

Original Research Article

Study on clinical profile of hyponatremia in patients admitted to the MIMS in Northern Andhra Pradesh, India

Anand Sankar Sastry*, Buridi Praneetha

Department of Medicine, Maharaja Institute of Medical Science, Vizianagaram, Andhra Pradesh, India

Received: 19 April 2019

Accepted: 30 April 2019

***Correspondence:**

Dr. Anand Sankar Sastry,

E-mail: dranandsastrymkcg@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Hyponatremia, most common electrolyte disorder has symptomatology ranging from asymptomatic to being comatose and etiologically from simple G.I. loss to chronic illnesses like CCF, CKD. Very sparse study has been done in this region on clinic-epidemiological profile of hyponatremia. The aims and objective of this study was to find out most common etiology, type, clinical features and outcome in hospitalised hyponatremic patients and to Correlate clinical profile and outcome with etiology, severity and treatment.

Methods: The present observational study was conducted in department of medicine, Maharajah's Institute of medical sciences, for two months. All patients aged ≥ 15 years having true hyponatremia were included. Detailed history, examination, relevant investigations including serum and urinary Na were done. Patients were classified to euvolemic, hypervolemic and hypovolemic depending on volume status and proper etiologies were determined in each group.

Results: Of 50 patients included, mean age was 50.12 ± 8.8 years. Hyponatremia was more common in older age group > 40 years ($P < 0.05$). CNS manifestations were more prevalent in patients with $\text{Na} < 125$ Meq. (80%) $P < 0.05$. Hypervolemic was most common type (50%) followed by hypovolemic (34%) and euvolemic (16%). CKD was the most common cause overall (24%) and also among hypervolemic type (40%).

Conclusions: Hyponatremia was more predominant in elderly age group ($P < 0.05$). It is more in 40-60 years age group. Hypervolemic type (50%) of hyponatremia is most common type of the hyponatremia and CKD (24%), to be most common cause of the hyponatremia attributed to Uddanam nephropathy in this region.

Keywords: CKD, Hypervolemic, Hyponatremia, Uddanam

INTRODUCTION

Hyponatremia defined as serum sodium less than 135 mEq/l, is the most common electrolyte disorder among hospitalized patients.¹⁻⁵ Symptomatology varies markedly ranging from asymptomatic to being comatose with mortality 5-50 % depending on severity, acuity of onset and associated illnesses.⁶ Hyponatremia occurs in patients with varieties of causes ranging from simple G.I. loss (vomiting and diarrhea), to chronic illnesses like CCF,

liver and renal failure. It affects all age groups and both sexes.

Hyponatraemia is important clinically because

- Acute severe hyponatraemia can cause substantial morbidity and mortality
- Prompt recognition and optimal management of hyponatremia reduce in-hospital mortality and symptom severity and

- overly rapid correction of chronic hyponatraemia can cause severe neurological deficit and death.
- Hyponatremia is not a homogenous disorder, depending upon the volume status, euvolemic, hypervolemic or hypovolemic and depending upon severity mild, moderate or severe.

The etiological profile, type, severity and outcome vary from region to region depending upon the climate, disease distribution pattern and peripheral services. Each etiology and type of hyponatremia requires a different approach to treatment. Although the most common cause of hyponatraemia in hospital inpatients is SIADH (Euvolemic) in most studies, but it varies especially in tropical regions (mainly hypovolemic) and also in patients with chronic diseases (hypervolemic).

Studies regarding clinico-etiological profile of hyponatremia are sparse in northern Andhra Pradesh which being a tropical region with most people being farmers and laborer's working in sun light. Again, there are plenty of patients with hypervolemic conditions like CCF and especially CKD which is widely prevalent known as Uddanam Nephropathy.^{7,8} Data on the clinical features, types and exact etiologies in patients with hyponatremia is lacking in this region. Hence this study has been planned to find out most common etiology, type, clinical features and outcome in hospitalised hyponatremic patients so as to enhance informations which will enlighten our approach towards early diagnosis, adequate management and prevention strategies of this highly prevalent and correctable metabolic disturbance.

The aim and objective of this study were based on this observational study is aimed to find out the most common etiology, type, clinical features and outcome in hospitalized hyponatremic patients.

The objectives of this study were based to find out type (hypo/hyper/euvolemic), etiology, and clinical profile of patients with hyponatremia, to record the clinical outcome with treatment, correlate the clinical profile and outcome with etiology, severity and treatment of hyponatremia.

