CLINICAL AND MANAGEMENT PROFILE OF HYPONATRAEMIA IN A TERTIARY HOSPITAL

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ABSTRACT

Hyponatraemia is an electrolyte disorder defined by blood sodium level < 135 mmol/L. It is a clinical emergency. It may be acute or chronic depending on duration and may be hypervolaemic, euvolaemic or hypovolaemic. In this observational study, a total of 111 patients were included. Out of them, 75% were male and 25% were female. Most patients were of 4th decade (72%). Among them, 22% in CKD stage II, 24% in stage III, 29% in stage IV and 25% were in stage V and 75% of patients presented with acute and severe hyponatraemia. Hiccup (38%) was the major symptom, followed by vomiting, dehydration, confusion. Among the modes of treatment used, 3% hypertonic saline was used in majority. Duration of treatment in acute and chronic hyponatraemia was average of 3 and 5 days respectively. Despite judicious treatment, 1 patient developed symptoms and signs of demyelination on next day of treatment. Patient was treated with Inj. methylprednisolone. Among the chronic hyponatraemia patients, 1 patient suffered from extrapontine myelinosis who recovered with supportive treatment. About 66% patients presented with hypovolaemic hyponatraemia due to exacerbating factors such as vomiting, infection, injudicious use of diuretic, dehydration of unknown cause.

KEYWORDS
Hyponatraemia, Hypovolaemic, Euvolaemic, Hypervolaemic, Chronic Kidney Disease, Dehydration.

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INTRODUCTION: Hyponatraemia is defined as a decrease in the serum sodium concentration to a level below 135 mmol per litre. Hyponatraemia can be associated with low, normal, or high tonicity.[2,3] It is the most common electrolyte disorder in hospitalised patients, with a prevalence of 30-40%.[4,5] Dilutional hyponatraemia is by far the most common form of disorder.

According to volume of distribution, it is of 3 types, hypovolaemic, hypervolaemic and euvolaemic. Hypovolaemic hyponatraemia has both a total body Na+ and a water deficit, with the Na+ deficit exceeding the water deficit caused by gastrointestinal and third space sequestered losses, injudicious use of diuretics, salt losing states.[1,2,3] In hypervolaemic hyponatraemia, the total body water is increased more than total body Na+ and hyponatraemia occurs, as in congestive heart failure (CHF), nephrotic syndrome, and cirrhosis.[2,3] In euvolaemic category, total body water increases but there is no change in total body Na+. It is seen in Glucocorticoid deficiency, Hypothyroidism, Stress, Syndrome of inappropriate ADH secretion (SIADH).[1,2]

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According to duration, hyponatraemia is of two types acute and chronic. In acute hyponatraemia, duration of hyponatraemia is of<48 hours. The major risk is an increase in intracranial pressure, which may lead to brain herniation.[1] Chronic hyponatraemia is defined as when hyponatraemia is present for >48 hours and there is no acute element.[1] The major risk is the development of osmotic demyelination[6,7,8] from too rapid a rise in the Na+. When an acute element of hyponatraemia is present in a patient with chronic hyponatraemia,[9] the Na must be raised quickly to lower intracranial pressure. But the rise should not exceed the desired upper limit for the increase in Na over a 24-hour period to avoid causing osmotic demyelination.[6,7,8]

Mild Hyponatraemia[10] is defined as sr. Na 130 mEq/L to < 135 MEq/L, Moderate Hyponatraemia[10] as 125 mEq/L - 129 mEq/L, and Severe Hyponatraemia[10] as<125 mEq/L.

Hypovolaemic Hyponatraemia responds readily to volume repletion and to hypertonic saline like 3% normal saline. The treatment of hypervolaemic hyponatraemia has been limited to fluid restriction[11] and correction of the underlying disorder. Treatment modalities[12,13] for euvolaemic hyponatraemia have included fluid, hypertonic saline, loop diuretics, demeclocycline. With the approval of the vasopressin-receptor antagonists conivaptan[14,15] and tolvaptan,[14,15] more targeted treatment for euvolaemic and hypervolaemic hyponatraemia became available.

