CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH HYPONATREMIA AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

BACKGROUND

Hyponatremia is defined as a serum sodium concentration less than 135 mmol/L and is the most common electrolyte disorder encountered in clinical practice.

MATERIALS AND METHODS

This was a retrospective, descriptive and data analysis study conducted over period of 12 month at a tertiary care centre, to study the clinical profile, aetiology, classification and outcome of hyponatremia. A total 115 consecutive cases who had serum sodium levels of <135 mmol/L were enrolled. The mean and standard deviation and percentage for numerical variables were calculated. Chi square test was used to analyse categorical variables.

RESULTS

Of a total of 115 patients, 73 (63.47%) were male and 42 (36.52%) were females. There was a predominance of Na⁺ levels of 115-134 mmol/L (mild hyponatremia) 59.13% [*p* < 0.001]. The majority of patients (42.61%) had nausea and/or vomiting (*p* < 0.001) and confusion, seizures and coma were associated with moderate to profound hyponatremia (*p* < 0.01). The SIADH (37.39%) was the commonest pathophysiological process observed in the present study [*p* < 0.0001]. Overall mortality was 9.57%. The patients with Sr. Na⁺ <105 mmol/L had (36.84%) significant mortality compared to >105 mmol/L [*p* < 0.002196]. The duration of hospital stay was inversely related to Sr. sodium level.

CONCLUSION

In present cohort of hyponatremia the SIADH was the commonest aetiology. Confusion, seizures and coma were associated with moderate to profound hyponatremia. The duration of hospital stay was inversely related to serum sodium level with overall mortality of 9.57% which was correlated with severity of hyponatremia.

KEY WORDS

Hyponatremia, SIADH, Serum Sodium Level, Seizures, Coma.

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BACKGROUND

Hyponatremia is defined as a serum sodium concentration less than 135 mmol/L and is the most common electrolyte abnormality encountered in clinical practice including intensive care unit. Mild hyponatremia has been estimated to occur in about 30%, whereas the prevalence of moderate to severe hyponatremia is about 7% among hospitalized patients. Hyponatremia especially severe associated significant morbidity and mortality. Acute severe hyponatremia is a medical emergency accompanied by severe neurological symptoms due to cerebral oedema and can be life-threatening if not recognized and appropriately treated.

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The rapid correction of chronic hyponatremia may results in osmotic demyelination syndrome (Central pontine myelinolysis).[1,2,3] The present study was conducted to evaluate clinical, etiological profile and outcome of patents presenting with hyponatremia at tertiary care centre.

MATERIALS AND METHODS

Aims and Objectives

To study clinical profile, aetiology, classification and outcome of Hyponatremia at a tertiary care center.

Study Design and Setting

This was a retrospective, descriptive; data analysis study of patients admitted over period of 12 month with diagnosis of hyponatremia, at a tertiary care center. The study was conducted at Krishna Institute of Medical Sciences and Deemed to be University, Karad, Maharashtra. The study was approved by the institutional ethics and protocol committee.

Inclusion Criteria

The patients of age 18 years or more and who were hyponatremia on admission were included in the study.

Exclusion Criteria

Patients who developed hyponatremia during hospital stay were excluded.

Detailed history including onset, duration, progression of symptoms, history of illnesses and detailed general and physical examinations of the patients were done.

Laboratory Investigation

The measurements of sodium (Na^+), potassium (K^+), urea, creatinine and glucose concentration were done by standard laboratory methods. Serum osmolality was measured using the formula $[2 \times (\text{Na} + \text{K})] + (\text{BUN}/2.8) + (\text{glucose}/18)]$.^[4] The urinary Na^+ was calculated as per standard protocol. The relevant other investigations were done as per need for the study.

A total 115 consecutive cases who had serum Sodium levels of <135 mmol/L were enrolled and studied admitted during a period of 12 months from July 2017 to June 2018. After establishing the diagnosis of hyponatremia, the patients were categorized based on the level of hyponatremia into mild, moderate and severe hyponatremia.^[1]

1. A 'Mild' hyponatremia: If serum sodium concentration between 130 and 134 mmol/L.
2. A 'moderate' hyponatremia: If serum sodium concentration between 125 and 129 mmol/L.
3. 'Profound' hyponatremia: serum sodium concentration <125 mmol/L
4. Acute hyponatremia, that is documented to exist <48 h. and chronic hyponatremia as hyponatremia that is documented to exist for at least 48 h.

