

Clinical Profile and Laboratory Spectrum of Hyponatremia in Patients Admitted In Tertiary Care Hospital

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Abstract

Background and Objectives

Hyponatremia is a common electrolyte disorder in adults. The underlying cause in them is often multi-factorial, a clear history may be difficult to obtain and clinical examination is unreliable. Established treatment modalities are often ineffective and carry considerable risks, especially if the diagnosis of underlying causes is incorrect which requires prompt diagnosis and effective therapy.

Data regarding the incidence of hyponatremia in elderly in our country is limited. This study is done to know the common clinical features and etiology of hyponatremia in adults in hospitalized patients and to manage such patients.

Objectives

1. To study the clinical features of hyponatremia in adults.
2. To identify and assess the risk factors of hyponatremia in adults.
3. Management of hyponatremia.

Methods

A descriptive study was conducted in a tertiary care hospital (SSMC, Tumkur) during the period of November 2016 to October 2018. Patients aged ≥ 18 years admitted with serum sodium < 135 mEq/L were included in the study. 107 patients were selected randomly. These patients were evaluated for the underlying cause for hyponatremia by a detailed history and physical examination and followed by appropriate lab investigations.

Results

107 patients were included in the study. 64.5% had presented with constitutional symptoms, 52.3% had confusion, 50.5% had other symptoms, 49.5% had fever, 41.1% had vomiting, 37.4% had respiratory symptoms, 36.4% had pain abdomen, 15% had loose stools, 4.7% were in coma, and 2.8% had convulsions. There was wide range of etiologies, most common being SIADH (32.7%), extra renal losses (22.4%), renal failure (13.1%), renal losses (12.1%), cirrhosis (11.2%), cardiac failure (4.7%), drug induced (2.8%) and glucocorticoid deficiency

(0.9%). Hypertonic saline was given to 43%, diuretics and fluid restriction was advised for 30.8%, 20.6% were given both hypertonic saline and vaptans and 5.6% were given only vaptans.

Conclusion

Hyponatremia is the most common electrolyte disorder in hospitalised patients particularly in adults. A systematic approach to the diagnosis of hyponatremia with the application of simple diagnostic algorithms, using history, clinical examination and laboratory findings to establish mechanism of hyponatremia can significantly improve the management and outcome of hyponatremia.

Keywords: hyponatremia, adult patients

Introduction

Hyponatremia is defined as a plasma sodium Na^+ concentration <135 meq/l. It is a very common electrolyte disorder occurring in about 22% of hospitalized patients.¹

Both hyponatremia and hypernatremia can cause substantial morbidity, mortality^{2,3} and ironically incorrect diagnosis and treatment can add to the problem. Under normal circumstances; the plasma sodium concentration is maintained within a narrow range despite wide variations in sodium and water intake. This is achieved through an integration of thirst, vasopressin secretion and renal responsiveness of the vasopressin.⁴

Sodium is the dominant cation in the extracellular fluid and is the main determinant of plasma osmolality.⁴

Osmolality is determined by the ratio of solute content to water. If total body water changes without an accompanying change in total body solute, plasma osmolality changes, and hyponatremia or hypernatremia results.⁴ Disturbances of plasma sodium concentration are therefore the result of alterations in water homeostasis. Alteration in sodium balance although not a direct cause of hypernatremia or hyponatremia, modulate water

homeostasis may contribute to the development of these disturbances.⁴

The incidence is much more in adults mainly owing to impaired ability to maintain water and electrolyte homeostasis in response to diet, drugs and environmental changes.⁵

The etiology is multifactorial. It can be classified on the basis of serum osmolality into hypertonic, isotonic and hypotonic type. Hypotonic hyponatremia is further classified into hypervolemic, euvolemic/normovolemic and hypovolemic.⁶

- Normovolemic disorders with a normal total body sodium and a modest total body water excess. (e.g. Syndrome of inappropriate ADH secretion (SIADH), Drug induced hyponatremia).
- Hypervolemic disorders with an excess of total body sodium and a larger excess of total body water. (e.g. Cardiac failure, hepatic cirrhosis, nephrotic syndrome).
- Hypovolemic disorders with a deficit of total body water and a larger deficit of total body sodium due to renal sodium loss. (e.g. Diuretics, osmotic diuresis due to glucose, urea etc).
- Hypovolemic disorders due to extra renal sodium loss. (e.g. Vomiting, Diarrhea, profuse sweating).