RAPID CORRECTION: Patients with severe hyponatraemia are at a risk of developing severe and potentially irreversible neurological damage and sometimes death.

Too rapid correction produces central pontine myelinosis or osmotic demyelination syndrome (ODS)[6,7,8] characterised by dysarthria, dysphagia, flaccid paresis, coma. (Rise in sodium > 25 mEq/L/48 hrs. or correction is made until normonatraemia, Sr Na+ 140 mEq/L).

Rapid correction is indicated in acute (<48 hrs.) symptomatic or severe (<125 mEq/L) hyponatraemia.[1,3]

In chronic hyponatraemia (>48 hrs.), rapid correction lead to ODS.

With this background, the present study was undertaken to study the clinical outcomes of treatment of hyponatraemia, at Department of Nephrology, SCB Medical College Cuttack, Odisha.

MATERIALS AND METHODS: Patients with hyponatraemia admitted in the Department of Nephrology, SCBMCH were taken for analysis between July 2015 to December 2015.

All patients with Sr. Na level < 135 mmol/L were included in the analysis and patients having hyperglycaemia and patients receiving RRT were excluded.

Data collected were symptoms and signs at admission, admitting diagnosis, Volume status, Time of hospitalisation, Demographics including age and gender, Severity of underlying condition, Aetiology of SIADH including tumour, CNS disorder, drugs, History of prior hyponatraemia, Acuity of onset of hyponatraemia, Hyponatraemia inducing medicines, Hyponatraemia symptoms. And monitoring of vitals such as Blood pressure and heart rate, hydration status, Daily weight and blood parameters such as Serum osmolality, Sr Na+, Blood Urea Nitrogen, Creatinine, and daily glucose values were recorded daily.

Na deficit calculated as =

(Desired Na-actual Na) x Total body water

Total body water -

= 0.60 x body weight (kg) in children and non-elderly man.

= 0.50 x body weight (kg) non-elderly woman and elderly male.

= 0.45 x body weight (kg) in elderly woman.

Change in serum sodium concentration =

Infusate Na-Serum Na/Total Body Water (L) + 1.

Or

Infusate (Na+K)-Serum Na/Total Body Water (L) + 1.

Rapid correction[6,7,8] of Na+

1. Done in hyponatraemia with severe neurological symptoms-
2. Rapid correction of [Na+] is defined as an increase >12 mEq/L in any 24-hr. interval or >18 mEq/L in any 48-hr. interval.
3. Initial rate of rise of Na concentration should be 1.5-2 mEq/L/hr. for the first 3-4 hrs.

Rate of change of [Na+] was calculated as the total increment in [Na+] during the period the treatment was utilized divided by the number of treatment days.

Various modes of treatment selected were hypertonic saline and normal saline, Water restriction, Water restriction and loop diuretics, Water restriction with Tolvaptan and average duration of treatment were calculated and any complication during treatment were carefully observed.

RESULTS: A total of 131 patients admitted between January 2015-July 2015 were taken in to study.

Patients excluded from the study-Hyperglycaemic-06, RRT-14.

The 111 patients were included in the analysis.

