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Original Research Article

A Clinical Study of Hyponatremia on Presentation and Its Prognostic Outcome in Patients Admitted to a Tertiary Care Hospital: A Cross Sectional Study

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Conflict of interest: Nil

Abstract:

Introduction: Hyponatremia, characterized by a lower-than-normal concentration of sodium in the blood, stands as one of the commonly encountered electrolyte imbalances in clinical settings. Its prevalence among hospitalized adults underscores its clinical significance and warrants the necessity for a deeper understanding of its manifestations and prognostic implications.

Aim: A clinical study of hyponatremia on presentation and its prognostic outcome in patients admitted to a tertiary care hospital.

Materials and Methods: It is a cross-sectional study done in the Department of General Medicine, Rohilkhand Medical College and Hospital Bareilly from 1 November 2022 to 31 October 2023. 100 patients with hyponatremia on presentation admitted to Medicine IPD were included in the study. They were evaluated for cause of hyponatremia based on history, clinical examination and laboratory investigations. Data was analyzed using descriptive statistics and appropriate tests.

Results: This study of 100 hyponatremia patients revealed a balanced gender distribution (1:1 male-to-female ratio) and a unique age profile, with the most common age group being 18-30 years, likely due to regional factors such as dengue fever and tuberculosis. Nausea and vomiting were the most prevalent symptoms, and patients presenting with these symptoms had a better prognosis compared to those with severe symptoms like altered sensorium or seizures. Euvolemic hyponatremia was most common, with tuberculosis being a major cause, and high urinary sodium levels (>20 mmol/L) were prevalent, aiding in diagnosis. Severe hyponatremia was more common than moderate, and treatment varied based on the underlying cause, including normal saline for hypovolemic cases and tolvaptan for hypervolemic cases.

Conclusion: In conclusion, this study provides valuable insights into the demographic, clinical, etiological and prognostic aspects of hyponatremia in a specific regional context. The clinical physician should always be aware to identify early on the patients presenting with hyponatremia and they should be intricately evaluated for etiology. A deep understanding of clinical presentation, pathophysiology and regional variations are key in management of hyponatremia.

Keywords: Hyponatremia, low sodium levels, SIADH, hyponatremia prognosis, serum sodium, tertiary care hospital.

Introduction

Hyponatremia presents a multifaceted clinical challenge, with diverse etiologies ranging from medication-induced to syndrome-associated and often complicating various medical conditions. Despite its prevalent occurrence, the clinical manifestations of hyponatremia can vary widely, encompassing a spectrum from subtle symptoms to life-threatening neurological complications. Understanding these nuances is paramount for timely recognition and effective management, thereby averting potential morbidities and mortalities associated with this electrolyte

disturbance. [1] Moreover, beyond its immediate clinical implications, hyponatremia has emerged as a significant predictor of adverse outcomes in hospitalized patients. Its association with prolonged hospital stays, increased healthcare resource utilization, and heightened mortality underscores the need for meticulous prognostic assessment and management strategies tailored to individual patient profiles. [1] Hyponatremia related risk of mortality showed a reciprocal relationship with serum sodium levels. [2]

The prognosis of the patient depends on a variety of factors with hyponatremia being an important factor. The spectrum of diseases in which hyponatremia was found to be an adverse prognostic factor was wide including conditions like myocardial infarction, cardiac failure, cirrhosis, pulmonary infections. Recent evidence favours mild chronic hyponatremia to be the causative factor for ataxia, frequent falls and bone loss in elderly persons. [1] Hyponatremia is particularly common in the hospitalised patients and with co-morbidities where access to water, renal handling and urinary dilution function of kidney are impaired. Patients often associated with multi-organ failure also contribute to morbidity and mortality. [2]

The economic impact and overall burden of hyponatremia on the patient and the health care facility is evidenced by longer duration of hospital stay, need of mechanical ventilation, higher risk of death, disability and cost of care. Yet, data regarding the clinical spectrum and prognostic outcome of hyponatremia in adults in our country is very limited. This study hence aims to delve into the intricate landscape of hyponatremia within the context of adult inpatient care, shedding light on its clinical features, etiology and prognostic outcomes. This study endeavours to contribute to the broader understanding of this electrolyte disorder.