Hyponatremia in patients with increased extracellular fluid (ECF) volume is generally attributable to congestive heart failure, liver failure, nephritic syndrome, or pregnancy. Patients who have hyponatremia with decreased ECF volume generally have excessive sweating, gastrointestinal losses, renal losses or bleeding as causes. Patients with normal ECF volume develop hyponatremia from cortisol deficiency or thyroid hormone deficiency or SIADH.⁷

Hyponatremia is a common problem encountered in patients presenting with non-specific symptoms. Symptomatology depends more on the rate of development of the electrolyte abnormality than on its severity.

Signs and symptoms include nausea and vomiting, headache, confusion, lethargy, fatigue, loss of appetite, irritability, muscle weakness, spasms or cramps, seizures, and drowsiness or coma.⁸

High incidences have been reported that hyponatremia is seen in upto 27% of patients admitted with acute heart failure^{9, 10, 11, 12} and that upto 50% of patients with cirrhosis and ascites to be found hyponatremic.^{13, 14}

Hyponatremia in moderate exercise is a potentially dangerous clinical scenario with only moderate water intake.¹⁵

Hyponatremia is almost always the resultant of dilution. It can be either Acute or Chronic.¹⁶

Untreated acute hyponatremia can cause osmotically induced cerebral edema and excessively rapid correction of chronic hyponatremia can cause severe neurologic impairment and death as a result of osmotic demyelination, which was first described in 1959 in patients who were both alcoholic and malnourished.⁷

Proper interpretation of the various laboratory tests helps to differentiate the various types of hyponatremia.¹⁷

Routine blood and urine investigations including complete blood count, renal function tests, electrolytes, liver function tests, serum osmolality, urine routine, urine osmolality, chest radiograph and imaging studies were done to rule out other co-morbid conditions. Serum cortisol level and Serum T3, T4 and TSH were done when indicated.

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. There have been several recent advances with revision in the guidelines for treatment and availability of vaptans.¹⁸ Judicious use of vaptans may help in treatment of hyponatremia.

Hyponatremia is one of the most common biochemical abnormalities in clinical practice.^{19, 20, 21} Due to the lack of large scale studies, limited data exists regarding the incidence of Hyponatremia in adults in India. Therefore this study was undertaken to establish the incidence of hyponatremia in a hospital setting.

Hyponatremia is associated with increased morbidity and mortality, especially in the adult population. As a result, an attempt has been made to identify the possible risk factors, clinical features and to manage such patients that will help in preventing the incidence of hyponatremia and subsequent morbidity.

Methodology

Source of Data

The present study was conducted from November 2016 to October 2018. In this period 107 patients with hyponatremia were taken into studies who were admitted to ICU, Emergency And Medical Wards Of Sri Siddhartha Medical College And Hospital, Tumkur. Patients aged \geq 18 with serum sodium $<$ 135 mEq/L were included in the study.

Inclusion Criteria

All cases of hyponatremia, irrespective of duration and type of treatment received will be included in the study.

Exclusion Criteria

Age less than 18 years of both sexes.

Materials and Method

Clinical Assessment

Detailed history: This included history of symptoms of hyponatremia, predisposing factors and pre-existing illness if present. The definition of symptomatic hyponatremia was based on clinical assessment of symptomatology including the presence of altered sensorium, postural dizziness, lethargy and seizures. Sensorium changes included acute confusional states, memory disturbances, stupor, delirium and coma. Drugs that can cause hyponatremia were recorded. History of illness causing hyponatremia such as CCF, CKD, CLD, hypothyroidism and other conditions which are associated with SIADH such as small cell carcinoma, CNS disease were taken. History of fluid loss as in vomiting, diarrhea, diuretic use, excessive sweating were taken in all patients.

Physical examination: Detailed clinical examination was done in every patient. Hydration status of the patient was determined by clinical examination. The signs of hypovolemia included tachycardia, decreased skin turgor, dry mucous membranes and decreased peripheral perfusion. Hypervolemic state was defined by the presence of anasarca, ascites, bilateral pitting pedal edema and raised JVP. Accordingly patients were divided into hypervolemic, hypovolemic and euvolemic.

At the time of diagnosis of hyponatremia, detailed CNS examination was done to document mental status of the patient and other focal neurological deficit. CNS examination was repeated after the correction of hyponatremia and the presence of symptoms such as dizziness, lethargy, altered sensorium and seizures were attributed to hyponatremia unless there was a co-existing medical condition or medication effect to account for these symptoms. Patients were screened for CPM based on clinical grounds that is development of confusion,

agitation and flaccid or spastic paralysis during or after correction of hyponatremia.

