# "HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL- A CROSS-SECTIONAL STUDY"

By

**Dr. HARSHITA G.** M.B.B.S

*Dissertation Submitted To*

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA**

*In Partial Fulfillment of the Requirements for the Degree of*

**DOCTOR OF MEDICINE**

**IN**

**GENERAL MEDICINE**

*Under the Guidance of*

**Dr. LAKSHMAIAH. V** D.CH, MD GENERAL MEDICINE

**Professor, Department of General Medicine.**

**DEPARTMENT OF GENERAL MEDICINE**
**SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR.**

**APRIL 2017**

**DEPARTMENT OF GENERAL MEDICINE**
**SRI DEVARAJ URS MEDICAL COLLEGE**
**TAMAKA, KOLAR-563101**

## DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL- A CROSS-SECTIONAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. LAKSHMAIAH V,** D.CH**,** M.D.GENERAL MEDICINE Professor, **DEPT OF GENERAL MEDICINE,** Sri Devaraj Urs Medical College, Kolar.

Date: **Dr. HARSHITA .G**

Place: Kolar

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA**

## CERTIFICATE BY THE GUIDE

This is to certify that the dissertation **"HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL - A CROSS-SECTIONAL STUDY"** is a bonafide and genuine research work carried out by **Dr. HARSHITA. G** in partial fulfillment of the requirement for the degree of **M.D** in **GENERAL MEDICINE.**

Date:

Place: Kolar

**SIGNATURE OF THE GUIDE**

**Dr. LAKSHMAIAH V** D.CH. M.D,

Professor
Department of General Medicine.
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA**

**ENDORSEMENT BY THE HOD,**

**PRINCIPAL / HEAD OF THE INSTITUTION**

This is to certify that the dissertation **"HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL- A CROSS-SECTIONAL STUDY"** is a bonafide research work done by **Dr. HARSHITA G** under the guidance of **Dr. LAKSHMAIAH V** D.CH, M.D Professor, Department Of General Medicine, Sri Devaraj Urs Medical College, Kolar, in partial fulfillment of University regulation for the award "**M.D. IN GENERAL MEDICINE.**"

**Dr. PRABHAKAR. K** MD
Professor and HOD
Department Of General Medicine
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

**Dr. HARENDRA KUMAR M.L** MD
Principal,
Sri Devaraj Urs Medical College
Tamaka, Kolar

Date:
Place: Kolar

Date:
Place: Kolar

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA**

## ETHICS COMMITTEE CERTIFICATE

This is to certify that the ethical committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved**, Dr. HARSHITA.G** student in the Department of General Medicine at Sri Devaraj Urs Medical College, Tamaka, Kolar to take up the dissertation work titled **"HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL- A CROSS-SECTIONAL STUDY"** to be submitted to Sri Devaraj Urs Academy of Higher Education and Research, Kolar.

Date: **Signature of Member Secretary**

Place: Kolar **Ethical Committee**

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA**

## COPY RIGHT

## DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research, Kolar, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic/research purpose.

Date: **Dr. HARSHITA.G**

Place: Kolar

# ACKNOWLEDGEMENT

*One of the joys of completion of this dissertation is to look over the journey past and remember and thank all the people who have helped and supported me along this long but fulfilling road. First and foremost, I thank the Almighty for giving me the strength and ability to carry out this study.*

*I am deeply indebted and grateful to my guide* ***Dr. Lakshmaiah V*** *D.Ch, MD, Professor, Department of General Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar, for his able guidance, support, timely advice and constant encouragement throughout the period of the study.*

*I am thankful to* ***Dr. Prabhakar K****, MD Professor, Head of the Department of General Medicine,* ***Dr.Raghavendra Prasad BN*** *MD,* ***Dr.Venkatarathnamma. P.N*** *MD,* ***Dr.Raveesha. A*** *MD Department of General Medicine, for their helpful guidance during my postgraduate career.*

*I thank my best friend and dear husband* ***Dr. Shravan Krishna Reddy. P*** *MD Paediatrics for his unending faith, unconditional love and support throughout this endeavor. I am extremely grateful for all his time, help, tireless effort in preparing this dissertation without which, it would not have been possible for me to complete this.*

*No words can express the deepest gratitude I feel towards my beloved parents,* ***Mr. Ravindra Reddy .G*** *and* ***Mrs. Sarala .G****, whose countless sacrifices and cherished blessings have made me who I am today in my life.*

*I also thank my dear brother* ***Mr. Dheeraj Reddy. G*** *for being a constant source of strength, encouragement and never ending support.*

*I am also thankful to my postgraduate colleagues, seniors, juniors and friends for their constant motivation and co-operation.*

*Last but not the least, I thank all my patients involved in this study, without whose co-operation, this study would not have been possible.*

*Signature of the candidate*

**Dr. HARSHITA.G**

# ABSTRACT

**BACKGROUND:** Hyponatremia is the commonest electrolyte disturbance encountered in the neurological and neurosurgical intensive care units. It can present with signs and symptoms mimicking a neurological disease and can worsen the existing neurological deficits

**OBJECTIVES:**

1. To assess the cognitive functions of patients with hyponatremia in acute neurological disorders by MMSE (Mini Mental State Examination) score.
2. To assess the cognitive functions by MMSE score after correction of hyponatremia.
3. To determine the correlation between cognitive functions and sodium levels among patients with neurological disorders.

**METHODS:** 57 patients of acute neurological disorders with hyponatremia were included in the study. These patients were clinically assessed by MMSE score and investigated as per protocol and were treated as per standardized regimen. These patients were clinically assessed by MMSE score on day 3 and day 5 after giving correction for hyponatremia.

**RESULTS:** 57 patients with hyponatremia were studied. The mean age of study population is 51.56 years. Among 57 patients with hyponatremia, 68.42% were males and 31.58% were females which shows male preponderance. The mean serum sodium level is 123.74mmol/L. 12.28% had mild hyponatremia (serum sodium levels between 130-134 mmol/l), 43.85% had moderate hyponatremia (serum sodium levels between 125-129

mmol/l), 43.85% had severe hyponatremia (serum sodium levels less than 125 mmol/l). All the patients had presented with altered sensorium. After hyponatremia correction, 52 patients (91.2%) had improvement in MMSE score.

**CONCLUSION:** In the present study, the treatment modality undertaken had an effect in improving cognition as well as managing hyponatremic condition. A better outcome to treatment and minimal or none complications related to correction of hyponatremia can be obtained by following a standardized regimen for treatment and keeping in mind the general guidelines of correction of hyponatremia.

Key words: Hyponatremia, MMSE, cognition

# LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| ACE | : | Angiotensin Converting Enzyme |
| ACTH | : | Adreno Corticotropic Hormone |
| ADH | : | Anti Diuretic Hormone |
| ANP | : | Atrial Natriuretic Peptide |
| ARB | : | Angiotensin Receptor Blocker |
| AVP | : | Arginine Vasopressin |
| BNP | : | Brain Natriuretic Peptide |
| CHF | : | Congestive Heart Failure |
| CNS | : | Central Nervous System |
| CSF | : | Cerebrospinal Fluid |
| CSW | : | Cerebral Salt Wasting |
| CVP | : | Central Venous Pressure |
| CT | : | Computed Tomography |
| DM | : | Type 2 Diabetes Mellitus |
| DNP | : | Dendroaspis Natriuretic peptide |
| ECF | : | Extra Cellular Fluid |
| GBS | : | Guillain – Barre Syndrome |
| HTN | : | Hypertension |
| ICU | : | Intensive Care Unit |
| K+ | : | Potassium |
| MMSE | : | Mini Mental State Examination |
| MRI | : | Magnetic Resonance Imaging |
| Na+ | : | Sodium |
| PCWP | : | Pulmonary Capillary Wedge Pressure |

| | | |
|---|---|---|
| SAH | : | Subarachnoid Hemorrhage |
| SIADH | : | Syndrome of Inappropriate Secretion of ADH |
| TBI | : | Traumatic Brain Injury |
| TBW | : | Total Body Water |
| TSH | : | Thyroid Stimulating Hormone |

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# INTRODUCTION

Disorders of sodium and water metabolism are common in hospitalized patients and are occasionally encountered in outpatients. Both hyponatremia and hypernatremia can cause substantial morbidity and mortality, and ironically incorrect treatment can add to the problem. Hyponatremia is defined as serum sodium levels of less than 135mEq/L[1].

Serum sodium levels and serum osmolality are normally under tight control of thirst, antidiuretic hormone and renin-angiotensin-aldosterone system.

There are various etiological factors for hyponatremia which depends upon patients volume status, his/her previous medical history, drug history etc. Many patients requires more extensive workup to know the cause of hyponatremia as each factor has its own treatment.

Hyponatremia is the commonest electrolyte disturbance encountered in the neurological and neurosurgical intensive care units. It can present with signs and symptoms mimicking a neurological disease and can worsen the existing neurological deficits. Hyponatremia in neurological disorders is usually of the hypo-osmolar type caused either due to the SIADH( Syndrome Of Inappropriate Antidiuretic Hormone Secretion) or Cerebral Salt Wasting Syndrome (CSWS) as a consequence of renal salt wasting, most likely attributable to an increased secretion of Brain Natriuretic Peptide (BNP) and Atrial Natriuretic Peptide (ANP).

Many central nervous system (CNS) disorders are associated with electrolyte disturbances disorders like stroke, infection, trauma, hemorrhage and psychosis enhance ADH release.

One of the symptoms often associated with hyponatremia is cognitive impairment, particularly in elderly populations. In cases of acute hyponatremia, the pathological mechanisms involved are well understood, with the neurological problems thought to be due to cerebral edema and hyponatremic Encephalopathy.

Clinical features of hyponatremia not just depends upon the absolute level of serum sodium but also depend upon the rapidity of its fall, so acute hyponatremia are more symptomatic than chronic hyponatremia. More over symptoms of hyponatremia is mainly cerebral due to hypoosmolality induced brain edema.

Treatment of hyponatremia mainly involves water restriction rather than sodium supplementation as hyponatremia is mainly due to excess of water rather than sodium loss. Acute and symptomatic hyponatremia requires early monitored treatment as a life saving measurement and at the same time rapid treatment has also a risk of central pontine myelinolysis. The prognosis of patient depends upon the etiology of hyponatremia, severity of hyponatremia and rapidity of development of hyponatremia, but in various studies it is shown that hyponatremia is associated with higher morbidity and mortality.

Treatment of hyponatremia at all levels was associated with improved cognitive function. Because hyponatremia is associated with changes in mentation, these findings suggest that careful monitoring of serum sodium levels is important in all patients, even in those with a mild degree of hyponatremia. Determining the etiology and attempting to correct mild, moderate and severe hyponatremia should be encouraged.

# AIMS AND OBJECTIVES

1. To assess the cognitive functions of patients with hyponatremia in acute neurological disorders by MMSE score.

2. To assess the cognitive functions by MMSE score after correction of hyponatremia.

**3.** To determine the correlation between cognitive functions and sodium levels among patients with neurological disorders.

# REVIEW OF LITERATURE

## HYPONATREMIA

Hyponatremia is common in both inpatients and outpatients.[1] It is the most common disorder among the hospitalized patients [2]. Both hyponatremia and hypernatremia can cause substantial morbidity and mortality, and ironically, incorrect treatment can add to the problem. Serum sodium concentration and serum osmolarity normally are maintained under precise control by homeostatic mechanisms involving thirst, antidiuretic hormone (ADH), and renal handling of filtered sodium.

About 40% of the body's sodium is contained in bone. Approximately 2-5% occurs within organs and cells and the remaining 55% is in blood plasma and other extra cellular fluids. The amount of sodium in blood plasma is typically 140mEq/L, a much higher amount than is found in intracellular sodium (about 5 mEq/L). This asymmetric distribution of sodium ions is essential for human life. It makes possible proper nerve conduction, the passage of various nutrients into cells, and the maintenance of blood pressure.[3]

Management of abnormalities in water homeostasis is frequently challenging. Because age-related changes and chronic diseases are often associated with impairment of water metabolism in elderly patients, it is absolutely essential to be aware of the pathophysiology of hyponatremia and hypernatremia in them. The sensation of thirst, renal function, concentrating abilities and hormonal modulators of salt and water balance are often impaired in the elderly, which makes such patients highly susceptible to morbid and iatrogenic events involving salt and water. A systematic approach in evaluating water and sodium problems, utilizing a comprehensive history and physical

examination, and a few directed laboratory tests are required to make the clinical diagnosis. Furthermore clinicians should have a clear appreciation of the roles that iatrogenic interventions and lapses in nutrition and nursing care frequently play in upsetting the homeostatic balance in elderly patients, particularly those who are in long-term institutional inpatient settings.[4]

## PREVALENCE AND INCIDENCE

Hyponatremia and hypernatremia are common in the elderly, particularly among those who are hospitalized or living in long-term care facilities. Hyponatremia is defined as a serum sodium concentration of less than 135 mEq per/L (135 mEq/L). It is estimated that nearly 7-11.4 percent of healthy elderly persons have serum sodium concentrations of 135 mEq per L or less which is increasing to 11-22.5% among the hospitalized patients.[4]

Cross sectional studies showed that hyponatremia may be present in 15 to 18 percent of patients in chronic care facilities. A 12-month longitudinal study showed that more than 50 percent of nursing home residents had at least one episode of hyponatremia. Thus, it would be an unusual day in many family physician's practices that at least one diagnostic or therapeutic issue related to water metabolism did not arise.[5]

**IN THE UNITED STATES:** Hyponatremia is the most common electrolyte disorder among hospitalized patients with the incidence of approximately 1 %.

**IN INDIA:** Incidence of hyponatremia is higher during the peak southwest monsoon season. Humidity and temperature may have important role in the manifestation of hyponatremia.

**AGE** Hyponatremia is more common in the very young and in the very old; these groups are less able to experience and express thirst and less able to regulate fluid intake autonomously. Specific high-risk groups include the following:

- Infants fed plain water in an effort to treat symptoms of gastroenteritis
- Elderly patients with diminished sense of thirst, especially when physical infirmity limits independent access to food and drink

## PATHOPHYSIOLOGY

Serum sodium is regulated by thirst, Antidiuretic hormone, the renin angiotensin aldosterone system, and variations in renal handling of filtered sodium. Increase in serum osmolarity above the normal range (280-300 mOsm/kg) stimulate hypothalamic osmoreceptors, which, in turn, cause an increase in thirst and in circulating levels of ADH.

ADH increases free water reabsorption from the urine, yielding low urine volumes of relatively high osmolarity and returning serum osmolarity towards normal. ADH also is secreted in response to hypovolemia, pain, fear, nausea, and hypoxia.

Aldosterone, synthesized by the adrenal cortex, is regulated primarily by serum potassium but also is released in response to hypovolemia through the renin-angiotensin-aldosterone axis. Aldosterone causes absorption of sodium at the distal renal tubule. Sodium retention obligates free water retention, helping to correct the hypovolemic state.

The healthy kidney regulates sodium balance independently of ADH or Aldosterone by varying the degree of sodium absorption at the distal tubule.

Hypovolemic states, such as hemorrhage or dehydration, prompt increases in sodium absorption in the proximal tubule. Increases in vascular volume suppress tubular sodium reabsorption, resulting in natriuresis and helping to restore normal vascular volume. Generally, disorders of sodium balance can be traced to a disturbance in thirst or water acquisition, ADH, Aldosterone, or renal sodium transport.

Hyponatremia is physiologically significant when it indicates a state of extracellular hypo-osmolarity and a tendency for free water to shift from the vascular space to the intracellular space. Although cellular edema is well tolerated by most tissues, it is not well tolerated within the rigid confines of the bony calvarium. Therefore, clinical manifestations of hyponatremia are related primarily to cerebral edema.

The rate of development of hyponatremia plays a critical role in its pathophysiology. When serum sodium falls slowly, over a period of several days or weeks, the brain is capable of compensating by extrusion of solutes and fluid to the extracellular space. Compensatory extrusion of solutes reduces the flow of free water into the intracellular space, and symptoms are much milder for a given degree of hyponatremia.

When serum sodium falls rapidly, over a period of 24-48 hours, this compensatory mechanism is overwhelmed and severe cerebral edema may ensue, resulting in brainstem herniation and death. [2]

**IMPACT OF AGING ON WATER METABOLISM:**

The age-related decrease in total-body water (relative and absolute) makes elderly persons markedly susceptible to stresses on water balance [6.] Average healthy 30- to 40-year-old persons have a total-body water content of 55 to 60 percent. By age

75 to 80 years, the total-body water content has declined to 50 percent, with even more of a decline in elderly women.[7,9,10,11]

Clearly, the thirst mechanism diminishes with age, which significantly impairs the ability to maintain homeostasis and increases the risk for dehydration.[8] There is also a clear age-related decrease in maximal urinary concentrating ability, which also increases the risk for dehydration.[9,10]

ADH release is not impaired with aging, but ADH levels are increased for any given plasma osmolality level, indicating a failure of the normal responsiveness of the kidney to ADH.[12,13]

The ability to excrete a water load is delayed in the elderly. This propensity may contribute to the frequently observed episodes of hyponatremia in hospitalized elderly patients who are receiving hypotonic intravenous fluids or whose fluid intake is not properly monitored .[13] Other changes in renal physiology and anatomy that increase the elderly patient's susceptibility to alterations of water imbalance include decreased renal mass [11], cortical blood flow[2] and glomerular filtration rate[12], as well as impaired responsiveness to sodium balance[13].

The impact of a lifetime of accumulated disease and co morbidities must also be duly considered in every clinical situation with an elderly patient, in addition to age-related physiologic changes. The elderly patient has a diminished reserve of water balance and an impaired regulatory mechanism. Thirst sensation, concentrating abilities and hormonal modulators of salt and water balance are sluggish and highly susceptible to being overtaken by morbid or iatrogenic events.

**Ageing changes that increases risk of dehydration:**

- Decreased Urinary concentrating ability.
- Impaired thirst mechanism.
- Inaccessibility to water, due to immobility and cognitive deficits.
- Less efficient sodium conservation.
- Decreased physiological reserve, due to decrease in ECF fluid volume

**Ageing changes that increase risk of water intoxication:**

- Osmoreceptors sensitivity in older adults with a higher set point for vasopressin secretion.
- Increased incidence of syndrome of inappropriate antidiuretic hormone.
- Decreased maximal urinary diluting capacity

**Electrolyte homeostasis by the aging kidney:**

Under normal circumstances, there is no change in the sodium, potassium, hydrogen ion concentration or extracellular fluid with age. However, when adaptive mechanisms are impaired, any acute illness, volume or electrolytes overload or depletion, or stress, can cause significant and prolonged derangements in fluid and electrolyte balance

**Sodium Metabolism**

The response to sodium loss is blunted in elderly. This is due to several different mechanisms as, increased nephron loss with age, decreased basal and

stimulated renin and aldosterone levels, decreased GFR with resultant plasma expansion, increased basal atrial natriuretic polypeptide.[14,15]

Response to sodium overload also is impaired in the elderly, and even in patients without myocardial disease, they are at increased risk of volume expansion. They take much longer time to excrete acute sodium overload as a decrease in GFR results in decreased delivery of fluid to the distal tubules.[14,16]

## ETIOLOGY AND PATHOGENESIS

Hyponatremia is defined as serum sodium levels <135mEq/L. Hyponatremia is not equal to sodium deficit but under most circumstances, hyponatremia is due to excess of water rather than the sodium deficit, so in the treatment of most of the etiology requires water restriction rather than sodium supplementation as the primary treatment.

