A DISSERTATION

ON

"PROSPECTIVE STUDY OF HYPONATREMIA IN DECOMPENSATED CHRONIC LIVER DISEASE AND ITS CORRELATION WITH SEVERITY''

Submitted to

THE TAMILNADU DR. M. G. R UNIVERSITY
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for the award of

M.D DEGREE IN GENERAL MEDICINE
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Ethical committee Meeting held on 30.07.2014 at 12 noon in the Dean's Chamber, Government Mohan kumaramangalam Medical College Hospital, Salem 01, The following members attended the meeting.

MEMBERS.

1. Dr.N. MOHAN MS., FICS., FAIS., FMMC.,Dean, Member secretary ECIRB
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8.	**Dr. Moogaambiga S** Final year MD (GM) Post graduate student, GMKMCH.Salem-30	Prospective study of hyponatremia in decompensated chronic liver disease and its correlation with severity	**Dr V.Sundaravel MD.,** Professor of General Medicine	**Approved**

The Ethical Committee examined the studies in detail and is pleased to accord Ethical Committee approval for the above Post Graduate of this college to carry out the studies with the following conditions.

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2. She should inform the institutional Ethical committee in case of any change of study or procedure site.
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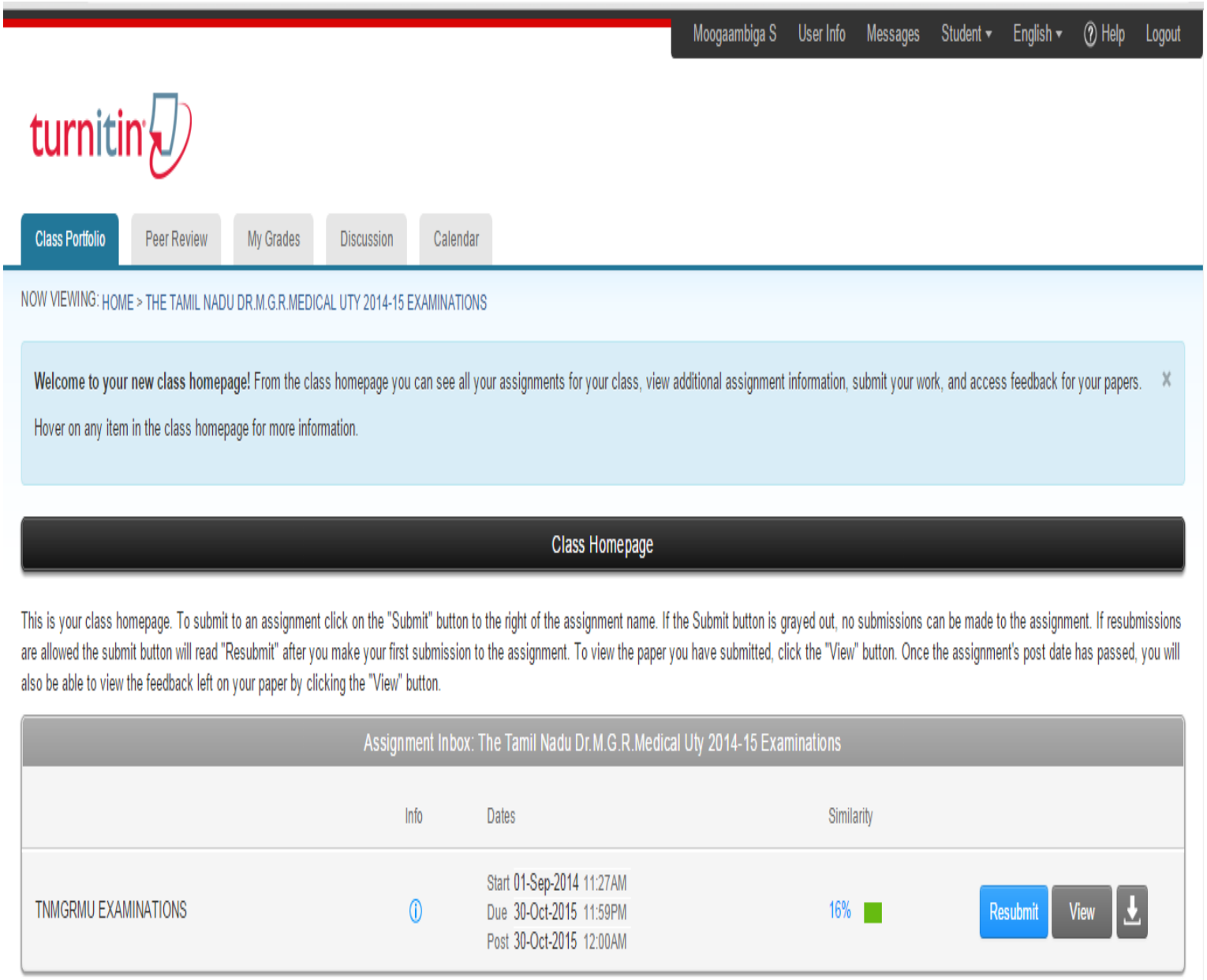
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LIST OF ABBREVATIONS

ECF	Extracellular fluid
ICF	Intracellular fluid
ADH	Anti-diuretic hormone
ACTH	Adrenocorticotropic hormone
cAMP	Cyclic adenosine monophosphate
Na^+	Sodium
Cl^-	Chloride
CNS	Central nervous system
SIADH	Syndrome of inappropriate antidiuretic hormone
CHF	Congestive heart failure
AVP	Arginine vasopressin
SSRI	Selective serotonin reuptake inhibitors
ODS	Osmotic demyelination syndrome
HVPG	Hepatic venous pressure gradient
SBP	Spontaneous bacterial peritonitis
HRS	Hepatorenal syndrome
NSAIDs	Non-steroidal antiflammatory drugs
CPS	Child pugh score
MELD	Model for endstage liver disease
INR	International normalised ratio
TIPSS	Transjugular intrahepatic portosystemic shunt
GFR	Glomerular filtration rate
SD	Standard deviation
PHT	Portal hypertension
HE	Hepatic encephalopathy
MRI	Magnetic resonance imaging

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INTRODUCTION

Sodium is the predominant cation of the extracellular compartment. It is the major contributing electrolye to serum osmolality. Hyponatremia is serum sodium<135meq/L. The prevalence of hyponatremia in general population is 4-7% whereas upto 30-40% of hospitalised patients have some degree of hyponatremia making it the most common electrolyte disorder(1,2). Since clinically symptomatic hyponatremia is rare, hyponatremia is frequently underdiagnosed.

In patients with cirrhosis hyponatremia is common due to disproportionate fluid retention in excess of sodium retention. Patients are hypervolemic but with reduced intravascular volume. Since hyponatremia is the outcome of compensatory mechanisms, the degree of hyponatremia can estimate the severity of underlying pathology. Recent studies show that sodium levels before liver transplantation predicted the outcome and development of neurological complications after transplant. Studying the importance of hyponatremia in cirrhosis can give an insight into usefulness of treating hyponatremia in cirrhotic patients in future. Hence we conducted this study in 100 cirrhosis patients in our hospital to find the prevalence of hyponatremia and its association with complications.

AIMS AND OBJECTIVES:

1. To study the prevalence of hyponatremia in cirrhotic patients
2. To study the association between hyponatremia and complications of cirrhosis and its correlation with severity of complications.

REVIEW OF LITERATURE

The major constituent of human body is water, which contributes to about 50% of body weight of average adult woman & 60% in men. Since fat contains less water, an obese person tends to have less amount of body water. About 55 – 75% of total body water is intracellular and 25 – 45% is extracellular. The ECF is further subdivided into Intravascular (plasma) and extravascular (interstitial) spaces in the ratio of 1:3(3).

The distribution of fluid across these spaces is determined by starling forces. According to Starling's hypothesis, the fluid movement across capillary is determined by the hydrostatic and osmotic pressure differences between intravascular and extravascular compartment.

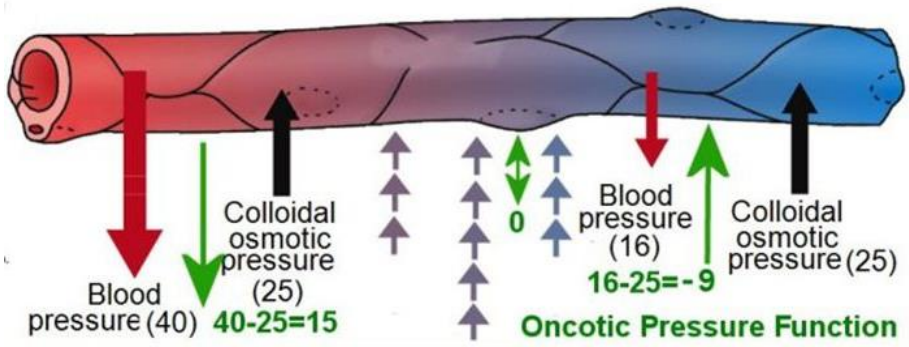


Figure1 – Starling hypothesis

The plasma ultrafiltrate moves into the extravascular space when the transcapillary hydraulic pressure gradient exceeds the oncotic pressure gradient. The return of fluid into the intravascular compartment occurs via lymphatics(4).

Osmolality of a fluid is defined as the solute or particle concentration of a fluid. It is expressed as milliosmoles per kg of water.

The major intacellular anions are phosphate, sulphate and protein and extracellular anions are chloride and bicarbonate. The major intracellular cation is potassium and extracellular cation is sodium.

Table 1 –Composition of electrolytes in body fluids(5)

Electrolytes(mEq/L)	**ECF**	**ICF**
Sodium	142	10
Potassium	4.3	140
Chloride	104	2
Bicarbonate	24	6

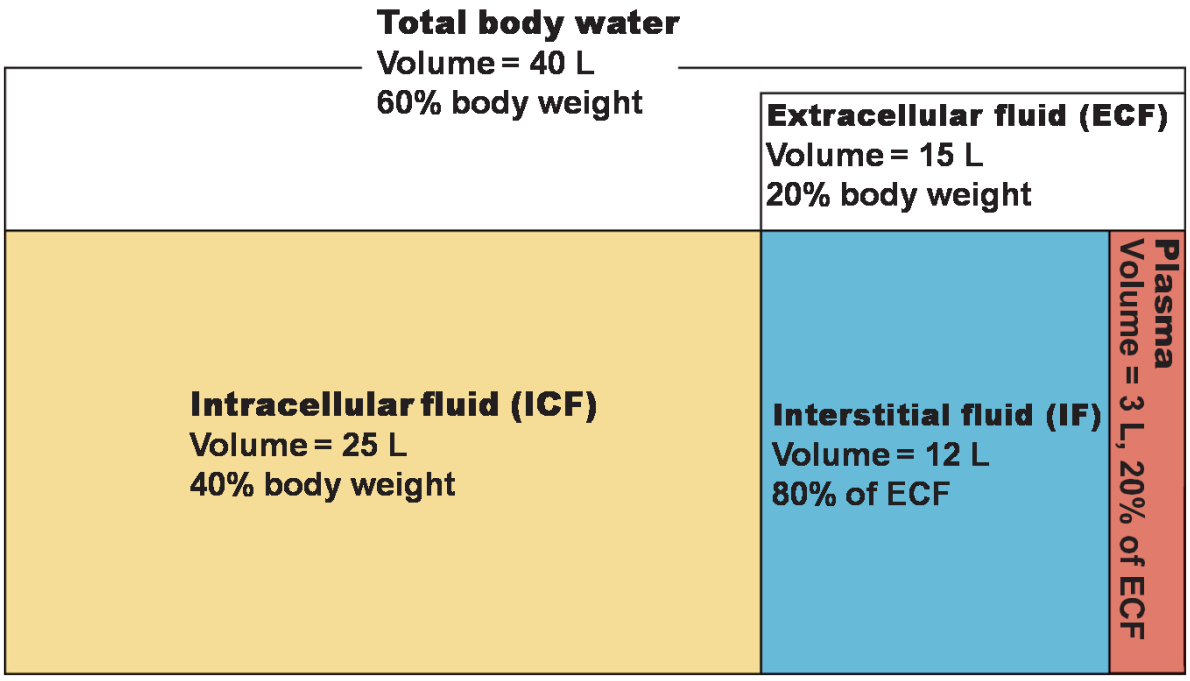


Figure 2 – Fluid composition of the body

REGULATION OF WATER BALANCE:

The human body fluid osmolality ranges normally between 280 and 295 mosm/kg. It is maintained within this narrow range by the following mechanisms(6),

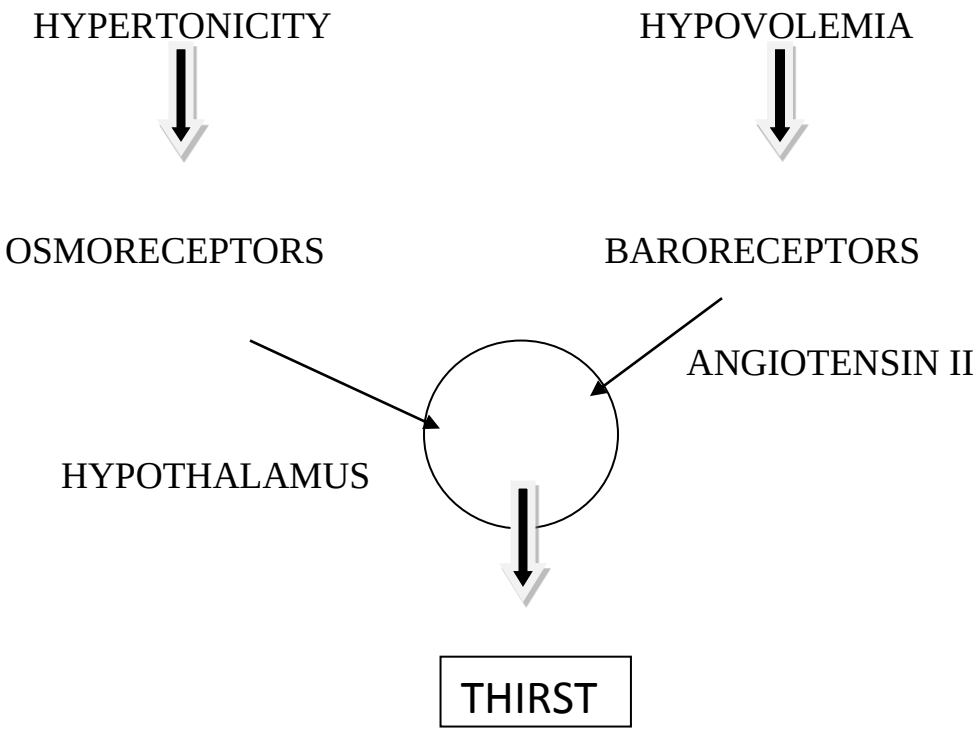
1). Thirst mechanism

2). Vasopressin secretion

3). Renal handling of sodium & water

1). THIRST MECHANISM:

Drinking or fluid intake is regulated by plasma osmolality and ECF volume. Water intake is increased by increase in effective osmotic pressure of the plasma, by decrease in ECF volume , by psychological and other factors.