Out of them 86 (75%) were male and 25 (25%) were female. Most patients were in their 4th decade i.e. 79 (72%). (Table and figure 1). Among them, 22% in CKD stage II, 24% in stage III, 29% in stage IV and 25% were in stage V and 75% of patient presented with acute and severe hyponatraemia. According to the duration of hyponatraemia, 67 (60%) patients were diagnosed as acute hyponatraemia and 44(40%) were as chronic. (Table and figure 2). Out of 111 patients 97(87%) patients had hyponatraemia at the time of hospital admission, 14 (13%) developed during hospital stay and 66 (60%) patients had severe hyponatraemia, 18 (10%) had mild hyponatraemia (Table and figure 3). Majority of patients were having hiccups 38% as the major symptom, followed by vomiting 31%, dehydration 22%, oedema 20%, disorientation 16%, confusion 15%, ascites 5%, anorexia 6%. Distribution of signs and symptoms were equal in both males and females except females had more anorexia and vomiting.(Table 04) Average duration of treatment in acute hyponatraemia was 3 days and in chronic hyponatraemia was 5 days. (Table and figure 2). According to volume of distribution 34(31%) were hypervolaemic, 66 (60%) were hypovolaemic and 11(9%) were euvolaemic. Considering the modes of treatment in hypovolaemic category 39 (60%) out of 66 patients responded to combined treatment of hypertonic saline and normal saline (Table and figure 6) and others responded to monotherapy of hypertonic saline or NS (Table 5). In hypervolaemic category, 14 (41%) responded to fluid restriction only, 08(23%) responded to fluid restriction and diuretic and 5 (15%) responded to Tablet Tolvaptan 15 mg OD for 5 days. (Table 08) And in euvolaemic category all patients responded to fluid restriction only. During the course of treatment 1 patient among acute hyponatraemia patients developed CPM syndrome and 1 patient among chronic category and both were treated and cured.

ETHICS: This is an observational study; however, ethical clearance has been granted by institutional ethical committee of SCB Medical College.

OBSERVATION:

Age	No	Male	Female
10-20 years	06	04	02
20-39 years	26	23	03
40-59 years	55	41	14
>60 years	24	18	06

Table 1: Demographic Data

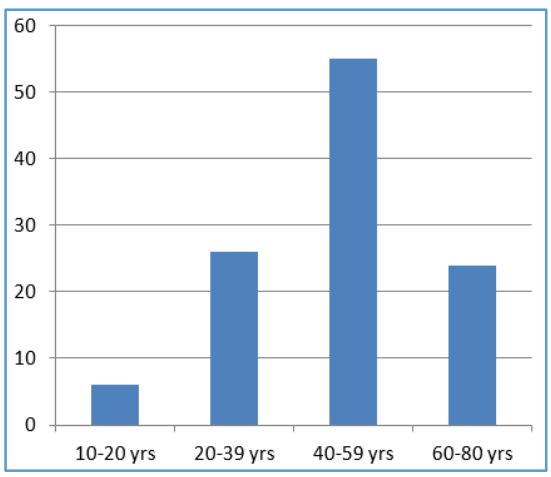

Figure 1

	No	Fluids	Dura-tion		
Acute (<48hr)	67	3% saline, IV fluids, fluid restriction	3 days	In 66 patients, Na corrected	1 patient had hyponatraemia with sequelae
Chronic (>48hr)	44	3% saline, IV fluids, fluid restriction	5 days	In 43 patients, Na corrected	1 patient had extrapontine myelinosis