As sodium is the most important ion in determining the plasma osmolality, true hyponatremia is associated with hypoosmolality while there are certain condition in which plasma osmolality is normal or even increased which is known as pseudohyponatremia. So, the etiology of true hyponatremia should be considered under the following three categories based on the hydration status of the individual.

A) **Hypovolemic hyponatremia** develops as sodium and free water are lost and replaced by inappropriately hypotonic fluids, such as tap water, half-normal saline, or dextrose in water. Sodium can be lost through renal or non renal routes. Non renal routes include GI losses, excessive sweating, third spacing of fluids ( Eg: Peritonitis, pancreatitis, Burns), and the cerebral salt-wasting syndrome.

- Excess fluid losses (eg, vomiting, diarrhea, excessive sweating, GI fistulas or drainage tubes, pancreatitis, burns) that have been replaced primarily by hypotonic fluids
- Addison's disease
- Salt-wasting nephropathy
- Cerebral salt-wasting syndrome seen in patients with traumatic brain injury, Aneurismal subarachnoid hemorrhage, and intracranial surgery.
- Prolonged exercise in a hot environment, especially in patients who hydrate aggressively with hypoosmolar fluids during exertion

B) **Euvolumic hyponatremia** implies normal sodium stores and a total body excess of free water. This occurs in patients who take in excess fluids.

- SIADH: Syndrome of Inappropriate ADH secretion.
- Psychogenic polydipsia, often in psychiatric patients
- Administration of hypotonic intravenous (IV) or irrigation fluids in the immediate postoperative period
- Glucocorticoid deficiency.
- Hypothyroidism
- Infants who may have been given inappropriate amounts of free water

C) **Hypervolumic hyponatremia** occurs when sodium stores increase inappropriately. This may result from renal causes, such as acute or chronic renal failure, when dysfunctional kidneys are unable to excrete the ingested sodium load. It also may occur in response to states of decreased effective intravascular volume.

- Renal Causes: Acute and chronic renal Failure
- Non-Renal Causes: Congestive cardiac failure, Liver cirrhosis, Nephrotic syndrome etc.

Hyponatremia can be caused by many medications. Known offenders include- acetazolamide, amiloride, amphotericin, atovaquone, thiazide diuretics, amiodarone, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, carbamazepine, carboplatin, cyclophosphamide, desmopressin, loop diuretics, oxcarbazepine, opiates, oxytocin, vincristine, selective serotonin reuptake inhibitors, sulfonylureas, tolbutamide.

## CLINICAL FEATURES

The clinical manifestations of hyponatremia depend upon the rapidity of development as well as severity of development of hyponatremia. The clinical symptoms are not primarily due to decrease in plasma sodium level but rather hypoosmolar state which it produces. Because of hypoosmolar state the water enters into cells causing cellular edema. In other tissues such as muscles it is of little clinical significance but in brain due to bony skull it produces symptoms. This is the reason why hyponatremia causes predominant cerebral symptoms. The clinical manifestations of hyponatremia are more evident when the decrease in serum sodium concentration is large or when the decrease occurs over a short period of time.[19]

Patients in whom the serum sodium concentration is greater than 130mEq/L are usually asymptomatic, whereas those in whom these values are lower may have symptoms that include headache, nausea, vomiting, muscle cramps, lethargy, restlessness, disorientation, and depressed reflexes. Severe and rapidly evolving

hyponatremia may present with seizures, coma, permanent brain damage, respiratory arrest, brainstem herniation, and death.[19]

The number and severity of symptoms increase with the degree of hyponatremia and the rapidity with which it develops. When serum sodium falls gradually, over a period of several days or weeks, sodium levels as low as 110 mEq/L may be reached with minimal symptomatology. In contrast, a fall in serum sodium over 24-48 hours may overwhelm compensatory mechanisms, leading to severe cerebral edema, coma, or brainstem herniation.

**History:**

- Symptoms may be limited to mild anorexia, headache, or muscle cramps, or the patient may present with obtundation, coma, or status epileptics.
- Hyponatremia is often seen in association with pulmonary / mediastinum disease or CNS disorders. The Emergency department physician should have an increased index of suspicion of hyponatremia in patients with pneumonia; active tuberculosis; pulmonary abscess; neoplasm; asthma; or in patients with CNS infection, trauma, or neoplasm. Patients with carcinoma of the nasopharynx, duodenum, stomach, pancreas, Ureter, prostate, or uterus also have an increased risk.
- Hyponatremia is associated with numerous medications. The patient's medication list should be examined for drugs known to cause hyponatremia.
- Hyponatremia has been noted in patients with poor dietary intake who consume large amounts of beer (called beer potomania) and after use of the recreational drug N-methyl-3,4- methylenedioxyamphetamine (i.e., MDMA or ecstasy).

- A history of hypothyroidism or adrenal insufficiency should be sought because each is associated with hypo-osmolar hyponatremia.
- Patients with clinically significant hyponatremia present with nonspecific symptoms attributable to cerebral edema. These symptoms, especially when coupled with a recent history of altered fluid balance, should suggest the possibility of hyponatremia. these symptoms include Anorexia, Nausea and vomiting, Difficulty concentrating, Confusion, Lethargy, Agitation, Headache, Seizures.

**Physical Finding:**

Physical findings are highly variable and dependent on the degree and the chronicity of hyponatremia. Patients with acutely developing hyponatremia are symptomatic at a level of 120 mEq/L. Those patients with chronic hyponatremia tolerate much lower levels

- Most abnormal findings on physical examination are neurologic in origin.
    - Level of alertness ranging from normal to agitation to coma
    - Variable degrees of cognitive impairment (e.g., difficulty with short- term recall; loss of orientation to person, place, or time; frank confusion or depression)
    - Focal or generalized seizure activity
    - In those patients with acute severe hyponatremia, signs of brainstem herniation, including coma; fixed, unilateral, dilated pupil: decorticate or decerebrate posturing; and respiratory arrest

- In addition to neurologic findings, patients may exhibit signs of hypovolemia or hypervolemia. Determining the hydration status of the patient may help establish the etiology of the hyponatremia and suggest the best treatment course.
    - Dry mucous membranes, tachycardia, diminished skin turgor, and orthostasis suggest hypovolemic hyponatremia due to excessive loss of body fluids and replacement with inappropriately dilute fluids
    - Pulmonary rales, S3 gallop, peripheral edema, or ascites suggest Hypervolemic hyponatremia due to excess retention of sodium and free water (i.e., cirrhosis, nephrotic syndrome, congestive heart failure).
    - Patients who lack findings of hypovolemia or hypervolemia are considered to have euvolemic hyponatremia, which is consistent with such etiologies as exogenous free water load, hypothyroidism, cortisol deficiency, or syndrome of inappropriate antidiuretic hormone (SIADH).
    - Other nonspecific signs include muscle weakness and cramping. Rhabdomyolysis is an occasional consequence of hyponatremia and should be considered in patients with muscle pain or tenderness.

## HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS

Hyponatremia is a common finding in acute brain disease. Hyponatremia is the commonest electrolyte disturbance encountered in the neurological and neurosurgical intensive care units. It can present with signs and symptoms mimicking a neurological disease and can worsen the existing neurological deficits. It is observed commonly in subarachnoid hemorrhage.

Early symptoms of headache, muscular weakness, nausea, lethargy, ataxia, and confusion can progress to seizures, irreversible neurological damage, coma and death, if unrecognized and untreated. One of the symptoms often associated with hyponatremia is cognitive impairment, particularly in elderly populations.

Hyponatremia in neurological disorders is usually of the hypo-osmolar type caused either due to the SIADH (Syndrome Of Inappropriate Antidiuretic Hormone) or Cerebral Salt Wasting Syndrome (CSWS) as a consequence of renal salt wasting, most likely attributable to an increased secretion of Brain Natriuretic Peptide (BNP) and Atrial Natriuretic Peptide (ANP). It is important to distinguish between these two disorders, as the treatment of the two differs to a large extent. In SIADH, the fluid intake is restricted, whereas in CSWS the treatment involves fluid and salt replacement. Many central nervous system (CNS) disorders are associated with electrolyte disturbances Disorders like stroke, infection, trauma, hemorrhage and psychosis enhance ADH release [19].

Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries. The ADH levels were elevated significantly in the stroke patients. Stroke patients are at risk for developing electrolyte disturbances, the common cause of hyponatraemia is SIADH. Hyponatraemia is associated with increased morbidity and mortality, but it is frequently under-recognized and undertreated[21].

## PATHOPHYSIOLOGY OF HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS

### SIADH (SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION):

SIADH was first described by Schwartz in 1957 in patients with bronchogenic carcinoma. SIADH consists of hyponatremia, inappropriately elevated urine osmolality (>100 mOsm/kg), and decreased serum osmolality in a euvolemic patient. SIADH should be diagnosed when these findings occur in the setting of otherwise normal cardiac, renal, adrenal, hepatic, and thyroid function; in the absence of diuretic therapy; and in absence of other factors known to stimulate ADH secretion, such as hypotension, severe pain, nausea, and stress.

In general, the plasma $Na^+$ concentration is the primary osmotic determinant of Arginine vasopressin (AVP) release. In persons with SIADH, the non-physiological secretion of AVP results in enhanced water reabsorption, leading to dilutional hyponatremia. While a large fraction of this water is intracellular, the extracellular fraction causes volume expansion. Volume receptors are activated and natriuretic peptides are secreted, which causes natriuresis and some degree of accompanying potassium excretion (kaliuresis). Eventually, a steady state is reached and the amount of $Na^+$ excreted in the urine matches Na intake. Ingestion of water is an essential prerequisite to the development of the syndrome; regardless of cause, hyponatremia does not occur if water intake is severely restricted.

In addition to the inappropriate AVP secretion, persons with this syndrome may also have an inappropriate thirst sensation, which leads to an intake of water that is in excess of free water excreted. This increase in water ingested may contribute to the

maintenance of hyponatremia.SIADH is associated with many conditions and these are best classified into four major categories: neoplasia, non-malignant lung disease, drugs and neurologic diseases. The most common causes in the neurologic group include meningitis/encephalitis, brain tumour, SAH and TBI. SIADH has also been reported following spinal surgery.[22]

**Neurologic manifestations:**

Neurologic complications in SIADH occur as a result of the brain's response to changes in osmolality. Hyponatremia and hypo-osmolality lead to acute edema of the brain cells. The rigid calvaria prevent expansion of brain volume beyond a certain point, after which the brain cells must adapt to persistent hypo-osmolality. However, a rapid increase in brain water content of more than 5-10% leads to severe cerebral edema and herniation and is fatal.

In response to a decrease in osmolality, brain ECF fluid moves into the CSF. The brain cells then lose potassium and intracellular organic osmolytes (amino acids, such as glutamate, glutamine, taurine, polyhydric alcohol, myoinositol, methylamine, and creatinine). This occurs concurrently to prevent excessive brain swelling.

Following correction of hyponatremia, the adaptive process does not match the extrusion kinetics. Electrolytes rapidly reaccumulate in the brain ECF within 24 hours, resulting in a significant overshoot above normal brain contents within the first 48 hours after correction. Organic osmolytes return to normal brain content very slowly over 5-7 days. Electrolyte brain content returns to normal levels by the fifth day after correction, when organic osmolytes return to normal.

Irreversible neurologic damage and death may occur when the rate of correction of $Na^+$ exceeds 0.5 mEq/L/h for patients with severe hyponatremia. At this rate of correction, osmolytes that have been lost in defense against brain edema during the development of hyponatremia cannot be restored as rapidly when hyponatremia is rapidly corrected. The brain cells are thus subject to osmotic injury, a condition termed osmotic demyelination. Certain factors such as hypokalemia, severe malnutrition, and advanced liver disease predispose patients to this devastating complication.[22]

**CEREBRAL SALT WASTING SYNDROME (CSWS):**

First described by Peters et al in 1950, cerebral salt-wasting syndrome is defined by the development of extracellular volume depletion due to a renal sodium transport abnormality in patients with intracranial disease and normal adrenal and thyroid function.[23]

Cerebral salt-wasting syndrome, or renal salt wasting, may be more common than SIADH and may even occur in the absence of cerebral disease. Contrary to SIADH, CSW is a volume-depleted state secondary to primary natriuresis.[24] Patients with CSW show a negative sodium balance. The mechanism responsible for the renal salt wasting is not fully understood, but the most likely site for impaired sodium reabsorption is the proximal nephron. Two main processes have been proposed to explain this derangement: decreased sympathetic input to the kidney and presence of circulating natriuretic factors.[24,25] The role of a brain ouabain-like compound in the pathogenesis of CSW is still largely speculative.[26]

Reduced sympathetic tone may explain the failure of renin and aldosterone levels to rise in patients with CSW despite volume depletion. The absence of

aldosterone response would then account for the lack of renal potassium excretion despite increased distal sodium load, explaining why hypokalemia is not encountered in patients with CSW. Meanwhile, the actions of potent natriuretic peptides could also contribute to the natriuresis by increasing glomerular filtration rate and blocking sodium reabsorption mainly in the inner medullary collecting duct. [27] These peptides also have inhibitory actions on aldosterone and are capable of decreasing autonomic flow through proposed effects on the brainstem.[28]

There are currently four recognized natriuretic peptides: atrial natriuretic peptide, brain natriuretic peptide, C- type natriuretic peptide, and the very recently discovered dendroaspis natriuretic peptide or DNP. Atrial natriuretic peptide is produced primarily by the heart atria, while brain natriuretic peptide predominates in the ventricles. In addition, all 3 peptides are produced in the brain, particularly the C-type, and have central as well as peripheral actions. In essence, these substances exert potent natriuretic, diuretic, and vasorelaxant activities. Currently available data suggest they do so by directly acting on renal tubules, increasing glomerular filtration rate, antagonizing the renal effects of ADH, suppressing the renin-angiotensin II-aldosterone axis, reducing sympathetic tone and the peripheral release of catecholamines, and centrally inhibiting salt appetite and thirst.[29]

There is some evidence suggesting that brain natriuretic peptide may be the more likely candidate to mediate renal salt wasting. Figure 1 illustrates the proposed mechanisms responsible for CSW syndrome.[29]

Once volume depletion is established, it stimulates ADH secretion overriding the usual inhibition exerted by the coexistent low serum osmolality.[30] Therefore, most patients with CSW have elevated circulating levels of ADH and meet the laboratory

criteria for SIADH. Failure to recognize volume contraction and a negative sodium balance in these patients will lead to the incorrect diagnosis of SIADH when, in fact, the elevation of ADH is actually appropriate for the clinical situation.

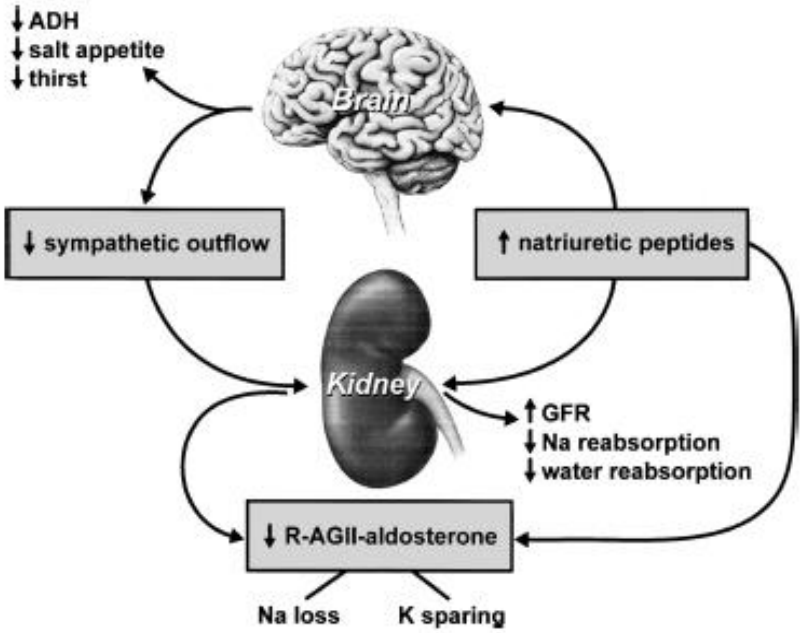



FIGURE 1. Proposed mechanisms responsible for the production of CSW syndrome. ADH, antidiuretic hormone; GFR, glomerular filtration rate; R-AG II, renin-angiotensin II; Na, sodium; K, potassium.

**SIADH VERSUS CSWS:**

Determination of the extracellular fluid volume remains the only reliable discriminatory element to differentiate SIADH and CSW.[31,32] Both disorders are commonly associated with intracranial diseases and their clinical presentations and laboratory features may overlap. However, extracellular fluid volume tends to be slightly increased in SIADH, whereas it is decreased in CSW. Table 1 displays a summary of the clinical features that can aid in the differentiation of SIADH and CSW.

| Variable | CSW | SIADH |
|---|---|---|
| Extracellular fluid volume | ↓ | ↑ |
| Body weight | ↓ | ↑ |
| Fluid balance | Negative | Negative |
| Urine volume | ↔ or ↑ | ↔ or ↓ |
| Tachycardia | + | − |
| Hematocrit | ↑ | ↔ |
| Albumin | ↑ | ↔ |
| Serum bicarbonate | ↑ | ↔ or ↓ |
| Blood urea nitrogen | ↑ | ↔ or ↓ |
| Serum uric acid | ↔ or ↓ | ↓ |
| Urinary sodium | ↑ | ↑ |
| Sodium balance | Negative | Neutral or + |
| Central venous pressure | ↓ (<6 cm $H_2O$) | ↔ or slightly ↑ (6–10 cm $H_2O$) |
| Wedge pressure | ↓ | ↔ or slightly ↑ |

**Table 1: Differences between CSW and SIADH**

## HYPONATREMIA IN SPECIFIC NEUROLOGIC AND NEUROSURGICAL DISEASES

### Hyponatremia in Patients with Aneurysmal Subarachnoid Hemorrhage:

Hyponatremia is the most common and severe electrolyte disturbance after aneurysmal subarachnoid hemorrhage (SAH). Serum sodium concentrations below 134 mmol/L have been reported in 34% of patients with SAH.[33] Severe hyponatremia (less than 120 mmol/L) though is rarely observed in these patients, and neurologic deterioration can seldom be primarily attributed to hyponatremia alone.[34] The decline in serum sodium levels tends to occur between the second and tenth days after the initial hemorrhage, closely paralleling the period of cerebral vasospasm. The risk of developing hyponatremia is significantly increased in patients with enlargement of the third ventricle (regardless of the size of the lateral ventricles)[35] or presence of suprasellar or intraventricular blood on initial computed tomography scan and patients with ruptured anterior communicating artery aneurysms.[36]

Hyponatremia in SAH was initially attributed to SIADH.[37] However, studies demonstrating volume contraction in patients with SAH and hyponatremia subsequently challenged this notion.The pathogenic role of CSW was further supported by a prospective study that measured plasma volume (using an isotope dilution technique) in 21 patients within the first week after SAH. Plasma volume was decreased in most patients with hyponatremia and negative sodium balance preceded the development of hyponatremia in all cases. Serum ADH levels were elevated early but declined during the first week regardless of the presence of hyponatremia.[38]

Circulating plasma natriuretic peptide concentrations are consistently increased after SAH. The presence of hyponatremia is significantly associated with the occurrence of cerebral infarctions from delayed cerebral ischemia.[39,40,41,42]

**Hyponatremia in Patients with Head Injury:**

Hyponatremia is fairly often observed after traumatic brain injury in clinical practice, although the incidence of this association has not been formally studied. Hyponatremia is more commonly seen days after the injury (although severe acute hyponatremia has been documented after head trauma in elderly patients)[43] while acute hypernatremia secondary to dehydration is frequently present shortly after trauma.[44] In this condition also, the mechanism responsible for the hyponatremia appears to be a combination of hormonal water retention and sodium wasting. Elevated levels of ADH are often found and they usually represent an appropriate response to decreased circulating blood volume [45,46] or other nonosmotic stimulants.

