osmolality. On basis of serum sodium levels, patients were classified into mild 125 to 135mEq/L, moderate 121 to 125 mEq/L, and severe less than 120mEq/L. The incidence and clinical profile of hyponatremia in hospitalized patients was studied and the clinical features were correlated with the biochemical profile of the patients. Also, patient's outcome of hyponatremia with various etiology and type was observed and recorded.

Statistical Analysis

All the data was recorded in a pre-designed study proforma. Qualitative data are represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test. Quantitative data are represented using Mean ± SD, Median and Interquartile range (IQR). Analysis of quantitative data between the two groups was done using unpaired t-test for normalized data and by Mann-Whitney Test for un-normalized data. A p value <0.05 was considered as significant value and SPSS software was used to execute all the statistical analysis.

RESULTS

Table 1 represents the demographic data of the study participants. Out of 100 participants, 57 were males and 43 were female. The average age for male was found to be 48.15 years which was at par with the average female age i.e., 49.13 years. Maximum subjects (35%) belonged to 41-50 years of age group. Further classification of the study subjects according to various parameters is presented in Table 2. On the basis of symptoms, the patients were classified as falling under the categories of asymptomatic, lethargy, dizziness, abnormal behavior, seizures, nausea/ vomiting, and coma. The symptoms of the patients varied from neurological to gastrointestinal to asymptomatic in this study, where the commonest symptom was revealed to be lethargy (21%), followed by postural dizziness (19%) and nausea or vomiting (19% each). Out of 100 patients, the most common cause of hyponatremia was SIADH (18%), whereas 15% had drug-induced hyponatremia, 13% had hypothyroidism, and 14% had GIT loss of water. The GCS score was more than 13 in 68% of patients, 8 to 12 in 22% of patients, and less than 8 in 10% of patients (Table 2). In the present study, 46% had mild hyponatremia, 35% had moderate hyponatremia, and 19% had severe hyponatremia. Furthermore, 51% had euvolemic hyponatremia, 18% had hypervolemic hyponatremia, and 31% had hypovolemic hyponatremia. A total of 13% of the subjects died, whereas the rest (87%) recovered. More death was seen in females than in males.

Various parameters and their percentages recorded as per the severity of the hyponatremia are displayed in Table 3. In the present study, severe hyponatremia was seen more frequently found in the age group from 41 to 70 years. The highest incidence was recorded in age limit of 41-50 years aged individual with 5% severity and 15% each mild and moderate hyponatremia case. The distribution of patients as per their disease severity was found to be statistically significant (p = 0.049). As per gender, 10% of the

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male and 9% of the female cases were severe, and hence the distribution was found to be statistically insignificant (p = 0.904). In this study, the majority of patients were asymptomatic, and the most common symptoms in severe cases were abnormal behavior and coma. Also, the GCS score was inversely proportional to the incidence of hyponatremia. The distribution of the individual as per the symptoms and GCS score versus severity of the disease was found to be statistically significant (p<0.001). Severe hyponatremia was associated with 4% of patients diagnosed with drug use (like diuretics), followed by SIADH and liver failure (3% each). The death rate was higher in patients who had moderate to severe hyponatremia. 19% had severe hyponatremia, of which 10% recovered and 9% died. The individual percentage difference in these groups were found to be statistically significant (p<0.001) (Table 4). This study aimed to evaluate hydration status and its association with the severity of hyponatremia. In this study, more severe hyponatremia was seen in euvolemic patients followed by hypovolemic patients, and the difference in the distribution was found to be statistically significant (p=0.465). With respect to co-morbidities, diabetes mellitus was investigated in 30% of patients, hypertension in 31%, and chronic kidney diseases in 12% of patients. Table 4 represents association of outcome according to age. Highest mortality was observed on age group of 61-70 years of patients. Further mean serum osmolarity, mean urinary osmolarity and mean urinary sodium level was also measured in all the patients in accordance to the severity levels (Table 5).

Table 1: Demographic of the study participants.

Demographic		Percentage (%)
Age (yrs)	18 to 30	10
	31 to 40	17
	41 to 50	35
	51 to 60	17
	61 to 70	14
	>70	7
Gender	Male	57
	Female	43

Table 2: Classification of the study subjects according to various parameters.

Parameters		Male (%)	Female (%)	Total (%)
Symptoms	Asymptomatic	9	5	14
	Lethargy	10	11	21
	Dizziness	15	4	19
	Abnormal behavior	6	9	15
	Seizures	3	2	5
	Nausea/ Vomiting	9	10	19
	Coma	5	2	7
	Total	57	43	100
Diagnosis	Adrenal insufficiency	5	2	7
	Cardiac failure	3	2	5
	Drugs	8	7	15
	GIT	8	6	14
	Hypothyroidism	6	7	13
	Liver failure	4	3	7
	Malignancy	1	1	2
	Meningitis	1	0	1
	Pneumonia	5	0	5
	Renal Failure	4	4	8
	Sepsis	4	1	5
	SIADH	8	10	18
	Total	57	43	100
GCS score	> 13	38	30	68
	8 to 12	12	10	22
	<8	7	3	10
	Total	57	43	100
Severity of hyponatremia	Mild	27	19	46
	Moderate	20	15	35
	Severe	10	9	19
	Total	57	43	100
Type of Hyponatremia	Euvolemic	27	24	51
	Hypervolemic	10	8	18
	Hypovolemic	20	11	31
	Total	57	43	100
Outcome	Recovered	52	35	87
	Death	5	8	13

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Table 3: Various parameters and their percentage recorded as per the severity of the hyponatremia.