The patients with hyponatremia were then further evaluated to find out the aetiology. Serum and urine osmolality was calculated [Normal osmolality: 275-295 mosm/kg H_2O]. They were then assessed clinically to find out the volume status clinically if they had low serum osmolality-

1. **Hypervolemia:** Presence of bilateral basal crepitation, raised jugular venous pressure, bilateral pitting pedal oedema and hepatomegaly.
2. **Hypovolemia:** Presence of tachycardia, postural hypotension, dry tongue, nature of skin turgor and urine output.
3. **Euvolemic:** Those patients who had no signs mentioned above were considered to be euvolemic.

Statistical Analysis

The mean and standard deviation and percentage for numerical variables were calculated. Chi-square test was used to analyze categorical variables. ANOVA was used to compare mean of duration of stay in patients with hyponatremia.

RESULTS

A total 115 patients fulfilling inclusion criteria of study with diagnosis of hyponatremia were enrolled, the mean and SD for age was 51.63 ± 13.73 years and sodium was 113.57 meq/L. A total 73 (63.47%) were male and 42 (36.52%) were females in present study. (Table 1) Of total 115 patients with hyponatremia, 18.26% had serum Na^+ levels <105 mmol/L (Severe hyponatremia), 22.60% had 105 – 115 mmol/L (Moderate Hyponatremia) and 59.13% had 115-134 mmol/L (Mild hyponatremia) with predominance of Na^+ level 115-134 mmol/L (Mild hyponatremia) [$p < 0.001$, DF:2]. (Table 2)

Variables	Mean	SD ($\pm$)
Age	51.63	13.73
Duration of Stay	13.5	6.3
Na^+	113.57	12.97
K^+	4.05	0.86
BSL	170.11	45.20
Serum Creatinine	1.45	0.50
Males: 73 (63.47%), Females: 42 (36.52%)		

Table 1. Mean and Standard Deviation of Patients with Hyponatremia

Severity of Hyponatremia according to Serum Sodium Levels	(n=115)	%
Severe Hyponatremia (Sr. $\text{Na}^+ < 105$ mmol/L)	21	18.26
Moderate Hyponatremia (Sr. $\text{Na}^+ 105 - 115$ mmol/L)	26	22.60
Mild Hyponatremia (Sr. $\text{Na}^+ 115 - 134$ mmol/L)	68	59.13
Total	115	100

Table 2. Total Number of Patients according to the Severity of Sr. Sodium

The majority of patients (42.61%) had nausea and or vomiting as presenting feature of hyponatremia ($p < 0.001$) with predominant mild to moderate' hyponatremia. The confusion, seizures and coma are the less common in present study and usually associated with moderate to profound hyponatremia ($p < 0.01$). The mild hyponatremia (59.13%) was common in present study followed by moderate (22.60%) and profound (18.26%) [$p = 0.0012$]. There was no significant statistical difference between severity of hyponatremia and volume status of the patients [$p = 0.7168$]. (Table 3)

Symptomatology		(n=115)		%				
Nausea and or Vomiting		49		42.61				
Lethargy		31		26.96				
Confusion		17		14.78				
Bizarre Behaviour		7		6.09				
Seizures		7		6.09				
Coma		4		3.48				
Total		115		100				
X ² ; DF:5; 'p' ['] < 0.001								
Classification of Hyponatremia	Mild %		Moderate %		Profound %		Total %	
Euvolemia	21	51.22	11	26.83	9	11.00	41	35.65
Hypervolemia	24	60.00	9	22.50	7	9.00	40	34.78
Hypovolemia	23	67.65	6	17.65	5	6.00	34	29.57
Total	68	59.13	26	22.60	21	18.26	115	100
X ² : 2.1033; DF: 4; 'p' ['] : 0.7168								
Table 3. Symptomatology, Severity of Hyponatremia and Volume Status of Patients with Hyponatremia								

The SIADH (37.39%) was the commonest aetiology observed in present study [$p < 0.0001$]. The diuretics (18.26%), cardiac (13.04%), gastrointestinal loss (7.83%) and chronic kidney disease (CKD) (7.83%) were the other disease condition associated with hyponatremia in present study. Of total 115 patients presented with hyponatremia 11

patients died with overall mortality of (9.57%). The patients with $\text{Sr. Na}^+ < 105 \text{ mmol/L}$ had (36.84%) significant mortality compared to $> 105 \text{ mmol/L}$ [$p' < 0.002196$]. (Table 4 and Graph 1) The duration of hospital stay was inversely related to Sr. Na^+ level in present study with negative correlation [$\text{Sr. Na}^+ < 105 \text{ mmol/L}$ 19.3 (± 9.5), 105 – 115 mmol/L 9.2 (± 5.9), 115-134 mmol/L 5.7 (± 2.4)]. (Table 4)