Investigations

1. CBC: Hb, TLC, DC, Platelet count.
2. URE, microscopic examination and specific gravity.
3. Serum sodium: serum sodium was done daily for symptomatic cases, alternate days for asymptomatic patients.
4. Serum BUN and glucose levels: For calculation of serum osmolality.
5. Serum osmolality was calculated by the formula
$$\text{Serum osmolality} = 2 (\text{sodium}) + \text{RBS}/18 + \text{BUN}/2.8$$

Patients were divided into

- Isotonic - 280-295 mOsm/l
 - Hypotonic - <280 mOsm/l
 - Hypertonic - >295 mOsm/l
6. Urine osmolality – in patients with hypotonic hyponatremia.
(normal range- 300-900 mOsm/kg)
 7. Urine sodium- in hypotonic hyponatremia patient.
(normal range- 40-220 mEq/L)
 8. Brain imaging and CSF analysis in patients presenting with altered sensorium to exclude structural abnormalities and meningeal infection.
 9. Serum protein and lipid profile to rule out pseudohyponatremia.

Management and Outcome Assessment

Patients with hyponatremia were classified based on serum sodium levels into following categories:

Category	Serum sodium levels
Mild	127-135 mEq/L
Moderate	121-126 mEq/L
Severe	< 120 mEq/L

Treatment Strategy

Decision on the treatment modality was based on the cause and severity of hyponatremia and presence of neurological symptoms of hyponatremia.

1. Fluid restriction – defined as total intake in 24 hrs equal to the volume of urine output of previous 24 hrs. It was advised in patients with hypervolemia and SIADH.
2. Normal saline (0.9%) – given to hypovolemic patients.
3. Loop diuretic – given for excretion of free water in cases of SIADH and hypervolemia.
4. 3% saline – in severe hyponatremic patients with neurological symptoms of hyponatremia.

Data Collection

For all patients clinical and demographic details, final diagnosis, investigations and management were recorded onto a standard data collection sheet as per the study proforma and later transferred to Microsoft excel spreadsheet for analysis.

Statistical Analysis

Analysis was done using SPSS for windows (version 18.0) and R environment ver.3.2.2. Statistical method used was descriptive statistics. Data are presented as frequency distribution and simple percentages.

Results

The study sample included 107 patients with hyponatremia were taken into studies who were admitted to ICU, emergency and medical wards of Sri Siddhartha Medical College and Hospital during the period of 2 years.

- The Mean age of patient admitted was 57 years with a range of 59 to 68 years.
- 71 patients were males and 36 patients were females with preponderance of hyponatremia in elderly sick males.

- 64.5% had presented with constitutional symptoms, 52.3% had confusion, 50.5% had other symptoms, 49.5% had fever, 41.1% had vomiting, 37.4% had respiratory symptoms, 36.4% had pain abdomen, 15% had loose stools, 4.7% were in coma, and 2.8% had convulsions.
- There was wide range of etiologies, most common being SIADH (32.7%), extra renal losses (22.4%), renal failure (13.1%), renal losses (12.1%), cirrhosis (11.2%), cardiac failure (4.7%), drug induced (2.8%) and glucocorticoid deficiency (0.9%).
- Hypertonic saline was given to 43%, diuretics and fluid restriction was advised for 30.8%, 20.6% were given both hypertonic saline and vaptans and 5.6% were given only vaptans.

Discussion

This study was undertaken keeping in view of frequent occurrence of hyponatremia in the adult sick patients who are at higher risk of development of electrolyte disturbance as these people have age related physiological changes in the function of kidneys and other multiple comorbid conditions.

In the study by Rao et al.²² 55 were females and 45 were males. In the study by Mahavir et al.²³ 64.3% were males and 53.7% were females. In the study by Rubio et al.²⁴ 52.7% were females and 47.3% were males. In the study by Vurghese et al.²⁵ males were 56% and females were 44%.

In the present study 107 patients were included. Out of 107, 71 (66.4%) were males and 36 (33.6%) were females.

In the study by Vurghese et al.²⁵ the commonest age group affected was 45-64 years.