Osmolality acts via osmoreceptors, receptors that sense the osmolality of the body fluids that are located in the anterior hypothalamus.

Decrease in ECF volume also stimulates thirst by a pathway independent of that mediating thirst in response to increase in plasma osmolality. The effect of hypovolemia on thirst is mediated in part via the renin - angiotensin system. Hypovolemia stimulates renin angiotensin axis. The Angiotensin II acts on the

subfornical organ in the diencephalon , to stimulate the neural areas that regulate thirst. There is also evidence suggesting that it acts on organum vasculosum of the lamina terminalis (OVLT) as well. These areas are located outside the blood brain barrier and highly permeable.

Baroreceptors in the heart & blood vessels also have a role on thirst control. When patients are in altered sensorium or when the disease process damages the thirst centre directly, fluid intake is reduced and this results in hypovolemia.

2). ROLE OF VASOPRESSIN :

Vasopressin or anti- diuretic hormone (ADH) is synthesized in the cell bodies of the magnocellular neurons in the supraoptic and paraventricular nuclei and transported down the axons of these neurons to their endings in the posterior lobe, where they are secreted in response to electrical activity in the nerve endings.

It is synthesized as precursor molecule, Prepro pressophysin, contains a 19 – amino acid and residue leader sequence followed by arginine vasopressin, neurophysin and a glycopeptide. Prepro pressophysin is synthesized in the ribosomes of cell bodies of neurons. The secretory granules are called herring bodies. They are secreted into circulation by means of exocytosis involving calcium.

VASOPRESSIN RECEPTORS :

There are three kinds of vasopressin receptors : V_{1A} , V_{1B} ,V_2 . V_{1a} recptors mediate vasoconstriction, myocardial hypertrophy. It also plays a role in glycogenolysis. V_{1b} receptors regulate the release of ACTH in the anterior pituitary. V_2 receptors mediate water reabsorption in the kidneys. They are also involved in release of von-willebrand factor(9).

ACTION OF VASOPRESSIN :

ADH acts on the V_2 receptors in the basolateral membrane of cells in the medullary and cortical collecting tubules . Normally apical membrane is impermeable to water in the absence of ADH , but basolateral membrane is freely permeable . Simple diffusion of water is augmented by the presence of water channels called AQUAPORINS .

Aquaporins 1,2,3 are present in the kidney , aquaporin 4 is found in the brain and aquaporin 5 in the salivary glands. The vasopressin responsive water channel in the collecting duct is Aquaporin- 2. The action of ADH at V_2 receptors activates Adenyl cyclase and cAMP is formed. This causes translocation of aquaporin-2 containing vesicles to the apical membrane. Thereby the apical membrane is rendered permeable to water. (figure 3)

In the absence of ADH , the apical membranes of the cells in the collecting tubules are impermeable to water. Large volumes of hypotonic urine will be produced. In the presence of ADH, water is reabsorbed in the collecting duct. The urine becomes hypertonic and its volume decreases. This results in increased retention of water compared to solutes which causes lowering of osmolarity. In the presence of ADH i.e, at maximum levels, less than 1% of the filtered water is excreted.

V_{1A} receptors mediate the vasoconstrictor effect of ADH. But large doses are required to increase blood pressure as it also acts on the brain to decrease cardiac output. V_{1A} receptors are also found in liver, where ADH causes glycogenolysis. The V_{1B} receptors are unique to pituitary, where they regulate ACTH secretion from the corticotrophs.

METABOLISM :

The half life of AVP in the circulation is only 30 minutes ,thus changes in the ECF volume or circulating osmolality can rapidly affect water metabolism .

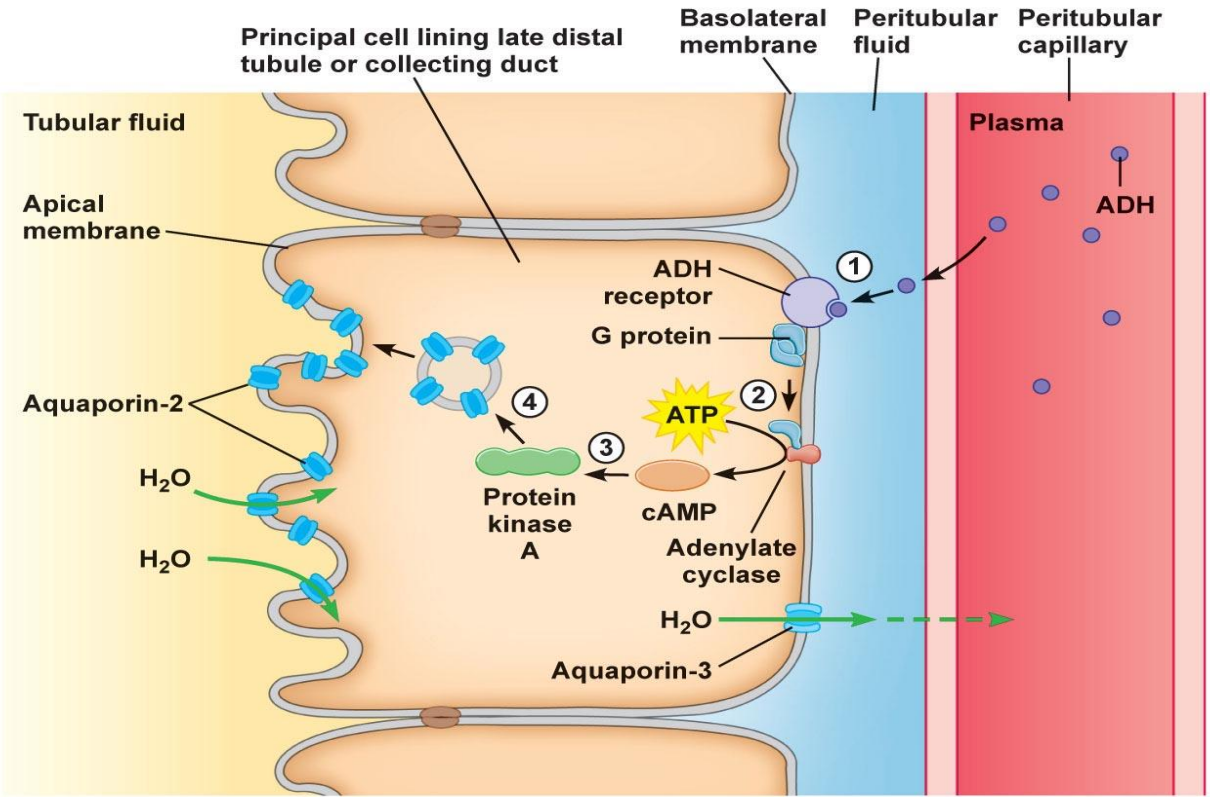


Figure 3 – Mechanism of action of vasopressin

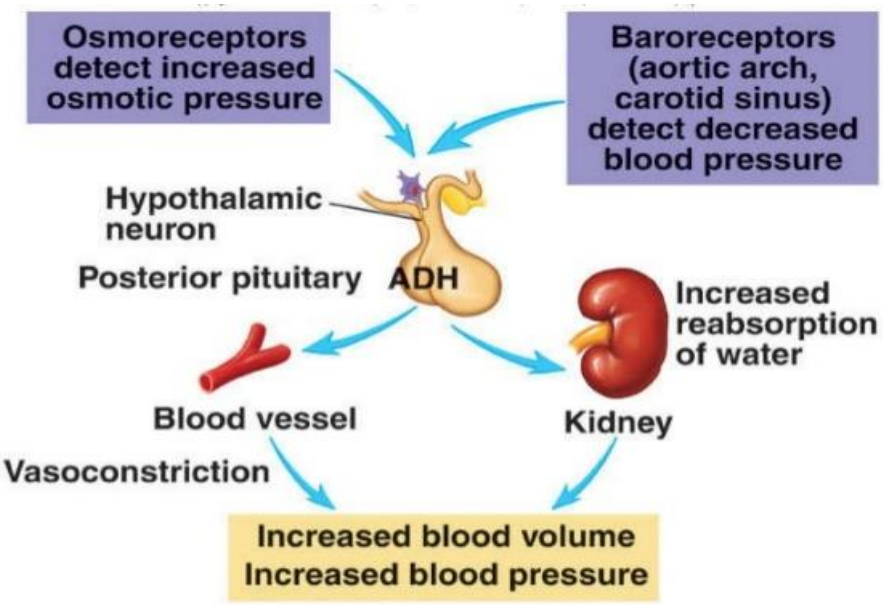


Figure 4 – Regulation of vasopressin secretion

REGULATION OF VASOPRESSIN SECRETION:

OSMOTIC STIMULI:

Vasopressin stimulation occurs when the plasma osmolality is more than 285 mosm/kg . Further,there is a linear relationship between osmolality and circulating vasopressin. Significant changes occur even the osmolality is changed as little as 1% . Vasopressin secretion is controlled by a delicate feedback mechanism (figure 4)that aims to maintain plasma osmolality in physiological range(10).

VOLUME EFFECTS:

The amount of vasopressin secretion is inversely related to the rate of discharge in afferents from stretch receptors of vascular system . The increase in vasopressin secretion in response to decrease in effective arterial pressure is exponential rather than linear .

There are also non-osmotic stimuli such as pain,emotion and exercise that cause increase in vasopressin secretion. Intake of alcohol causes decreases vasopressin secretion. Drugs like clofibrate, carbamazepine cause increased secretion of vasopressin.

3)RENAL HANDLING OF WATER AND SODIUM:

Normally ,180 L of fluid is filtered through the glomeruli each day , while the average daily urine volume is 1 L.

In the proximal tubule, 60-70% of water moves by passive transport along osmotic gradient due to active transport of solutes and isotonicity is maintained. The descending limb of loop of Henle is permeable to water, but the ascending limb is impermeable. The fluid becomes hypertonic in the descending limb and hypotonic to plasma in the ascending limb. $Na^{+}K^{+}2Cl^{-}$ cotransporter in the basolateral membrane is responsible for the transport of sodium from lumen to the cell(11).

The distal tubule is relatively impermeable to water and 5% of filtered water is removed here. The collecting duct under the influence of vasopressin as explained above reabsorbs further 10% of filtered water through Aquaporin2.

The concentrating mechanism depends on the maintainence of gradient of increasing osmolality along the medullary pyramids. The gradient is produced by the constant circulation of fluid and electrolytes across the loop of Henle that functions as countercurrent multipliers and is maintained by the operation of vasarecta as countercurrent exchangers.