Hyponatremia, when severe, can be symptomatic in certain patients with acute head injury. It can also be associated with increased risk of symptomatic vasospasm in patients with traumatic SAH. The effects of hyponatremia on cognitive outcome after

traumatic brain injury remain to be defined.[47] However, experimental data from animal studies suggest that acute hyponatremia potentiates secondary brain damage in severe traumatic brain injury by augmentation of both focal contusion and diffuse axonal injury.[48]

**Hyponatremia in Patients with Guillain-Barre´ Syndrome:**

Hyponatremia may occur in up to one-third of patients with Guillain-Barre´ syndrome (GBS), but it is rarely symptomatic.[49] In a prospective series, hyponatremia was more common on ventilated patients (42% vs. 19%), and it appeared on average 10 days after intubation (range, 1 to 23 days).[49] Seizures never occurred and hyponatremia resolved after fluid restriction, thus suggesting SIADH. In another study, ADH levels were increased in patients with GBS (especially those ventilated) compared with controls; atrial natriuretic peptide levels were only elevated in a subgroup of patients with dysautonomia and extreme blood pressure changes.[50] Several hypotheses have been offered to explain the occurrence of SIADH in GBS, including downward osmotic resetting[51] and enhanced renal tubular sensitivity to ADH[52], but the exact mechanism remains to be elucidated.

**Hyponatremia in Patients with Meningitis:**

Hyponatremia has been reported in 7 to 32% of patients with different forms of meningitis.[53,54] Hyponatremia in patients with meningitis has been traditionally thought to be a consequence of SIADH.[55,56] Evidence favoring CSW has emerged in more recent years. The discussion regarding the underlying mechanism of hyponatremia in patients with meningitis has vital practical implications. Prophylactic fluid restriction has been traditionally recommended to counter the presumed threat of SIADH and reduce the risk of cerebral edema. However, no evidence supports that

restricting fluid intake reduces the incidence or severity of cerebral edema. Furthermore, in the only prospective, controlled study evaluating fluid therapy in patients with meningitis, fluid restriction did not improve outcome and contraction of the extracellular volume was associated with greater likelihood of adverse outcome. Therefore, not only should prophylactic fluid restriction be discouraged in patients with meningitis but also hypovolemia should be treated with fluid therapy aiming at iso-osmolality to avoid cerebral hypoperfusion. [57]

## HYPONATREMIA AND COGNITION:

One of the symptoms often associated with hyponatremia is cognitive impairment, particularly in elderly populations. In cases of acute hyponatremia, the pathological mechanisms involved are well understood, with the neurological problems thought to be due to cerebral edema and hyponatremic encephalopathy.[58] However, understanding of such mechanisms in the more prevalent, chronic hyponatremia is poor. Several studies have recently found an association between cognitive impairment and chronic hyponatremia, even at a mild to moderate level. In chronic hyponatremia, serum sodium levels decline gradually, allowing the body time to adapt. To prevent swelling initially, the glial cells use the Na+-K+-ATPase system to move sodium out of cells whilst also expelling osmolytes.[59] This adaptation results in water leaving the brain following an osmotic gradient, preventing the accumulation of fluid in cells and thus preserving function. [60] Therefore, any cognitive impairment associated with chronic hyponatremia is due to a different pathological mechanism than is the case for acute hyponatremia.

**INVESTIGATIONS:**

The goals of investigations [19,20] in a hyponatremic patient in the admitted patients are to establish:

1. Serum Osmolality and Urine Osmolality
2. Assessment of Volume status: This can be assessed by measurement of the Central Venous Pressure (CVP), Pulmonary Capillary Wedge Pressure (PCWP) or by radioisotope scanning.
3. Documentation of Renal sodium loss: Urine Spot Sodium
4. Routine blood investigations which include blood sugars, serum creatinine, blood urea, uric acid.
5. To rule out hypothyroidism and adrenal insufficiency (especially in severe head injury and post operative patients undergoing hypothalamic/pituitary surgery)

- The diagnosis of hyponatremia depends entirely upon the ability to properly obtain a sample of the patient's serum and to accurately measure its concentration of sodium.
- When interpreting serum sodium levels, always consider the possibility of sampling error, especially when the reported value does not seem consistent with the history or physical findings.
  - Was the patient's blood sample properly labeled?
  - Was it obtained from a venous site proximal to an infusion of hypotonic saline or dextrose in water?
  - Is laboratory measurement or reporting in error?

- If an error is suspected, a second sample should be submitted for testing before therapeutic measures are initiated.

- In addition to sampling and analysis errors, several physiologic states exist in which correct laboratory analysis yields low serum sodium levels, but these levels do not reflect a true hypo-osmolar state. The most common example is serum hyperglycemia.
- Accumulation of extracellular glucose induces shift of free water from the intracellular space to the extracellular space.
- Serum sodium is diluted by a factor of 1.6 mEq/L for each 100 mg/dL increase in serum glucose.
- Systemic osmolarity is normal or even increased, not decreased as in true (i.e., hypo-osmolar) hyponatremia.
- This hypertonic hyponatremia has no physiologic significance. and serum sodium corrects as normoglycemia is reestablished.
    - A similar phenomenon is observed in patients treated with glycerol or mannitol in an effort to control acute glaucoma or intracranial hypertension. This phenomenon is also seen in patients with advanced renal disease who receive radio contrast agents for diagnostic testing.
    - Hyponatremia may be noted in patients whose serum contains unusually large quantities of protein or lipid.
- In these patients, an expanded plasma protein or lipid fraction leads to a decrease in the plasma water fraction in which sodium is dissolved.

- Laboratory techniques that measure absolute sodium content per unit of plasma water report low sodium levels despite the fact that the concentration of sodium in serum water remains within the normal range.
- This phenomenon, known as pseudohyponatremia.
- Serum osmolarity remains undisturbed, and attempts at correcting serum sodium are not indicated.
- Hyperlipidemia that is severe enough to produce pseudohyponatremia almost always is accompanied by a lipemic appearance of the serum sample.
- Hyperproteinemia of sufficient magnitude to induce pseudohyponatremia commonly is due to coexisting multiple myeloma.
- Serum osmolarity is helpful in establishing the diagnosis of true hypo-osmolar hyponatremia.
- Serum osmolarity is abnormally low in patients with hypo-osmolar hyponatremia, but it is normal in patients with pseudohyponatremia due to hyperlipidemia or hyperproteinemia and normal or elevated in patients with hypertonic hyponatremia due to serum hyperglycemia.
- Urine sodium levels are helpful in distinguishing renal causes of hyponatremia from nonrenal causes.
    - Patients with hypovolemic hyponatremia due to nonrenal causes (e.g., vomiting, diarrhea, fistulas, GI drainage, third spacing of fluids) have avid renal absorption of tubular sodium and urine sodium levels of less than 20 mEq/L, whereas those with hypovolemic hyponatremia due to renal causes (e.g., diuretics, salt-losing nephropathy, Aldosterone

deficiency) have inappropriately elevated urine sodium levels in excess of 20 mEq/L.

  - Patients with hypervolemic hyponatremia due to decreases in effective circulating volume (e.g., cirrhosis, nephrotic syndrome, congestive heart failure) have urine sodium levels of less than 20 mEq/L, whereas those with renal causes of hypervolemic hyponatremia or with SIADH have urine sodium levels in excess of 20 mEq/L.

- Urine osmolarity may be helpful in establishing the diagnosis of SIADH.
  - Typically, patients with SIADH have inappropriately concentrated urine with urine osmolarity in excess of 100 mOsm/L.
  - Patients with other forms of hyponatremia and appropriately depressed levels of ADH have urine osmolarity below 100 mOsm/L.
- Serum thyroid-stimulating hormone (TSH) and free thyroxin should be checked if the clinical presentation is consistent with hypothyroidism.
- Adrenal function should be assessed, via random serum cortisol levels or adrenocorticotropic hormone (ACTH) stimulation test, in patients who recently have taken oral steroids or in any patient suspected of having cortisol deficiency.
- **Imaging Studies:** Imaging studies may be indicated depending upon the underlying etiology of the hyponatremia (e.g., chest radiograph in a patient with CHF). Usually, a head CT scan is indicated in the patient with altered mental status to ensure that no other underlying cause for the mental status is present.

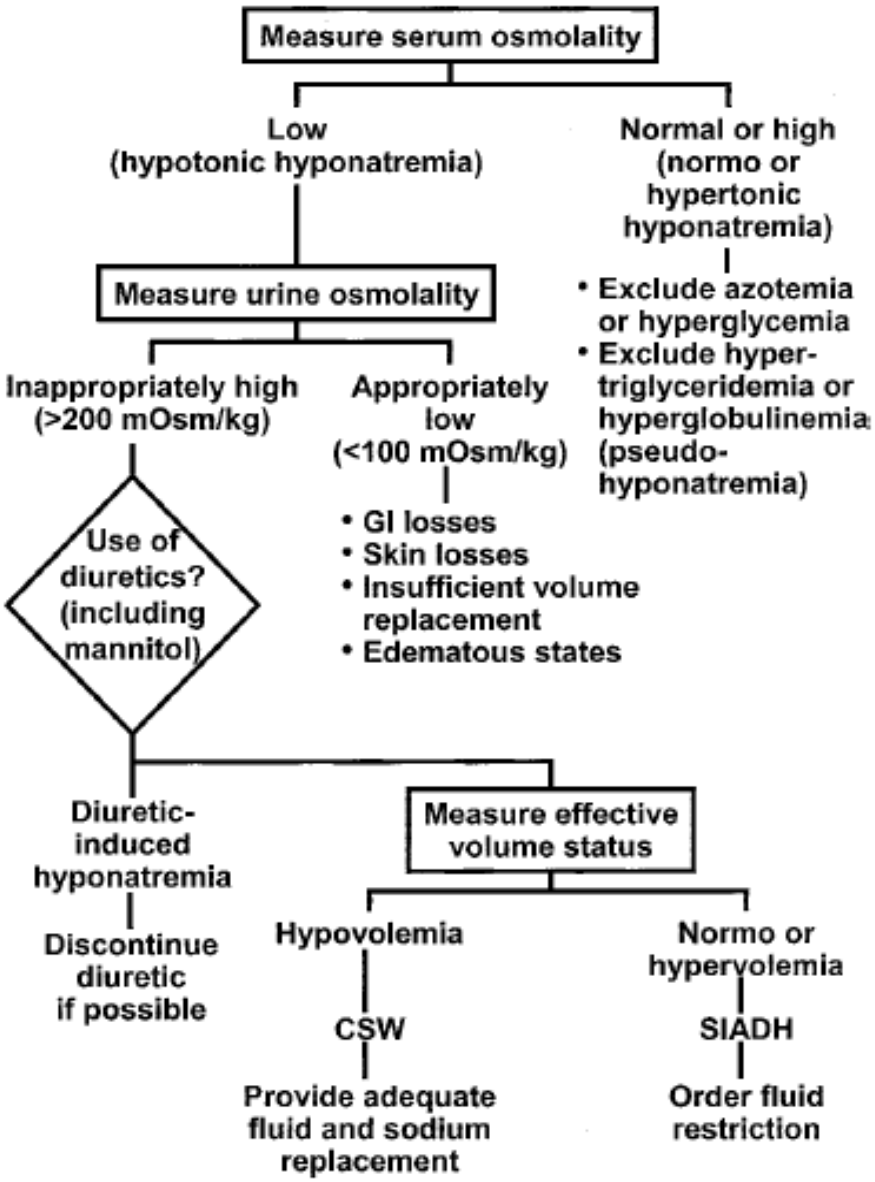



FIGURE 2. Decision tree for the evaluation and management of hyponatremia in critically ill neurologic patients. CSW, cerebral salt wasting; SIADH, syndrome of inappropriate secretion of antidiuretic hormone.

## MANAGEMENT

Treatment of hyponatremia is depends upon various factors like whether patient is symptomatic for hyponatremia or not whether hyponatremia is acute or chronic & volume status. As most commonly hyponatremia is of hypervolemic or euvolemic the hyponatremia is usually due to water retention rather than due to sodium retention so treatment usually involves water restriction as a first line of treatment rather than sodium supplement.

As patients with hyponatremia presents with cerebral symptoms treatment of same is important and the same time it is also important to recognize that rapidly treatment also carries a risk of central pontine myelinolysis.[1,21,22] So it is utmost important to balance between this risk & benefit. This condition is demyelination of the pons, which can lead to mutism, dysphasia, spastic quadriparesis, pseudo bulbar palsy, delirium, coma, and even death. On the basis of observations in both animals and humans. It appears that aggressive treatment of hyponatremia that has been present for longer than 24 to 48 hours is responsible for development of central pontine myelinolysis. Raising the serum sodium concentration more than 25 mEq/L or to a normal or above-normal level in the first 48 hours increases the likelihood of central pontine myelinolysis. In addition, certain patients have a greater propensity for the disorder (e.g., alcoholics, elderly women taking thiazide diuretics, patients who are malnourished or hypokalemic, burn patients). [1,23]

Treatment of hyponatremia varies depending on whether symptoms are present.[1,23-26]

**In asymptomatic patients:** When symptoms are absent, the focus of therapy should be on identifying and correcting the underlying cause of hyponatremia. If a patient is judged to be hypovolemic on the basis of clinical assessment and urine sodium concentration, normal saline solution should be administered initially to correct the extracellular fluid volume deficit. If a patient is hypervolemic, salt and water restriction is key. Most patients with CHF or nephrotic syndrome maintain a serum sodium concentration of more than 125 mEq/L, even with marked increase in ADH levels. Patients with CHF can be treated with inotropes, afterload reduction, and loop diuretics in addition to salt and water restriction. Loop diuretics are the mainstay of therapy in patients with nephrotic syndrome, and if these agents are unsuccessful, dialysis may be warranted.

For patients who are euvolemic and hyponatremic, therapy consists primarily of water restriction. Again, treating the underlying cause is important (e.g., withdrawing drug, initiating hormone therapy for hypothyroidism or adrenal insufficiency) and may correct the hyponatremia. When the cause of the syndrome of inappropriate ADH is unknown or not treatable, other methods can be used, including increased dietary protein and salt and use of urea, loop diuretics and. rarely. demeclocycline hydrochloride.

**In symptomatic patients:** Patients with acute symptomatic hyponatremia are candidates for aggressive treatment. [1,23-26] In this condition, acute hyponatremia develops so quickly (within 48 hours) that the brain has little time for adaptation. It more commonly occurs in elderly patients, in patients with preexisting brain injury, alcoholics, young menstruating women seem to be particularly susceptible to hyponatrernic encephalopathy.[1,27]

Hyponatremia can be corrected with administration of hypertonic saline solution (3%). The rate of correction can be calculated by following formula:

Change in serum sodium concentration= Infusate Na/L-Serum Na/TBW+1

Here Infusate (3% Nacl) Na= 513mEq/L and TBW= Total Body Water which is 0.5*weight (kg) for elderly men & 0.45* weight (kg) for elderly women.

It will give idea about the change in serum sodium level by transfusing one lit. of 3% Nac1. The rate of correction for acute hyponatremia should not be greater than 1.0-1.5mEq/L & no more than10mEq/L of sodium correction in first day. More over the tae target serum sodium should not to normalize the serum sodium but rather to a safe level (upto125mEq/L) to alleviate patients acute neurological symptoms. This decreases the chances of central Pontine myelinolysis. A loop diuretic may be added to enhance water excretion if urine osmolality is greater than 300 mOsmlkg. As a loop diuretic abolishes positive as well as negative gradient within renal parenchyma it causes loss of water more than loss of sodium so it is particularly helpful in patients with hypervolemic hyponatremia.

| Intravenous solution | Intravenous solution |
|---|---|
| 5% Dextrose in water | 0 |
| 0.45% NaCl in water | 77 |
| 0.45% NaCl in water | 130 |
| 0.9% NaCl in water | 154 |
| 0.9% NaCl in water | 256 |
| 0.9% NaCl in water | 513 |

**TABLE 2: SODIUM CONCENTRATIONS IN COMMONLY USED INTRAVENOUS SOLUTIONS**

The serum sodium concentration should be raised no more than 25 mEq/L in the first 48 hours, at a rate of no more than 1.5 mEq/L per hour and the target goal should be 120 to 125 mEq/L. Treatment with hypertonic saline solution is advocated only for patients with severe hyponatremia who have profound neurologic symptoms. The main conroversy in the literature surrounds treatment of chronic symptomatic hyponatremia because, as mentioned, central pontine myelinolysis may result if the condition is corrected too rapidly .Therefore, although treatment in these patients is similar to that just described, the rate of correction should be slower (0.5 to 1 mEq/L per hour). Aggressive therapy should be discontinued when the serum sodium concentration is raised 10% or symptoms abate. Regardless of whether a symptomatic patient presents with acute or chronic hyponatremia, the key to successful management is frequent monitoring of serum electrolytes to ensure adherence to the guidelines outlined. In general, the serum sodium concentration should be reassessed every 2 to 4 hours during active intervention.[61]

**TREATMENT OF SIADH AND CSW:**

The first step in the treatment of SIADH or CSW is to identify the cause and then reverse or treat it. The most common reversible causes of SIADH include medications, such as carbamazepine, oxcarbazine, cyclophosphamide, and selective serotonin reuptake inhibitors, and pulmonary disease, such as pneumonia.[62] Medication- induced SIADH can be reversed by discontinuing the medication, and SIADH caused by pneumonia can be reversed by treating the pneumonia. Unfortunately, many common causes of SIADH and CSW, such as subarachnoid hemorrhage and malignancy, are irreversible, at least in the short term. The next step is

initiation of hyponatremia treatment. Treatment options are outlined in Table 3, along with dosing and monitoring considerations.[63]

| Treatment | Use | Dose | Monitoring[a] |
|---|---|---|---|
| Fluid restriction | SIADH | 800-1200 mL/d | Volume status, intake, output, and dehydration (eg, heart rate, blood gas pressure) |
| Isotonic saline | CSW | 100-200 mL/h IV (correction rate of 0.5 mEq/L) | Volume status, intake, and output |
| Salt tablets | CSW | Up to 12 g/d orally in divided doses | Volume status, intake, and output |
| Hypertonic saline | SIADH<br>CSW (with caution) | 0.5 mL/kg/h IV | Volume status, intake, output, and central catheter status |
| Furosemide | SIADH | 20-120 mg IV/orally | Volume status, urine output, salt intake, and renally excreted electrolytes (ie, potassium, chloride, and magnesium) |
| Demeclocycline | SIADH | 600-1200 mg/d orally in divided doses | BUN, SCr, and urine output |
| Lithium | SIADH | 900 mg/d orally | Mental status, tremor, electrolytes, BUN, SCr, urine output, thyroid function, CBC, weight, vomiting, and diarrhea |
| Urea | SIADH | 30 g/d orally | Nausea, vomiting, mental status, and BUN |
| Fludrocortisone | CSW | 200 mcg twice daily orally | Respiratory function, potassium, and glucose |
| Conivaptan | SIADH | 20 mg IV over 30 min, then 20-40 mg/d continuous infusion over 96 h | Constipation, urine output, and thirst |
| Tolvaptan | SIADH | 15, 30, or 60 mg/d orally | Edema, potassium, urine output, and thirst |

Abbreviations: BUN, blood urea nitrogen; CBC, complete blood cell; CSW, cerebral salt wasting; IV, intravenous; SCr, serum creatinine; SIADH, syndrome of inappropriate antidiuretic hormone.