Material and Method

Place of Study: This study was be carried out in department of General Medicine, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh

Type of Study: Cross sectional study

Time of Study: 1st November 2022 to 31st October 2023

Study Duration: 1 year.

Subjects: All adult patients.

Sample Size: In our study a total of 100 patients were taken Sample size has been calculated using formula $N= 4 \times p \times q/L^2$, p= 93.5 [22] q=100-p (100-93.5) = 6.5 , L: Allowable error (5%)

Inclusion Criteria:

1. Patients aged ≥18 years
2. Patients with moderate-to severe-hyponatremia ("≤125 mmol/L") admitted to the Medicine IPD.

Exclusion Criteria:

1. Patients with hyperglycemia, hyperlipidemia, and paraproteinemias.
2. Patients with mild hyponatremia (130-134 mmol/L)

Statistical Analysis: The data was entered in the SSPS (Statistical Package for social sciences) licensed version 23.0. Descriptive analysis was done by calculating proportions, means & standard deviation.

Appropriate statistical test was applied depending on type & the distribution and type of data. P<0.05 was considered significant.

Observations & Results

Table 1: Etiology Vs Type of Hyponatremia

	Type of Hyponatremia						
Etiology	**Euvolemic**		**Hypervolemic**		**Hypovolemic**		**P-Value**
	Number	**%**	**Number**	**%**	**Number**	**%**	
Acute Gastroenteritis	2	33.3	0	0.0	4	66.7	0.000*
CKD	2	8.3	22	91.7	0	0.0	
CHF	2	33.3	3	50.0	1	16.7	
CLD	5	38.5	8	61.5	0	0.0	
KOCH'S	21	100.0	0	0.0	0	0.0	
Dengue Fever	1	4.5	1	4.5	20	90.9	
SEPSIS	6	75.0	0	0.0	2	25.0	
Total	39	39.0	34	34.0	27	27.0	

***P<0.05(statistically significant)**

Table 2: Clinical Presentation Vs Prognostic Outcome

Clinical Presentation	Prognostic Outcome						P-Value
	Death		Recovery		Total		
	Number	%	Number	%	Number	%	
Vomiting/nausea	2	5.6	34	94.4	36	100.0	0.038*
altered sensorium	6	26.1	17	73.9	23	100.0	
asymptomatic	0	0.0	1	100.0	1	100.0	
Coma	4	33.3	8	66.7	12	100.0	
lethargy	1	5.3	18	94.7	19	100.0	
postural dizziness	0	0.0	2	100.0	2	100.0	
seizure	3	42.9	4	57.1	7	100.0	
Total	16	16.0	84	84.0	100	100.0	

*P<0.05(statistically significant)

Gender-wise Distribution: A statistically significant differences in the types of hyponatremias observed between males and females, with euvolemic hyponatremia being more common in females and hypervolemic hyponatremia more common in males. This suggests potential gender-specific factors influencing the pathophysiology or clinical presentation of hyponatremia.

Age-wise Distribution: Contrary to previous studies, the most common age group presenting with hyponatremia in this study was between 18-30 years, which can be attributed to regional epidemics such as dengue fever and tuberculosis affecting younger populations.

Clinical Presentations: Nausea and vomiting were the most common symptoms experienced by patients with hyponatremia in this study, followed by altered sensorium and lethargy. The presence of nausea and vomiting was found to be associated with a higher likelihood of recovery compared to other symptoms.

Distribution According to Type of Hyponatremia: Euvolemic hyponatremia was the commonest type observed, with SIADH being a predominant cause, particularly associated with pulmonary tuberculosis and TB meningitis.

Distribution According to Etiology of Hyponatremia: The underlying causes of hyponatremia varied across different types, with acute gastroenteritis, CKD, CHF, CLD, Koch's, and sepsis predominantly leading to hypovolemic hyponatremia. Tuberculosis was mainly linked to Euvolemic hyponatremia, while dengue fever cases were mostly hypovolemic.