In the present study, majority of the cases i.e., 34 (31.8%) were in the age group of 59-68, 19 (17.8%) cases were in

the age group of 49-58, 15 (14%) cases were in the age group of 69-78, 13 (12.1%) cases were in the age group of 39-48, 10 (9.3%) cases in the age group of 29-38 and 79-88, 5 (4.7%) cases were in the age group of 18-28 and only 1 (0.9%) case in the age group of 89-99.

Out of 71 males 20 (28.2%) falls in the age group of 59-68. Out of 36 females 14 (38.9%) falls in the age group of 59-68. There was only 1 (0.9%) male and no females in the age group of 89-99.

In the study Rao et al.,²² lethargy, drowsiness with slow response and irrelevant talk were the common presenting symptoms. 4% had seizures. In the study Mahavir et al.,²³ confusion was present in 30% and altered sensorium in 17.1%. 2% had seizures. 14% were asymptomatic. In the study done by Hochman²⁶, there were 43.4% patients with asymptomatic, 39.9% who had mild symptoms and 16.7% patients has severe neurological symptoms with stupor and coma.

In the present study out of 107 cases, 69 (64.5%) had presented with constitutional symptoms, 56 (52.3%) had confusion, 54 (50.5%) had other symptoms, 53 (49.5%) had fever, 44 (41.1%) had vomiting, 40 (37.4%) had respiratory symptoms, 39 (36.4%) had pain abdomen, 16 (15%) had loose stools, 5 (4.7%) were in coma, 3 (2.8%) had convulsions. All the 3 patients had GTCS, had recovered when serum sodium normalized.

In the study by Rao et al.²² common causes were SIADH (30%) followed by drugs. In the study Nandini Chatterjee et al.,²⁷ gastro-intestinal fluid loss was the most common cause for hyponatremia followed by cerebrovascular accidents and pulmonary sepsis. In the study by Vurghese et al.²⁵ most common etiology was SIADH (34.8%), CKD (19.69%), CCF (18.18%), 6% of DM, HTN, cirrhosis and 3% acute gastroenteritis. In the study by Mahavir et al.²³ decreased intake (82.9%) was the most common etiology,

increased loss (65.7%) was also present as second most common cause.

In the present study out of 107 patients, most common risk factor was SIADH, 35 (32.7%). 24 (22.4%) was due to extra renal losses, 14 (13.1%) was due to renal failure, 13 (12.1%) was due to renal losses, 12 (11.2%) was due to cirrhosis, 5 (4.7%) was due to cardiac failure, 3 (2.8%) was drug induced, 1 (0.9%) was due to glucocorticoid deficiency. None of the patients were having hypothyroidism and nephrotic syndrome as a risk factor.

In the study by Rao et al.²² 61% were euvolemic, 23% were overloaded and 16% dehydrated. The commonest type of hyponatremia noted in this study was isovolemic Hypo-osmolar hyponatremia. In the study by Miyashita et al.²⁸ 95% had hypotonic hyponatremia out of which 63% had hypovolemia, 5% had hypervolemia and 32% euvolemia.

In the present study out of 107 patients all were having hypotonic hyponatremia. Out of that 37 (34.6%) were hypovolemic, 38 (35.5%) were euvolemic and 32 (29.9%) were hypervolemic. Most common type in this study was euvolemic hyponatremia. Most common age group is 59-68 years with a total number of 34 (31.8%) patients, in which 9 (24.3%) were hypovolemic, 13 (34.2%) were euvolemic and 12 (37.5%) were hypervolemic.

In the study done by Mahavir et al.,²³ 3% saline was given for 48.5%, normal saline for 48.6%, fluid restriction was given for 40%.

In the present study out of 107 cases, 46 (43%) were received 3% NaCl, 33 (30.8%) were received other treatment like diuretics and fluid restriction, 22 (20.6%) were received both 3% NaCl and vaptans and 6 (5.6%) received only vaptans.