[a]In addition to serum sodium level monitoring.

**Table 3: Treatment options for SIADH and CSW**

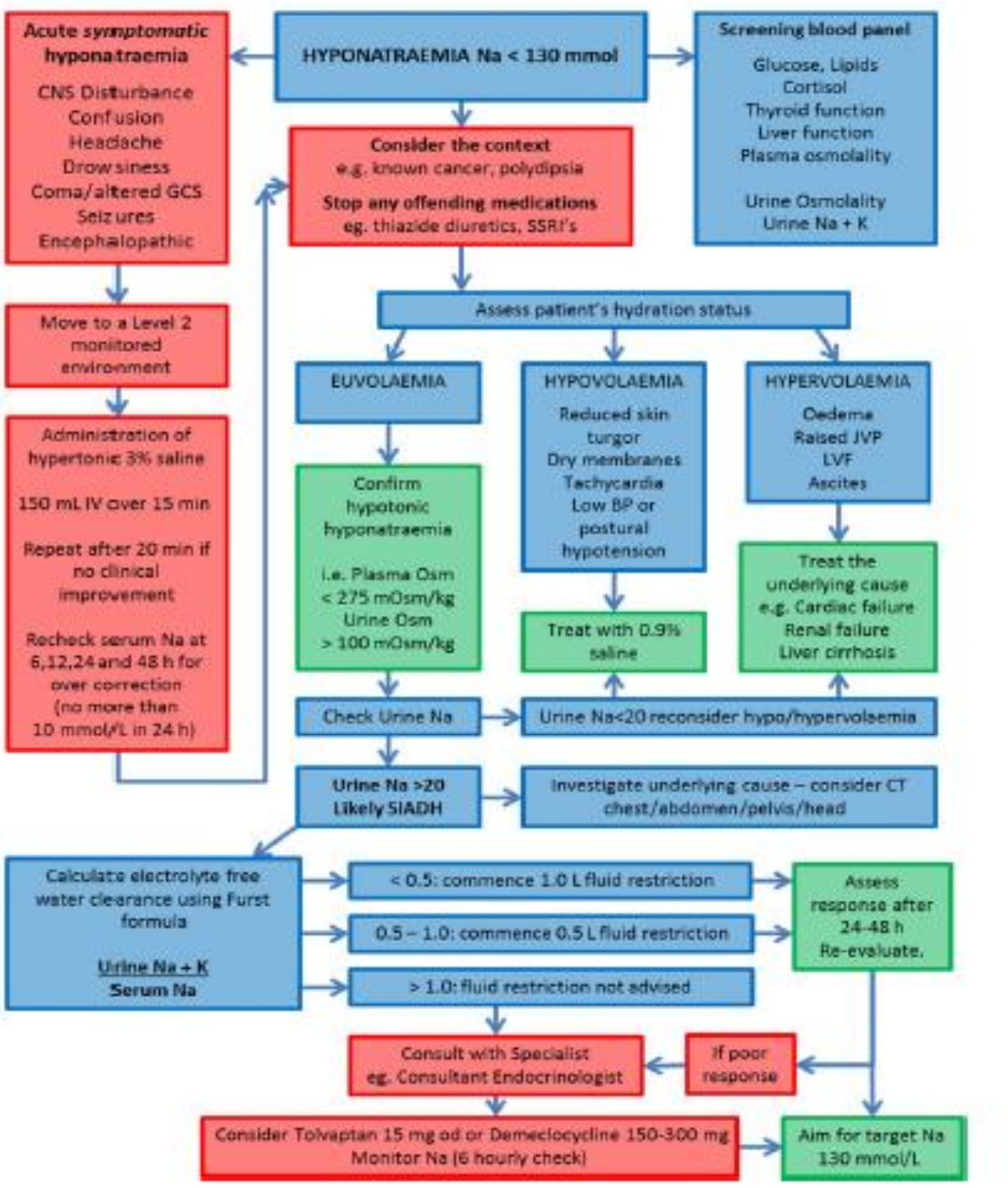



**Figure 3:** Algorithm for management of inpatients with hyponatraemia. CNS, central nervous system; CT, computed tomography; GCS, Glasgow Coma Score; IV, intravenous; JVP, jugular venous pressure; K, potassium; LVF, left ventricular fibrillation; Na, sodium; od, once daily; Osm, osmolality; SSRI, selective serotonin reuptake inhibitor

# MATERIALS AND METHODS

**SOURCE OF DATA:**

Patients age more than 18years admitted in RL Jalappa hospital and research centre, Tamaka, Kolar, from January 2015 to January 2016. 57 patients with hyponatremia were included in the study.

**METHOD OF COLLECTION OF DATA:**

The following data was collected from the selected subjects

a) Required routine/ specific investigations relevant to evaluate as per admission diagnosis

b) Serum sodium levels- at admission , every day during correction period, then as and when indicated.

c) Mini mental state examination (MMSE) score was assessed on the day of admission, on day 3 and day 5.

d) MMSE score is a 30-point questionnaire that is used to measure cognitive impairment.

e) Patients with MMSE score <28 were defined as cognitive impaired.

f) CT brain/MRI brain was done to know the neurological cause for hyponatremia

g) Other investigations like Electrocardiogram, Thyroid function tests , Liver function tests was done to rule out other causes of hyponatremia

h) Treatment is given as per prevalent practice in ICU

**INCLUSION CRITERIA:**

a) Age more than 18years

b) Neuro infection (meningitis, encephalitis)

c) Acute cerebrovascular accidents

d) Head injury

**EXCLUSION CRITERIA:**

a) Patients on drugs causing hyponatremia

b) Patients who are not conscious enough and unable to perform motor functions

c) Hypothyroid patients

**SEVERITY OF HYPONATREMIA:**

a) Mild Hyponatraemia – serum sodium level 130–134 mmol/l,

b) Moderate hyponatremia- serum sodium level 125–129 mmol/l,

c) Severe hyponatremia- serum sodium level <125 mmol/l.

**METHODS:**

All patients with acute neurological disorders with age more than 18 years, 3-5 ml of venous blood was collected in a yellow top vaccutainer. Routine blood investigations like complete blood count, renal function tests, random blood sugar, serum electrolytes (serum sodium and potassium), liver function tests, thyroid function tests, electrocardiogram was done. Serum Sodium was measured by potentiometric method. CT brain /MRI brain was done to know the neurological cause for hyponatremia. Patients with serum sodium level less than 135mmol/L were enrolled in the study. Clinical assessment of patients of acute neurological disorders with

hyponatremia is done by Mini Mental State Examination (MMSE) on day 1. Patients with MMSE score <28 were defined as cognitive impaired. Hyponatremia correction was given according to the following guidelines and formulas. Cognitive functions were assessed by MMSE scores on day 3 and day 5. Inference was drawn accordingly.


**Figure 4: Serum Sodium level Biochemical Analyser**

**CLASSIC FORMULAS:**

| **HYPONATREMIA** |
|---|
| $Na^+$ requirement (mmol) = total body water X ( desired $Na^+$- serum $Na^+$ ) |
| Rate of infusion (cc/hr) = $\frac{Na^+ \text{ requirement (mmol) X } 1000}{\text{Infusate } Na^+ \text{ (mmol/L) x time (hours)}}$ |

| **ADROGUE FORMULA** |
|---|
| Change in serum $Na^+$ = $\frac{(\text{infusate } Na^+ + \text{infusate } K^+) - \text{serum } Na^+}{\text{Total body water} + 1}$ |

| Infusate | Infusate $Na^+$ (mmol/L) |
|---|---|
| 5% Nacl | 855 |
| 3% Nacl | 513 |
| 0.9% Nacl (NS) | 154 |
| Ringer's Lactate | 130 |
| 0.45% Nacl (1/2 NS) | 77 |
| 0.2% Nacl (1/4 NS) | 34 |
| 5% Dextrose in water | 0 |

| **Total Body Water (in liters) :** | |
|---|---|
| Children | 0.6 x weight |
| Women | 0.5 x weight |
| Men | 0.6 x weight |
| Elderly Women | 0.45 x weight |
| Elderly Men | 0.5 x weight |

# RESULTS

Total number of patients with hyponatremia (serum sodium $\leq$ 135 mmol/l)- 57 patients

**AGE DISTRIBUTION OF THE STUDY POPULATION:**

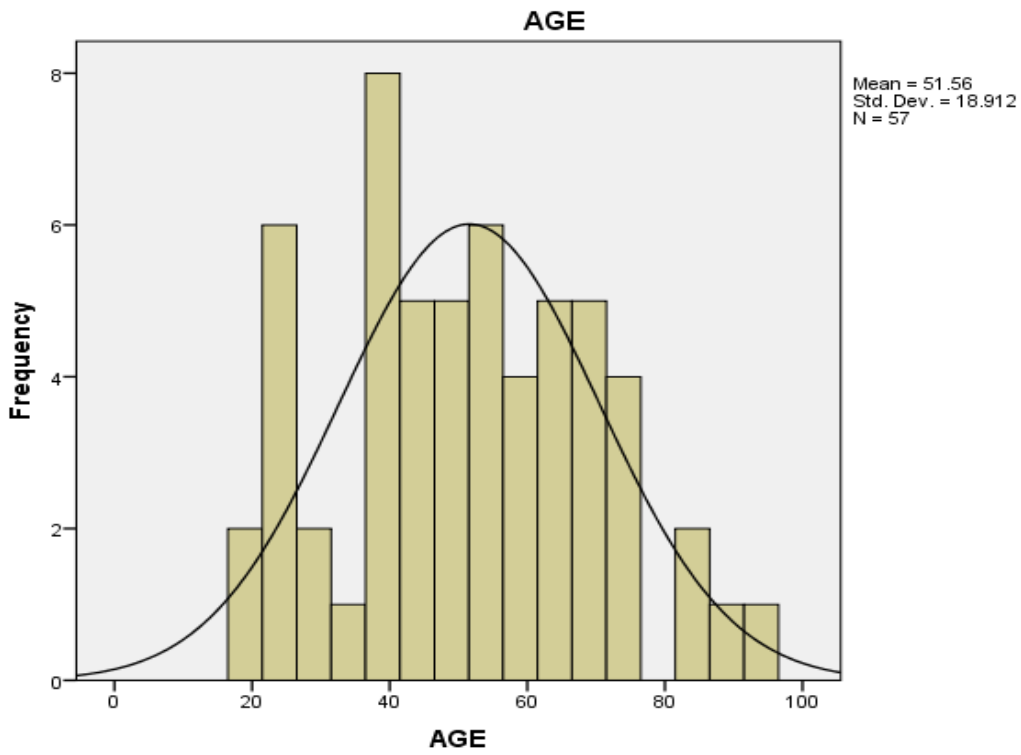



**Figure 5: The mean age of the patients admitted is 52 years. Patients with age 40 years are mostly admitted.**

**GENDER DISTRIBUTION AMONG STUDY POPULATION:**

**Table 4: Gender distribution**

| GENDER | FREQUENCY | PERCENT |
|---|---|---|
| MALES | 39 | 68.42% |
| FEMALES | 18 | 31.58% |

Among 57 patients who had hyponatremia, 39 patients (68.42%) were males and 18 patients (31.58%) were females which shows male preponderance

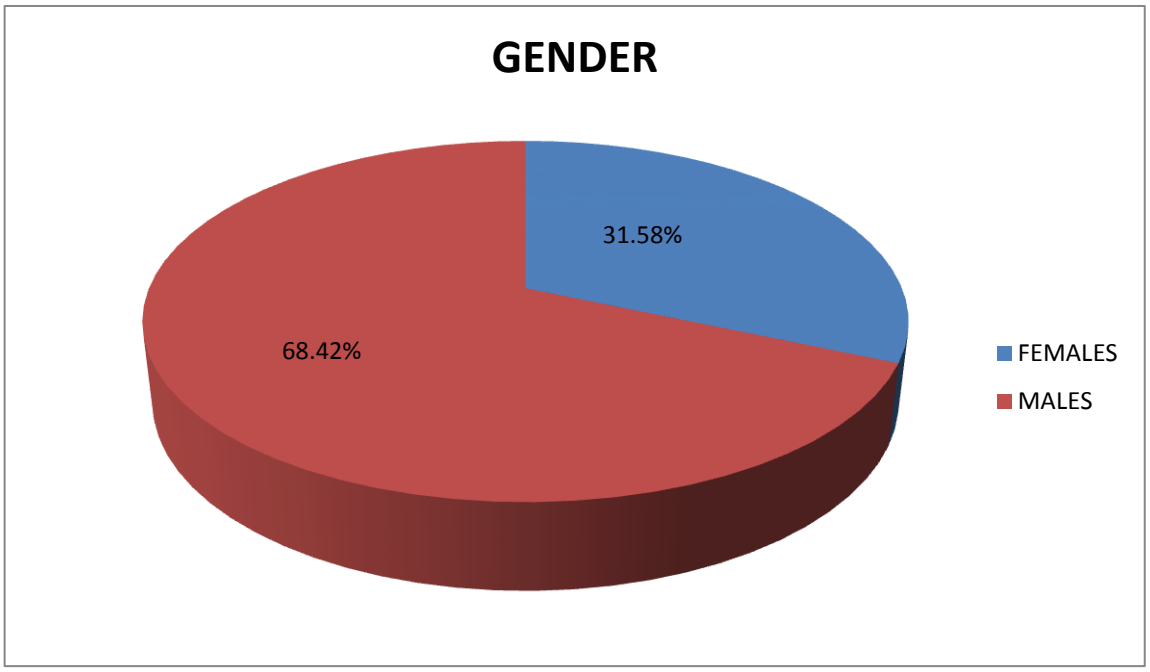



**Figure 6: Gender distribution**

**CO-MORBIDITIES AMONG STUDY POPULATION:**

**Table 5: Comorbidities among study population**

| Comorbidities | Number Of Patients | Percentage |
|---|---|---|
| Diabetes Mellitus | 9 | 16% |
| Hypertension | 15 | 26% |
| Both Diabetes And Hypertension | 1 | 1.7% |
| Neither Diabetes Or Hypertension | 32 | 56% |

Among 57 patients, 32 patients (56%) had neither diabetes nor hypertension, 15 patients (26%) had hypertension, 9 patients (16%) had diabetes mellitus and 1 patient (1.7%) had both diabetes and hypertension.

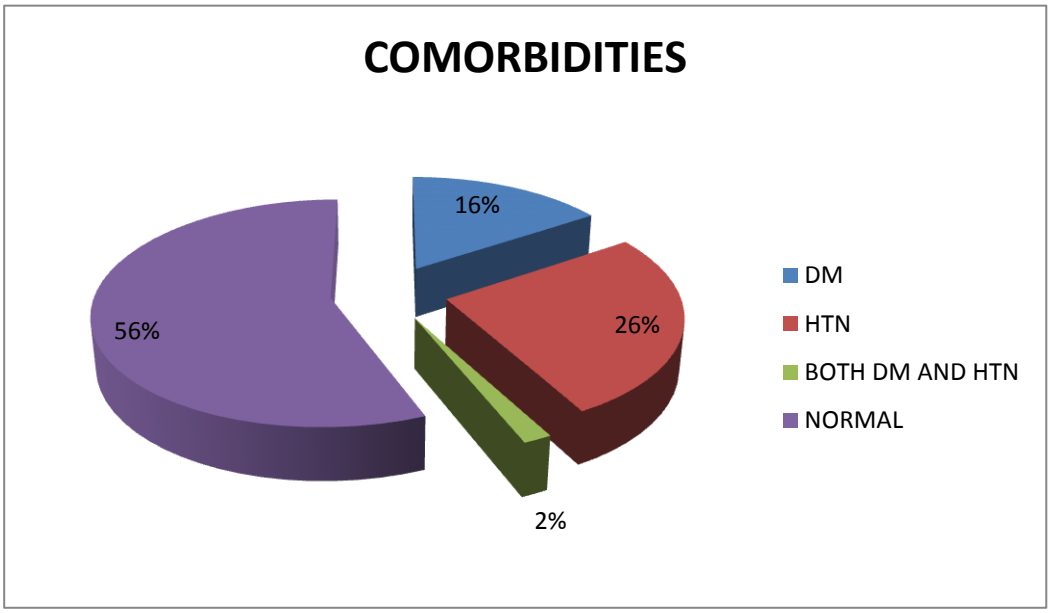



**Figure 7: Comorbidities among study population**

**ADDICTIONS:**

**Table 6: Addictions among study population**

| Addiction | Number of patients | Percentage |
|---|---|---|
| Smoking | 10 | 18% |
| Alcohol | 6 | 11% |
| Both | 2 | 3% |
| None | 39 | 68% |

Among 57 patients, 39 patients (68%) had neither smoking nor alcohol addiction, 10 patients (18%) had smoking addiction, 6 patients (11%) had alcohol addiction , 2 patients ( 3%) had both smoking and alcohol addiction.

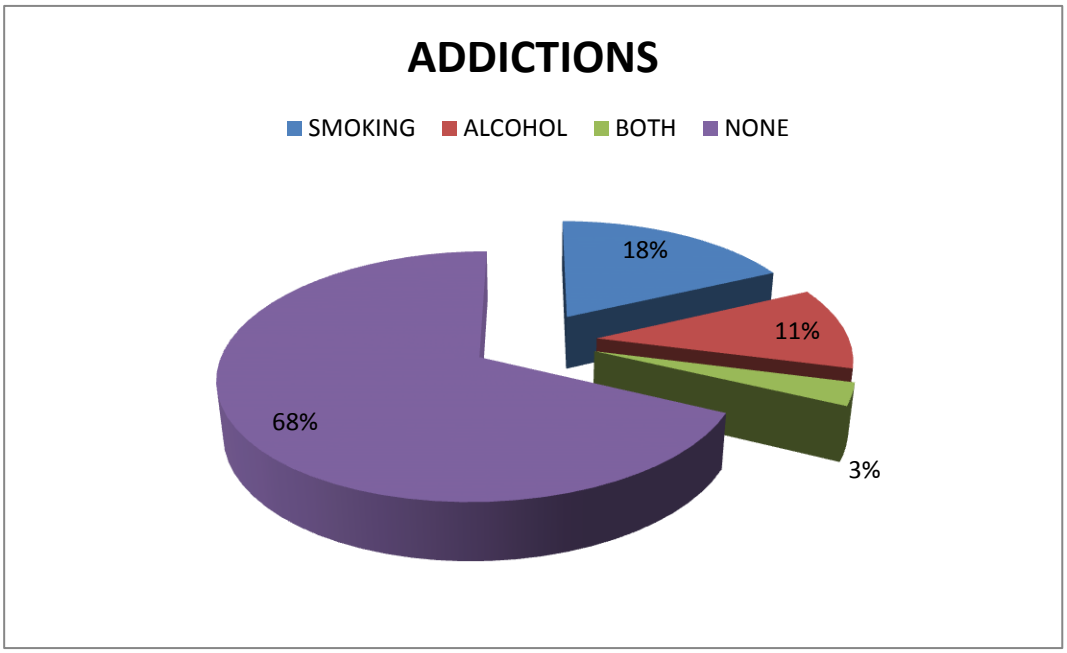



**Figure 8: Addictions among study population**

**CT BRAIN FINDINGS AMONG STUDY POPULATION:**

**Table 7: CT brain findings among study population**

| CT Brain | Number of Patients | Percentage |
|---|---|---|
| Infarct | 21 | 37% |
| Hemorrhage | 14 | 24% |
| Normal | 22 | 39% |

Among 57 patients, 21 patients (37%) had infarct on CT brain , 14 patients (24%) had hemorrhage, 22 patients (39%) had normal CT brain. normal CT brain suggests that the underlying etiology for hyponatremia is  either meningitis or enchepalitis.