Table 2: Duration of Treatment

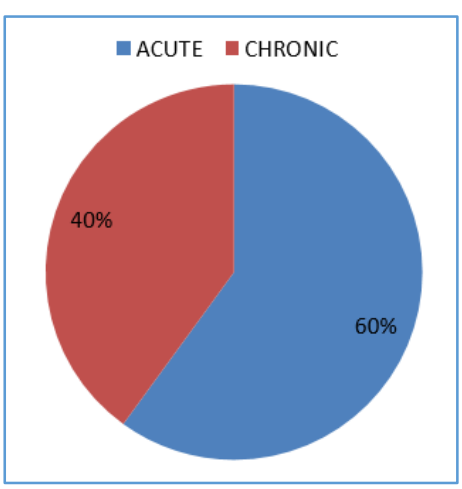

Figure 2

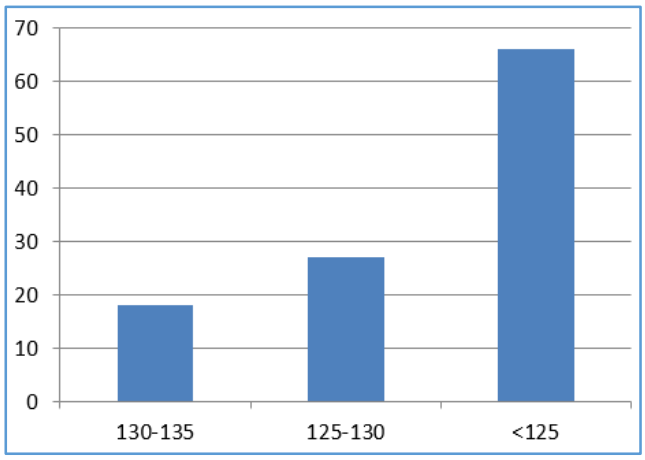

Figure 3: Serum Sodium Conc. and no. of Patients

Table 3: Na + Concentration:

1. Mild-135-130 mEq/L-18 Patients.
2. Moderate-130-125 mEq/L-27 Patients.
3. Severe-<125 mEq/L-66 Patients.
4. Previous h/o of Hyponatraemia- 12.
5. Hyponatraemia at admission-97 patients.

Symptoms/ signs	No of patients	Male	Female	% of Patients
Dehydration	24	14	10	21.6
Vomiting	34	14	20	30.6
Hiccups	42	22	20	37.8
Nausea	22	12	10	20
Confusion	18	10	8	16
Disorientation	16	8	8	14.4
Convulsion	8	5	3	7.2
Oedema	22	15	7	19.8
JVP raised	7	4	3	6.3
Ascites	5	4	1	4.5
Anorexia	6	2	4	5.4

Table 4: Clinical Features

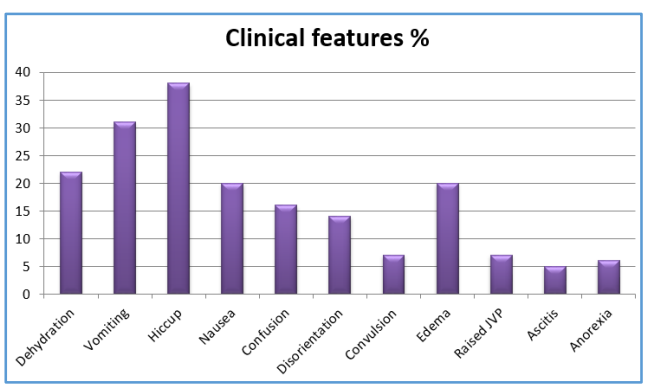

Figure 4

	Median baseline sodium	Median rate of Na+ change mEq/L	Mean duration of treatment
Fluid restriction	125 (121-128)	2 mEq/L	4
Normal saline	123 (120-127)	3 mEq/L	3
Hypertonic saline	112 (106-118)	5 mEq/L	2
Tolvaptan	124 (120-128)	4 mEq/L	4

Table 5: Response to Monotherapy

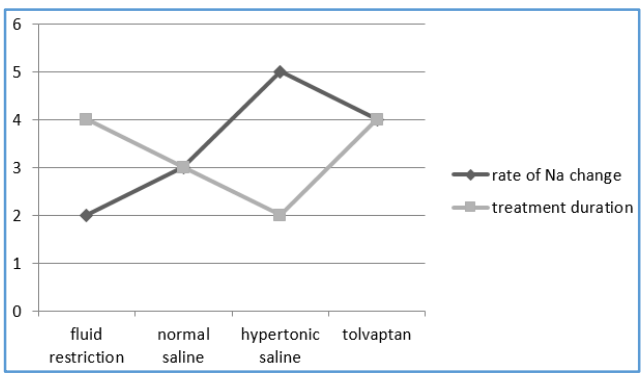

Figure 5

Individual Therapy Mode:

Treatment	No. of Patients	Mean Duration	Outcome
Hypertonic saline	08	2 days	Corrected
Hypertonic saline with NS	39	4 days	Corrected but 2 patients had complication
NS	19	04 days	Corrected