METHODS

The present study was conducted in department of medicine, Maharajah's Institute of Medical Sciences, Vizianagaram, A.P, India for a period of two months i.e., from 1-05-2017 to 30-06-2017 with size of 50 samples after approval of the ethical committee and ICMR.

Inclusion criteria

- Patients aged ≥ 15 years,
- Patients with true hyponatraemia (low plasma osmolality < 260 mOsm/kg) either on admission or at any point of time during hospitalization.

Exclusion criteria

- Patients aged ≤ 15 years,
- Patients having Pseudo hyponatremia,
- Patients with hyperosmolar hyponatremia,
- Patients not willing to participate in the study.

Detailed history

This included, detail history including onset, duration and progression of symptoms of hyponatremia, predisposing factors and pre-existing illnesses if present.

History of illnesses causing hyponatremia such as congestive heart failure, chronic kidney disease, chronic liver disease, hypothyroidism and other conditions which are associated with SIADH such as small cell lung carcinoma, CNS disease, and pulmonary disease were taken and recorded. History of fluid loss as in vomiting, diarrhea was noted.

Drug history causing hyponatremia like diuretics (loop and thiazide), antidepressants (SSRI, TCA), anticonvulsants, chemotherapeutic agents and NSAID's were taken.

Physical examination

Detailed clinical evaluation was done in every patient. Hydration status of the patient was determined by clinical examination to determine type of hyponatremia (hyper/hypo/euvolemic).

The signs of hypovolemia included tachycardia, orthostatic fall in blood pressure, decreased skin turgor, dry mucous membranes and decreased peripheral perfusion with a delayed capillary refill more than three seconds.

Hypervolemic state will be defined by the presence of anasarca, ascites, symmetrical and pitting pedal edema and raised jugular venous pressure (JVP).

Investigations

Apart from the routine investigations like hemoglobin, total count, differential count, erythrocyte sedimentation rate, electrocardiogram, chest x-ray, other tests like Serum creatinine, potassium, uric acid, blood glucose, albumin, serum osmolality, urine osmolality, urinary electrolytes, thyroid function tests, cortisol and lipid profile were performed on these patients to determine the probable and underlying causes for hyponatremia.

Serum sodium levels were noted on admission, every 24 hours (where available) and the last value before discharge. The electrolyte analysis was done by ion sensitive electrode method in ESCHWEILER combi line machine. Serum electrolytes were recorded and successively repeated until it becomes normal.

Patients suspected with other causes were also investigated accordingly. Other investigations like CSF analysis, thyroid function, cortisol levels, abdominal sonography, and computer tomographic scans were performed on some patients depending on the clinical suspicion,

First, based on serum osmolality patients

- Pseudo hyponatremia: (normal serum osmolality, 275-295 mOsm/kg) In high content of plasma proteins and lipid proteins
- Hyperosmolar hyponatremia: (plasma osmolality >295 mOsm/kg) in hyperglycemia, mannitol administration, etc.
- Patients with true hyponatraemia: (Low plasma osmolality <275 mOsm/kg)

Based on serum sodium level, these patients were divided into

- Mild hyponatremia with serum sodium 125-134 mEq/L,
- Moderate hyponatremia with serum sodium 115-124 mEq/L and,
- Severe hyponatremia with serum sodium less than or equal to 115 mEq/L.

Based on fluid status and urinary sodium these cases were further divided into

- Euvolemic hyponatremia
- Hypervolemic hyponatremia and
- Hypovolemic hyponatremia

Based on clinical status and other parameters, patients were categorized etiologically

SIADH as defined by the classic criteria introduced by Bartter and Schwartz

Patients with clinical euvolemia, serum osmolality <275 mmol/kg, urine osmolality <100 mmol/kg, urine Na⁺>40 mmol/l, serum uric acid ≤4 mg/dl, no diuretic use, normal renal function (serum creatinine and blood urea) and absence of thyroid or pituitary insufficiency were:

- Hyponatremia due to renal loss: Renal sodium excretion of >20 mmol/L,
- Hyponatremia due to extra-renal loss: renal sodium excretion of <0.05).
- Heart failure- Induced hyponatremia: evidence of heart failure (clinically as well as by echocardiography), urine sodium of less than 10 mEq/l in the absence of liver cirrhosis, renal failure and other causes of hyponatremia.
- Liver cirrhosis hyponatremia: Liver cirrhosis with ascites, with hypervolaemic status and urine sodium of less 10 meq/l.