Distribution Based on Severity of Hyponatremia: Severe hyponatremia was more prevalent than moderate hyponatremia in this study, with most recoveries occurring within a mean timeframe of 6 days.

Distribution of Comorbidities in Hyponatremic Patients: Hypertension, CKD, and diabetes were the most prevalent comorbidities observed in patients with hyponatremia, highlighting the importance of managing underlying conditions in conjunction with hyponatremia treatment.

Distribution Based on Urinary Sodium Levels: High urinary sodium levels (>20mmol/L) were predominant, indicating underlying causes such as SIADH and renal losses, while low urinary sodium levels (<20mmol/L) were less common, mainly associated with dengue fever cases.

Prognostic Outcome and Recovery Time: Patients presenting with vomiting/nausea had a significantly higher likelihood of recovery compared to other symptoms. The mean recovery time was 6 days, with the majority of recoveries occurring within this time frame.

Climate Influence: The study observed an increased incidence of hyponatremia during the monsoon season, attributed to regional epidemics such as dengue fever and acute gastroenteritis.

Association with Hypothyroidism: Hypothyroidism was found to be associated with hyponatremia, emphasizing the need for electrolyte evaluation in patients with hypothyroidism and early treatment to avoid complications.

Correction of Hyponatremia: Various correction methods were used, including Tolvaptan, IV fluids, oral salt capsules, 3% NaCl, and hemodialysis, with mean sodium increment of 10 mmol/L after 24 hours. The study highlights the importance of cautious correction to avoid adverse effects such as osmotic demyelination syndrome and to avoid correction of more than 10 mmol/L Day.

Discussion

Gender Wise Distribution: In our study of 100 patients admitted with hyponatremia in IPD, 50% were male and rest 50% female. With no preponderance toward either sex. The male to female ratio was 1:1. Chandregowda et al. (2021) [5] and Murkut G. et al. (2022) [11] also had an almost equal distribution of male to female, i.e. 48% women, 52% men and 53% men, 47% female respectively. We had found statistically significant results on comparing sex with type of

hyponatremia indicating that the distribution of hyponatremia types differs significantly between males and females. In females euvolemic hyponatremia was more common while in males hypervolemic hyponatremia was more common. This can be explained by the hypothesis that metabolic diseases cause higher incidence of hypervolemic hyponatremia and metabolic diseases being more common in men [15] (T2DM, HTN) hence explains incidence of hypervolemic hyponatremia to be higher in men. This suggests potential gender-specific factors influencing the pathophysiology or clinical presentation of hyponatremia, warranting further investigation to better understand and address these disparities in patient management.

Age Wise Distribution: In this study the most common age group presenting with hyponatremia was between 18-30 years (26%) followed by 31-40 years (21%) and 41 to 50 years (20%). This is a unique finding in our study since all the studies done until now have shown the most common age group to be between 60 to 70 years, as warranted by Murkut G. et al. (2022) [11] and Naik MK et al. (2017) [12]. This unique feature of our study can be explained by the dengue epidemic that hits northern India soon after the spring season between Junes to September every year. Our study located in Bareilly also faces a similar epidemic each year. Amongst the most common age groups affected by DF each year is the age group between 20 to 40 years as seen by Chandrasekaran et al. (2017) [13]. Another common disease in this region is that of tuberculosis – both pulmonary and extra-pulmonary. According to RNTCP census 2018 the maximum cases of tuberculosis was arising from the age group of 20 to 24 years. Hence a majority of cases presenting to our tertiary care hospital in Bareilly were in this age group owing to these two diseases in the region i.e. TB and DF. In both these diseases hyponatremia is very commonly manifested.

Distribution of Clinical Presentation: The distribution of clinical presentations of hyponatremia reveals nausea and vomiting to be the most common symptom experienced by patients (36%). Nausea & vomiting was also seen to be most common in studies conducted by Chandregowda et al. (2021) [5], Babliche et al. (2017) [6] and Rani RU et al. (2020) [7]. This establishes the fact that out of all the symptoms experienced by patients with hyponatremia, nausea and vomiting in fact should ring most alarm bells so as to consider hyponatremia amongst a likely diagnosis or associated disturbance. In our study altered sensorium (23%) and lethargy (19%) follows closely behind as a presenting symptom. This was in coherence to the study conducted by Sood et al. (2020) [8].