Aetiology	(n=115)	%
SIADH	43	37.39
Drugs (Diuretics)	21	18.26
Renal Salt Wasting	7	6.09
Gastrointestinal Loss	9	7.83
Endocrine Disorders	5	4.35
Cardiac	15	13.04
Cirrhosis of Liver	6	5.22
CKD	9	7.83
Total	115	100

$X^2: 66.48; \text{DF: } 7; 'p': < 0.0001$		
Serum Sodium Level	Mean Duration of Stay	SD ($\pm$)
Serum Sodium $< 105 \text{ mmol/L}$ (n=21)	19.3	9.5
Serum Sodium 105 – 115 mmol/L (n=26)	9.2	5.9
Serum Sodium 115-134 mmol/L (n=68)	5.7	2.4
Mortality	(n=11)	%
$\text{Sr. Na}^+ < 105 \text{ mmol/L}$	7	33.33
$\text{Sr. Na}^+ 105-115 \text{ mmol/L}$	3	11.53
$\text{Sr. Na}^+ 115-134 \text{ mmol/L}$	1	1.4
Total	11	9.57
$X^2: 7.63; \text{DF: } 2; 'p': < 0.00219$		
Table 4. Aetiology and Relation of Serum Sodium Levels with Duration of Hospital Stay and Mortality

Graph 1. Distribution of Patients with Hyponatremia and Mortality

Of total 115 patients presented with hyponatremia, CVA (9.57%), diabetes mellitus, hypertension (7.83%) and diabetes mellitus (7.83%) were the relatively frequent diagnosis in present study. (Table 5)

Diagnosis	n	%	Diagnosis	n	%	Diagnosis	n	%
CKD	9	7.83	Malignancy	3	2.61	DM and HTN	9	7.83
AKI	7	6.09	UTI	5	4.35	COPD	4	3.48
Collagen VD	8	6.96	AMI	7	6.09	Anaemia	2	1.74
CCF	8	6.96	PTE	1	0.87	Cirrhosis	6	5.22
Pneumonia	8	6.96	Seizure	3	2.61	BEP	2	1.74
CVA	11	9.57	Jaundice	1	0.87	Psychiatric D.	1	0.87
AGE	3	2.61	Atrial fibrillation	3	2.61	Pulmonary HTN	1	0.87
Hypertension	1	0.87	RVD	1	0.87	RA	1	0.87
DM	9	7.83	PTB	1	0.87			
Table 5. Diagnosis and Co-Morbidities associated with Hyponatremia								

Abbreviations

CKD: Chronic kidney disease, AKI: Acute Kidney Injury, PTE: pulmonary thrombo-embolism, RVD: retroviral Disease, PTB: pulmonary tuberculosis, AMI: acute myocardial infarction, BEP: benign enlargement of prostate, RA: rheumatoid arthritis)

Of total 115 patients with hyponatremia Renal disease was present in 18.26%, CNS in 13.04%, infections in 16.52%, HTN and DM in 15.65% and cardiovascular diseases were present in 15.65%. (Table 6)

Systems Affected	(n=115)	%
Renal Disease	21	18.26
Liver Disease	7	6.09
Infection	19	16.52
CNS	15	13.04
HTN and DM	18	15.65
Pulmonary	6	5.22
Haematological	2	1.74
Collagen Vascular	9	7.83
Cardiovascular	18	15.65
Total	115	100
Table 6. Systems Association with Hyponatremia		

DISCUSSION

Hyponatremia occurs in up to 8% of the general population and in up to 60% of hospitalized patients. Acute profound hyponatremia can cause brain oedema, but also chronic mild hyponatremia is associated with poor health outcomes. Even when co-morbid conditions are taken into account, people with a mildly decreased serum sodium concentration have a 30% higher risk of death and are hospitalized 14% longer relative to those without hyponatremia.^[5] Hyponatremia is often iatrogenic in in patients and severe sodium disturbances are associated with considerable morbidity and mortality. The management of Hyponatremia is always associated with diversity of aetiology and volume status of the patients and different disease conditions. The hyponatremia is managed by clinicians with a broad variety of backgrounds have diverse institution specialty based approaches to manage the same.^[6]