- Diuretics: Urine sodium is more than 20 meq/l in hypovolemic or apparently euvolemic patients excluding other causes of hyponatraemia.

The data review also included input/output fluid balance records and management done (fluid restriction, fluid resuscitation or diuretic use) during the hospital course. Final outcome (death or discharge) was also noted.

The qualitative data are expressed in proportion and percentages and the quantitative data as mean and standard deviation. The difference in proportion is analyzed by using chi-square test and Fisher exact test wherever applicable and the difference in means is analyzed by using student t test (unpaired). Significance level for tests has been determined as 95% (p <0.05). The difference is significant if p<0.05.

RESULTS

This project was done for two months from 1st May 2017 to 30th June 2017 with sample size of 50.

Table 1: Patient demographics.

Total no. of hyponatremic patients	50
Mean age (years)	50.12±8.85 (Range 18-75 years)
Age distribution	
15-40 years	14 (28%) M-14, F-0
40-60 years	22(44%) M-12, F-10
>60 years	14(28%) M-8, F-6
Gender distribution	M-35(70%), F-15(30%) ratio 7:3
Volumic status	
Euvolemic	8 (16%)
Hypovolemic	17(34%)
Hypervolemic	25(50%)
Clinical diagnosis	
Chronic kidney disease	12 (24%)
Chronic liver disease	8 (16%)
Heart diseases	8 (16%)
CHF	6 (12%)
CAD	4 (8%)
Hypertension	4 (8%)
Cardiomyopathy	2 (4%)
Lung diseases	10 (20%)
COPD	4(8%)
Pneumonia	2 (4%)
Tuberculosis	4 (8%)
CNS diseases	3(6%)
Hydrocephalous	2 (4%)
CVA with right hemi paresis	1 (2%)
Miscellaneous causes	9(18%)

Table 1 shows demographics; no. of male patients was 35 (70%) and female are 15 (30%) with a ratio of 7:3 and the

mean age was 50.12±8.85(range 18-75 years). With age group of 18-40 years, 28% (14) cases were seen with all males and no female. Maximum number, i.e, 44% (22) cases were seen in the people with age group of 40-60 years with male and female 12 and 10 respectively. 28 (14%) cases were seen in the people with age group of >60 years within this male and female 8 and 6 six respectively

It also reveals that patients with hypervolemic type of presentation being most common was seen in 25 (50%) of the cases. Patients with hypovolemic type of presentation was seen in 17 (34%) of the cases, and patients with euvoletic type of presentation was seen in 8 (16%) of the cases.

Table 2: Distribution of hyponatremia in older (>40) and younger (<40) patients.

Age of the patient	(n=50)	Significance
Patients more than 40 years	36(72%)	P<0.05%
Patients less than 40 years	14(28%)	

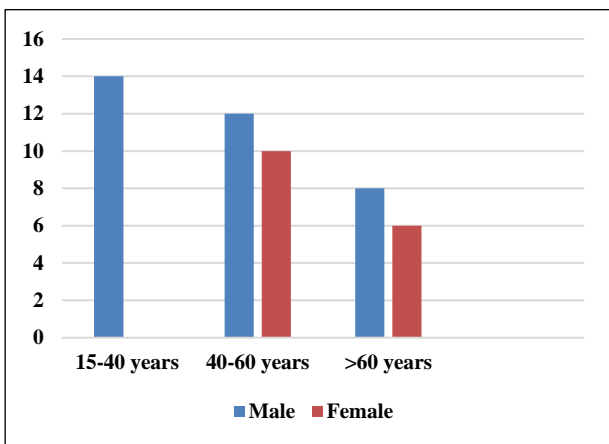


Figure 1: Distribution of male and female with hyponatremia.

Table 2 shows that 36 out of 50 patients were older than 40 years, only 14 were less than 40 years age. Hence, hyponatremia is most common after 40 years of age (72%) compared to those <40 years (28%) with p <0.05% which is statistically significant.

Table 4: Correlation of clinical symptomology with severity of hyponatremia.