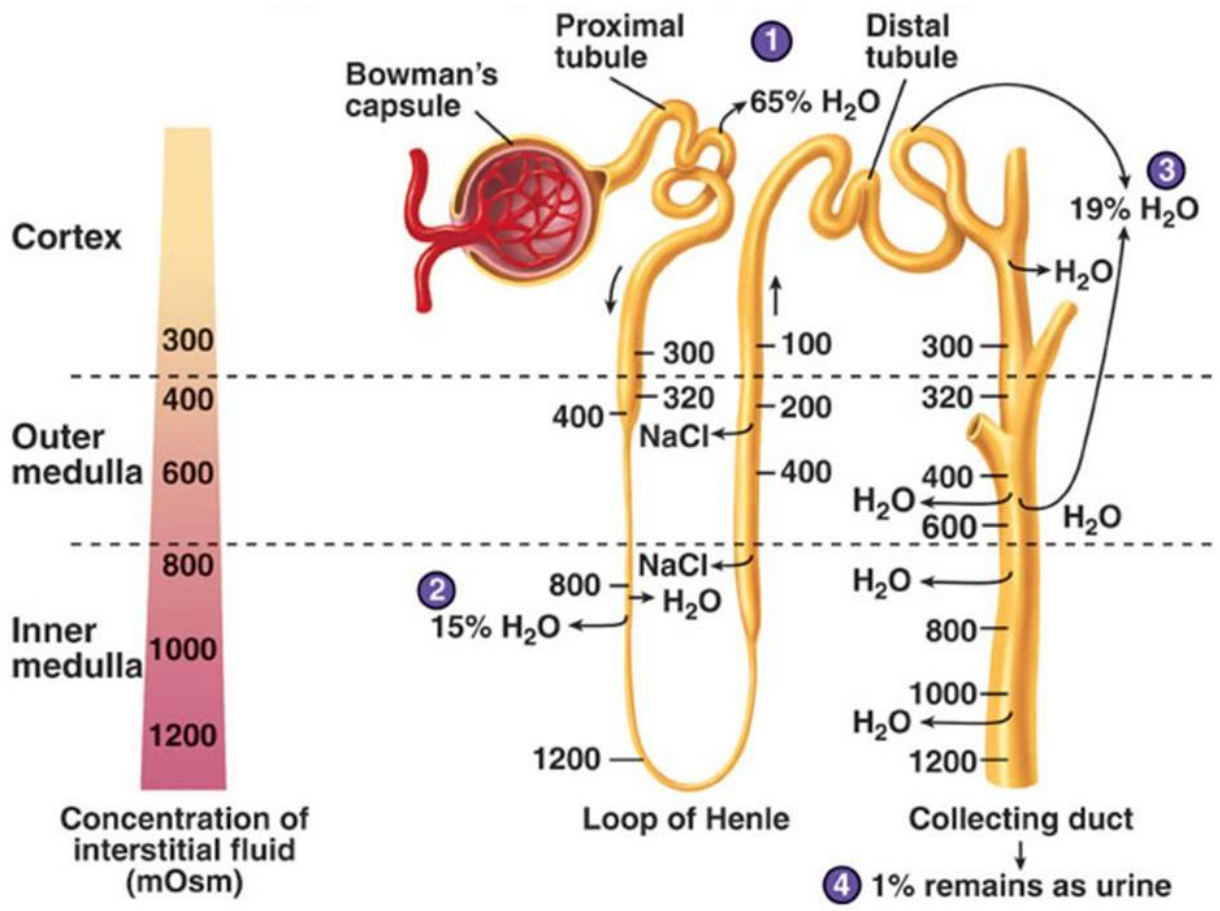


Figure 5 – Renal handling of water

The operation of each loop of Henle as a countercurrent multiplier depends on the active transport of Na^+ and Cl^- out of its thick ascending limb, and its contents equilibriate with the interstitium. But fluid containing 300mosm/kg of water is continuously entering from proximal tubule, so the gradient against which the Na^+ and Cl^- are pumped is reduced and more enters the interstitium.

This process continues repeatedly, and the end result is a gradient of osmolality from the top to the bottom of the Henle's loop. The osmotic gradient in

the medullary pyramids is maintained as the solutes remain in the pyramids primarily due to vasarecta operating as countercurrent exchangers(3).

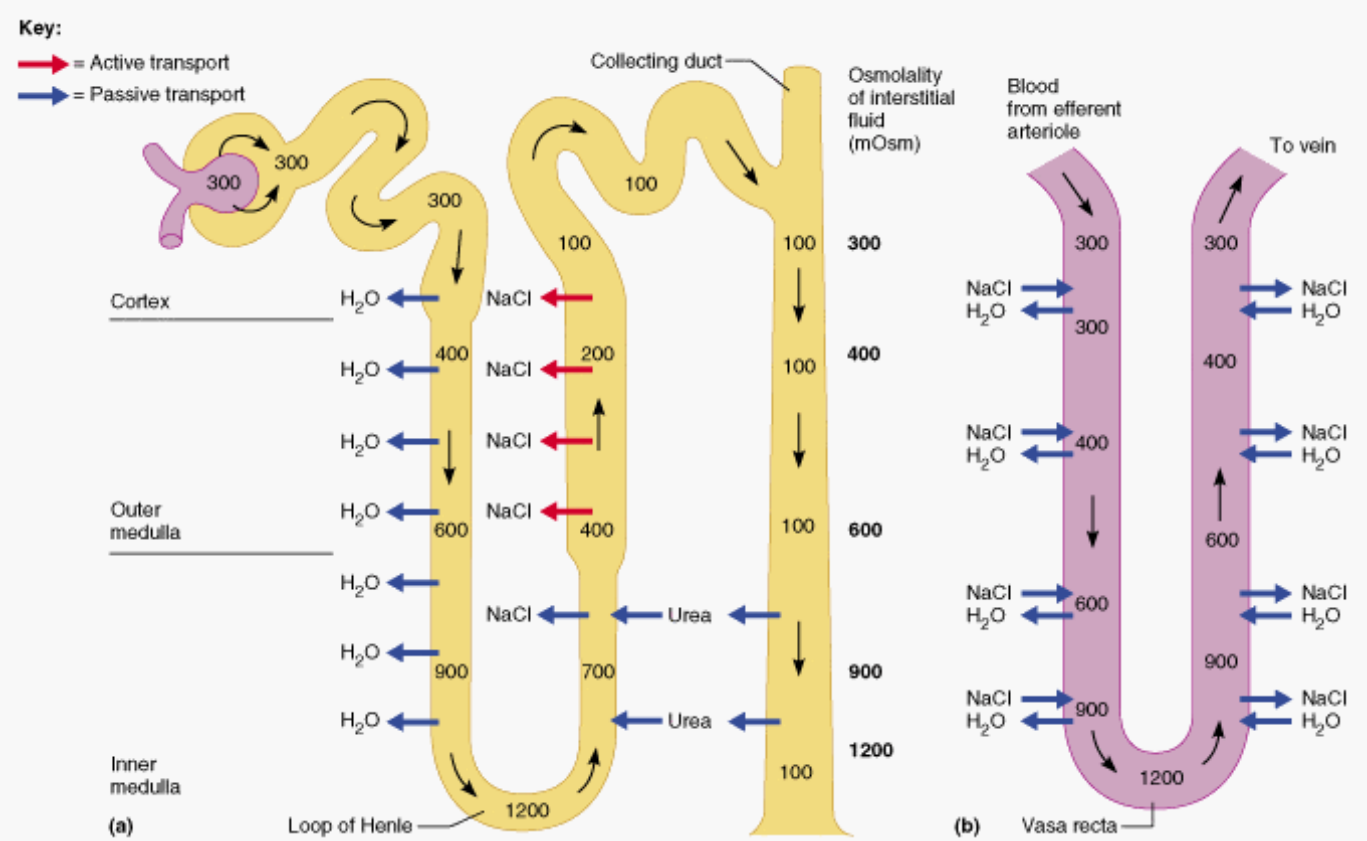


Figure 6-Countercurrent multiplier and countercurrent exchanger

The daily solute load of our body can be excreted in a urine volume as low as 500ml with a concentration of 1400mosm/kg. If not for the countercurrent mechanism, action of vasopressin, the solutes will be excreted in a volume of about 23L with a concentration of 30mosm/kg.

RENAL REGULATION OF Na^+ EXCRETION:

In the kidneys, sodium is freely filtered in large amounts, but it is actively reabsorbed throughout the tubule except the thin loop of Henle. Out of the total 96%-99% of the filtered Na^+ 65% is reabsorbed in proximal tubule and 25% in thick ascending loop of Henle. Through action of multiple mechanisms, the amount of Na^+ excreted is adjusted according to daily intake to maintain normal sodium levels. Thus, urinary Na^+ output ranges from less than 1meq/d on a low salt diet to 400meq/d or more when dietary intake of Na^+ is high.

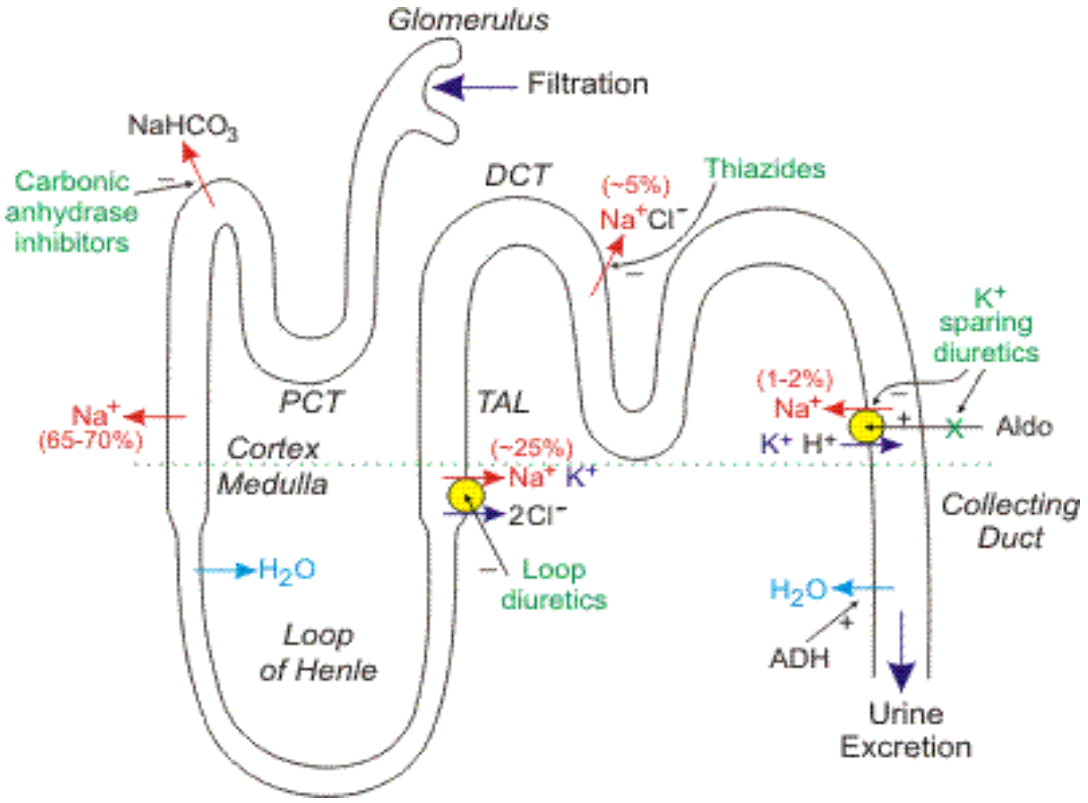


Figure 7 – Renal handling of sodium

Factors affecting Na^+ reabsorption are,

-Aldosterone and other adrenocortical hormones

-Atrial natriuretic peptide and other natriuretic hormones

-Rate of tubular secretion of H^+ and K^+

HYPONATREMIA

Sodium is the most abundant cation in the ECF and Na^+ salts account for over 90% of the osmotically active solute in the plasma and interstitial fluid. Therefore, the amount of Na^+ in the body is the prime determinant of ECF volume.

The normal serum sodium ranges from 135-145meq/L.

Types of hyponatremia:

Hypovolemic hyponatremia

Hypervolemic hyponatremia

Euvolemic hyponatremia

Redistributive hyponatremia

Pseudohyponatremia

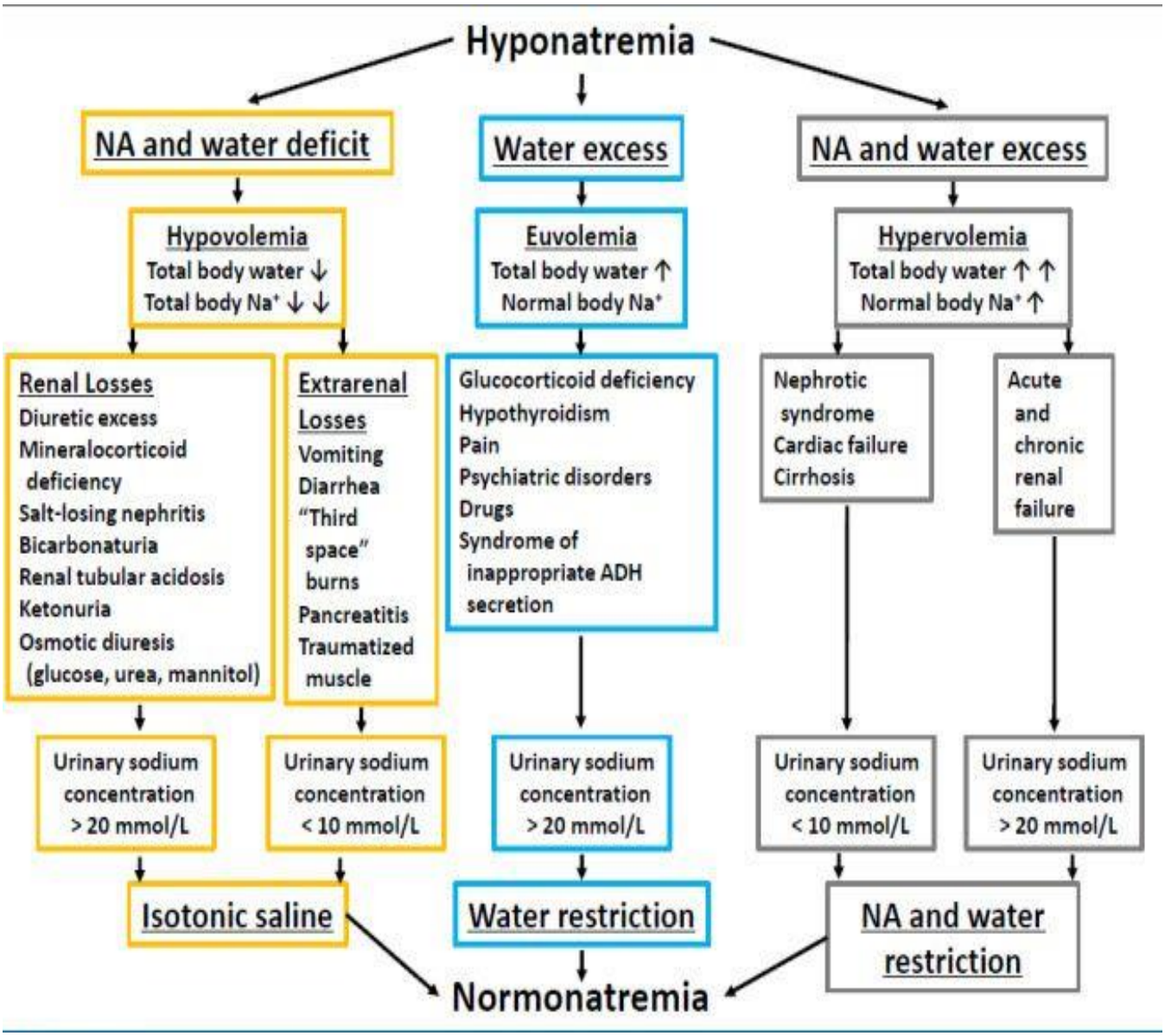


Figure 8- Types of hyponatremia

HYPOVOLEMIC HYPONATREMIA:

It occurs as the result of decrease in total body water. Total body sodium decreases to a relatively greater extent. The ECF volume is decreased. It occurs due to following reasons.