In current study on cohort of hyponatremia, 63.47% were males and 36.52% were females with mean age of 51.63±13.73 years with predominance of male population. The majority of patients (42.61%) had nausea and or vomiting ($p < 0.001$). The confusion, seizures and coma are the less common in present study and associated with moderate to profound hyponatremia ($p < 0.01$). The SIADH (37.39%) was the commonest pathophysiological process observed [$p < 0.0001$] for hyponatremia. Similarly, Nandakumar et al reported drowsiness was commonest symptom (53.2%) followed by vomiting, hiccoughs and seizures. About half of the patients had euvolemic hyponatremia 39% had hypovolemic hyponatremia and SIADH was the commonest cause of hyponatremia. Hyponatremia was common in elderly. Seizures were present only in severe hyponatremia.^[7] Mittal M et al studied 250 patients with mean age of 53.9 years predominated by males with 61.6% patients had euvolemic 21.2% hypervolemic and 17.2% hypovolemic hyponatremia. The most common causes for hyponatremia were CNS infections, CLD and acute gastroenteritis. Neurologic symptoms were more common in severe hyponatremia and seizures were attributable to hyponatremia were in 17.6% patients, all with severe hyponatremia. Deaths were more frequently seen in patients with severe hyponatremia as compared to patients with mild hyponatremia with overall mortality was 14%.^[8] Similarly in present study the patients with $Sr. Na^+ < 105$ mmol/L had (36.84%) significant mortality compared to > 105 mmol/L [$p < 0.002196$]. In current cohort of hyponatremia, total 73 (63.47%) were males and 42 (36.52%) were females with mean age of 51.63±13.73 years with predominance of male. The diuretics (18.26%), cardiac (13.04%), gastrointestinal loss (7.83%) and chronic kidney disease (CKD) (7.83%) CVA (9.57%), diabetes mellitus and hypertension (7.83%) were the relatively frequent diagnosis in present study. There was no significant statistical difference between severity of hyponatremia and volume status of the patients [$p = 0.7168$]

with predominance of euvolemia. Similarly, Mary Grace et al studied a total of 100 consecutive patients, hyponatremia (55% male 45% female) with a mean age of 60±16 years. The most common precipitating factor were neurological and lung conditions. Majority of the patients were asymptomatic and euvolemic at the time of detecting hyponatremia.^[9] In present study the duration of hospital stay was inversely related to $Sr. Na^+$ level with negative correlation [$Sr. Na^+ < 105$ mmol/L 19.3 (±9.5) days, 105 – 115 mmol/L 9.2 (±5.9) days, 115-134 mmol/L 5.7 (±2.4) days] ($p = 0.0014$); similarly Lochan Karki et al (2016) quoted that, the hyponatremia was a common occurrence at hospital admission with an incidence of 36.11% and associated with a longer hospital stay in cured CAP patients.^[10] Khalid Ali et al (2016) quoted that the patients on salt restriction, on chronic diuretic treatment, and with impaired renal function at admission were found to be highly affected with hyponatremia with increased in-hospital mortality ($p = 0.008$) and longer hospital stay (16.6 vs 12 days, $P < 0.001$).^[11] Similarly diuretics (18.26%), cardiac (13.04%), gastrointestinal loss (7.83%) and chronic kidney disease (CKD) (7.83%) were the other aetiologies or disease condition associated with hyponatremia and severity of hyponatremia was proportional longer duration of stay and mortality in present study. Thomas Antony et al (2017) in their study of 89 patients, 50 patients had serum sodium level of less than 125 mEq/L (M:56% and F:44%) of them 64% of the patients were euvolaemic and 24% were hypervolaemic with SIADH was the commonest cause for hyponatremia (18%) and Thiazide diuretics was the second (12%) with mortality rate of 0.89%.^[12] These findings are comparable with present study in which, the SIADH was the commonest pathophysiological process observed (37.39%) [$p < 0.0001$] for hyponatremia and diuretics intake was present in 18.26% patients with overall mortality of (9.57%).

Hyponatremia is seen in 15-30% in Intensive care units setting. The aetiology is multifactorial. Hyponatremia may be euvolemic, hypovolemic or hypervolemic. Proper interpretation of the various laboratory tests helps to differentiate the various types of hyponatremia. A urinary sodium level below 20 mmol/l is suggestive of an extra renal cause of hypovolaemic hyponatremia. Disorientation, weakness and confusion are typically seen in chronically hyponatremia patients with sodium levels between 130-125 mmol/l. Treatment varies with the nature of onset -acute or chronic, severity and symptoms. Normal saline forms the mainstay of treatment for hypovolemic hyponatremia while 3% NaCl and fluid restriction are important for euvolemic hyponatremia. Hypervolemic hyponatremia responds well to fluid restriction and diuretics.^[6] There have been several recent advances in the last year with revision in the guidelines for treatment and availability of vaptans. Judicious use of vaptans may help in treatment of hyponatremia. We compared various studies with present study. (Table 7)