Symptoms	In mild hyponatremia(N=40)	In moderate hyponatremia(N=08)	In severe hyponatremia(N=02)
CNS manifestations (N=24)	16 (40%)	06 (75%)	02 (100%)
G.I manifestations (N=26)	20 (50%)	04 (50%)	02 (100%)
CVS manifestations (N=24)	20 (50%)	03 (37.5%)	01 (50%)
Respiratory manifestations (N=30)	24 (60%)	05 (62.5%)	01 (50%)

Figure 1 shows that with age group of 18-40 years, 28% (14) cases were seen with all males and no female. Maximum number, i.e,44% (22) cases were seen in the people with age group of 40-60 years with male and female 12 and 10 respectively.28 (14%) cases were seen in the people with age group of >60 years within this male and female 8 and 6 six respectively.

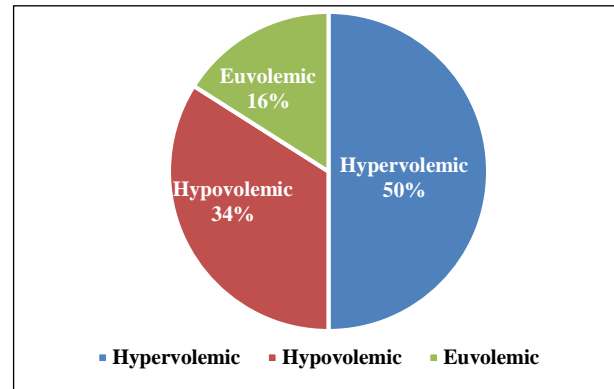


Figure 2: Distribution of type of hyponatremia.

Figure 2 reveals that patients with hypervolemic type of presentation being most common was seen in 25 (50%) of the cases. Patients with hypovolemic type of presentation was seen in 17 (34%) of the cases, and patients with euvoletic type of presentation was seen in 8 (16%) of the cases.

Table 3: Distribution of patients (as per degree of hyponatremia /serum Na⁺ level (mmol/L).

Hyponatremia	N (no. of patients)
Mild hyponatremia (125-134mEq/l)	40 (80%)
Moderate hyponatremia (124-115mEq/)	8 (16%)
Severe hyponatremia(<115mEq/l)	2 (4%)

Table 4 reveals CNS manifestations like altered sensorium, seizures, etc. were present in 16 patients (40%) of mild hyponatremia, 6 patients (75%) of moderate hyponatremia whereas all 2 patients (100%) of severe hyponatremia had neurological symptoms. CNS manifestations are more common with moderate and severe hyponatremia with Na<125 (80%) than with mild hyponatremia (40%) with P<0.05% being statistically significant.

Table 5 shows CKD is most common disease producing hyponatremia found in 12 patients (hyper volemia-10, hypovolemic-2), next common CLD found in 8 patients all hypervolemic, others being heart disease (Hypervolemic-7, Hypovolemic-1), Lung disease (Euvolemic-8, Hypovolemic-2), Drug induced (Hypovolemic-2).

Table 5: Underlying major disease contributing to hyponatremia.

CKD induced	12 (24%)	Hyper volemia-10 Hypovolemic-2
Chronic liver diseases induced	8 (16%)	Hypervolemic-8
Heart diseases induced	8 (16%)	Hypervolemic- 7 Hypovolemic-1
Lung diseases induced	10 (20%)	Euvolemic-8 Hypovolemic-2
Drug induced	2 (4%)	Hypovolemic -2

Table 6 reveals that commonest hypervolemic type (50%) was seen in CKD 10 (40%), heart diseases 7 (28%), liver diseases 8 (32%). For the hypovolemic type of hyponatremia (50%), it is seen in G.I. loss 10 (58.8%), lung diseases 2 (11.7%), drug induced 3 (17.6%), CKD 2 (11.7%), heart disease (5.9%) euvolemic type of hyponatremia is seen only in the lung diseases like TB and pneumonia (100%). Two patients of CKD were hypovolemic due to vomiting and use of diuretics. 1 patient of heart disease was dehydrated due to excessive diuretic use.

Table 6: Distribution of etiology causing each type of hyponatremia.