- Nonrenal loss:

  In these cases urine sodium is less than 20mM. It may be due excessive sweating, vomiting or loose stools, fluid leak into various serous cavities and also in burns, muscle injury, pancreatitis.

- Cerebral salt-wasting syndrome: (13-15)

  Occurs in patients with CNS diseases such as meningitis, subarachnoid hemorrhage, head injury and surgeries. In contrast with SIADH, these patients respond to aggressive Na^+ and Cl^- replacement.

- Renal Loss

  In Acute or chronic renal insufficiency, there is impairment of excretion of solute free water due to renal malfunction.

Salt-wasting nephropathies(16) may lead to hyponatremia when sodium intake is reduced due to impaired renal tubular function- typical causes include reflux nephropathy, interstitial nephropathies, post-obstructive uropathy, medullary cystic

disease, and the recovery phase of acute tubular necrosis. Urine Na^+ concentration is typically>20mM

HYPERVOLEMIC HYPONATREMIA:

In hypervolemic hyponatremia,patients develop an increase in total body Na^+-Cl^- that is accompanied by a proportionately greater increase in total body water, leading to a reduced plasma Na^+ concentration. It can be categorised into two according to urine sodium excretion .

- Acute or chronic renal failure uniquely associated with an increase in urine Na^+ concentration >20.
- Sodium-avid edematous disorders are associated with decrease in urinary sodium excretion. Some of these disorders are nephrotic syndrome,congestive cardiac failure and cirrhosis.(17)

The pathophysiology of hyponatremia is similar in these conditions except that arterial filling and circulatory integrity are decreased due to the specific etiologic factors, e.g., cardiac dysfunction in CHF and peripheral vasodilation in cirrhosis(18). Urine Na^+ concentration is typically very low, i.e., <10 m*M*, even after hydration with normal saline; this Na^+-avid state may be obscured by diuretic therapy. The degree of hyponatremia provides an indirect index of the associated

neurohumoral activation and is an important prognostic indicator in hypervolemic hyponatremia.

EUVOLEMIC HYPONATREMIA:

In this case the patient clinically has no edema. It can occur due to severe hypothyroidism, secondary adrenal deficiency, pituitary disease and glucocorticoid deficiency. The most common cause of euvolemic hyponatremia is Syndrome of inappropriate antidiuretic hormone (SIADH). The generation of hyponatremia requires an intake of free water which is persistent even at serum osmolalities lower than the usual thirst threshold. There are 4 types of AVP secretion in SIADH.

Table 2 –Types of AVP secretion

Type A	Unregulated erratic AVP secretion irrespective of serum osmolality
Type B "reset osmostat"	Patients with lower osmolality threshold
Type C	Failure of secretion of AVP at lower osmolality
Type D	Patients with an antidiuretic substance distinct from AVP

Serum uric acid is usually low(<4mg/dl) in patients with SIADH, due to suppressed proximal tubular transport in the setting of increased distal tubular water and electrolyte transport. But patients with hypovolemic hyponatremia are often hyperuricemic, due to shared activation of proximal tubular $Na^{+}Cl^{-}$ and urate transport.

Table 3- Common causes of SIADH

Pulmonary diseases	Pneumonia, tuberculosis, pleural effusion, respiratory failure with positive pressure ventilation
Malignant diseases	Lung carcinomas(small-cell ca), gastrointestinal and oropharyngeal malignancies
CNS diseases	Tumours, subarachnoid hemorrhage, meningitis
drugs	Drugs that stimulate release of AVP or enhance its action, chlorpropamide, carbamazepine, clofibrate, antipsychotic drugs,oxytocin, SSRIs

SIADH is diagnosed by exclusion. SIADH is characterised by hypotonic hyponatremia in the setting of clinical euvolemia and an inappropriately elevated urinary osmolality. Conditions such as hypothyroidism(19) and adrenal insufficiency(20) should be ruled out for a diagnosis of SIADH to be made.

REDISTRIBUTIVE HYPONATREMIA

The total body water and sodium levels do not change,but there is relative hyponatremia. It is due to the movement of water from inside the cells to extracellular space. It occurs due to hyperglycemia and mannitol administration.

PSEUDOHYPONATREMIA

Here also the total body water and sodium is unchanged. But the extracellular fluid is diluted with excess of lipids or proteins. It is seen in conditions like multiple myeloma and hypertriglyceridemia.

APPROACH TO HYPONATREMIA

The specific type of hyponatremia is identified by a systemic approach assessing serum osmolarity, volume status and renal sodium excretion in a step by step approach.

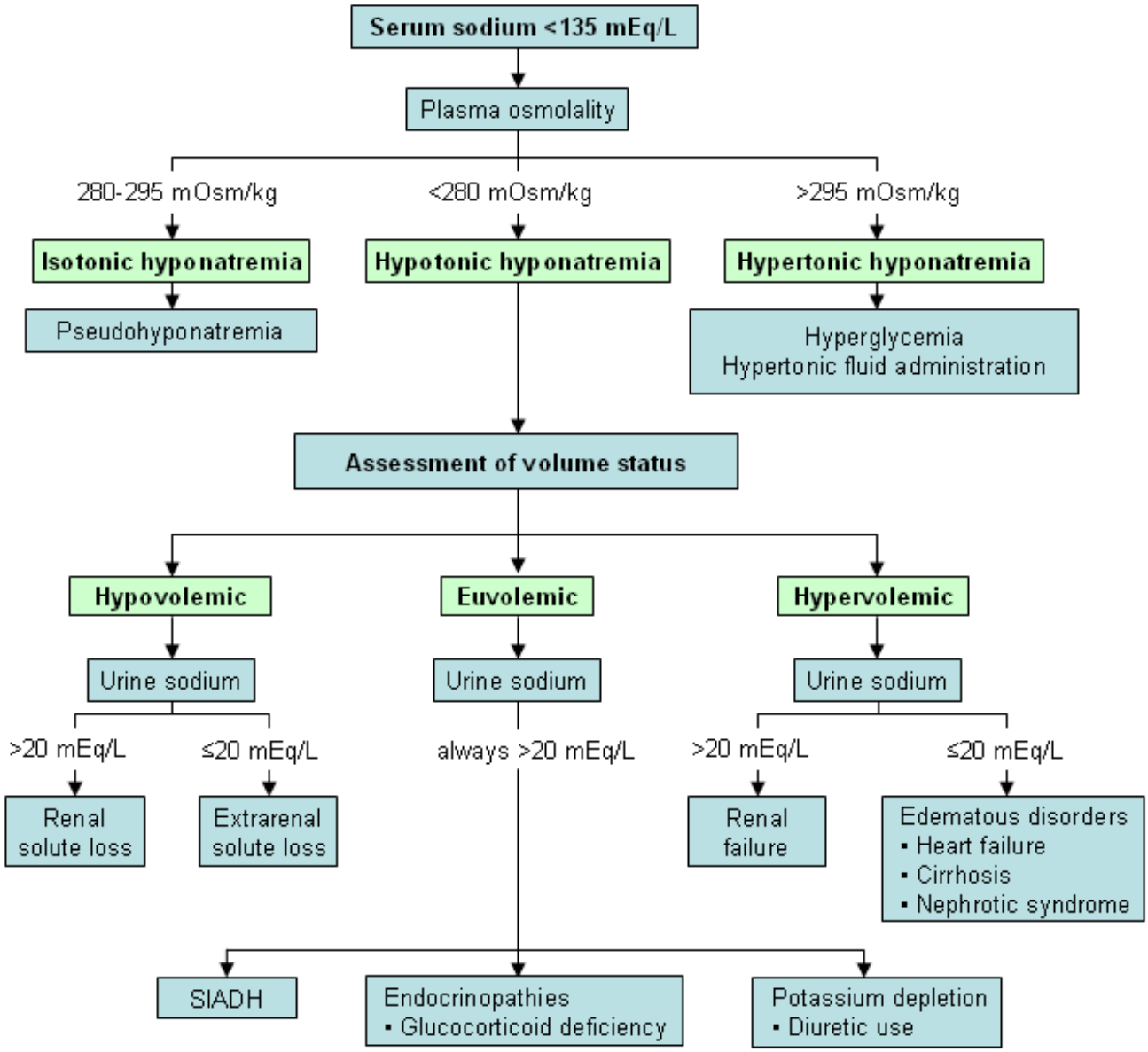


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Figure 9- Approach to hyponatremia

CLINICAL FEATURES OF HYPONATREMIA

The severity of symptoms depends upon the severity of hyponatremia and the rate of lowering of serum sodium. So acute and severe hyponatremia is symptomatic but chronic and mild hyponatremia is well tolerated. Patients with extremes of age are more symptomatic.

Table 4-Clinical features of hyponatremia

MILD	MODERATE	SEVERE
Anorexia	Personality changes	Drowsiness
Headache	Muscle cramps	Diminished reflexes
Nausea	Muscular weakness	Convulsions
Vomiting	Confusion	Coma
lethargy	Ataxia	Death

The extracellular sodium is the principal determinant of the extracellular osmolarity and the ECF osmolarity is the crucial determinant of many processes essential for brain function including excitability, myelination and volume regulation. So brain is the most commonly affected organ in hyponatremia.

Cerebral adaptation to hyponatremia:

The mechanism of brain adaptation to acute and chronic hyponatremia can be viewed as a part of the same physiological continuum.

Acute hyponatremia is defined as a duration of hyponatremia less than 24-48 hours. During the first few hours of hyponatremia at the CNS level,the rapid decrease in sodium level is followed by an attempt to counterbalance the water entry into the cells. A decrease in the extracellular volume and and a quick loss of intracellular electrolytes are the first changes seen after acute hyponatremia(21).

In spite of these changes crebral edema may sometimes occur due to

a)faster rate of decline in serum sodium than the rate of brain loss of electrolytes.

b)situations where the magnitude of hyponatremia exceeds the brain's capacity to adapt.

The mechanism of rapid brain adaptation by electrolyte extrusion is exhausted by 3 hours and the absence of cerebral edema despite continuation of hyponatremia is due to other mechanisms that act in chronic hyponatremia.

The brain will also use non-ionic osmotic substances to preserve intracellular brain water content. The depletion of these "organic osmolytes" starts as early as 4 hours after hyponatremia and reaches its maximum by 4 days. The

main organic osmolytes that are depleted in the brain are myoinositol, taurine,betaine, glutamate and glycerophosocholine.(22)

Hyponatremic encephalopathy:

The clinical syndrome resulting from the effect of hyponatremia on the brain is termed as hyponatremic encephalopathy.

Risk factors:

Acuteness and severity of onset of hyponatremia.

Extremes of age-children and elderly.

Females are more susceptible.

Concurrent hypoxia may can impede the mechanism of brain adaptation to hyponatremia.

To summarise, the clinical features of hyponatremia depend on whether its acute or chronic(23).