Study	Sample Size	Symptoms	Aetiology/ Outcome
Nandakumar et al ^[7] (2013)	n=60	Drowsiness by vomiting, hiccoughs and seizures	48.3% patients had euvolemic hyponatremia. SIADH was the commonest cause of hyponatremia (38.3%)
Mittal M et al ^[8] (2016)	Males:140 Females:110, 53.9±16.4 yr	Seizures 17.6%	Deaths were more in patients with severe hyponatremia
Mary Grace	n=100 (55% male 45%	The precipitating factor for	Majority of the patients were

et al ^[9] (2016)	female) [60+/-16]	hyponatremia was neurological and lung conditions	asymptomatic and were euvolemic at the time of detection of hyponatremia
Lochan Karki et al ^[10] (2016)	n=72 F:61;M:39	Incidence: 36.11%	Mortality of 13.7%, mean length of hospital stay: 4.3 days
Khalid Ali et al (2016) ^[11]	n=152	Salt restriction, on chronic diuretic treatment	Patients with hyponatremia had increased in-hospital mortality and longer hospital stay
Padhi R et al (2014) ^[13]	Mean age was 60.4 ± 17.2. Frequency: 34.3%, 58.96%	SIADH criteria was met in 36.25%, pneumonia being the leading cause of SIADH / euvolemic	The hyponatremia group a longer stay, longer ventilator days and had more mortality
Babaliche P et al ^[14] (2017)	n=100 Prospective cross-sectional study	S/S: Vomiting confusion. SIADH& euvolemic renal dysfunction& Drug	Hyponatremia infectious cause should be meticulously screened for tuberculosis
Patil S et al ^[15] (2016)	Cross-sectional n=100, Hyponatremia: 100 non-hyponatremia 50	66% patients had seizures, reduced consciousness level, confusion, unsteadiness, and falls	Most aetiology was severe sepsis, renal failure, liver cirrhosis, trauma, hypothyroidism, hypocortisolism. Longer duration stay in ICU with higher mortality rate
Paniker GI et al ^[16] (2014)	n=100	Confusion	Commonest aetiology was SIADH and pneumonia. Mortality: 4%
Gopinath H et al ^[17] (2016)	n=50	Hypertension and diuretics and excessive renal loss	Diabetes mellitus and dyslipidaemia were important co-morbidities of hyponatremia
Parijat P et al ^[18] (2015)		Nausea, vomiting and drowsiness are the commonest symptoms	Increasing age, hypertension, diabetes mellitus and use of drugs (diuretics). Hyponatremia acts as a poor prognostic marker
Present study	n=115; Males: 73 (63.47%), Females: 42(36.52%)	Confusion, seizures and coma were associated with moderate to profound hyponatremia	Mild hyponatremia was common and the SIADH was the commonest aetiology. The duration of hospital stay was inversely related to Na ⁺ levels. Overall mortality of 9.57% correlated with severity of hyponatremia

Table 7. Comparison of Various Studies with Present Study

Rao MY et al studied 100 patients with hyponatremia with CNS manifestations with mortality rate of 9.09% with SIADH was the aetiology with hypertension and DM was the frequent co-morbidity these findings are comparable with present study.^[19] In the evaluation of the hyponatremia patient, history taking should focus on identifying the potential cause, duration and symptomatology. Clinical examination should include assessment of volume status. Acute hyponatremia of less than 48 h duration requires prompt correction.^[20]

CONCLUSION

Hyponatremia is a frequent electrolyte eccentricity found in the present study. All the symptomatic cases had moderate to severe hyponatremia. Cerebrovascular accident was the frequent diagnosis of patients with hyponatremia and diabetes mellitus and the hypertension was the common co-morbidity in the present study. The most common aetiology was euvolemia with SIADH. Hyponatremia was found to be related to multiple aetiological factors in a large number of patients. There was significant alliance between serum sodium levels and symptoms and outcome of the patients. Central nervous system symptoms were often seen in severe hyponatremia. The mortality and prolonged duration of stay and mortality was often correlated with severity of hyponatremia. A well-structured approach to the diagnosis of hyponatremia with the application of simple diagnostic algorithms, using history, clinical examination and laboratory findings to establish protocol of hyponatremia can significantly improve the outcome of hyponatremia.

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