Euvolemic (n=8,16%)	Hypovolemic (n=17, 34%)	Hypervolemic (n=25, 50%)
	GI loss (58.80%)	CKD (40%)
Lung disease induced (100%)	Drug induced (17.60%)	Liver disease induced (32%)
	CKD (11.7%)	Heart disease induced (28%)
	Heart disease induced (5.9%)	

DISCUSSION

Among 50 hospitalized patients, it was more commonly seen in the middle age groups (40-60years) and more prevalent in males than in females. No. of male patients were 35 (70%) and female are 15 (30%) with a ratio of male and female with hyponatremia in 7:3 and the mean age was 50.12±8.85(range 18-75years). With age group of 18-40 years, 28% (14) cases were seen with all males and no female. Maximum number, i.e,44% (22) cases were seen in the people with age group of 40-60 years with male and female 12 and 10 respectively. 28 (14%)

cases were seen in the people with age group of >60 years within this male and female 8 and 6 six respectively. Hyponatremia is most common after 40 years of age (72%) compared to those <40 years (28%) with p <0.05% with male predominance. In study by Agarwal SM et al, mean age of patients was 48.1±16.1 years and in study by Rahil A I et al, in Qatar mean age was 56±20 years, almost similar to present study.^{9,10}

Regarding study of volemia status among the three types (hypervolemic, hypovolemic, euvolemic), patients with hypervolemic type of presentation being most common was seen in 25 (50%) of the cases. Patients with hypovolemic type of presentation was seen in 17 (34%) of the cases, and patients with euvolemic type of presentation was seen in 8 (16%) of the cases. In Agarwal SM et al, study and Rahil AI et al, study, hypovolemic type was common (decreased salt intake and extra-renal loss respectively) where as in Nauman Tarif study, hypervolemic was common (CKD) and in Padma V et al, study, euvolemic type (SIADH) was common.⁹⁻¹² Hypervolemic type being most common in present study may be attributable to more prevalence of heart failure, chronic liver disease and especially CKD in this region (Uddanam nephropathy).^{6,7} Hypovolemic is 2nd most common type due to the tropical climate and increased incidence of gastroenteritis (G.I. loss).

Coming to the study on etiology causing the hyponatremia, among the many factors causing the hyponatremia, CKD 24% (12) is the most common cause of hyponatremia in present study. In this northern Andhra Pradesh region (Srikakulam and Vizianagaram Districts), prevalence of chronic kidney diseases is high (Uddanam Nephropathy) compared to other surrounding region.^{6,7} Only Tarif N et al, in Pakistan study had a similar finding of CKD being most common cause as in present study.¹¹ In Agarwal SM et al, study, Decreased salt intake and in Rahil AI et al, study, extra-renal loss was most common etiology.^{9,10} In Padma V et al, study, SIADH was most common.¹² G.I. loss was 2nd most common in present study 20% (10) due to tropical climate.

Correlating the data about etiology of hyponatremia with the type of hyponatremia (hyper, hypo, euvolemic), Commonest hypervolemic type (50%) was seen in CKD 10 (40%), heart diseases 7 (28%), liver diseases 8 (32%). For the hypovolemic type of hyponatremia, it is seen in G.I. loss 10 (58.8%), lung diseases 2 (11.7%), Drug induced 3 (17.6%), CKD 2 (11.7%). Hypovolemic type in CKD are attributable to those who were on dialysis with high doses of diuretics and those with severe nausea and vomiting. Euvolemic type of hyponatremia is seen only in the lung diseases like TB and pneumonia in this study due to more ADH secretions in these lung conditions. Study by Mittal M et al, reveals euvolemic to be most common type, SIADH due to CNS infections being MC cause.¹³ CLD and acute gastroenteritis were MC causes

for, hypervolemic, and hypovolemic hyponatremia respectively.

Among the cases 24 (48%) were presented with CNS manifestations like altered sensorium (Drowsy, Stuporous and Comatose), seizures, delirium. 26 (52%) cases were presented with G.I. manifestations, 30 (60%) cases were presented with respiratory manifestations, 24 (48%) cases were presented with CVS manifestations, 8 (16%) cases were presented with urinary manifestations, and 12 (24%) cases were presented with fever. There were no cases causing mortality among these patients. CNS manifestations are more common with moderate and severe hyponatremia with Na <125 (80%) than with mild hyponatremia (40%) with P <0.05%. Other studies like Agarwal SM et al, study and Rahil AI et al, study showed similar results.^{9,10} All patients recovered with adequate treatment of hyponatremia and of the etiology.