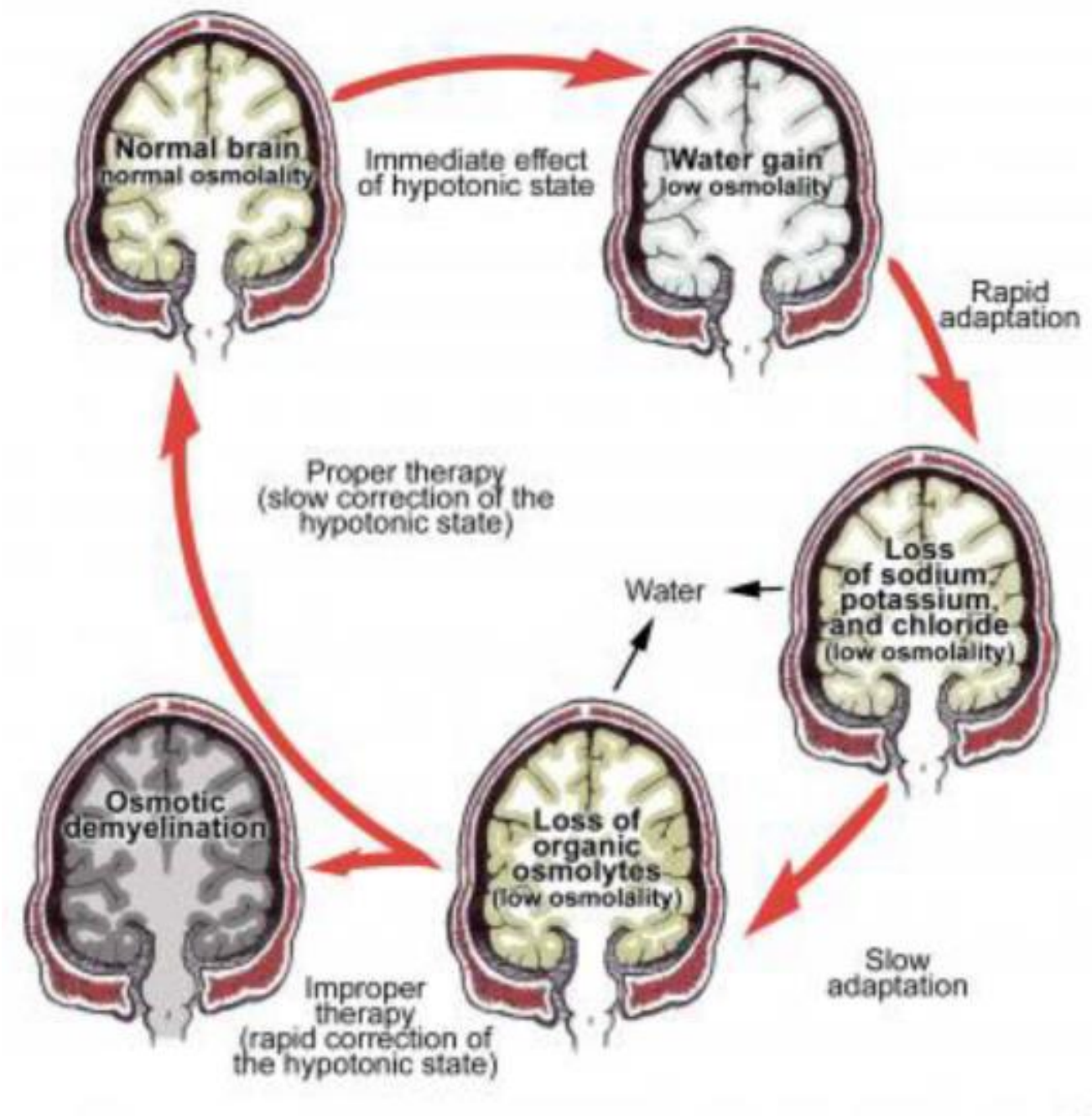

Figure 10 – Adaptation of brain to hyponatremia

Table 5- Clinical features of Acute and Chronic hyponatremia

Acute hyponatremia **<48 hours**	**Chronic hyponatremia** **>48 hours**
Nausea and vomiting Headache Disorientation Seizures Coma Respiratory arrest Death	Fatigue Confusion Somnolence Gait deficit Attention deficit Frequent falls

TREATMENT OF HYPONATREMIA :

Treatment of hyponatremia must meet three goals :

- Plasma sodium concentration must not decrease further.
- Increase in plasma sodium should be just enough to prevent complications.
- Avoid iatrogenic neurological injury caused by rapid or excessive correction.

Different types of hyponatremia can be managed as per the following guidelines,

1). Mild asymptomatic hyponatremia – requires no treatment.

2). Hypovolemic hyponatremia

– These patients require fluid and salt supplementation generally in the form of isotonic saline at a rate appropriate for estimated volume depletion.

- Fluids like 0.45 % NaCl , Isolyte – M, 5% dextrose must be avoided as it aggravates hyponatremia.
- Diuretics induced hyponatremia is treated with saline with potassium supplementation (30 – 40 meq/L).

3). Hypervolemic hyponatremia

- Restriction of sodium and water intake.
- Loop diuretics causes promotion of water loss in excess of Sodium.
- Correction of hypokalemia
- Treatment of etiology
- Restriction of dietary water to less than urine output

4). Euvolemic hyponatremia

In these patients, fluid restriction is the most important treatment.

5). Acute hyponatremic with neurological symptoms

Rapid correction of plasma sodium with hypertonic saline is needed. Initial rise of sodium should be 1.5 – 2 meq/L for the first 3 to 4 hours or until severe neurological symptoms improve. Once symptoms have improved or seizures stop, the correction should not exceed 10 – 12 meq in first 24 hrs. The targeted rate of plasma sodium inrease should not be greater than 0.5 meq/L/hr(24).

Increase in plasma sodium by giving 1 litre of different infusate can be calculated as

Change in serum Na^+ =

$$\frac{\text{Infusate } Na^+(meq/L) + \text{Infusate } K^+(meq/L) - \text{Plasma } Na^+(meq/L)}{\text{Total body water (L)} + 1}$$

Where total body water is

= 0.6 * body weight (kg) in children & non elderly man

= 0.5 * body weight (kg) in non elderly woman & elderly man

= 0.45 * body weight (kg) in elderly woman

Table 6:Composition of various I.V fluids

Solution	Na+	K+	Ca+	Mg+	Cl^-	HCO_3	Glu	Osm
0.9%NaCl(NS)	154	-	-	-	154	-	-	308
D5/0.9%NaCl	154	-	-	-	154	-	50	560
0.45%NaCl(1/2NS)	77	-	-	-	77	-	-	560
D5/0.45% NaCl	77	-	-	-	77	-	50	406
0.225% NaCl(1/4)	38.5	-	-	-	38.5	-	-	77
D5/0.225% NaCl	38.5	-	-	-	38.5	-	50	329
LR	130	4	3	-	109	28	-	273
3.0% NaCl(hypertonic)	513	-	-	-	513	-	-	1026

Osmotic demyelination syndrome:

Rapid correction of hyponatremia (>8-10meq/L in 24 hours or 18meq/L in 48 hours) is associated with a disruption in the integrity of blood brain barrier, allowing the entry of immune mediators that may contribute to demyelination. When the hyponatremia is rapidly corrected there is a delay in the reaccumulation of organic osmolytes by brain cells as osmolarity increases with correction of hyponatremia. The demyelination is more pronounced in pons, but can also occur in other structures. Osmotic demyelination syndrome(ODS) can occur as early as 12 hours but is usually delayed by 2-3 days after the correction of hyponatremia.Neurological manifestations of ODS are as follows(25).

Table 7:Manifestations of osmotic demyelination syndrome

Motor & sensory	Neuropsychiatric
• seizures, coma • dysarthria, dysphagia • dysmetria, tremors • paraplegia • locked in syndrome • ocular movement disorders • cortical blindness	• dementia • altered sensorium • depression • decreased concentration • altered memory • catatonia

The early diagnosis depends on clinical suspicion & examination in conjunction with laboratory analysis and imaging. MRI shows hyperdense lesions in T_2 – weighted images and hypodense non – enhancing lesions on T_1 – weighted images. Pathological findings include a breakdown of blood brain barrier and astrocyte loss.

ODS can be prevented by slowly correcting hyponatremia not exceeding 10 – 12 meq/L on the first day and less than 18 meq/L over first 48 hrs. After rapid correction, relowering of sodium can prevent neurological symptoms but should be started within first 24 hrs.

LIVER

The normal adult liver weighs 1.4 to 1.6 kg, constituting approximately 2.5% of total body weight. The liver has a variety of functions- synthesis of albumin, clotting factors, metabolic functions, detoxification and storage functions.

CIRRHOSIS

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. The entire architecture of the liver is distorted. There is periportal inflammation and bridging fibrosis connecting the portal triads. Nodules develop during the process of regeneration.(26)

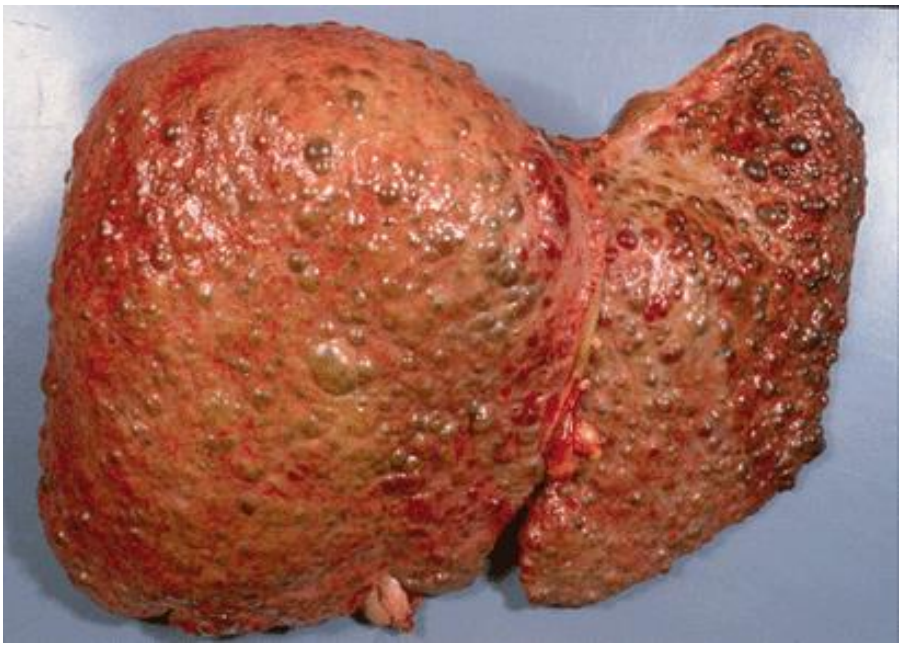

Figure 11: Cirrhotic liver with coarse nodules

CAUSES OF CIRRHOSIS:

The causes include alcohol, infections, autoimmune, metabolic and other causes such as cardiac cirrhosis, non alcoholic fatty liver disease,etc. Cryptogenic cirrhosis occurs without any identifiable etiology. Drugs like amiodarone, methyldopa and methotrexate can cause cirrhosis. Although the causes are many, the pathological changes and end result is the same.

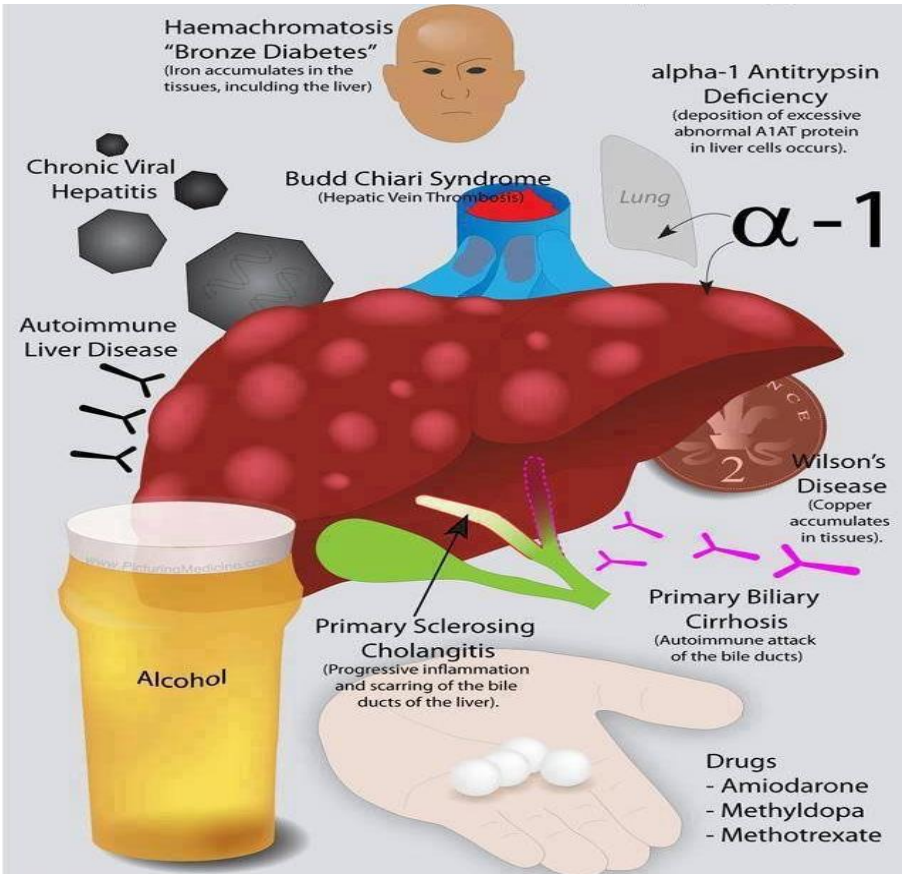

Figure 12- Causes of cirrhosis

CLINICAL MANIFESTATIONS OF CIRRHOSIS:

Clinical manifestations depend upon whether the patient has compensated disease or decompensated disease. Patients are usually malnourished and anemic. Bitot spots and night blindness may develop due to vitamin A deficiency. Anemia may be nutritional, due to hypersplenism, chronic blood loss or a combination of all these factors. Platelets are reduced both in number and function. Patients usually have mild to moderate jaundice. Hypoalbuminemia and coagulopathy occur as a result of impaired synthetic functions of liver.