Table 6: Hypovolaemia with Hyponatraemia

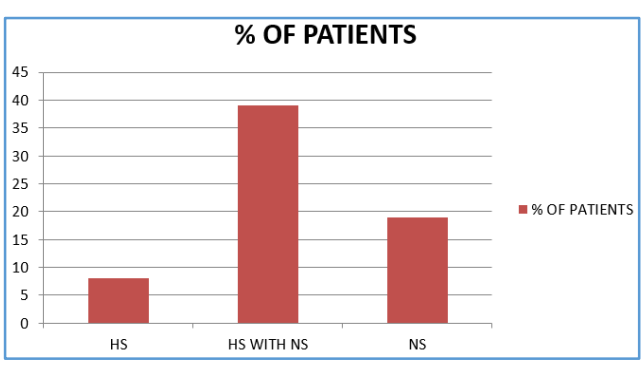

Figure 6

Out of 2 patients, 1 had hyponatraemia with sequelae treated with inj. methylprednisolone 1 g for 3 days and other patient had extrapontine myelinosis. Both patients improved and discharged.

Treatment	No. of Patients	Average duration	Outcome
Fluid restriction	14	03 days	Corrected
Fluid restriction with diuretic	08	04 days	Corrected
Fluid and Salt restriction	07	04 days	Corrected
Tolvaptan	05	04 days	Corrected

Table 7: Hypervolaemia

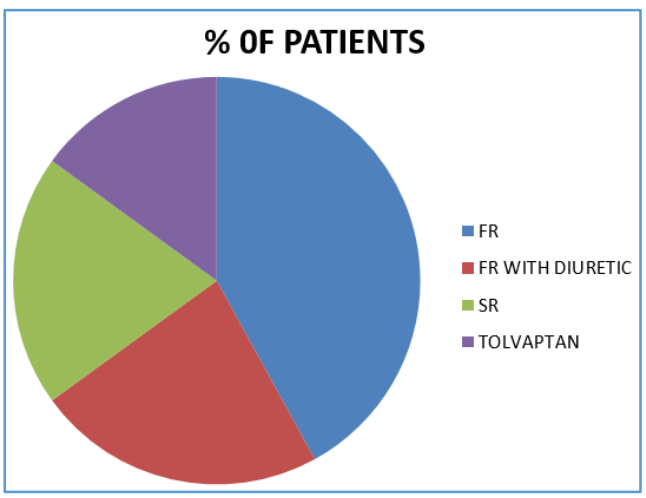

Figure 7

Treatment	No. of patients	Average duration	Outcome
Fluid restriction	11	04 days	corrected

Table 8: Euvolaemia

DISCUSSION: The demographic profile of this study showed 75% male and 25% female and most patients were in their 4th decade i.e. 72% which is similar to the study taken by Miller et al[16] with incidence of 7%-53% in institutional geriatric patients; and in a study 4123 patients aged 65 or more admitted to a community hospital had more incidence of death compared to normonatraemic (RR 1.95:P<.05). CKD staging showed 22% in CKD stage II, 24% in stage III, 29% in stage IV and 25% were in stage V which is deviated from majority of studies for e.g by Wallia et Al[17] which showed decreased incidence of hyponatraemia due to homeostasis of diluting and concentrating capacity of kidney with advanced stage. 60% patients were diagnosed as acute hyponatraemia and 40% were as chronic, and 60% presented with severe hyponatraemia< 125 mmol/L similar to the review literature by Upadhyaya A, Jaber BL Semin Nephrol 2009. Majority of patients were having hiccups 38% as the major symptom, followed by vomiting 31%, dehydration 22%, oedema 20%, etc. This finding is deviated from most of the studies and review literature published by Vervalis JG et al,[18] Richard H Stern.[9] Hence, hiccup is a prominent finding in our study. Hypovolaemic