CONCLUSION

This study reveals that hyponatremia was more predominant in the elderly age group (more seen in group of 40-60 years) than the younger group which is statistically significant (P<0.05%) with a more frequency in males than in females. Hypervolemic type (50%) is most common and CKD (24%), is most common cause. Among the three types, CKD (40%) major cause for hypervolemic, G.I. loss (58.8%) for hypovolemic type and lung diseases for the euvolemic type. CNS manifestations were more common with Na level less than 125 Meq which is statistically significant (P<0.05%).

Hyponatremia being the most common electrolyte disorder among the hospitalized patients, must be actively looked for and corrected early as the delay in starting treatment worsens the hyponatremia and prolongs the hospital stay. Determining the type of hyponatremia by history, clinical examinations and adequate investigations like urinary osmolarity and urinary sodium is very vital with regards to treatment, which is very different in hypervolemic type, most common in present study (CKD). In CKD, water restriction, removal of excess free fluid by dialysis and ADH antagonists like tolvaptan are the mainstay of treatment rather than sodium replacements.

CKD should be thought as an important cause of hyponatremia in this region due to Uddanam nephropathy as evidenced in present study. Uddanam nephropathy is a public health issue in India and more research should focus to establish its causes and adequate training among both medical and paramedical workers must take place to help proper renal care and prevent and treat complications like hyponatremia.

Care must be taken in CKD patients who are on maintenance dialysis and taking high dose of diuretics or having severe vomiting as hyponatremia in these patients

may be hypovolemic in spite of CKD and may require sodium replacement. Urine osmolarity and Urinary Sodium should be more frequently used for evaluation of hyponatremia in these patients.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Oh MS. Management of hyponatremia and clinical use of vasopressin antagonists. *Am J Med Sci.* 2007;333(2):101-5.
2. Montain SJ, Sawka MN, Wenger CB. Hyponatremia associated with exercise: risk factors and pathogenesis. *Exercise Sport Scienc Reviews.* 2001;29(3):113-7.
3. Gonc NE, Kandemir N, Sen Y, Yordam N, Hyponatremia can be a presenting finding of multiple pituitary hormone deficiency in children: report of a case and review of literature. *Clin Pediatr.* 2005;44:623-8.
4. Bhananker SM, Paek R, Vavilala MS. Water intoxication and symptomatic hyponatremia after outpatient surgery. *Anesthes Analges.* 2004;98(5):1294-6.
5. Coenraad MJ, Meinders AE, Vandebroucke JP, Frölich M, Taal JC, Bolk JH. Causes of hyponatremia in the departments of internal medicine and neurosurgery. *European J Int Med.* 2003;14(5):302-9.
6. Douglas I. Hyponatremia: why it matters, how it presents, how we can manage it. *Clevel Clin J Med.* 2006;73(3):S4.
7. Ganguli A. Uddanam nephropathy/regional nephropathy in India: preliminary findings and a plea for further research. *Am J Kidney Dis.* 2016;68(3):344-8.
8. Gadde P, Sanikommu S, Manumanthu R, Akkaloori A. Uddanam nephropathy in India: a challenge for epidemiologists. *Bull World Health Org.* 2017;95(12):848.
9. Agarwal SM, Agrawal A. A comparative study of the clinico-aetiological profile of hyponatremia at presentation with that developing in the hospital. *Indian J Med Res.* 2011;134(1):118.
10. Rahil AI, Khan FY, Al Badri MM. Clinical profile of hyponatraemia in adult patients admitted to Hamad general hospital, Qatar: Experience with 53 Cases. *J Clin Diag Res.* 2009;3:1419-25.
11. Tarif N, Sabir O, Niaz A, Akhtar R, Rafique K, Rizvi N. Hyponatraemia: epidemiology and aetiology in a tertiary care centre in Pakistan. *J Pak Med Assoc.* 2016;66(11):1436-9.
12. Padma V, Javid SM, Narendran D, Anand K, Karthikeyan D. Study of symptomatic hyponatremia in elderly patients. *Int J Pharm Bio Sci.* 2016;7:434-0.

13. Mittal M, Deepshikha KH. Profile of hyponatremia in a tertiary care centre in North India. *Int J Adv Med.* 2016;3(4):1011-5.

Cite this article as: Sastry AS, Praneetha B. Study on clinical profile of hyponatremia in patients admitted to the MIMS in Northern Andhra Pradesh, India. *Int J Res Med Sci* 2019;7:2055-61.