Patients are prone to develop infections due to decreased immunity. Eventually portal hypertension develops and patient develops ascites, extensive portosystemic collaterals and splenomegaly. Loss of axillary hair, gynaecomastia and testicular atrophy occurs due to hyperestrogenemia. Due to long standing abdominal distension, the skin is stretched and shiny. Umbilical hernia may develop. Collaterals can be seen around the umbilicus. Spider naevi are seen in the front of chest. Long standing cirrhosis is a risk factor to develop hepatocellular carcinoma.

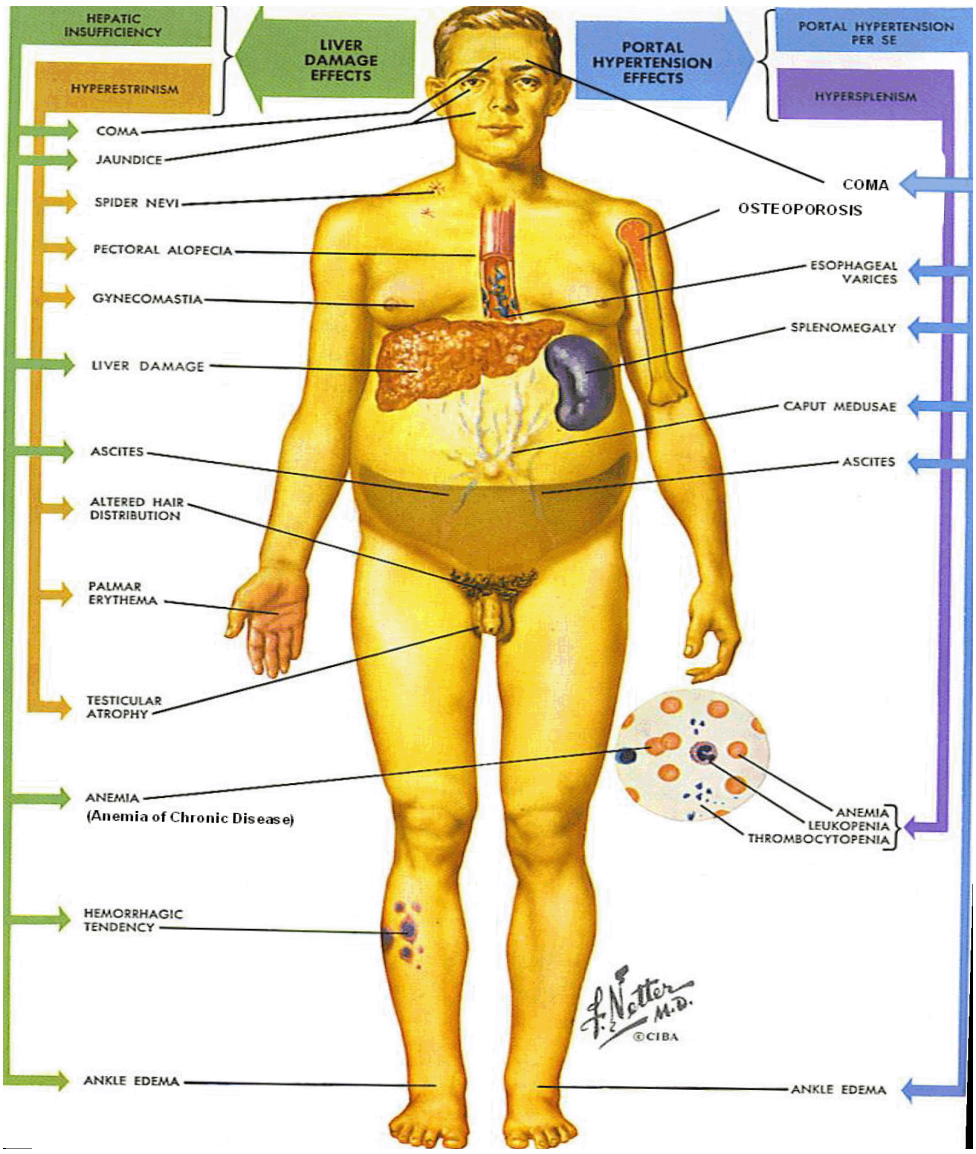

Figure 13: Clinical manifestations of cirrhosis

Figure 14: Stages of cirrhosis

COMPLICATIONS OF CIRRHOSIS(27):

Portal hypertension

- Ascites
- Variceal bleeding
- Splenomegaly
- Portal hypertensive gastropathy

Spontaneous bacterial peritonitis

Hepatorenal syndrome

Hepatopulmonary syndrome

Hepatic encephalopathy

Coagulopathy

Hepatocellular carcinoma

Malnutrition

Haematological abnormalities

PORTAL HYPERTENSION:

PH refers to an elevated hepatic venous pressure gradient (HVPG) >5mmHg and cirrhosis is the most common cause of portal hypertension. In cirrhosis there is increased resistance to portal blood flow. The resistance is both mechanical and dynamic. Mechanical resistance is due to fibrosis,altered architecture and collagen deposition in the space of disse. The cardinal features of portal hypertension are ascites, splenomegaly and variceal bleeding. Varices develop at sites of portosystemic collaterals. Varices are commonly present at lower end of esophagus, fundus, stomach and also lower part of rectum.

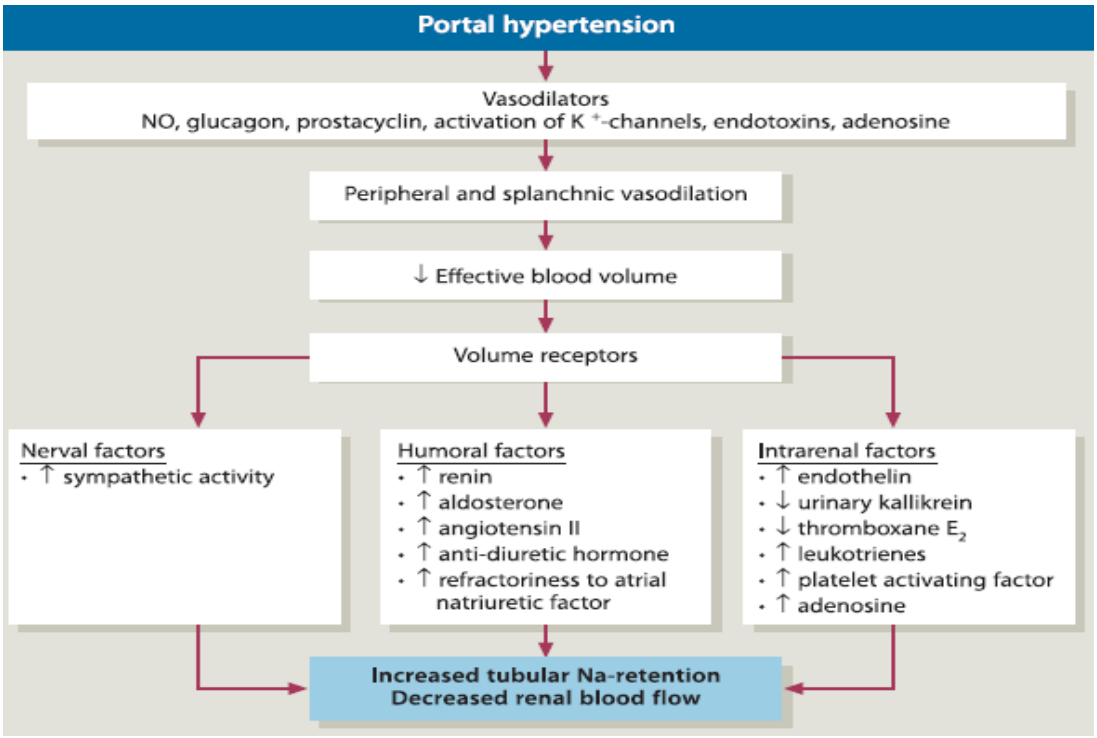

Figure 15: Pathogenic mechanisms in portal hypertension

ASCITES:

Ascites is caused due to splanchnic vasodilation occurring as a result of increase in portal pressure. There is increased hepatic lymph production. Decreased synthesis of albumin as a result of liver damage further contributes to volume overload and free fluid in the abdomen. The kidneys develop a tendency to retain sodium due to drop in effective intravascular volume. All these proposed mechanisms involve inappropriate renal sodium and water retention, either secondary to intravascular hypovolemia (underfill and peripheral arterial vasodilatation theory) or as a primary event (overfill theory).

Refractory ascites(28) is defined as ascites that cannot be reduced or which reaccumulates in spite of continuous maximal medical therapy and diet restriction. It is of 2 types.

- Diuretic resistant: no response to maximum diuretic dose
- Diuretic intractable: patients do not tolerate diuretics due to complications.

CLASSIFICATION OF ASCITES

GRADE	PRESENTATION
Grade 1	Mild ascites detectable only by ultrasound examination
Grade 2	Moderate ascites manifested by moderate distention of the abdomen
Grade 3	Large or gross ascites with marked abdominal distention

Figure 16: Classification of ascites

SPONTANEOUS BACTERIAL PERITONITIS(SBP):

About 8% patients with ascites develop spontaneous bacterial peritonitis(29). There is immune dysfunction and decreased opsonins in the ascitic fluid that causes translocation of gut organisms resulting in spontaneous infection. Infection is usually monomicrobial and gram negative. Ascitic protein <1g/dl indictes higher risk. Ascitic fluid polymorphs >250/mm^3 is indicative of SBP. Mortality is 50% in patients with spontaneous bacterial peritonitis. 69% of patients

recur in one year. These patients are at more risk of developing hepatorenal syndrome and encephalopathy.

HEPATORENAL SYNDROME:

Hepato-renal syndrome is the development of functional renal failure in patients with severe liver disease in the absence of any identifiable renal pathology.

It occurs secondary to decreased renal perfusion and renal vasoconstriction. About 20% of cirrhotic patients with ascites and normal renal function develop the syndrome after 1 year of follow-up, and 39% at 5 years. Based on the time course of development and precipitating factors it is classified into 4 types.

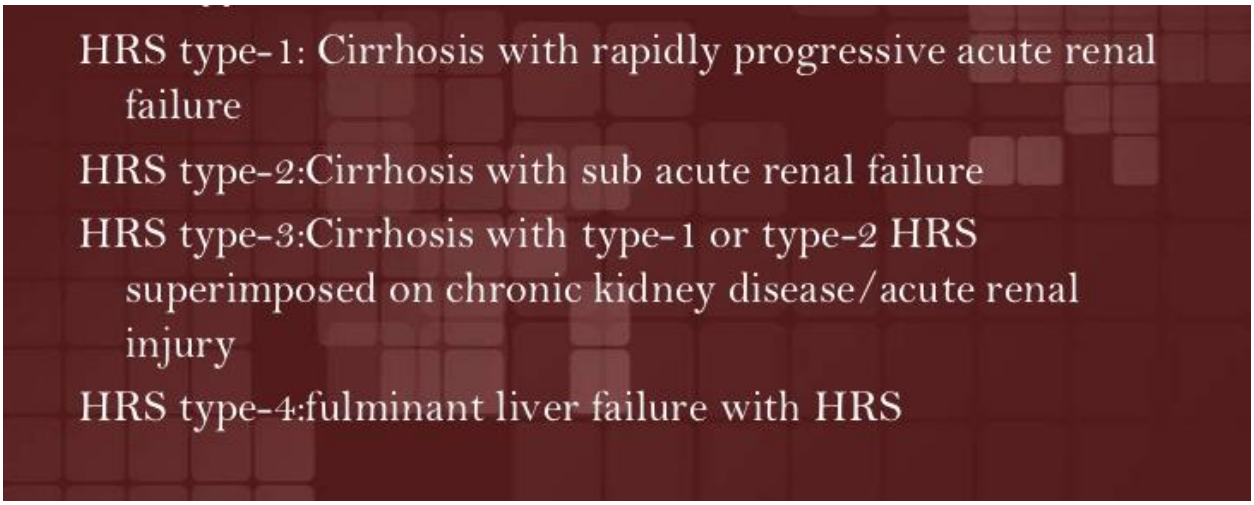

Figure17: Types of hepatorenal syndrome

The 2 week mortality is as high as 80% in patients with type 1 hepatorenal syndrome.

. **HEPATIC ENCEPHALOPATHY:**

Hepatic encephalopathy is a reversible neuropsychiatric complication of advanced cirrhosis. It occurs due to increased ammonia in the brain as a result of depressed urea cycle. There is an imbalance between inhibitory and excitatory neurotransmitters. Clinical features depends upon the severity of encephalopathy and varies from sleep disturbances, disorientation, decreased concentration to drowsiness and deep coma. Patients can be categorised according to severity on the basis of West havens grading of hepatic encephalopathy. Precipitating factors for hepatic encephalopathy are alcohol intake, variceal bleed, constipation, infections, electrolyte imbalances and drugs like diuretics and sedatives.

HYPONATREMIA IN CIRRHOTICS

Patients with cirrhosis and ascites have a functional renal failure and inability to excrete solute free water. This disorder leads to a disproportionate retention of water in relation to sodium which leads to dilutional state and hypo-osmolarity.