	Severity of hyponatremia				Total
		Mild (%)	Moderate (%)	Severe (%)	
Age group	18 to 30	8	1	1	10
	31 to 40	12	4	1	17
	41 to 50	15	15	5	35
	51 to 60	7	5	5	17
	61 to 70	2	7	5	14
	>70	2	3	2	7
	Total	46	35	19	100
Gender	Male	27	20	10	57
	Female	19	15	9	43
	Total	46	35	19	100
Symptoms	Asymptomatic	14	0	0	14
	Lethargy	10	11	0	21
	Postural dizziness	8	11	0	19
	Abnormal behavior	1	4	10	15
	Seizures	0	3	2	5
	Nausea/Vomiting	13	6	0	19
	Coma	0	0	7	7
	Total	46	35	19	100
GCS score	> 13	46	22	0	68
	8 to 12	0	13	9	22
	<8	0	0	10	10
	Total	46	35	19	100
Diagnosis	Adrenal insufficiency	1	5	1	7
	Cardiac failure	3	0	2	5
	Drugs	7	4	4	15
	GIT	7	5	2	14
	Hypothyroidism	12	1	0	13
	Liver failure	0	4	3	7
	Malignancy	0	1	1	2
	Meningitis	1	0	0	1
	Pneumonia	4	0	1	5
	Renal Failure	2	4	2	8
	Sepsis	0	5	0	5
	SIADH	9	6	3	18
	Total	46	35	19	100
Outcome	Recovered	46	31	10	87
	Death	0	4	9	13
Type of Hyponatremia	Euvolemic	21	21	9	51
	Hypervolemic	7	7	4	18
	Hypovolemic	18	7	6	31
	Total	46	35	19	100
Co-morbidities					
Diabetes Mellitus	Yes	8	10	12	30
	No	38	25	7	70
Hypertension	Yes	11	12	8	31
	No	35	23	11	69
CKD	Yes	1	4	7	12
	No	45	31	12	88

CKD- chronic kidney disease.

Table 4: Association of outcome according to age wise.

Age group	Outcome (%)		Mortality age wise (%)
	Survive	Death	
18 to 30	10	0	0
31 to 40	14	3	17
41 to 50	34	1	2.8
51 to 60	13	4	23.52
61 to 70	10	4	28.57
>70	6	1	14.28
Total	87	13	100

Table 5: Mean serum osmolarity, mean urinary osmolarity and mean urinary sodium level in hyponatremia

Parameters	Mild (%)	Moderate (%)	Severe (%)	Mean
Serum osmolarity (275-295 mOsm/kg)	245.4 ±11.9	247.7 ±12.5	240.8 ±14.7	245.4 ±12.8
Urine osmolarity (500-850mIsm/kg)	338.8 ± 91.3	318.4 ± 70.8	329.9 ± 81.9	329.9 ± 81.9
Urinary sodium (20-220mEq)	59.3 ± 22.7	54.8 ± 19.1	51.8 ± 21.4	56.3 ± 21.2

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DISCUSSION

Hyponatremia is a common electrolyte abnormality found in hospitalised patients. Most often, this occurs because of a failure to suppress antidiuretic hormone, resulting in decreased free water excretion (ADH). A high-water intake that exceeds the kidney's maximum diluting ability is another possible cause of polydipsia.[15] As per our data, the incidence of hyponatremia was more commonly seen in males as compared to females and in the middle age group between 40 and 60 years of age. As age increases, the severity of hyponatremia also increases. The majority of patients had mild hyponatremia, followed by moderate and severe. The findings of our study are consistent with those of Babaliche and the team, who found that 59% of their participants were male and 41% were female.[16] Patients were mostly between the ages of 61 and 70 (29%), with a mean age of 58.94 ± 16.10 years old (1.43 men to 1 woman). Rahil and co-researchers also documented a similar gender ratio, finding that 62.3% of their hyponatremia patients were male and 37.7% were female.[17] As a result of age-related impairments in water and electrolyte homeostasis brought on by dietary and environmental factors, the elderly is disproportionately affected by hyponatremia. In agreement with prior studies, we found that hyponatremia was more common in individuals who were middle-aged or older than in those who were younger. [18,19]