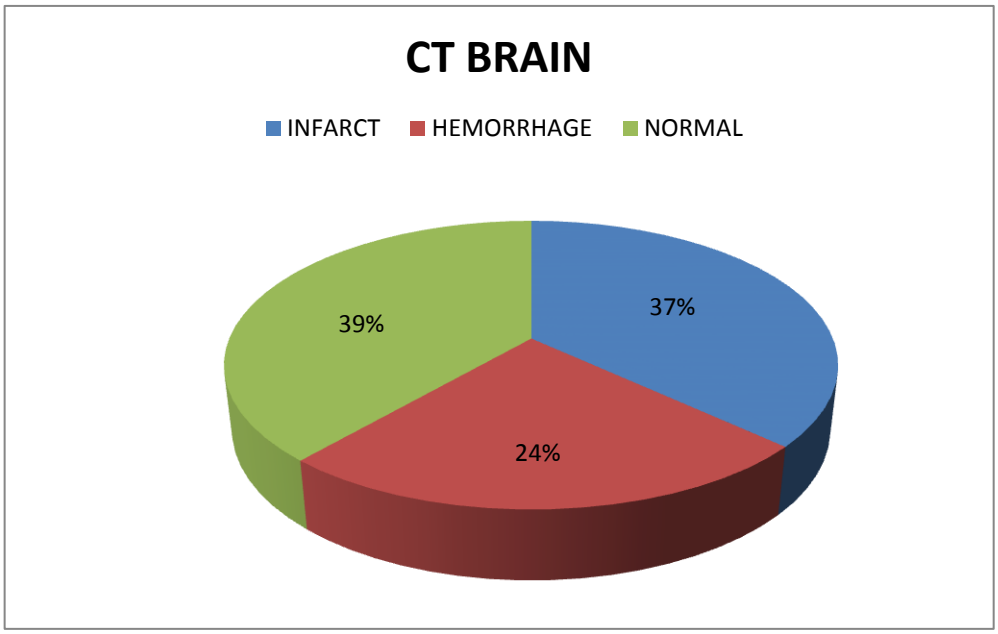



**Figure 9: CT brain findings among study population**

**PULSE RATE AMONG STUDY POPULATION:**

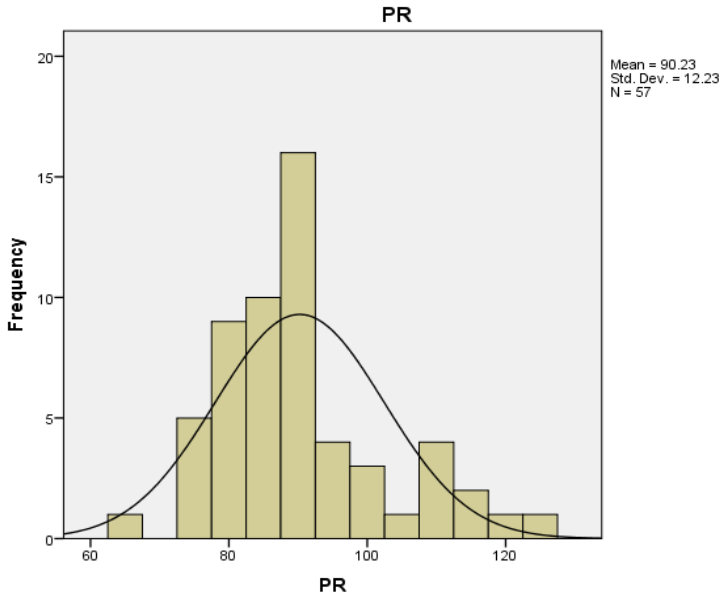



**Figure 10: Pulse rate among study population**

The mean pulse rate of study population is 90.23 beats per minute.

**SERUM SODIUM LEVELS AMONG STUDY POPULATION:**

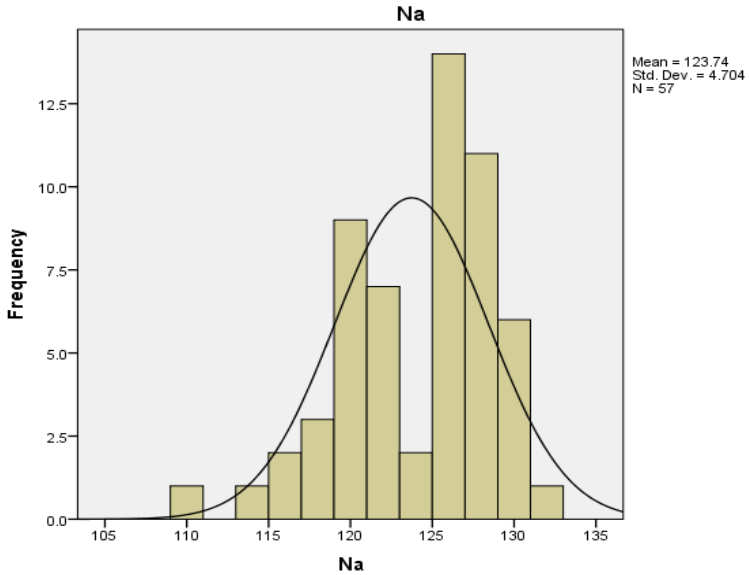



**Figure 11: Serum sodium levels among study population**

The mean serum sodium among study population is 123.74 mmol/l. most frequency occur at 125-126

**SERUM POTASSIUM LEVELS AMONG STUDY POPULATION:**

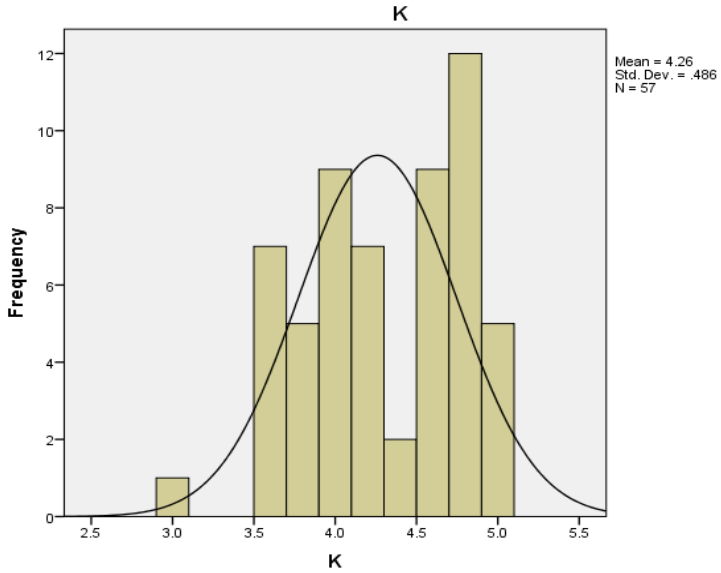



**Figure 12: Serum potassium levels among study population**

The mean serum potassium levels among study population is 4.26mmol/l

**SEVERITY OF HYPONATREMIA:**

**Table 8: Severity of hyponatremia**

| | Mild Hyponatremia | Moderate Hyponatremia | Severe Hyponatremia |
|---|---|---|---|
| Number of Patients | 7 | 25 | 25 |
| Percentage | 12.28% | 43.85% | 43.85% |

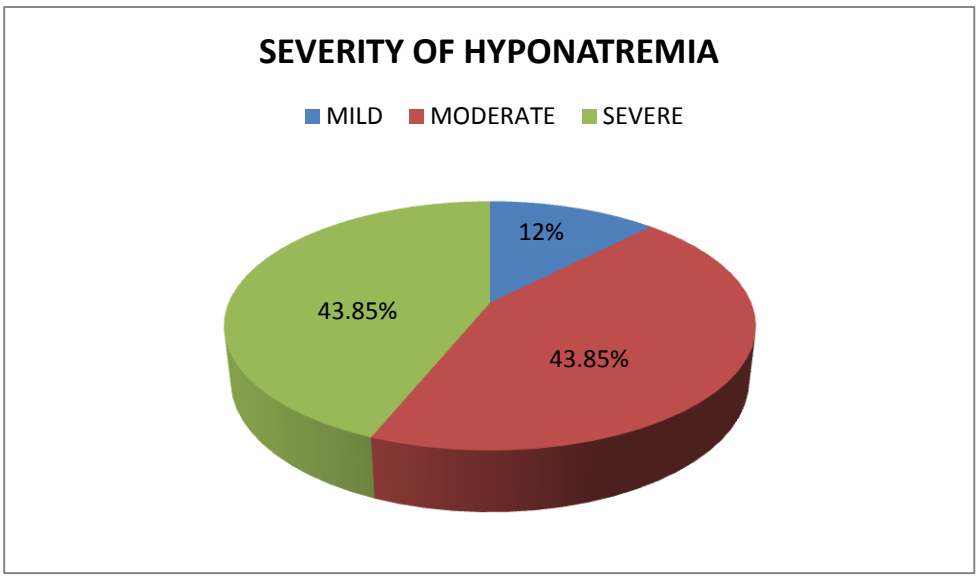



**Figure 13: Severity of hyponatremia**

Among 57 patients with hyponatremia, 7 patients had mild hyponatremia, 25 patients had moderate hyponatremia, 25 patients had severe hyponatremia.

**SEVERITY OF HYPONATREMIA: COMPARISON OF GENDER AND SEVERITY OF HYPONATREMIA**

**Table 9: Comparison of gender and severity of hyponatremia**

| Gender | Mild Hyponatremia | Moderate Hyponatremia | Severe Hyponatremia |
|---|---|---|---|
| Females | 2 (11.1%) | 9 (50%) | 7 (38.9%) |
| Males | 5 (12.9%) | 16 (41%) | 18 (46.1%) |

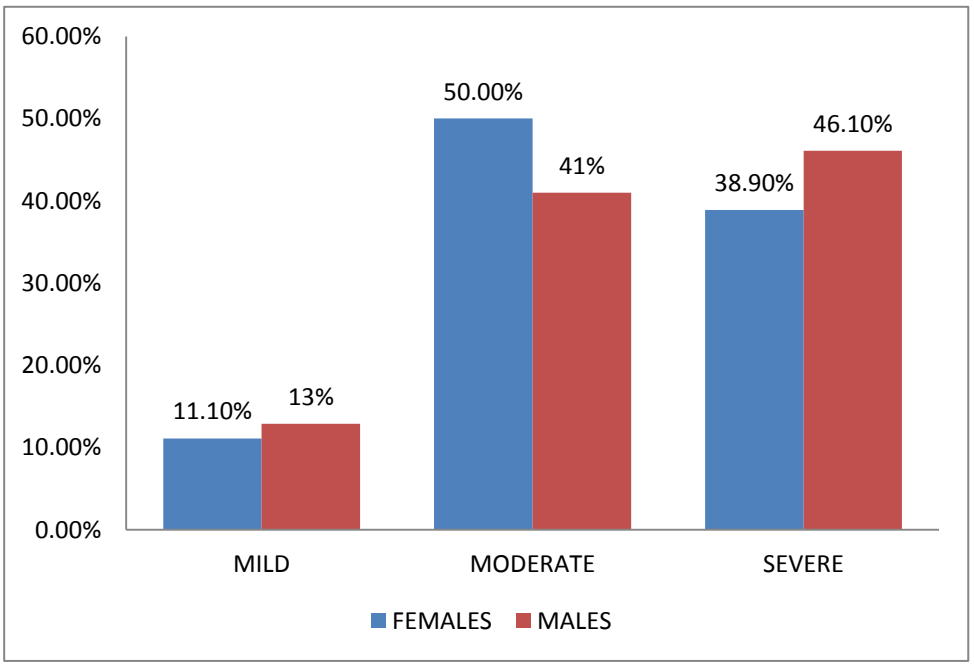



**Figure 14: Comparison of gender and severity of hyponatremia**

Among 18 females patients with hyponatremia, 2 patients had mild hyponatremia ( serum sodium levels between 130-134 mmol/l), 9 patients had moderate hyponatremia( serum sodium levels between 125-129 mmol/l), 7 patients had severe hyponatremia (serum sodium levels less than 125 mmol/l) .

Among male patients with hyponatremia, 5 patients had mild hyponatremia, 16 patients had moderate hyponatremia, 18 patients had severe hyponatremia.

**SEVERITY OF HYPONATREMIA AMONG DIFFERENT AGE GROUPS:**

**Table 10: Severity of hyponatremia among different age groups**

| Age Groups | Mild Hyponatremia | Moderate Hyponatremia | Severe Hyponatremia | Total |
|---|---|---|---|---|
| 18-30 YEARS | 3 ( 5.2%) | 4 (7%) | 2 (3.5%) | 9 (15.8%) |
| 31-50 YEARS | 3 (5.2%) | 11 (19.2%) | 6 (10.5%) | 20 ( 35%) |
| 51-65 YEARS | 1 (1.7%) | 9 (15.7%) | 5 (8.7%) | 15 (26.3%) |
| >65 YEARS | 0 | 1 (1.7%) | 12 (21%) | 13 (22.8%) |

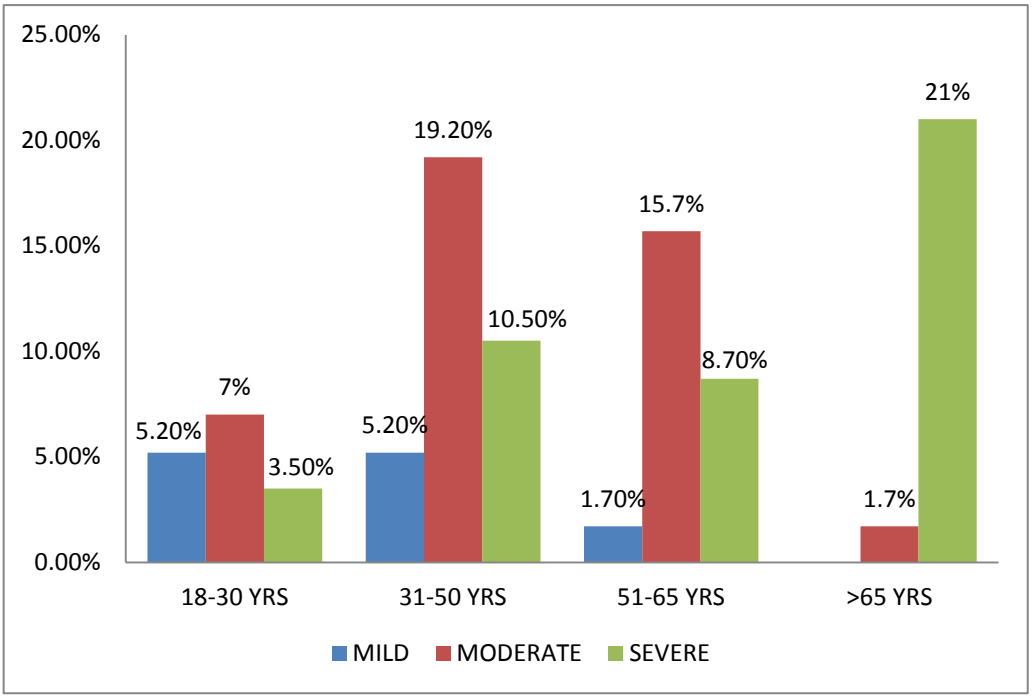



**Figure 15: Severity of hyponatremia among different age groups:**

Among 18-30 years age group, 3 patients had mild hyponatremia, 4 patients had moderate hyponatremia, 2 patients had severe hyponatremia.

Among 31-50 years age group, 3 patients had mild hyponatremia, 11 patients had moderate hyponatremia, 6 patients had severe hyponatremia.

Among 51-65 years age group, 1 patient had mild hyponatremia, 9 patients had moderate hyponatremia, 5 patients had severe hyponatremia.

Among >65 years age group, 1 patient had moderate hyponatremia, 12 patients had severe hyponatremia.

The above graph suggests that most of the elderly patients are severely hyponatremic.

**MMSE SCORE AMONG STUDY POPULATION:**

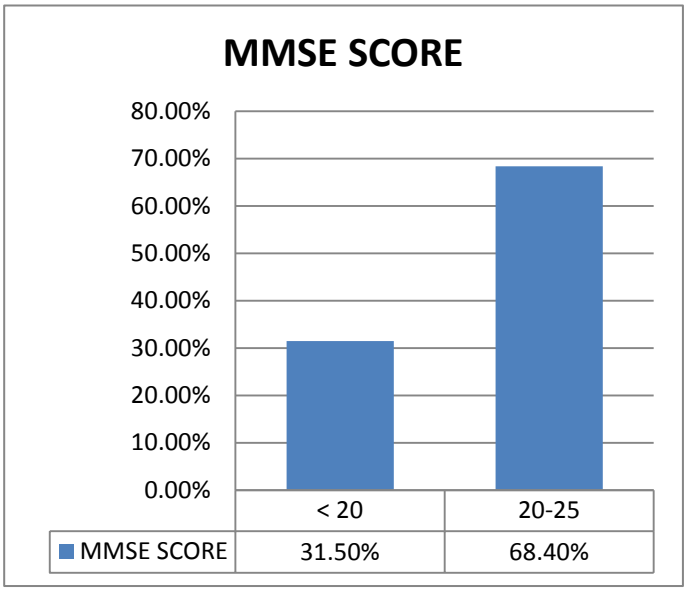
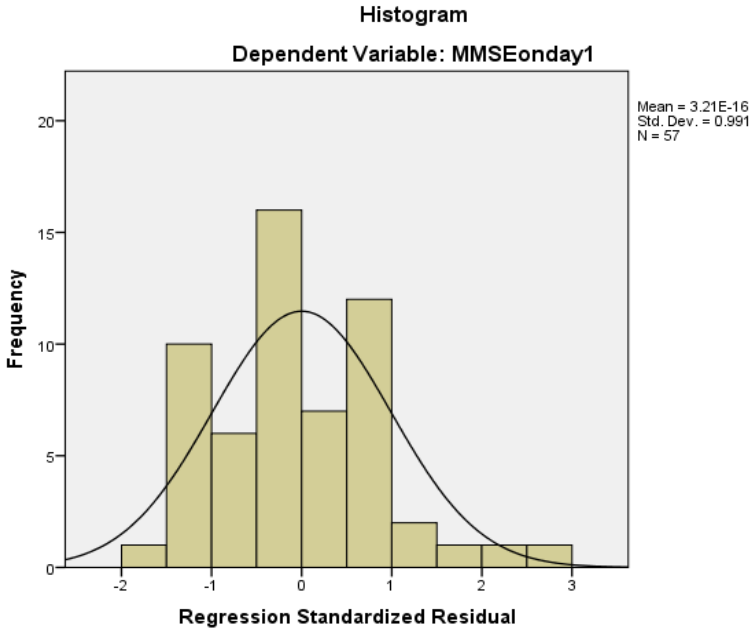



**Figure 16: MMSE score among study population**

Among 57 patients with hyponatremia, 18 patients (31.5%) had MMSE score <20, 39 patients (68.4%) had MMSE score 20-25.