DEFINITION AND PREVALENCE:

Hyponatremia in the general population is defined as serum sodium less than 135mEq/L(30). However, hyponatremia in cirrhosis is defined as serum sodium less than 130mEq/L in the presence of ascites or edema. A significant proportion

of cirrhotic patients have serum sodium between 130-135 mEq/L and these patients may display pathogenetic and clinical features similar to but less pronounced than with patients with serum sodium less than 130mEq/L. In patients with cirrhosis and ascites, the 5 year probability of developing hyponatremia is 37% with 25% probability of survival at 1 year. It is estimated that 22% of patients with advanced cirrhosis have serum sodium levels less than 130mEq/L, however in patients with refractory ascites and hepatorenal syndrome, the prevalence may increase upto 50%(31). If the cutoff level of 135mEq/L is used then the prevalence goes upto 49.4%.

TYPES OF HYPONATREMIA:

Table 8: Types of hyponatremia

	HYPOVOLEMIC HYPONATREMIA	HYPERVOLEMIC HYPONATREMIA
CAUSES	Excessive Diuretic use Diarrhea (Loss of fluid)	Marked impairment of **renal solute-free water excretion**, resulting in **disproportionate renal retention of water with respect to sodium retention.**
FEATURES	***Lack of edema and ascites, signs of dehydration present***	***Presence of ascites and edema***

Patients with cirrhosis may develop two types of hyponatremia as explained above(32).

PATHOGENESIS OF HYPONATREMIA IN CIRRHOSIS:

Patients with cirrrhosis usually have impaired ability to excrete solute free water. The degree of impairment varies and patients with moderate impairment can be detected by measuring urine volume after water loading test. In cirrhosis there is splanchnic vasodilation and extensive peripheral vasodilation. This causes reduced effective circulatory volume leading to activation of baroreceptors and non-osmotic secretion of vasopressin. Other vasopressor systems and antidiuretic systems are also activated(33). In initial stages of disease this compensatory neurohemoral mechanism restores the intravascular volume. The compensatory mechanisms are transient(34). In advanced disease, there is compensatory mechanism failure and persistent activation of vasoconstrictors leading to renal sodium retention, edema and hyponatremia.

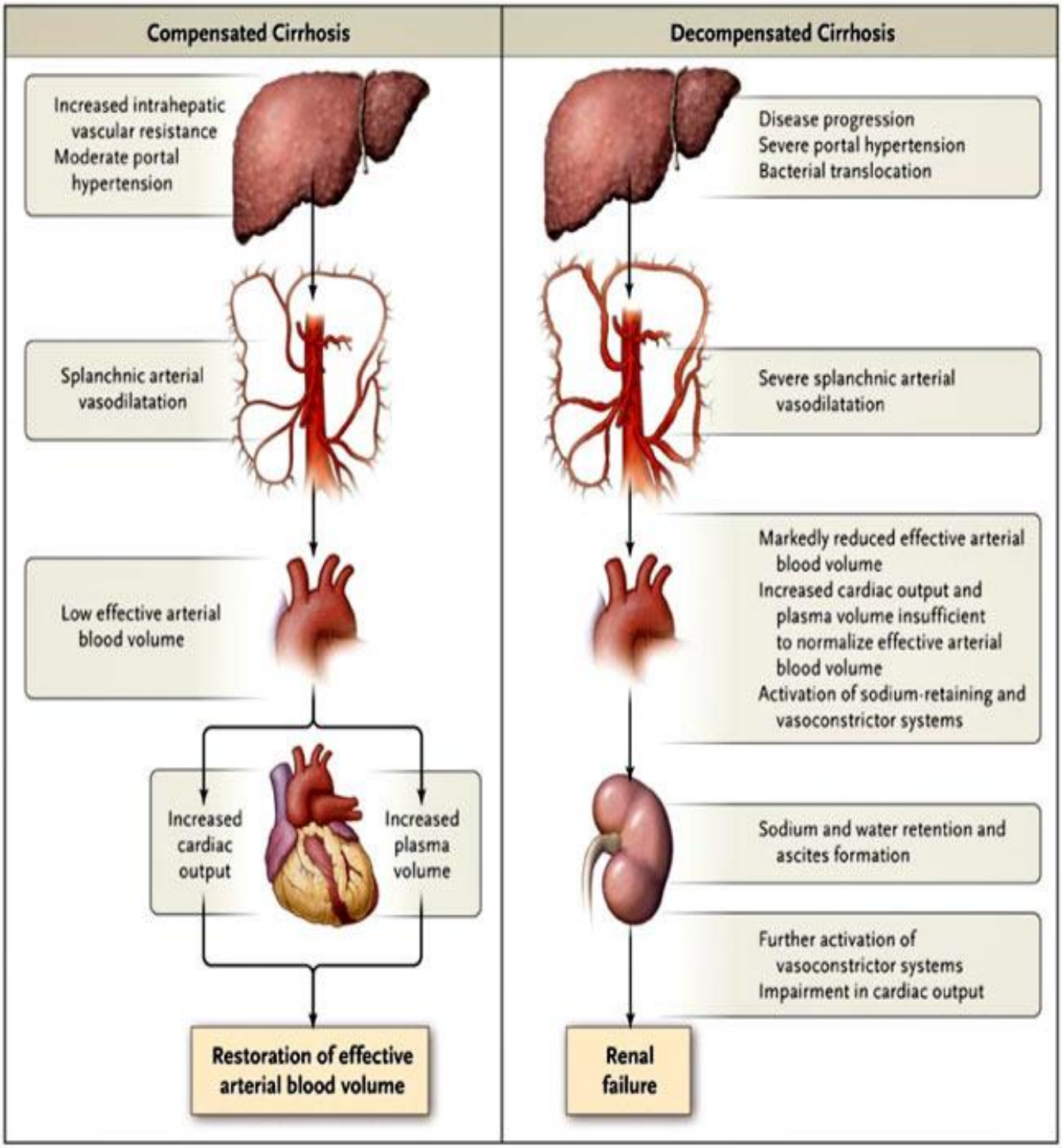

Figure 18: Compensatory mechanisms in cirrhosis

MECHANISMS OF WATER RETENTION AND DILUTIONAL HYPONATREMIA IN CIRRHOSIS(32):

1.NON OSMOTIC SECRETION OF AVP(ARGININE-VASOPRESSIN)

Increased free water intake in patients with decreased capacity to excrete solute free water results in dilutional hyponatremia. Water load test is the standard method to estimate renal capacity of free water clearance. About 20 mL/kg of body weight of fluid is administered over 45 minutes.

In healthy people after fluid loading the serum osmolality falls due to dilution in excess of water. This is sensed by the osmoreceptors and there is suppression of vasopressin release from hypothalamus. Due to short half life (30 min) of vasopressin.there is immediate response to changes in osmolality. Due to decreased vasopressin, the urine is maximally diluted to upto 40-50 milliosmoles/kg. Persons with normal free water clearance excrete more amount of diluted urine in 2 hours. This is the normal physiological response. This response can be seen even in patients with stable compensated cirrhosis. However in patients with advanced decompensated disease, there is impairment of excretion of solute free water. The reduction in free water clearance can be correlated with severity of the disease, patients with severe disease are unable to produce diluted urine. Electrolyte free water clearance can be used to determine the degree of water

restriction required to cause negative water balance. It is also used to predict the effectiveness and feasibility of using fluid restriction as a mode of treatment.

Bichet et al(35) selected cirrhotic patients with ascites and subjected them to water load test. Plasma vasopressin concentrations were measured before and after water load. He classified these patients according to the amount of water excreted after 5 hours. “Excretors” were those who excreted 80% or more of water load and those who were unable to do so called as “non-excretors”. Non excretors had basal vasopressin levels minimally higher than that of secretors. In nonexcretors there was no fall in vasopressin in response to change in osmolality and vasopressin levels continued to be high independent of hypoosmolality. The amount of water excreted was inversely related with vasopressin levels. Higher vasopressin levels were found in patients with severe water retention.

Another similar study(35) classified patients into 2 groups according to water excretion after a water challenge test and measured their plasma levels of various vasomediators. Group of patients unable to excrete solute free water had higher levels of vasopressin confirming its role in causing water retention. Moreover these patients had increased plasma renin, aldosterone and nor epinephrine levels compared to the other group. This shows the role played by pathological hyperstimulation of sympathetic system and renin angiotensin system in response to decreased circulatory volume. These two studies proposed a

nonosmotic stimulation for VP release in cirrhotic patients with impaired water excretion.

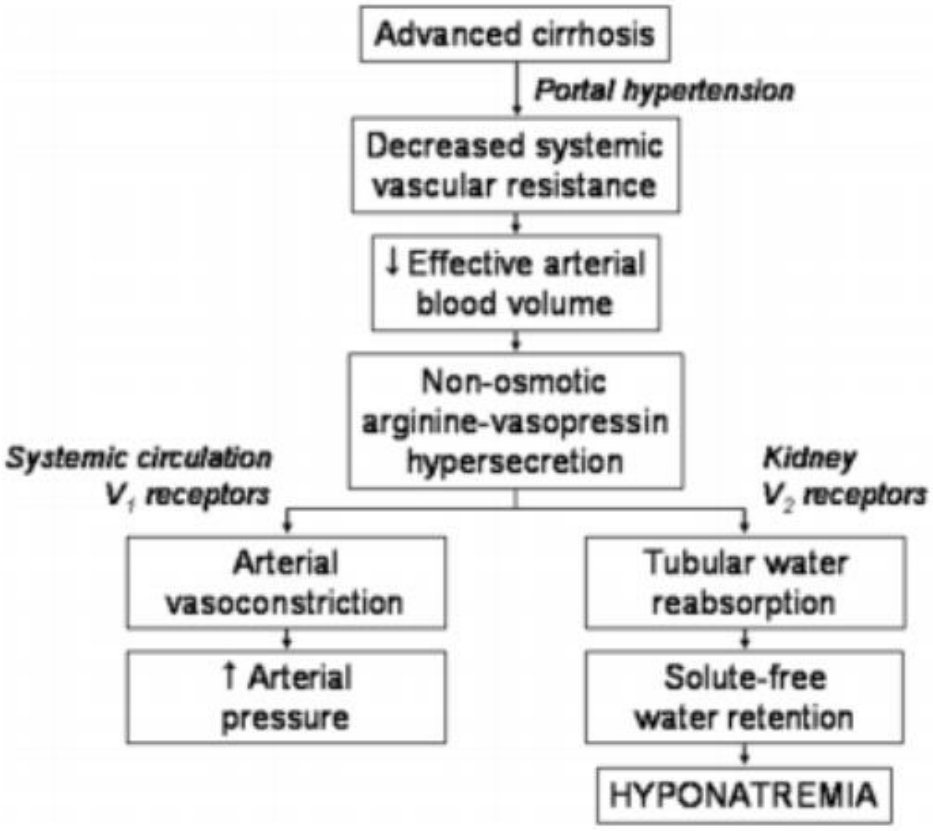

Figure 19: Role of vasopresssin

Studies using vasopressin antagonists (vaptans)for the treatment of hypervolemic hyponatremia in cirrhosis showed that vaptans caused an increase in serum sodium in about 60-70% of patients(36). This strongly emphasises that hypersecretion of vasopressin plays a major role in the pathology of hyponatremia. But in a small percentage of patients vaptans could not increase the sodium levels

suggesting that other mechanisms are also involved in water retention other than vasopressin.

2.DECREASED METABOLISM OF VASOPRESSIN:

Vasopressin is metabolised in the liver and kidneys(37). In cirrhosis, the functions of liver are deranged. The normal half life of VP is only 30 minutes. Due to liver dysfunction the half life of VP may be prolonged causing pathological reabsorption of excess water. This prolonged action in addition to increased secretion can act synergistically to cause antidiuresis.

3.DECREASED DISTAL SODIUM DELIVERY:

Normally 60-75% of sodium is reabsorbed in proximal tubules, but in cirrhosis there is excessive reabsorption due to decreased renal perfusion. The amount of fluid delivered to the distal segment is reduced progressively due to decline in glomerular filtration. The upper limits of urine output is determined by the amount of fluid reaching the distal tubules. Due to renin angiotensin activation, excess aldosterone causes increased sodium reabsorption. In physiological states, along with sodium, fluid is also reabsorbed and there is increased fluid delivery to distal tubule resulting in pressure natriuresis. This is called aldosterone escape. This is impaired in cirrhosis due to decreased filtrate reaching the distal portion of the nephron. This is also a contributing factor for reduced response to atrial

natriuretic peptide in patients with cirrhosis. Researchers calculated distal fluid delivery by using lithium clearances in cirrhosis and found a significant reduction(38).

4.REDUCTION IN RENAL PROSTAGLANDINS(39):

Prostaglandins are secreted in the kidney by glomerular and vascular endothelium. These have local actions but no systemic effect. These are endogenously produced vasodilators that try to maintain renal blood flow and glomerular filtration. In cirrhosis patients, the renal hemodynamics is altered more towards vasoconstriction. Prostaglandins act as a defence against vasoconstrictive effects of angiotensin II, vasopressin and norepinephrine that are found in high levels in cirrhosis. There are studies which propose that prostaglandins inhibit VP-stimulated water reabsorption. Effects of non-steroidal anti inflammatory drugs(NSAIDs) in cirrhosis causing deterioration of renal function is an indirect evidence of the role played by prostaglandins(40). It is probably due to loss of protective role of prostaglandins due to inhibition of production by NSAIDs. In cirrhosis patients there is impaired production of renal prostaglandins.