In our study, most patients with mild hyponatremia were asymptomatic. Patients with moderate to severe hyponatremia presented with neurological and GI symptoms. Lethargy and dizziness were the most common complaints, followed by nausea and vomiting. As the severity of hyponatremia increased, serious symptoms such as abnormal behaviour, seizures, and coma were seen in the patients. Previous study also supports that nausea and vomiting are most common gastrointestinal symptoms whereas headache, giddiness, slurred speech and drowsiness are most common neurological symptoms of hyponatremia.[1] Our study results can be compared with the study conducted by Babaliche and colleagues in which most frequent presenting complaint was vomiting (28%) followed by confusion (26%), seizure (9%), and coma (4%).[16]

In our study, SIADH followed by GI loss of water was one of the common causes of hyponatremia. Other causes were hypothyroidism, adrenal insufficiency, cardiac failure, liver failure, renal failure, drugs, malignancy, pneumonia, meningitis, and sepsis. A relatively large number of patients had endocrine abnormalities such as hypothyroidism, adrenal insufficiency, and pituitary abnormalities associated with hyponatremia. Previous study have also reported SIADH as the most common cause of hyponatremia.[16] A prospective research in a general medical-surgical setting found that 66 patients (34%) had euvolemic hyponatremia, 38 (19%) had hypervolemic hyponatremia linked with oedematous illnesses, and 33 (17%) had hypovolemic situations, primarily due to gastrointestinal fluid loss or diuretic usage.[20] Extra-renal fluid loss, including vomiting, diarrhoea, or diaphoresis, was shown to be the most common cause of hyponatremia in 33.9% of patients and in 20.7% of the cases, SIADH was suspected to be the cause.[17] Also our finding corroborates with previously published research where SIADH was revealed to be the most common cause of euvolemic hyponatremia.[21] Another study by Panicker and Joseph on the clinical profile of hyponatremia in ICU hospitalized patients has also reported SIADH as a predominant cause for hyponatremia.[5]

Inverse relation was observed between severity of hyponatremia and GCS score in our study. Severe the hyponatremia poor the GCS. According to hydration status, patients were classified into euvolemic, hypovolemic, and hypervolemic states, of which euvolemic hyponatremia was the most common type observed in study patients, but slightly higher mortality was observed in patients with hypovolemic hyponatremia. Our study is in agreement with the previous published research. [16,22] Our results also stand in contradiction when compared to the data published by Hochman and group, where hypovolemic hyponatremia was more common than hypervolemic in their study population.[23] In our study, 87% of the participants recovered following treatment, while 13 died. Hyponatremia is observed in 15 to 30% of hospitalised patients, particularly in intensive care units.[24] Correction of hyponatremia must take into account the condition's chronicity. Acute hyponatremia (less than 48 hours) can be treated more safely and quickly than chronic hyponatremia. Rapid correction of serum sodium, on the other hand, can result in serious neurological sequelae. Conversely, significant hyponatremia (125 mEq/l) has a greater mortality rate, which can surpass 50% if serum sodium levels fall below 105 mEq/l.[23] Doshi et al. discovered that hyponatremia and hypernatremia were linked with an elevated risk of all-cause mortality in patients with CKD that was independent to cardiovascular events or malignancy.[25] A meta-regression study revealed that the risk of overall mortality associated with hyponatremia was inversely related to serum sodium. After correcting for age, gender, and diabetes mellitus as an associated morbidity, this link was confirmed in a multiple regression model.[26] The incidence of osmotic demyelination syndrome (ODS) following treatment has been very rare.[27] There was no such complication in our study.

Our study also suggests that the severity of hyponatremia increases with increasing age. Similar results were observed by other researchers in their study, who have shown that elderly patients are more susceptible to hyponatremia. Comorbidities such as diabetes mellitus and hypertension had a significant impact on the severity of hyponatremia. Our study is comparable to the other research work where 80% of patients had one or more co morbid condition,

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commonest being hypertension (51%) and diabetes mellitus (42%).[1] Treatment with hypertonic saline was restricted for severe hyponatremia and those with neurological symptoms with proper monitoring to avoid complication of over correction like osmotic demyelination syndrome. Vasopressin receptor agonists are a potential tool in the management of mild to moderate hyponatremia. Fluid restriction and salt supplementation were the other modalities used for treatment. Early and accurate identification and treatment of hyponatremia will help in decreasing morbidity and mortality.

Limitation

The current limitation of the study is its small sample size. In addition, only short-term mortality and morbidity are considered. Long-term morbidity, such as readmission, and long-term death, are not evaluated. The pathogenesis of hyponatremia in the elderly is multifaceted, with patients exhibiting dubious indicators of hydration. Patients seeking medical attention in a tertiary care centre comprised the study population, which may not be representative of the broader population.

CONCLUSION

The most prevalent electrolyte problem in hospitalised patients, particularly the elderly, is hyponatremia. Because of the possible morbidity, mortality, and economic burden on the patient and health care, hyponatremia must be recognised. Researcher community should come together and conduct multi-centric study with larger sample population to unfold hyponatremia's origin, risk factors, and clinical profile in hospitalised patients which further shall aid in lowering its incidence and minimising the problems associated with hyponatremia.

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