**SERUM SODIUM VS MMSE ON DAY 1:**



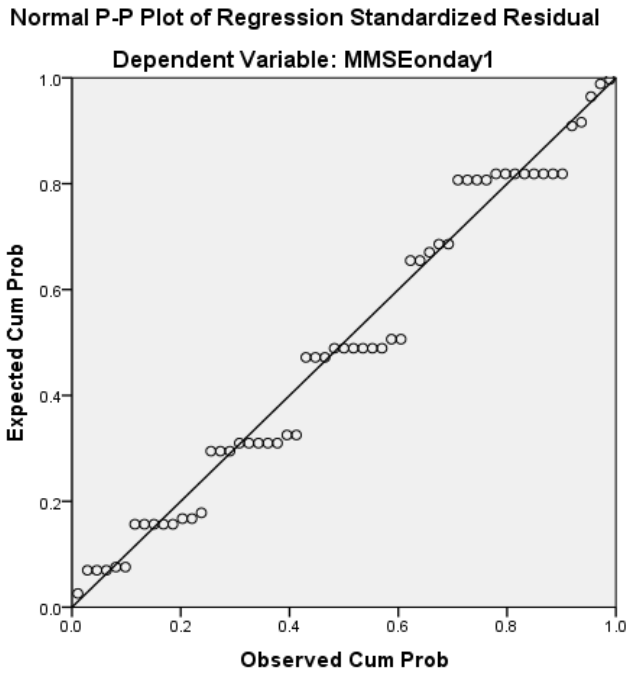




**Figure 17a AND 17b: Serum sodium vs MMSE on day 1**

The P-P plots between expected and observed probabilities on MMSE day 1 signifies linear regression.

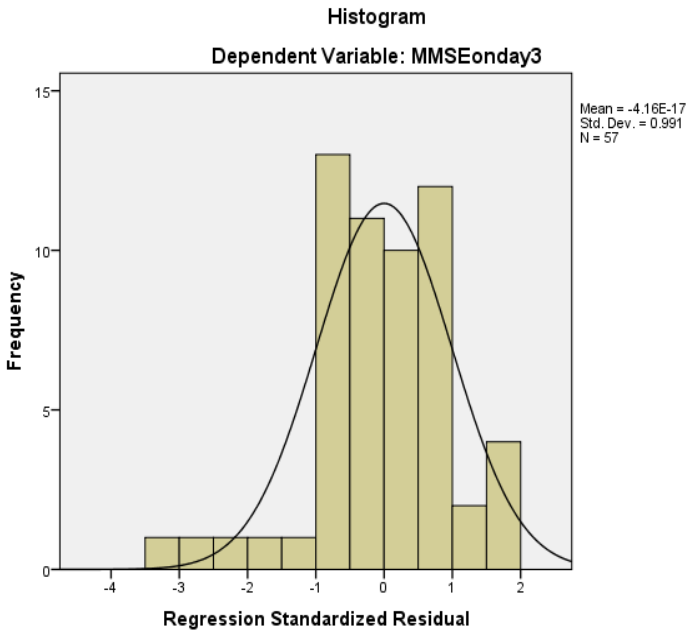
**Table 11: correlation between sodium before treatment and MMSE day 1 is p<0.05.**

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 218.247[a] | 160 | 0.002 |
| Likelihood Ratio | 129.962 | 160 | 0.961 |
| Linear-by-Linear Association | 23.678 | 1 | 0.000 |
| N of Valid Cases | 57 | | |

a. 187 cells (100.0%) have expected count less than 5. The minimum expected count is .02.

**SERUM SODIUM VS MMSE ON DAY 3:**



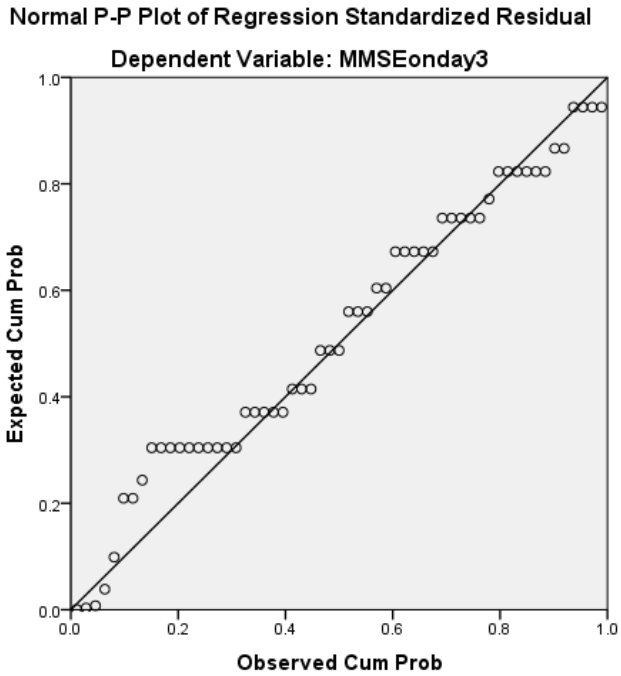



**Figure 18a AND 18b: Serum sodium vs MMSE on day 3**

The P-P plots between expected and observed probabilities on MMSE day 3 signifies linear regression

**Table 12: Correlation between sodium before treatment and mmse day 3 is p<0.05.**

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 197.401[a] | 160 | 0.024 |
| Likelihood Ratio | 113.610 | 160 | 0.998 |
| Linear-by-Linear Association | 13.457 | 1 | 0.000 |
| N of Valid Cases | 57 | | |

a. 187 cells (100.0%) have expected count less than 5. The minimum expected count is .02.

**SERUM SODIUM VS MMSE ON DAY 5:**

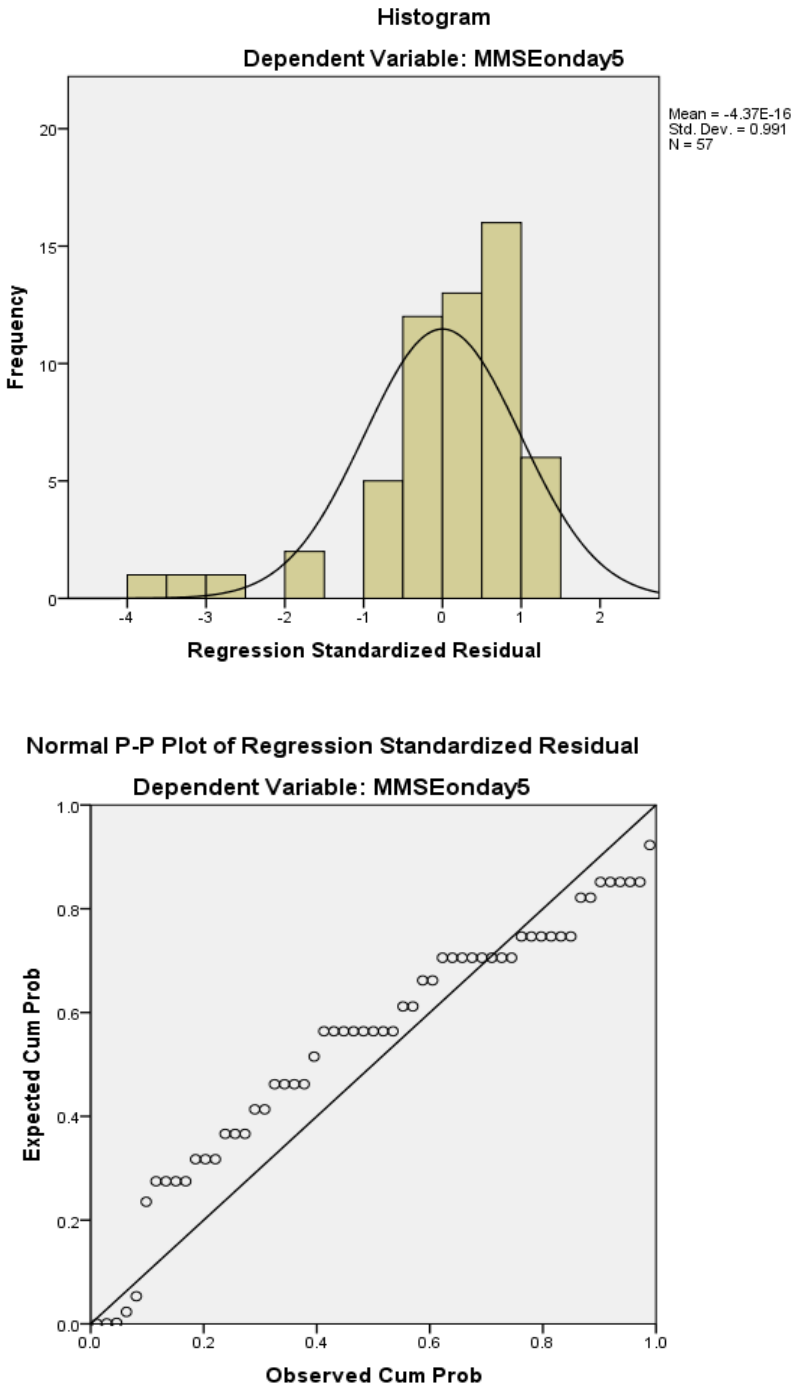



**Figure 19a AND 19b: Serum sodium vs MMSE on day 5**

The P-P plots between expected and observed probabilities on MMSE day 5 signifies linear regression.

**Table 13: Correlation between sodium before treatment and MMSE day 5 is p<0.05.**

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 205.327[a] | 160 | 0.009 |
| Likelihood Ratio | 107.225 | 160 | 1.000 |
| Linear-by-Linear Association | 7.556 | 1 | 0.006 |
| N of Valid Cases | 57 | | |

a. 187 cells (100.0%) have expected count less than 5. The minimum expected count is .02.

**Table 14: The mean MMSE score was 20.46, 23.63, 26.16 on day 1,day 3 and day 5 respectively.**

**Descriptive Statistics**

| | Mean | Std. Deviation | N |
|---|---|---|---|
| Na | 2.32 | 0.686 | 57 |
| MMSEonday1 | 20.46 | 2.486 | 57 |
| MMSEonday3 | 23.63 | 2.273 | 57 |
| MMSEonday5 | 26.16 | 2.763 | 57 |

**SERUM SODIUM LEVELS BEFORE AND AFTER TREATMENT OF HYPONATREMIA:**

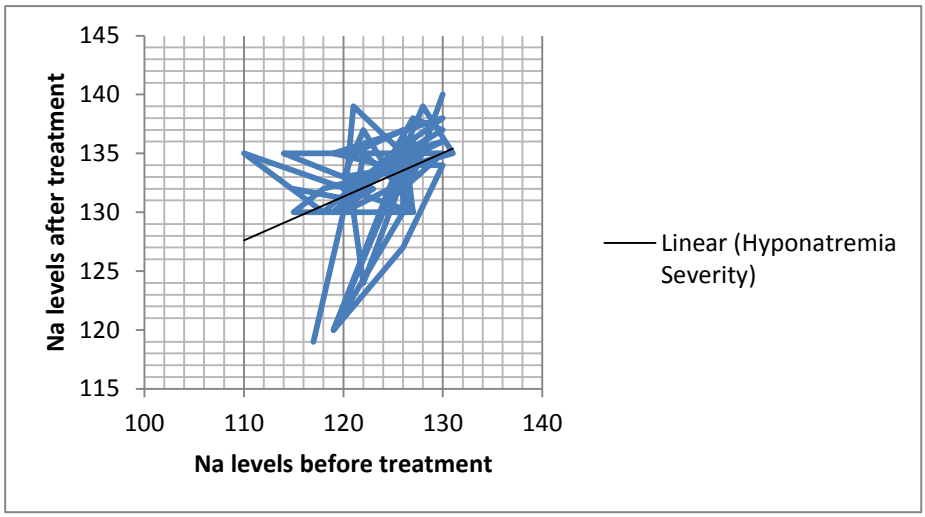



**Figure 20: Serum sodium levels before and after treatment of hyponatremia**

The treatment modality undertaken has an effect in improving cognition as well as managing hyponatremic condition. The linear line signifies this.

**TABLE 15: Serum sodium levels before and after treatment of hyponatremia**

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 229.630[a] | 224 | 0.384 |
| Likelihood Ratio | 126.715 | 224 | 1.000 |
| Linear-by-Linear Association | 9.057 | 1 | 0.003 |
| N of Valid Cases | 57 | | |

a. 255 cells (100.0%) have expected count less than 5. The minimum expected count is .02.

Pearson correlation signifies the treatment modality has positive effect on patients

**ANOVA TABLE:**

**Table 16a : Correlations between serum sodium and MMSE scores on day 1, day 3, day 5**

**ANOVA Table**

| | | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|---|
| MMSE on day1 * Na after correction | Between Groups | (Combined) | 135.737 | 14 | 9.696 | 1.935 | 0.050 |
| | | Linearity | 64.442 | 1 | 64.442 | 12.864 | 0.001 |
| | | Deviation from Linearity | 71.295 | 13 | 5.484 | 1.095 | 0.390 |
| | Within Groups | | 210.403 | 42 | 5.010 | | |
| | Total | | 346.140 | 56 | | | |
| MMSE on day3 * Na after correction | Between Groups | (Combined) | 195.666 | 14 | 13.976 | 6.272 | 0.000 |
| | | Linearity | 137.084 | 1 | 137.084 | 61.514 | 0.000 |
| | | Deviation from Linearity | 58.583 | 13 | 4.506 | 2.022 | 0.043 |
| | Within Groups | | 93.597 | 42 | 2.228 | | |
| | Total | | 289.263 | 56 | | | |
| MMSE on day5 * Na after correction | Between Groups | (Combined) | 343.154 | 14 | 24.511 | 12.194 | 0.000 |
| | | Linearity | 236.455 | 1 | 236.455 | 117.632 | 0.000 |
| | | Deviation from Linearity | 106.698 | 13 | 8.208 | 4.083 | 0.000 |
| | Within Groups | | 84.425 | 42 | 2.010 | | |
| | Total | | 427.579 | 56 | | | |

The ANOVA tables signifies that between the groups, P value is significant.

**Table 16b: Correlations between serum sodium and MMSE scores on day 1, day 3, day 5**

**Measures of Association**

| | R | R Squared | Eta | Eta Squared |
|---|---|---|---|---|
| MMSE on day1 * Na after correction | 0.431 | 0.186 | 0.626 | 0.392 |
| MMSE on day3 * Na after correction | 0.688 | 0.474 | 0.822 | 0.676 |
| MMSE on day5 * Na after correction | 0.744 | 0.553 | 0.896 | 0.803 |

R value was increasing on day 1,3,5 and it was approaching 0.3 to 0.8 i.e, it was moving towards 1 which implies that the treatment had positive effect over the patients prognosis

# DISCUSSION

This study was conducted at a tertiary care centre. This study was undertaken keeping in view the frequent occurrence of hyponatremia in acute neurological disorders.

In this study a total of 57 patients with acute neurological disorders with hyponatremia were included. The mean age of study population is 51.56 years. The maximum frequency of patients were in 31-50 years age group (35%). Among 57 patients with hyponatremia, 68.42% were males and 31.58% were females which shows male preponderance. In a study done by Xu et al, the mean age with hyponatremia was found to be 55.9 $\pm$ 13.2 years.[64]

Among 57 patients 56% had neither diabetes or hypertension, 26% had hypertension, 16% had diabetes mellitus and 1.7% had both diabetes and hypertension. In a study done by Xu et al, 23.7% of patients with hyponatremia had diabetes.[64]

In the present study, mean serum sodium level is 123.74mmol/L. Among 57 patients with hyponatremia, 7 patients (12.28%) had mild hyponatremia ( serum sodium levels between 130-134 mmol/l), 25 patients (43.85%) had moderate hyponatremia( serum sodium levels between 125-129 mmol/l), 25 patients (43.85%) had severe hyponatremia (serum sodium levels less than 125 mmol/l). All the patients had presented with altered sensorium. After hyponatremia correction, 52 patients (91.2% ) had improvement in MMSE score.

Vaghasiya et al, conducted a study evaluating the performance of hyponatremic participants in the Mini Mental State Examination (MMSE), with the assessment being repeated again after correction of the electrolyte disorder in the same participants. There was an increase in MMSE score following improvement in serum sodium concentration in 93% of patients ($p$ = 0.001).[65]

In the present study, among 18 female patients with hyponatremia, 11.1% had mild hyponatremia, 50% had moderate hyponatremia, 38.9% had severe hyponatremia . Among male patients with hyponatremia, 12.9% had mild hyponatremia, 41% had moderate hyponatremia, 46.1% had severe hyponatremia. Yumoto T et al, studied the Prevalence, Risk Factors, and Short-term Consequences of Traumatic Brain Injury-associated Hyponatremia. The prevalence of hyponatremia has been reported to be as high as 30-40% among ICU patients and upto 50% of neurosurgical patients are affected by the condition. In this study, incidence of hyponatremia (serum sodium level <135meq/L) was 51% and that of severe hyponatremia (serum sodium level <130 meq/L) was 20%.[66]

In this study, among 57 patients, 15.8% patients were in 18-30 years age group out of which 5.2% had mild hyponatremia, 7% had moderate hyponatremia, 3.5% had severe hyponatremia. 35% patients were among 31-50 years age group out of which 5.2% had mild hyponatremia, 19.2% had moderate hyponatremia, 10.5% had severe hyponatremia. 26.3% patients were among 51-65 years age group, out of which 1.7% had mild hyponatremia, 15.7% had moderate hyponatremia, 8.7% had severe hyponatremia. 22.8% were among >65 years age group out of which 1.7% had moderate hyponatremia, 21% had severe hyponatremia. Most of the elderly patients were severely hyponatremic.

In this study, out of 57 patients 37% had infarct on CT brain, 24% had hemorrhage on CT brain, and 39% had normal CT brain.

In the present study, among 57 patients with hyponatremia 31.5% had MMSE score <20, 68.4% had MMSE score 20-25. The mean MMSE score was 20.46, 23.63, 26.16 on day 1,day 3 and day 5 respectively. In this study, 52 patients showed increase in MMSE score after correction of hyponatremia.

All patients were treated according to a standardized regimen based on recommendation in various studies. In this study, patients were treated with intravenous 3% saline infusion to raise their serum sodium levels by 0.5mmol/L /hour to a maximum of 12mmol/L increase in serum sodium per day. Though pontine demyelination is described as a rare complication associated with symptomatic hyponatremia, animal data have shown that correction of hyponatremia by > 20-25 mEq/L can result in pontine demyelination.

In the present study, the treatment modality undertaken has an effect in improving cognition as well as managing hyponatremic condition.