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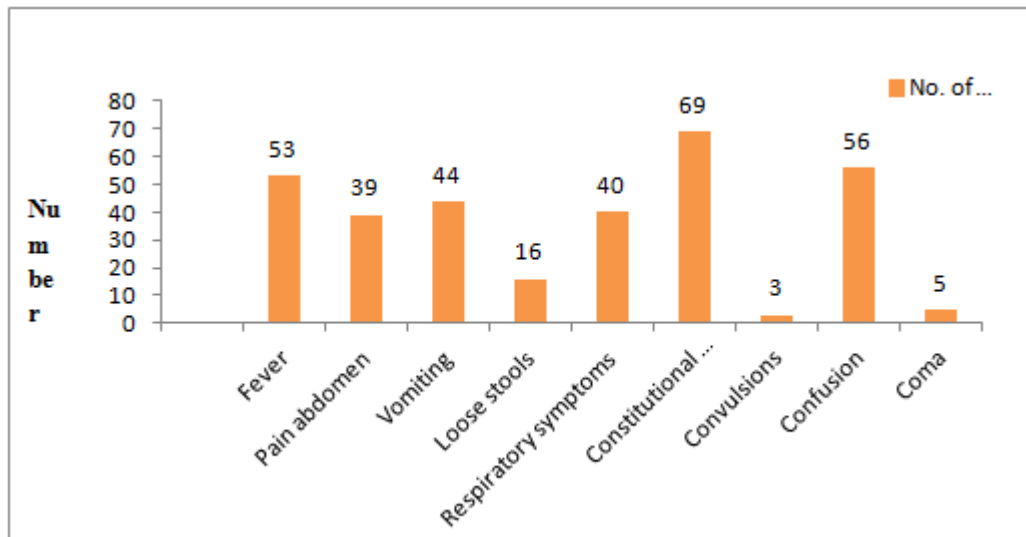
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Tables And Figures

Table 1: Distribution of clinical features in cases of hyponatremia

Clinical features	Total (n=107)	Percentage
Fever	53	49.5
Pain abdomen	39	36.4
Vomiting	44	41.1
Loose stools	16	15
Respiratory symptoms	40	37.4
Constitutional symptoms	69	64.5
Convulsions	3	2.8
Confusion	56	52.3
Coma	5	4.7
Others	54	50.5

Graph 1: Distribution of clinical features in cases of hyponatremia

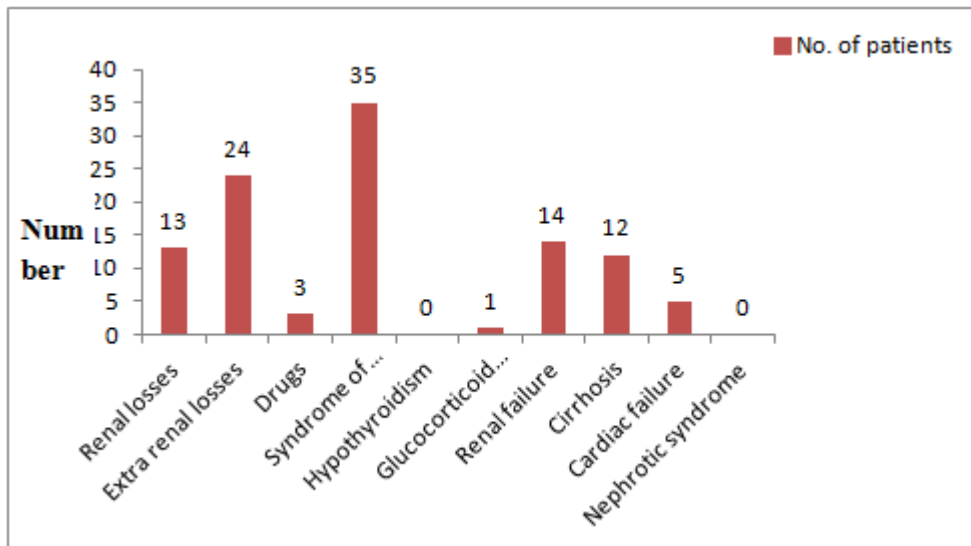


In the study out of 107 cases, 69 (64.5%) had presented with constitutional symptoms, 56 (52.3%) had confusion, 54 (50.5%) had other symptoms, 53 (49.5%) had fever, 44 (41.1%) had vomiting, 40 (37.4%) had respiratory symptoms, 39 (36.4%) had pain abdomen, 16 (15%) had loose stools, 5 (4.7%) were in coma, 3 (2.8%) had convulsions.