We also compared clinical presentations with the prognostic outcome of patients with hyponatremia and found patients presenting with vomiting/nausea have a significantly higher (p=0.038) likelihood of recovery (Table 2). However, other clinical presentations, such as altered sensorium, coma, lethargy, postural dizziness and seizure had poorer prognostic outcomes. The results were statistically significant. This suggests that while patients presenting with only vomiting/nausea may serve as a positive prognostic indicator, other symptoms may not have a significant impact on prognostic outcomes in patients with hyponatremia. Further investigation may be necessary to explore additional factors influencing prognostic outcomes in this context. This was also an unique feature of our study since no other study done in recent times could find an association between clinical presentation and outcome of hyponatremic patients.

Distribution According to Type of Hyponatremia: The type of hyponatremia that we observed most commonly was euvolemic hyponatremia which was seen in 39% patients, this was also seen in studies conducted by Chandregowda. et al. (2021) [5], Babliche P. et al. (2017) [6] and Sood N. et al. (2020)[8]. All these studies like ours was conducted in tier 3 type of cities which had a mixed population of urban and rural. The most common cause of euvolemic hyponatremia was SIADH and the most common cause of SIADH were: Pulmonary TB (12%) and TB Meningitis (9%) also observed by Nandakumar et al. (2013) [4].

Distribution According to Etiology of Hyponatremia: Our study presents the association between different etiologies of hyponatremia and the type of hyponatremia (euvolemic, hypervolemic, or hypovolemic). Various causes such as acute gastroenteritis, CKD, CHF, CLD, Koch's, dengue fever, and sepsis are listed, along with the corresponding numbers and percentages of cases within each type of hyponatremia and the total number of cases. Etiologies such as acute gastroenteritis, CHF, and sepsis predominantly lead to hypovolemic hyponatremia. Chronic liver disease is associated with a mix of hypervolemic and euvolemic hyponatremia. Tuberculosis is predominantly linked to euvolemic hyponatremia. Meanwhile, dengue fever cases are mainly hypovolemic. Statistical analysis between type of hyponatremia and causes of hyponatremia (Table 1) shows a significant statistic. This was coherent with the study conducted by Babliche et al. (2017) [6].

This suggests that the underlying cause of hyponatremia may influence the volume status of the patient, which is crucial for determining appropriate management strategies. Further investigation may be necessary to understand the mechanisms

underlying these associations and their clinical implications.

Distribution Based on Severity of Hyponatremia: Only the moderate and severe levels of hyponatremia were considered in the study. Moderate (125-129 mmol/L) was seen a smaller percentage of patients (18%) and the remaining were severe (82%) (<125 mmol/L).

Severe hyponatremia was found to be more prevalent compared to moderate hyponatremia, according to Babliche et al.'s (2017) [6] study investigating patients admitted to a medical College in Karnataka in 2017, in their findings, out of 100 micu patients with moderate-to-severe hyponatremia, moderate hyponatremia was observed in 46% of cases, while severe hyponatremia was observed in 54% of cases. [6] This is in coherence to our study where severe hyponatremia (82%) was also more prevalent. This can thus conclude that in patients with severe hyonatremia need more often the need for hospitalisation than moderate hyponatremia as they tend to be less symptomatic than severe hyponatremic patients. Sundar et al. (2023) [9] stated that the severity of hyponatremia increases with age, this was not seen in our study due to a statistical error of sampling, where most of our patients admitted with hyponatremia were in the younger age group as described above.

There was no association between age and sex with the severity of hyponatremia in any of the previous studies so we tried establishing a comparison but the statistical output (p=1.0 & p=0.554) came to be insignificant.

Distribution of Comorbidities in Hyponatremia: The prevalence of comorbidities among hyponatremia cases is notable, with hypertension being the most common (32%), followed by CKD at 20%, and DM at 14%. This aligns with findings from Nandakumar et al. (2013) [10], which observed a higher likelihood of comorbid conditions such as diabetes, hypertension, and ischemic heart disease in elderly cases, consistent with our study.