Gosch et al, studied whether geriatric patients with mild to moderate hyponatremia ($\leq$ 131 mmol/l) reveal different outcomes in structured tests for functional and cognitive impairments, depression and malnutrition compared to normonatremic patients. Two tests were applied to evaluate cognitive function, the Mini Mental State Examination (MMSE), a sufficient screening instrument for cognitive impairment, and the Clock Completion (CC) test, a sensitive test concerning practical cognitive skills. The MMSE scores of 129 (100%) hyponatremic patients were analyzed and the mean MMSE value was 26.05 $\pm$ 3.64 points. The mean MMSE score was significantly higher in the control group (27.18 $\pm$ 3.15 points; $p = 0.003$) compared to the hyponatremic patients. A significant positive correlation of the MMSE results was found with age ($p < 0.001$).[67]

Gunathilake et al, used the Audio Recorded Cognitive Screening Tool to compare the cognition of hyponatremic participants to a control group. They concluded that the scores of the group with mild hyponatremia were on average 4.67 units lower than the control group ($p$ = 0.01, 95% CI 1.56–7.79). Interestingly, the significant

reduction in cognitive performance occurred when sodium levels decreased by as little as 5 mmol/L.[68]

Ahluwalia V et al, studied the effect of tolvaptan on serum sodium, cognition, companion burden, and brain MRI in cirrhotics with hyponatremia. Out of 17 patients, Cognitive function and companion burden only improved in these 14 patients after tolvaptan.[69]

Saleem et al, study in a tertiary care hospital in Srinagar, India to determine the incidence and etiology of hyponatremia in patients of stroke admitted in the hospital. Incidence of hyponatremia in this population was 35%. Out of 353 patients with hyponatremia, 238 (67%) had SIADH and 115 (33%) had CSWS. SIADH was seen in 83 patients who had ischemic stroke and 155 patients of hemorrhagic stroke. CSWS was found in 38 patients with ischemic stroke and 77 patients with hemorrhagic stroke.[70]

Hyponatremia is one of the important causes of persistent altered sensorium in stroke patients. It can also give various other neurological sign and symptoms like seizures, which can further deteriorate level of consciousness and outcome. There are many precipitating factors for hyponatremia in stroke like dietary restriction of sodium for control of hypertension, use of diuretics and infections like aspiration pneumonia. Hyponatremia in stroke is usually of the hypoosmolal type caused either due to SIADH or CSWS.

# CONCLUSION

The mean age of study population was 51.56 years. The maximum frequency of patients were in 31-50 years age group (35%). There were 39 (68.42%) males and 18 (31.58%) were females which showed male preponderance. 56% had neither diabetes or hypertension, 26% had hypertension, 16% have diabetes mellitus and 1.7% had both diabetes and hypertension.

The mean serum sodium level was 123.74mmol/L. 12.28% had mild hyponatremia (serum sodium levels between 130-134 mmol/l), 43.85% had moderate hyponatremia ( serum sodium levels between 125-129 mmol/l), 43.85% had severe hyponatremia (serum sodium levels less than 125 mmol/l).

All the patients had presented with altered sensorium. After hyponatremia correction, 52 patients (91.2%) had improvement in MMSE score.

Among 18 female patients with hyponatremia, 11.1% had mild hyponatremia , 50% had moderate hyponatremia, 38.9% had severe hyponatremia. Among male patients with hyponatremia, 12.9% had mild hyponatremia, 41% had moderate hyponatremia, 46.1% had severe hyponatremia.

Among 57 patients, 15.8% were in 18-30 years age group , 35% patients were among 31-50 years age group , 26.3% were among 51-65 years age group, 22.8% were among >65 years age group. 37% had infarct on CT brain, 24% had hemorrhage on CT brain, and 39% had normal CT brain.

31.5% had MMSE score <20, 68.4% had MMSE score 20-25. The mean MMSE score was 20.46, 23.63, 26.16 on day 1,day 3 and day 5 respectively. In this study, 52 patients (91.2%) showed increase in MMSE score after correction of hyponatremia.

In the present study, the treatment modality undertaken had an effect in improving cognition as well as managing hyponatremic condition.

# SUMMARY

This is a hospital based cross sectional study of adults conducted in a tertiary care centre. A total of 57 patients with acute neurological disorders with hyponatremia were studied. For these patients a detailed history recording, clinical examination, MMSE Score assessment and appropriate investigations as per protocol were done. They were treated as per standardized treatment regimen taking in to consideration the general guidelines for treatment of hyponatremia.

The mean age of study population was 51.56 years. The maximum frequency of patients were in 31-50 years age group. There were 68.42% males and 31.58% were females which showed male preponderance. The mean serum sodium level was 123.74mmol/L. All the patients had presented with altered sensorium. After hyponatremia correction, 52 patients (91.2%) had improvement in MMSE score. In the present study, the treatment modality undertaken had an effect in improving cognition as well as managing hyponatremic condition. A better outcome to treatment and minimal or none complications related to correction of hyponatremia can be obtained by following a standardized regimen for treatment and keeping in mind the general guidelines of correction of hyponatremia. Clinicians need to be aware about the common occurrence of hyponatremia in acute neurological disorders and it being one of the reasons for altered sensorium.

# BIBLIOGRAPHY


1. Yeates KE, Singer M, Morton AR. Salt and water: a simple approach to hyponatremia CMAJ 2004; 170(3) : 365-9.

2. Callahan MA, Do HT, Caplan DW, Yoon-Flannery K. Economic impact of hyponatremia in hospitalized patients: a retrospective cohort study. Post grad Med 2009 Mar; 121(2):186-91.

3. Fried LF, and Palevsky PM . "Hyponatremia and Hypernatremia." Medical Clinics of North America 1997; 81: 585-609.

4. Kugler JP et al. "Hyponatremia and Hypernatremia in the Elderly" American family physician 2000 ; 61: 3623-30.

5. Anita R, Palani G, Sathiyasekaran BWC. Morbidity profile of elders in old age homes in chennai. Natl J Community Med 2012; 3(3) : 458-64.

6. Ayus JC, Arieff Al. Abnormalities of water metabolism in the elderly. Semin Nephrol 1996; 16: 277-88.

7. Fulop T Jr, Worum I, Csongor J, Foris G, Leovey A. Body composition in elderly people. l. Determination of body composition by multiisotope method and the elimination kinetics of these isotopes in healthy elderly subjects. Gerontology 1985; 31: 6-14.

8. Phillips PA, Rolls BJ, Ledingham JG, Forsling ML, Morton JJ, Crowe MJ et al. Reduced thirst after water deprivation in healthy elderly men. N Engl J Med 1984; 311:753-9.

9. Rowe JW, Shock NW, DeFronzo RA. The influence of age on the renal response to water deprivation in man. Nephron 1976; 17: 270-8.

10. Faun CM, Holmes C, Baylis PH. Water balance in elderly people: is there a deficiency of vasopressin? Age Ageing 1993; 22 :114-20.

11. McLachlan M, Wasserman P. Changes in sizes and distensibility of the aging kidney. Br J Radiol 1981;54:488-91.

12. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. J Am Geriatr Soc 1985; 33 :278-85.

13. Beck LH. Changes in renal function with aging. Clin Geriatr Med 1998; 14:199¬209.

14. Mehrotra A et.al. Sodium homeostasis in Elderly : Diagnosis and Management. Journal of Internal Medicine of India 1999; 2: 262 - 266.

15. Ohashi M et.al. Pharmacokinetics of synthetic and human ANP in man and effects on aging. Regul. Pept 1987; 19: 265.

16. Lindeman RD, Tobin RD , Shock NW. Longitudinal studies on the rate of decline in renal function with age. Am J Geriatr Soc 1985; 33: 278.

17. Berl T, Treating Hyponatremia : Damned it we do and damned if we donot. Kidney int; 37: 1006 -1018.

18. Chakrapani M, Shenoy D, Pillai A. Seasonal Variation in the Incidence of Hyponatremia. J Assoc Physicians India 2002;50:559-562.

19. Lath R. Hyponatremia in neurological diseases in ICU. Indian J Crit Care Med [serial online] 2005; 9:47-51.

20. Milionis HJ, Liamis GL, Elisaf MS. The hyponatremic patient: A systematic approach to laboratory diagnosis. Review. CMAJ 2002; 166: 1052-62.

21. Hoorn EJ, Halperin ML, Zietse R. Diagnostic approach to a patient with hyponatraemia: traditional versus physiology-based options. QJM 2005; 98: 529–540.

22. Elhassan EA, Schrier RW. Hyponatremia: diagnosis, complications, and management including V2 receptor antagonists. *Curr Opin Nephrol Hypertens* 2011; 20(2): 161-8.

23. Peters JP, Welt LG, Sims EA, Orloff J, Needham J. A salt-wasting syndrome associated with cerebral disease. Trans Assoc Am Physicians 1950 ;63: 57–64.

24. Palmer BF. Hyponatraemia in a neurosurgical patient: syndrome of inappropriate antidiuretic hormone secretion versus cerebral salt wasting. Nephrol Dial Transplant 2000;15:262–268.

25. Schwartz WB, Bennett W, Curelop S et al. A syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone. Am J Med 1957;23:529.

26. Harrigan MR. Cerebral salt wasting syndrome. Crit Care Clin 2001; 17:125–138.

27. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med 1998; 339:321–328.

28. Steele MK, Gardner DG, Xie PL et al. Interactions between ANP and ANG II in regulating blood pressure and sympathetic outflow. Am J Physiol 1991; 260: R1145–R1151.

29. Berendes E, Walter M, Cullen P et al. Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage. Lancet 1997; 349 :245–249.

30. Robertson GL, Athar S. The interaction of blood osmolality and blood volume in regulating plasma vasopressin in man. J Clin Endocrinol Metab 1976; 42 :613–620.

31. Albanese A, Hindmarsh P, Stanhope R. Management of hyponatraemia in patients with acute cerebral insults. Arch Dis Child 2001; 85: 246–251.

32. Coenraad MJ, Meinders AE, Taal JC et al. Hyponatremia in intracranial disorders. Neth J Med 2001; 58 :123–127.

33. Hasan D, Wijdicks EF, Vermeulen M. Hyponatremia is associated with cerebral ischemia in patients with aneurysmal subarachnoid hemorrhage. Ann Neurol 1990; 27 :106–108.

34. Wijdicks EFM. Acid-base disorder and sodium handling. In: The Clinical Practice of Critical Care Neurology. New York, NY. Oxford University Press, 2003:501–516.

35. Wijdicks EF, Vermeulen M, van Brummelen P et al. The effect of fludrocortisone acetate on plasma volume and natriuresis in patients with aneurysmal subarachnoid hemorrhage. Clin Neurol Neurosurg. 1988; 90:209–214.

36. Sayama T, Inamura T, Matsushima T et al. High incidence of hyponatremia in patients with ruptured anterior communicating artery aneurysms. Neurol Res. 2000;22:151–155.

37. Doczi T, Bende J, Huszka E et al. Syndrome of inappropriate secretion of antidiuretic hormone after subarachnoid hemorrhage. Neurosurgery 1981;9:394.

38. Wijdicks EF, Vermeulen M, Haaf JA et al. Volume depletion and natriuresis in patients with a ruptured intracranial aneurysm. Ann Neurol 1985;18:211–216.

39. Sviri GE, Feinsod M, Soustiel JF. Brain natriuretic peptide and cerebral vasospasm in subarachnoid hemorrhage. Clinical and TCD correlations. Stroke 2000 ;31:118–122.

40. Tomida M, Muraki M, Uemura K et al. Plasma concentrations of brain natriuretic peptide in patients with subarachnoid hemorrhage. Stroke 1998;29:1584–1587.

41. Wijdicks EF, Ropper AH, Hunnicutt EJ et al. Atrial natriuretic factor and salt wasting after aneurysmal subarachnoid hemorrhage. Stroke 1991;22:1519–1524.

42. Diringer MN, Wu KC, Verbalis JG et al. Hypervolemic therapy prevents volume contraction but not hyponatremia following subarachnoid hemorrhage. Ann Neurol 1992;31:543–550.

43. Ishikawa SE, Saito T, Kaneko K et al. Hyponatremia responsive to fludrocortisone acetate in elderly patients after head injury. Ann Intern Med 1987; 106: 187–191.

44. Steinbok P, Thompson GB. Metabolic disturbances after head injury: abnormalities of sodium and water balance with special reference to the effects of alcohol intoxication. Neurosurgery 1978; 3 :9–15.

45. Penney MD, Walters G, Wilkins DG. Hyponatraemia in patients with head injury. Intensive Care Med. 1979; 5: 23–26.

46. Vingerhoets F, de Tribolet N. Hyponatremia hypo-osmolarity in neurosurgical patients. “Appropriate secretion of ADH” and “cerebral salt wasting syndrome”. Acta Neurochir (Wien) 1988; 91:50–54.

47. Atchison JW, Wachendorf J, Haddock D et al. Hyponatremia associated cognitive impairment in traumatic brain injury. Brain Inj 1993; 7 :347–352.

48. Ke C, Poon WS, Ng HK et al. The impact of acute hyponatraemia on severe traumatic brain injury in rats. Acta Neurochir Suppl. 2000;76: 405–408.

49. Ropper AH, Wijdicks EFM, Truax BT eds. Guillain-Barre´ Syndrome. Philadelphia, PA: FA Davis Company; 1991.

50. Wijdicks EFM, Ropper AH, Hathanson JA. Atrial natriuretic factor and blood pressure fluctuations in Guillain-Barre´ Syndrome (letter). Ann Neurol 1990; 27 :337.

51. Penney MD, Murphy D, Walters G. Resetting of osmoreceptor response as cause of hyponatremia in acute idiopathic polyneuritis. Br Med J 1979; 2 :1474–1476.

52. Cooke CR, Latif KA, Huch KM, et al. Inappropriate antidiuresis and hyponatremia with suppressible vasopressin in Guillain-Barre´ syndrome. Am J Nephrol 1998; 18 :71–76.

53. Dodge PR, Swartz MN. Bacterial meningitis—a review of selected aspects. II. Special neurologic problems, postmeningitis complications and clinicopathological correlations. N Engl J Med 1965; 272: 954.

54. Karandanis D, Shulman JA. Recent survey of infectious meningitis in adults: review of laboratory findings in bacterial, tuberculous, and aseptic meningitis. South Med J 1976; 69: 449–457.

55. Feigin RD, Kaplan S. Inappropriate secretion of antidiuretic hormone in children with bacterial meningitis. Am J Clin Nutr 1977; 30 :1482– 1484.

56. Kaplan SL, Feigin RD. The syndrome of inappropriate secretion of antidiuretic hormone in children with bacterial meningitis. J Pediatr 1978; 92 :758–761.

57. M[swsl]oller K, Larsen FS, Bie P et al. The syndrome of inappropriate secretion of antidiuretic hormone and fluid restriction in meningitis—how strong is the evidence? Scand J Infect Dis 2001; 33 :13–26.

58. Ayus JC, Arieff AI. Pathogenesis and prevention of hyponatremic encephalopathy. Endocrinol. Metab. Clin. N. Am 1993; *22*: 425–446.

59. Ayus, JC, Achinger SG, Arieff A. Brain cell volume regulation in hyponatremia: Role of sex, age, vasopressin, and hypoxia. Am J Physiol Ren Physiol 2008; *295*: doi:10.1152/ajprenal.00502.2007.

60. Cordoba J, García R , Simón M. Hyponatremic and hepatic encephalopathies: Similarities, differences and coexistence. Metab Brain Dis 2010 ;*25* :73–80.

61. Chung HM, Kluge R, Schrier RW et al. Clinical assessment of extracellular fluid volume in hyponatremia. Am J Med 1987; 83:905–908.

62. Doczi T, Tarjanyi J, Huszka E et al. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) after head injury. Neurosurgery 1982; 10: 685–688.

63. Born JD, Hans P, Smitz S et al. Syndrome of inappropriate secretion of antidiuretic hormone after severe head injury. Surg Neurol 1985; 23: 383–387.

64. Xu et al. Hyponatremia and Cognitive Impairment in patients treated with peritoneal dialysis. Clin J Am Soc Nephrol 2015; doi: 10.2215/CJN.02240215.

65. Vaghasiya RP, DeVita MV, Panagopoulos G , Michelis MF. Hyponatremic patients demonstrate improved cognition after an increase in serum sodium. In Proceedings of the Poster Presented at NKF Annual Meeting, Orlando, FL, USA, 6–10 April, 2010.

66. Yumoto T et al. Prevalence, Risk Factors, and Short-term Consequences of Traumatic Brain Injury-associated Hyponatremia**.** Acta Med Okayama 2015; 69:213-218.

67. Gosch M et al. Hyponatremia in Geriatric Inhospital Patients: Effects on Results of a Comprehensive Geriatric Assessment. Gerontology 2012; 58 :430–440.

68. Gunathilake R et al. Mild hyponatremia is associated with impaired cognition and falls in community-dwelling older persons. J. Am. Geriatr Soc 2013 ;61 : 1838–1839.

69. Ahluwalia et al. Correction of Hyponatremia Improves Cognition, Quality of Life, and Brain Edema in Cirrhosis. J Hepatol 2015 ; 62(1): 75–82.