Table 2: Distribution of Hyponatremia based on risk factors

Risk Factors	Total (n=107)	Percentage
Renal losses	13	12.1
Extra renal losses	24	22.4
Drugs	3	2.8
Syndrome of Inappropriate antidiuretic hormone	35	32.7
Hypothyroidism	0	0
Glucocorticoid deficiency	1	0.9
Renal failure	14	13.1
Cirrhosis	12	11.2
Cardiac failure	5	4.7
Nephrotic syndrome	0	0

Graph 2: Distribution of Hyponatremia based on risk factors



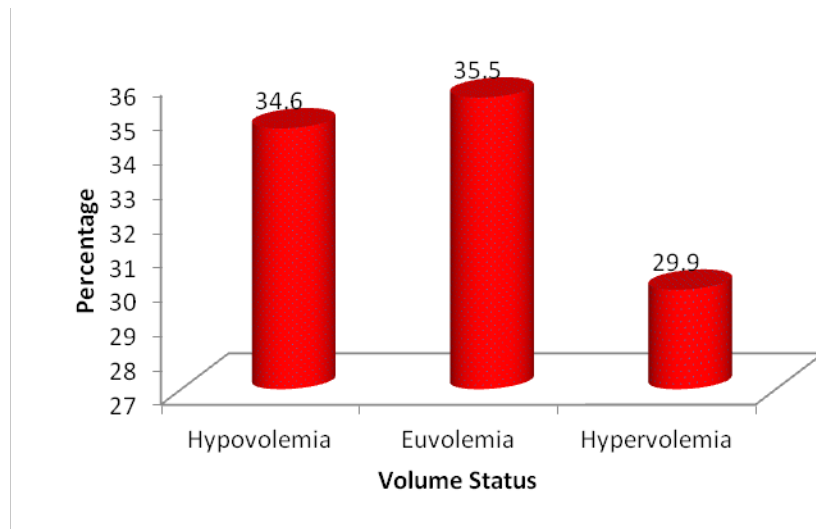
Out of 107 patients, most common risk factor was SIADH, 35 (32.7%). 24 (22.4%) was due to extra renal losses, 14 (13.1%) was due to renal failure, 13 (12.1%) was due to renal losses, 12 (11.2%) was due to cirrhosis, 5 (4.7%) was due to

cardiac failure, 3 (2.8%) was drug induced, 1 (0.9%) was due to glucocorticoid deficiency. None of the patients were having hypothyroidism and nephrotic syndrome as a risk factor.

Table 3: Volume status of patients with Hyponatremia

Volume Status	No. of patients	Percentage
Hypovolemia	37	34.6
Euvolemia	38	35.5
Hypervolemia	32	29.9
Total	107	100.0

Graph 3: Volume status of patients with Hyponatremia

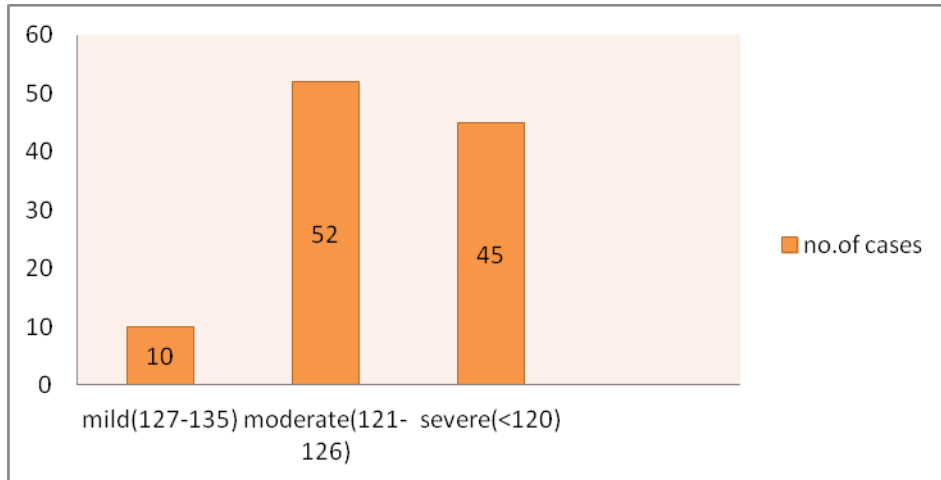


Out of 107 patients all were having hypotonic hyponatremia. Out of that 37 (34.6%) were hypovolemic, 38 (35.5%) were euvolemic and 32 (29.9%) were hypervolemic.

Table 4: Severity of hyponatremia

Serum sodium mEq/L	Total (n=107)
<120 (Severe)	45(42.1%)
121-126 (Moderate)	52(48.6%)
127-135 (Mild)	10(9.3%)

Graph 4: Severity of Hyponatremia



Out of 107 cases, 52 (48.6%) were having moderate hyponatremia, 45 (42.1%) were having severe hyponatremia, 10(9.3%) were having mild hyponatremia.