In the study by Sumit Mohan et al. (2013) [14], hyponatremia was found to be more prevalent in individuals with hypertension, diabetes, coronary artery disease, stroke, copd, cancer, and psychiatric disorders, while being less common in those without comorbidities.

Hyponatremic hypertensive syndrome is a recognized condition, often associated with essential hypertension patients receiving diuretics (10%). These medications can disrupt electrolyte metabolism, leading to electrolyte imbalances. Thiazide diuretics, for example, impact the sodium chloride cotransporter channel and trigger the nonosmotic release of vasopressin. [18]

CKD (20%) was observed to be the second most common cause of hyponatremia in this study which was also observed by Jain AK (2019) et al [3]. Our study had been conducted in a 3rd tier city which had a mix population of urban and rural. This explains the rise of metabolic diseases increasingly owing to sedentary lifestyle and unhealthy eating practices in not only the urban but rural population as well. Another factor that was seen in many patients presenting with hyponatremia was that of a poor diet (53%) due to the low socio economic status in this region, 53 patients out of the 100 studied had some form of poor nutrition which ultimately also contributed to them developing hyponatremia. This was also observed by Jain et al. (2019) [3]. This underscores the role played by diet in our general well-being and the need to eat clean and balanced food with adequate water intake.

Distribution Based on Urinary Sodium Levels: A majority of patients with hyponatremia exhibited a high urinary sodium concentration (>20mmol/L), while only a small percentage (9%) had low urinary sodium (<20mmol/L). This disparity in urinary sodium concentration aids in distinguishing between hyponatremia secondary to hypovolemia and the SIADH.

In cases of SIADH and salt-wasting syndrome, urinary sodium levels typically exceed 20 mmol/L. Conversely, in hypovolemic conditions, urinary sodium levels are usually below 20 mmol/L. Among euvolemic patients, 39% exhibited increased urinary sodium due to SIADH, while among hypervolemic patients, 34% showed elevated urinary sodium levels due to renal losses. In hypovolemic patients, which were predominantly associated with conditions like dengue fever and renal impairment, urinary sodium losses were observed, with only 9% of patients exhibiting urinary sodium levels less than 20 mmol/L out of the total 100 patients studied.

Uniquely, in our study there is a statistically significant difference in urinary sodium levels across different causes of hyponatremia. Specifically, acute gastroenteritis, CKD, CHF, CLD, Koch's, and sepsis are associated with urinary sodium levels greater than or equal to 20, whereas dengue fever shows a mixed pattern with some cases having urinary sodium levels less than 20. This suggests that the underlying cause of hyponatremia may influence urinary sodium levels, which can be an important diagnostic indicator in determining the etiology of hyponatremia. Further investigation may be warranted to explore the mechanisms underlying these associations and their clinical implications.

Prognostic Outcome and Recovery Time: In our study 16% cases resulted in mortality while a majority of 84% recovered. A prospective observa-

tional study of 100 patients was conducted in a medical college at Navi Mumbai (2023) [9] which was a "Study on the clinical profile and outcome in patients of hyponatremia" showed a similar outcome of 13% mortality and recovery of 87% of cases. There is a statistically significant difference in prognostic outcomes associated with vomiting/nausea (Table 2). Specifically, patients presenting with vomiting/nausea have a significantly higher likelihood of recovery compared to death. However, for other symptoms, such as altered sensorium, coma, lethargy, postural dizziness, and seizure, there doesn't seem to be a significant difference in prognostic outcomes. This suggests that while vomiting/nausea may serve as a positive prognostic indicator, other symptoms may not have a significant impact on prognostic outcomes in patients with hyponatremia.