70. Saleem et al. Hyponatremia in stroke. Ann Indian Acad Neurol 2014; 17(1): 55–57.

# ANNEXURE I

# PROFORMA

OP/IP No.: Date:

Serial No.:

Name: Age: Gender:

Occupation:

Address

Chief Complaints:

Past history:

Family history:

Personal History:

General Physical Examination:

PR: BP: HEIGHT:

WEIGHT:

Pallor: Icterus: Cyanosis:

Clubbing: Lymphdenopathy: Oedema

Systemic examination:

CVS:

RS:

PA:

CNS:

INVESTIGATIONS:

CBC

BLOOD UREA

SERUM CREATININE

RBS

SERUM SODIUM

SERUM POTASSIUM

Thyroid function tests

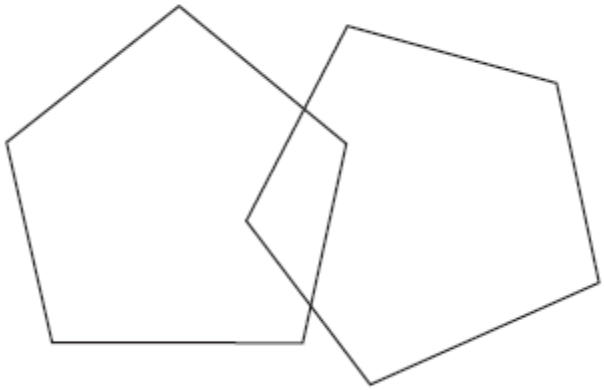
Liver function tests

CT BRAIN/MRI BRAIN-

PROVISIONAL DIAGNOSIS:

**STANDARDIZED MINI-MENTAL STATE EXAMINATION (SMMSE)**

| QUESTION | | TIME ALLOWED | SCORE |
|---|---|---|---|
| 1 | a. ***What year is this?*** | 10 seconds | /1 |
| b. ***Which season is this?*** | | 10 seconds | /1 |
| c. ***What month is this?*** | | 10 seconds | /1 |
| d. ***What is today's date?*** | | 10 seconds | /1 |
| e. ***What day of the week is this?*** | | 10 seconds | /1 |
| 2 | a. ***What country are we in?*** | 10 seconds | /1 |
| b. ***What province are we in?*** | | 10 seconds | /1 |
| c. ***What city/town are we in?*** | | 10 seconds | /1 |
| d. ***IN HOME – What is the street address of this house?*** ***IN FACILITY – What is the name of this building?*** | | 10 seconds | / 1 |
| e. ***IN HOME – What room are we in? IN FACILITY – What floor are we on?*** | | 10 seconds | / 1 |
| 3 | **SAY:** ***I am going to name three objects. When I am finished, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes.*** Say the following words slowly at 1-second intervals **- ball/ car/ man** | 20 seconds | /3 |
| 4 | ***Spell the word WORLD. Now spell it backwards.*** | 30 seconds | /5 |
| 5 | ***Now what were the three objects I asked you to remember?*** | 10 seconds | /3 |
| 6 | **SHOW** wristwatch. **ASK:** ***What is this called?*** | 10 seconds | /1 |
| 7 | **SHOW** pencil. **ASK**: ***What is this called?*** | 10 seconds | /1 |
| 8 | **SAY:** ***I would like you to repeat this phrase after me: No ifs, ands or buts.*** | 10 seconds | /1 |
| 9 | **SAY:** ***Read the words on the page and then do what it says.*** Then hand the person the sheet with CLOSE YOUR EYES on it. If the subject reads and does not | 10 seconds | /1 |

| | | | |
|---|---|---|---|
| | close their eyes, repeat up to three times. Score only if subject closes eyes | | |
| 10 | **HAND** the person a pencil and paper. **SAY:** ***Write any complete sentence on that piece of paper.*** (Note: The sentence must make sense. Ignore spelling errors) | 30 seconds | /1 |
| 11 | **PLACE** design, eraser and pencil in front of the person. **SAY**: ***Copy this design please.***<br>  <br>Allow multiple tries. Wait until person is finished and hands it back. Score only for correctly copied diagram with a 4-sided figure between two 5-sided figures. | 1 minute | /1 |
| 12 | **ASK** the person if he is right or left-handed. Take a piece of paper and hold it up in front of the person. **SAY**: ***Take this paper in your right/left hand*** (whichever is non-dominant), ***fold the paper in half once with both hands and put the paper down on the floor*** . Score 1 point for each instruction executed correctly.<br>Takes paper correctly in hand<br>Folds it in half<br>Puts it on the floor | 30 seconds | /1<br>/1<br>/1 |
| | **TOTAL TEST SCORE** | **/30** | |

# ANNEXURE II

# PATIENT INFORMATION SHEET

**Study Title: HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL – A CROSS-SECTIONAL STUDY**

**Study site:** R.L.Jalappa hospital, Tamaka, Kolar

**Aim:** 1. To assess the cognitive functions of patients with hyponatremia in acute neurological disorders by MMSE score.
2. To assess the cognitive functions by MMSE score after correction of hyponatremia.
3. To determine the correlation between cognitive functions and sodium levels among patients with neurological disorders

Hyponatremia is a common finding in acute brain disease. Early symptoms of headache, muscular weakness, nausea, lethargy, ataxia, and confusion can progress to seizures, irreversible neurological damage, coma and death, if unrecognized and untreated. One of the symptoms often associated with hyponatremia is cognitive impairment, particularly in elderly populations. Hence, early diagnosis and correction of hyponatremia is required for better improvement of cognitive functions in acute neurological diseases.

Complete history will be taken and investigations which will be done are CT Scan brain/ MRI brain, complete hemogram ,renal function tests, ECG. This information is intended to give you the general background of the study. Please read the following information and discuss with your family members. If you agree to participate in this, we will collect information from you or a person responsible for you or both. This information collected will be used only for poster presentation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. There is no compulsion to agree for this. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

# ANNEXURE III

# CONSENT FORM

**Study Title**: **HYPONATREMIA IN ACUTE NEUROLOGICAL DISORDERS AMONG ADULTS IN A TERTIARY CARE HOSPITAL – A CROSS-SECTIONAL STUDY**

**Chief Researcher/ PG guide's name:** DR. LAKSHMAIAH.V

**Principal investigator:** DR. HARSHITA. G

Hyponatremia in acute neurological diseases have impact on cognitive functions. Hence, early diagnosis and correction of hyponatremia is required for better improvement of cognitive functions in acute neurological diseases.If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. We will collect the treatment and relevant details from your hospital record. This information collected will be used for only dissertation and publication. This study has been reviewed by the institutional ethical committee. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

I understand that I remain free to withdraw from the study at any time and this will not change my future care. I have read or have been read to me and understood the purpose of the study, the procedure that will be used, the risk and benefits associated with my involvement in the study and the nature of information that will be collected and disclosed during the study. I have had the opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction. I,the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information for dissertation.

Subject name (Parents / Guardians name)

DATE:

SIGNATURE /THUMB IMPRESSION

Name and signature of person taking consent

# ANNEXURE IV

# KEY TO MASTER CHART

1. S.NO : Serial number
2. H.NO : Hospital number
3. AGE (YRS) : age in years
4. SEX: M-MALE F-FEMALE
5. ALTERED SENSORIUM: P-PRESENT A-ABSENT
6. PAST HISTORY:

   Diabetes Mellitus- DM

   Hypertension- HTN

   No comorbidities- N
7. PR- Pulse Rate in beats per minute
8. BP- Blood Pressure in mm/Hg
9. CT Brain- Computed Tomography of Brain
10. MRI Brain- Magnetic Resonance Imaging of Brain
11. Na - Serum Sodium in meq/L
12. K- Serum Potassium in meq/L
13. BU- Blood urea in mg/dl
14. SC- serum creatinine in mg/dl
15. LFT- Liver Function Tests N- Normal
16. TFT- Thyroid Function Tests N-Normal
17. MMSE – Mini Mental State Examination

# ANNEXURE V

# MASTER CHART

| S.No | H.No | Age | Sex | Altered Sensorium | Past History | Personal History | PR | BP | CT Brain/MRI Brain | Na | K | BU | SC | LFT | TFT | MMSE on Day 1 | MMSE on Day 3 | MMSE on Day 5 | Na After Correction |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 118340 | 45 | F | Y | DM | N | 78 | 110/80 | RIGHT MCA INFARCT | 127 | 3.8 | 28 | 0.7 | N | N | 20 | 23 | 27 | 133 |
| 2 | 181059 | 55 | M | Y | N | ALCOHOLIC | 110 | 130/70 | N / (PYOGENIC MENINGITIS) | 130 | 3.6 | 34 | 1.1 | N | N | 22 | 24 | 27 | 140 |
| 3 | 180944 | 56 | F | Y | HTN | N | 90 | 190/110 | RIGHT THALAMIC ICH | 127 | 4.2 | 35 | 0.8 | N | N | 22 | 26 | 28 | 130 |
| 4 | 171627 | 75 | M | Y | DM | SMOKER ALCOHOLIC | 85 | 110/70 | ACUTE INFARCT IN RIGHT PARIETAL REGION | 115 | 4.6 | 30 | 0.5 | N | N | 16 | 22 | 24 | 130 |
| 5 | 181915 | 75 | M | Y | DM | SMOKER | 80 | 120/60 | RIGHT MCA INFARCT | 118 | 4.8 | 39 | 1.2 | N | N | 17 | 22 | 25 | 132 |
| 6 | 180795 | 25 | M | Y | N | N | 78 | 110/70 | N( TB MENINGITIS) | 131 | 4.5 | 32 | 0.8 | N | N | 21 | 25 | 26 | 135 |
| 7 | 180922 | 25 | M | Y | N | N | 89 | 110/80 | SDH IN LEFT OCCIPITAL AND PARIETAL REGION | 128 | 4.2 | 34 | 0.6 | N | N | 23 | 26 | 27 | 139 |
| 8 | 180403 | 49 | M | Y | N | N | 86 | 130/70 | INTRAPARENCHYMAL BLEED IN RIGHT PARIETO OCCIPITAL REGION | 126 | 4.7 | 30 | 0.9 | N | N | 23 | 25 | 26 | 135 |
| 9 | 179435 | 40 | F | Y | N | N | 89 | 130/90 | N (TB MENINGITIS) | 130 | 4.5 | 34 | 4.2 | N | N | 23 | 25 | 27 | 136 |
| 10 | 175141 | 48 | M | Y | N | ALCOHOLIC | 96 | 130/90 | RIGHT TEMPOROPARIETAL EDH,SDH WITH LEFT TEMPEROPARIETAL SDH | 120 | 4 | 30 | 1 | N | N | 16 | 22 | 25 | 132 |
| 11 | 173683 | 40 | M | Y | N | ALCOHOLIC | 78 | 190/110 | EXTRA AXIAL HEMORRHAGE IN RIGHT PARIETOTEMOPORAL REGION | 128 | 3.9 | 28 | 0.9 | N | N | 23 | 26 | 28 | 135 |
| 12 | 174117 | 38 | M | Y | N | N | 89 | 180/120 | HEMORRHAGIC INFARCT IN POSTERIIOR FOSSA | 120 | 3 | 36 | 1.2 | N | N | 17 | 23 | 26 | 132 |
| 13 | 156536 | 22 | M | Y | N | N | 90 | 100/70 | LEFT SIDE INTRAPARENCHYMAL BLEED | 130 | 4.2 | 30 | 0.9 | N | N | 24 | 26 | 28 | 137 |
| 14 | 157148 | 23 | M | Y | N | N | 85 | 110/70 | SDH IN LEFT PARIETAL REGION. | 127 | 4 | 38 | 0.8 | N | N | 21 | 24 | 26 | 138 |
| 15 | 173091 | 31 | M | Y | N | N | 89 | 120/90 | SDH IN RIGHT FRONTOPARIETAL REGION | 125 | 4 | 30 | 1 | N | N | 19 | 23 | 25 | 135 |

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 180204 | 67 | M | Y | N | SMOKER | 90 | 110/90 | ACUTE INFARCT IN LEFT TEMPOROPARIETAL CORTICAL REGION | 118 | 5 | 28 | 0.6 | N | N | 17 | 22 | 24 | 130 |
| 17 | 180960 | 68 | M | Y | N | N | 89 | 140/80 | N(TB MENINGITIS) | 110 | 4 | 38 | 0.9 | N | N | 15 | 19 | 24 | 135 |
| 18 | 180400 | 50 | F | Y | HTN | N | 86 | 190/100 | RIGHT BASAL GANGLIA INFARCT | 127 | 4.7 | 39 | 0.7 | N | N | 24 | 24 | 25 | 130 |
| 19 | 179467 | 70 | F | Y | N | N | 89 | 130/80 | ACUTE INFARCT IN LEFT PARIETAL CORTICAL/SUBCORTICAL REGION | 122 | 4.9 | 89 | 1.9 | N | N | 20 | 24 | 26 | 137 |
| 20 | 175130 | 65 | M | Y | N | N | 90 | 130/80 | LEFT TEMPOROPARIETAL INFARCT | 120 | 4 | 30 | 1 | N | N | 18 | 21 | 25 | 133 |
| 21 | 167564 | 70 | M | Y | HTN | N | 87 | 180/100 | LEFT BASAL GANGLIA INFARCT | 127 | 3.7 | 35 | 1.2 | N | N | 23 | 26 | 27 | 134 |
| 22 | 217376 | 24 | M | Y | N | N | 80 | 110/70 | SDH IN LEFT PARIETOTEMPORAL REGION | 126 | 4.2 | 20 | 0.6 | N | N | 20 | 23 | 27 | 130 |
| 23 | 218419 | 55 | M | Y | DM | SMOKER | 94 | 180/110 | SAH IN B/L FRONTOPARIETAL REGION | 126 | 4.7 | 28 | 0.9 | N | N | 18 | 24 | 28 | 132 |
| 24 | 173683 | 40 | M | Y | N | ALCOHOLIC | 76 | 160/110 | SDH IN RIGHT PARIETOTEMPORAL REGION | 130 | 4.2 | 35 | 1.1 | N | N | 22 | 25 | 27 | 135 |
| 25 | 241032 | 62 | M | Y | HTN | SMOKER | 73 | 120/90 | INTRAVENTRICULAR HEMORRHAGE IN B/L LATERAL VENTRICLES | 114 | 4.8 | 36 | 0.9 | N | N | 17 | 24 | 27 | 135 |
| 26 | 241419 | 40 | M | Y | N | N | 85 | 110/80 | N( VIRAL ENCEPHALITIS) | 123 | 4.6 | 37 | 1.2 | N | N | 21 | 24 | 28 | 132 |
| 27 | 219372 | 22 | F | Y | N | N | 90 | 130/70 | N (TB MENINGITIS) | 121 | 3.8 | 24 | 1 | N | N | 19 | 24 | 27 | 131 |
| 28 | 236094 | 60 | M | Y | HTN | N | 75 | 110/70 | ACUTE INFARCT IN RIGHT TEMPEROPARIETAL REGION | 115 | 3.5 | 37 | 1.1 | N | N | 21 | 25 | 28 | 132 |
| 29 | 238061 | 95 | F | Y | DM | N | 120 | 120/90 | VIRAL ENCEPHALITIS | 121 | 4.4 | 39 | 0.8 | N | N | 22 | 26 | 29 | 135 |
| 30 | 237999 | 65 | F | Y | HTN | N | 90 | 140/110 | HEMORRHAGIC INFARCT IN LEFT FRONTOPARIETAL REGION | 126 | 4.8 | 37 | 0.9 | N | N | 21 | 23 | 28 | 137 |
| 31 | 236088 | 55 | F | Y | N | N | 80 | 110/80 | N( VIRAL MENINGITIS) | 127 | 4.3 | 26 | 0.8 | N | N | 23 | 23 | 25 | 130 |
| 32 | 235566 | 42 | F | Y | N | N | 110 | 140/70 | N( VIRAL MENINGOENCEPHALITIS) | 126 | 4.9 | 38 | 0.7 | N | N | 20 | 23 | 28 | 132 |
| 33 | 229338 | 28 | F | Y | N | N | 116 | 100/70 | N(TB MENINGITIS) | 122 | 4.2 | 35 | 1.2 | N | N | 21 | 25 | 27 | 135 |
| 34 | 243916 | 38 | M | Y | N | N | 123 | 120/80 | N(VIRAL MENINGITIS) | 121 | 4.8 | 35 | 0.77 | N | N | 18 | 23 | 27 | 130 |
| 35 | 223683 | 85 | M | Y | HTN | SMOKER | 87 | 110/70 | ACUTE INFARCT IN LEFT MCA TERRITORY | 122 | 4.5 | 36 | 1.1 | N | N | 20 | 20 | 20 | 124 |
| 36 | 238031 | 19 | M | Y | N | N | 96 | 130/80 | N(PYOGENIC MENINGITIS) | 126 | 3.9 | 29 | 0.5 | N | N | 21 | 25 | 29 | 133 |
| 37 | 227432 | 42 | M | Y | N | N | 101 | 110/70 | N (VIRAL ENCEPALITIS) | 126 | 3.9 | 39 | 1.2 | N | N | 23 | 25 | 28 | 134 |

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 38 | 216293 | 21 | F | Y | N | N | 109 | 120/70 | N (VIRAL ENCEPHALITIS) | 130 | 4.9 | 38 | 0.5 | N | N | 23 | 26 | 29 | 134 |
| 39 | 222511 | 60 | M | Y | HTN | SMOKER ALCOHOLIC | 96 | 140/70 | HEMORRHAGIC INFARCT IN RIGHT FRONTOPARIETAL REGION | 126 | 4.7 | 38 | 0.7 | N | N | 19 | 19 | 19 | 127 |
| 40 | 223750 | 89 | M | Y | N | N | 87 | 140/80 | SDH IN RIGHT PARIENTAL REGION | 119 | 4.6 | 26 | 0.8 | N | N | 17 | 17 | 17 | 120 |
| 41 | 216256 | 65 | M | Y | DM | N | 92 | 140/90 | N( VIRAL ENCEPHALITIS) | 126 | 4.2 | 38 | 0.9 | N | N | 21 | 23 | 28 | 135 |
| 42 | 219605 | 47 | F | Y | N | N | 79 | 100/80 | N(VIRAL MENINGITIS) | 126 | 4.7 | 37 | 1 | N | N | 20 | 26 | 27 | 134 |
| 43 | 222118 | 70 | F | Y | HTN | N | 79 | 150/90 | ACUTE INFARCT IN RIGHT CAPSULOGANGLIONIC REGION | 119 | 4.6 | 36 | 0.77 | N | N | 16 | 16 | 16 | 120 |
| 44 | 242240 | 58 | M | Y | HTN | SMOKER | 89 | 110/80 | ACUTE INFARCT IN LEFT MCA TERRITORY | 126 | 4.7 | 38 | 1.2 | N | N | 18 | 23 | 27 | 130 |
| 45 | 320332 | 65 | M | Y | N | N | 75 | 100/70 | N( VIRAL ENCHEPHALITIS) | 127 | 4.8 | 24 | 1.3 | N | N | 21 | 23 | 25 | 136 |
| 46 | 334450 | 57 | F | Y | HTN | N | 76 | 110/80 | ACUTE INFARCT IN RIGHT PARIETAL REGION | 126 | 5 | 26 | 1 | N | N | 23 | 25 | 28 | 135 |
| 47 | 321345 | 56 | M | Y | DM | N | 113 | 110/90 | N (VIRAL MENINGITIS) | 121 | 3.7 | 24 | 0.8 | N | N | 25 | 26 | 28 | 139 |
| 48 | 340413 | 75 | M | Y | HTN | SMOKER | 79 | 150/100 | ACUTE INFARCT IN LEFT MCA TERRITORY | 120 | 4.5 | 27 | 1.1 | N | N | 23 | 26 | 28 | 130 |
| 49 | 330996 | 56 | F | Y | DM | N | 87 | 110/86 | N(VIRAL ENCEPHALITIS) | 124 | 3.6 | 29 | 1.3 | N | N | 24 | 26 | 28 | 134 |
| 50 | 342667 | 45 | M | Y | N | N | 89 | 130/90 | N(VIRAL MENINGOENCEPHALITIS) | 119 | 3.6 | 37 | 1.1 | N | N | 19 | 23 | 27 | 135 |
| 51 | 341660 | 40 | M | Y | HTN | SMOKER | 92 | 210/120 | ACUTE INFARCT IN RIGHT INTERNAL CAPSULE | 130 | 3.9 | 29 | 0.8 | N | N | 24 | 27 | 29 | 138 |
| 52 | 340004 | 39 | M | Y | N | ALCOHOLIC | 98 | 160/100 | ACUTE INFARCT IN LEFT CEREBELLAR HEMISPHERE | 125 | 3.5 | 39 | 0.6 | N | N | 23 | 26 | 27 | 135 |
| 53 | 328827 | 45 | F | Y | HTN, DM | N | 86 | 150/110 | ACUTE INFARCT IN RIGHT MCA TERRITORY | 119 | 4.5 | 40 | 1.2 | N | N | 19 | 24 | 27 | 130 |
| 54 | 314988 | 32 | F | Y | N | N | 110 | 12070 | N(VIRAL MENINGITIS ) | 128 | 4.7 | 39 | 1.1 | N | N | 21 | 25 | 29 | 136 |
| 55 | 339505 | 50 | M | Y | HTN | SMOKER | 98 | 170/120 | ACUTE INFARCT IN RIGHT CEREBELLAR HEMISPHERE | 127 | 3.7 | 30 | 1.4 | N | N | 20 | 23 | 27 | 133 |
| 56 | 332422 | 75 | M | Y | DM | ALCOHOLIC | 105 | 160/100 | N(VIRAL MENINGOENCEPHALITIS) | 120 | 3.5 | 45 | 1.5 | N | N | 18 | 22 | 25 | 130 |
| 57 | 324444 | 85 | M | Y | HTN | SMOKER | 65 | 180/120 | SDH IN RIGHT FRONTOPARIETAL REGION | 117 | 3.6 | 40 | 1.1 | N | N | 21 | 21 | 21 | 119 |