hyponatraemic patients were 60%, 31% were hypervolaemic, 9% were euvolaemic, these results were similar to studies elsewhere like Vervalis JG et al,[18] Richard H Stern,[9] Upadhyaya[5] Fifty eight% hypovolaemic hyponatraemic patients responded to 3% hypertonic saline and normal saline and the average treatment duration was of 4 days similar to study by Worthley et al[19] 1986, Mohmand[20] et al, Woo et al[21] who found it in 74 % cases of their study, few patients responded to only normal saline as they had mild hyponatraemia. Fluid restriction was the treatment of choice in 42% hypervolaemic hyponatraemic patients and few patients responded to fluid restriction and diuretics and few to Tolvaptan. Similar result was seen in study by Vervalis JG et al,[19] who shows role of fluid restriction and furosemide in case of hyponatraemia among CHF patients, and role of Tolvaptan from 15 mg OD to 60 mg OD according to Active and Everest trial). Correction of hyponatraemia in selected patients e.g. CHF is associated with improved survival, and improved long-term survival following correction of in hyponatraemia patients in general has been observed. Experimentally, hyponatraemia has been shown to have direct effects on cardiac fibrosis and myocyte function. (Vervalis JG et al,[19] Castello[22] et al 23 patients) (Upadhyaya A, Jaber BL Semin Nephrol 2009).[5]

One patient, despite of judicious treatment, Sr Na got raised >10 mEq/L per day and patient suffered from hyponatraemia with sequelae similar to incidence in a case series published by Worthley et al[16]1986, Mohmand[17] et al, Woo et al.[18] Patient was treated with 3 days of high dose of Inj. methylprednisolone 1 g and other supportive treatments. Patients improved after 2 weeks, similar to results seen in a case series by Kenneth Musan and Seven H Yale[23]. Among the chronic hyponatraemia patients, 1 patient having hypovolaemic hyponatraemia treated with hypertonic saline had extrapontine myelinosis. Patient's sodium raised >10 MEq/L per day. Patient was treated only supportively and improved after 2 weeks. All 11 euvolaemic hyponatraemia patients responded to fluid restriction, similar results with Vervalis JG et al.[19] Determining the cause of hyponatraemia is the first step in evaluating patients with hyponatraemia and is crucial to guiding correct management.

CONCLUSION: A total of 111 patients were included in the analysis. 75% were male and 25 (25%) were female. Most patients were in their 4th decade i.e. 72%. Among them, 22% in CKD stage II, 24% in stage III, 29% in stage IV and 25% were in stage V and 75% of patients presented with acute and severe hyponatraemia. Though similar incidence was in all stages, slightly more in stage IV which is a major deviation from most studies. Majority of patients were having hiccups 38% as the major symptom, followed by vomiting, dehydration, oedema, disorientation, confusion, ascites, anorexia. Hiccups even though is not described in many literatures, we have found is one of the early and persistent features of hyponatraemia, which disappears on correction of Na level. Distribution of signs and symptoms were equal in both males and females except females had more anorexia and vomiting. Average duration of treatment in acute hyponatraemia was 3 days and in chronic hyponatraemia was 5 days. According to volume of distribution, most patients were hypovolaemic (60%), followed by hypervolaemic and euvolaemic. Fifty eight% hypovolaemic hyponatraemic patients responded to 3% hypertonic saline and normal saline and the average treatment duration was of 4 days, fluid restriction was the treatment of choice in 42% hypervolaemic hyponatraemic patients and all 11 euvolaemic hyponatraemia patients responded to fluid restriction. One patient, despite judicious treatment, Sr. Na got raised > 10 MEq/L per day and patient suffered from hyponatraemia with sequelae, treated with 3 days of high dose of Inj. methylprednisolone 1 g and other supportive treatments. Patients improved after 2 weeks. Among the chronic hyponatraemia patients, 1 patient having hypovolaemic hyponatraemia treated with hypertonic saline had extrapontine myelinosis. Patient's sodium was raised >10 mEq/L per day. Patient was treated only supportively and improved after 2 weeks.

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