We also tried to establish an association between the prognostic outcome and etiology but the results were statistically insignificant p=0.12. The type of hyponatremia was compared to prognostic outcome, p=0.573 but a statistical association was not found. Association between age and sex with prognostic outcome was also statistically insignificant p=0.127 & p=1.0 respectively. Among the recorded recovery periods, the most common timeframe is 4 days, representing 18% of cases. Following closely are recovery days of 5 and 6 days, each comprising 12% of the total. Instances of 3, 7, and 8 days account for 5%, 10%, and 8% of the recoveries, respectively. Longer recovery durations, such as those beyond 10 days, exhibit lower representation, suggesting that the majority of recoveries occur within a shorter timeframe with a mean recovery time of 6 days.

Climate and Its Influence: An Indian study conducted by Chakrapani et al. (2002) [15] over a span of two years revealed an increased incidence of hyponatremia, particularly during the monsoon season. Our own study also covered a monsoon period during which cases of dengue fever (22%) and acute gastroenteritis (6%) peaked, suggesting that tropical weather conditions may contribute to the prevalence of hyponatremia. However, there are contrasting findings in some studies, such as Atluntus et al. (2021) [22], which propose that hyponatremia tends to occur more frequently during the summer season. This discrepancy in findings may be attributed to factors such as insensible losses, dehydration, and excessive drinking of hypotonic fluids during hot weather conditions.

Hypothyroidism & Hyponatremia: Hypothyroidism can lead to hyponatremia through several mechanisms. Firstly, it can decrease renal blood flow and glomerular filtration rate, resulting in reduced sodium excretion and water retention. Secondly, alterations in antidiuretic hormone (ADH) secretion may lead to increased water reabsorption in the kidneys. Thirdly, changes in fluid distribution within the body, including increased interstitial fluid volume, can dilute sodium concentrations. Additionally, hypothyroidism is associated with decreased cardiac output, which can stimulate ADH and aldosterone release, further contributing to water retention and hyponatremia. Lastly, reduced sensitivity to natriuretic peptides may impair sodium excretion. Overall, hypothyroidism disrupts the delicate balance of fluid and electrolytes, ultimately predisposing individuals to hyponatremia through multiple pathways involving renal function, hormone regulation, and fluid dynamics. [16]

In our study as well 4% cases were hypothyroid; this emphasizes the need to evaluate electrolytes in a patient with hypothyroidism and treating it early to avoid complications. This was also affirmed by a study conducted in Navi Mumbai [17]; it suggested that blood sodium investigation should be done in any patient with hypothyroidism.

Correction of Hyponatremia & Level after 24 Hours: There were mainly 5 modes of correction, i.e. IVF-NS (33%), Oral tolvaptan (10%), 3% NaCl (13%), salt capsules (7%) and hemodialysis (21%). Tolvaptan was used in hypervolemic patient's i.e CLD, CHF and SIADH. Tolvaptan represents a ground-breaking approach to treating hyponatremia by directly addressing the elevated levels of antidiuretic hormone associated with conditions such as syndrome of inappropriate secretion of antidiuretic hormone, congestive heart failure, and liver cirrhosis. IVF NS was used especially in hypovolemic conditions as it would not only correct the sodium reuirement but also replenish dehydration. Oral salt capsules were given in patients who could take oral intake and in correct moderate hyponatremia of euvolemic and hypovolemic kind. 3% NaCl was used in patients with severe hyponatremia of euvolemic and hypovolemic kind. Hemodialysis was done in patients who met the criteria for need of hemodialysis [19] wherein collaterally sodium also got corrected so there was no need for other modes of therapeutic correction.

Conclusion

The study on hyponatremia reveals significant insights into its epidemiology, presentation, and management. It highlights gender-specific differences in hyponatremia types, with euvolemic cases more common in females and hypervolemic in males, and underscores a shift in age distribution towards younger adults, likely due to regional epidemics. Clinical presentations frequently include nausea and vomiting, which correlate with a better recovery prognosis. The predominant type of hyponatremia is euvolemic, often linked to conditions like SIADH and tuberculosis, while severe cases are more common than moderate ones. Comorbidities such as hypertension and CKD are

prevalent, and urinary sodium levels help differentiates types of hyponatremia. Seasonal variations and associations with hypothyroidism further impact the incidence and management of hyponatremia. Overall, the study emphasizes the importance of tailored treatment strategies and careful correction methods to avoid complications and improve patient outcomes.

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