PROGNOSIS OF CIRRHOTIC PATIENTS:

Cirrhosis is a chronic disease and hence a standard prognostic tool is required in order to understand the severity and staging of disease and predict mortality and morbidity based on previous data. Moreover prognostic categorisation of patients is required to make treatment decisions, estimate risk involved in interventions, surgeries and shunt procedures. They are also used to determine the threshold for listing patients for liver transplantation, predict survival following transplant and to select patients waiting for transplant. Current scores available are:

1.CHILD PUGH TURCOTTE SCORE(CPS)

2.MODEL FOR END STAGE LIVER DISEASE SCORE(MELD)

CHILD PUGH TURCOTTE SCORE:

The scoring system was first proposed by Dr C.G.Child and Dr J.G.Turcotte of University of Michigan in 1964 and originally used to predict mortality during surgery(41). It used 5 variables ascites, bilirubin, albumin, hepatic encephalopathy and malnutrition. The selection was based on observations made by clinical experience. In 1972 it was modified by Pugh et al, nutritional status was replaced by elevation in prothrombin time or INR. Each variable was assigned scores1-3 and a total for 15 is made.

Child-Turcotte-Pugh Classification

	1 point	2 points	3 points
Encephalopathy	0	1-2	3-4
Ascites	none	slight	moderate
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
PT prolonged (s)	1-4	5-6	>6
(INR)	<1.7	1.8-2.3	>2.3

Figure 20:MODIFIED CHILD PUGH SCORE

Based on total points, Child A = 5–6 points, Child B = 7–9 points, Child C = 10–15 points.

INTERPRETATION

Based on the category the survival is predicted as follows(42).

Points	Class	Life Expectancy	Perioperative Mortality
5-6	A	15-50 yrs	10%
7-9	B	Candidate for transplant	30%
10-15	C	1-3 months	82%
Score: 5-6 (Child's A), 7-9 (Child's B), 10-15 (Child's C)			

Figure 21: Interpretation of child pugh score

MELD SCORE:

It was originally developed by Dr Patrick Kamath at mayo clinic to predict the likelihood of survival in cirrhotic patients with refractory ascites undergoing transjugular intrahepatic portosystemic shunt (TIPSS)(43). Researchers discovered the four objective variables capable of independently predicting survival in these patients in a multivariate Cox model. These were bilirubin, creatinine, INR and cause of cirrhosis (alcohol and cholestatic versus

other causes). It is calculated using the formula

MELD= 3.78 × log[serum bilirubin(mg/dl)] + 11.2 × log[INR] + 9.57×log[serum creatinine(mg/dl)] + 6.43×[etiology]

Etiology:0-cholestatic/alcohol,1-others.

Each variable was log transformed and had a regression coefficient attached relative to its individual contribution to the model. Then years later, it was also used to allocate patients for liver transplantation based on severity.(44) Later studies found out that the etiology turned out to be relatively unimportant and the score was calculated as

MELD= 3.78 × log[serum bilirubin(mg/dl)] + 11.2 × log[INR] + 9.57×log[serum creatinine(mg/dl)] + 6.43.

This score was also extensively studied in hospitalized cirrhotic patients, ambulatory patients without cholestasis, patients with Primary Biliary Cirrhosis and a large unselected patient cohort from the 1980s.

Interpretation:

The 3 month mortality based on MELD score in hospitalised patients is

Table 9: Interpretation of MELD.

Score	Mortality in%
40 or more	71.3
30-39	52.6
20-29	19.6
10-19	6.0
<9	1.9

Caveats within score:

- The maximum score given for MELD is 40. All values higher than 40 are given a score of 40.

- Maximum value for creatinine was 4 and if the patient has underwent dialysis twice within the last week, the value for serum creatinine used should be 4.0.
- Any value less than one is given a value of one (i.e. if bilirubin is 0.8, a value of 1.0 is used).

PROGNOSTIC VALUE OF SODIUM(49):

Hyponatremia in cirrhosis is a chronic process and this allows the brain to adapt to the hypo-osmolality of the extracellular fluid. Patients with cirrhosis and hyponatremia are less likely to have severe neurologic symptoms due to the fact that hyponatremia develops very slowly(32). However, hyponatremia may pose a additional insult to cerebral edema and astrocyte swelling, in addition to the astrocyte dysfunction caused by increased intracellular glutamine concentration from ammonia metabolism, thereby precipitating hepatic encephalopathy.

The quality of life is poor in patients with cirrhosis and hyponatremia due to the requirement for strict fluid restriction. Hyponatremia has been found to be an independent predictive factor of the impaired health related quality of life(45) as well as hepatic encephalopathy(46). Many studies suggest that the extent of hyponatremia and severity of ascites can be used to determine disease severity and

prognosis in cirrhosis. The degree of hyponatremia is proportional to the circulatory dysfunction and secondary sympathetic system activation. In one study, the serum sodium level before the onset of spontaneous bacterial peritonitis (SBP) was an independent predictor of renal failure triggered by SBP. It has also been suggested that serum sodium is more sensitive test than serum creatinine to detect circulatory dysfunction resulting in renal failure or death. Sodium levels rose even before creatinine level raised. Although patients with hyponatremia are at a very high risk for developing hepatorenal syndrome, low serum sodium in hepatorenal syndrome is not only due to high ADH levels but also due to decreased GFR and proximal sodium reabsorption.

Patients with hyponatremia were found to have a higher risk of early death before transplantation independent of the severity of cirrhosis as assessed by the MELD scores. Sodium and MELD score proved to be independent prognostic factors. Hence, some investigators have advocated a prioritised liver transplantation under a ‘sickest first’ model based on sodium values in cirrhotic patients with MELD scores below 21, persistent ascites and hyponatremia. These studies formed the basis of a suggestion that serum sodium could be incorporated into the MELD score(47), and this may provide a more accurate survival prediction than MELD alone.(48)

MATERIALS AND METHODS

Source of the study:

The study was conducted on 100 patients admitted in Government Mohan Kumaramangalam Medical College Hospital diagnosed to have cirrhosis during the study period August 2014- August 2015.

Method of collection of data:

The data of the patients was collected in a well designed proforma. Informed consent was obtained from all the patients. Patients diagnosed to have cirrhosis based on clinical examination and investigations were selected. A detailed history was taken and all essential investigations done. Serum sodium was measured in all the patients. Based on investigation results, Child-Pugh score and MELD score was calculated for all patients to assess severity of cirrhosis. Complications present in all the patients was documented.

Inclusion criteria:

Patients with cirrhosis

Both sexes included

Exclusion criteria:

Patients with cardiac disease

Patients with chronic kidney disease

Patients on diuretics

Statistical analysis:

Tabulation and statistical analysis were performed using Microsoft excel and SPSS v.17.0 software. Numerical data were summarised by measures of central tendency:mean and standard deviation. Qualitative data was analysed with descriptive statistics & a two way univariate analysis was used for comparison of study variables. If p value < 0.05 at 95% confidence interval it is taken as statistically significant.

OBSERVATIONS AND RESULTS

The study included 100 patients with cirrhosis out of which 93 patients were males and 7 patients were females. The mean age of the patients was 48.27±10.85 years. The basic demographic details of the patients is given in the table below.

Table 10:Basic demographic details of the patients

S.NO	PARAMETER	N=100
1	Age(years)(Mean±SD)	48.27±10.85
2	Sex: (number)(%) Males females	 93 7
3	Cause of cirrhosis(no)(%) Alcohol Hepatitis B Hepatitis C	 96 2 2
4	MELD score (Mean±SD)	22.53±8.16
5	Serum Na^+ (Meq/L)(Mean±SD) a) ≤130Meq/L b)131-135 Meq/L c) ≥136 Meq/L (Number%)	131.38±9.38 31(31%) 21(21%) 48(48%)

About 96% of the cirrhosis patients were due to alcohol, 2% of cirrhosis was due to hepatitis B infection, 2% were due to hepatitis C infection. Alcohol was the most common cause contributing to about 96% of cirrhosis. The MELD score of the patients ranged from 9-46, the mean MELD score was found to be 22.53±8.16.

The serum sodium level of the patients ranged from 108 to 145 Meq/L. The mean sodium score of the patients was 131.38±9.38. Based on the diagnostic criteria of hyponatremia in cirrhosis 31(31%) patients had serum sodium ≤ 130 Meq/L. 21(21%) patients had mild hyponatremia with serum sodium between 131-135 Meq/L. The remaining 48 patients had serum sodium ≥136 Meq/L.

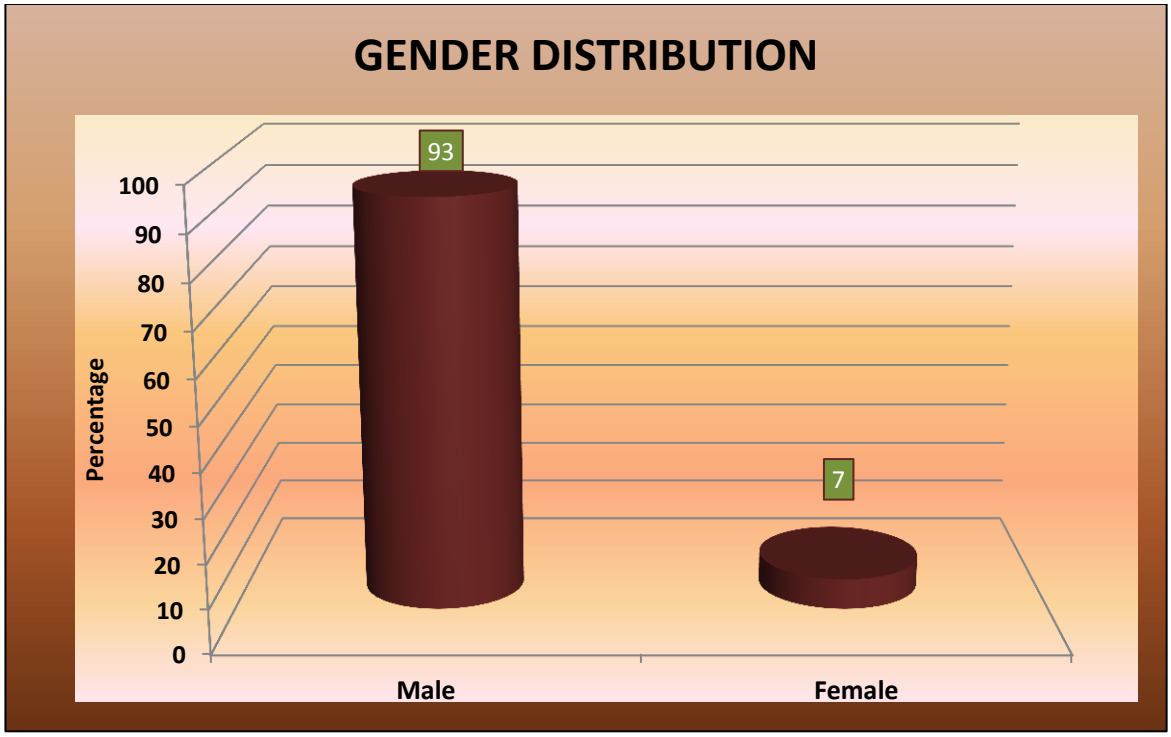

Figure 22:Bar diagram showing sex distribution of cirrhotic patients

The male :female sex ratio is around 13.2:1 in our study. Male preponderance for cirrhosis is due to the increased alcohol intake in males compared to females.

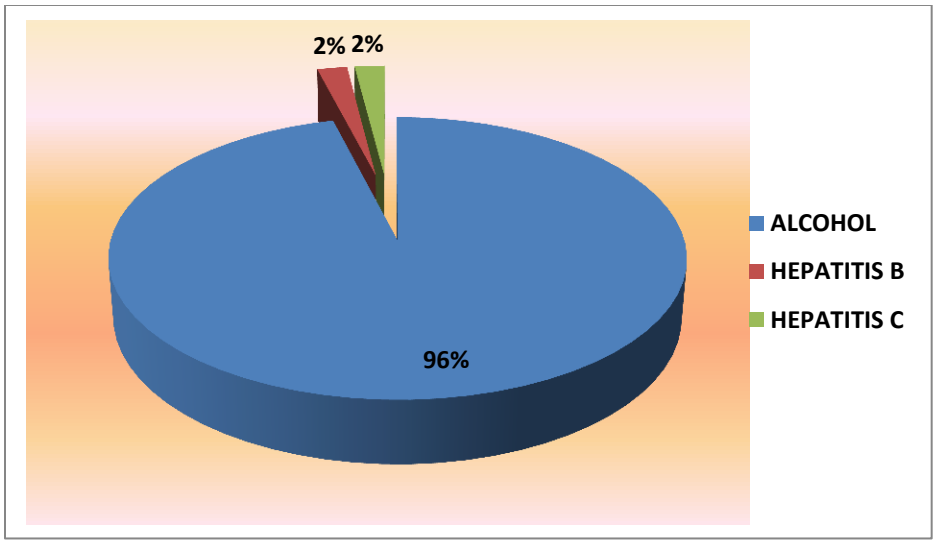

Figure 23:Pie chart showing etiological causes of cirrhosis

96% of the cases were due to alcohol and 2 cases were due to Hepatitis B and Hepatitis C infection each.

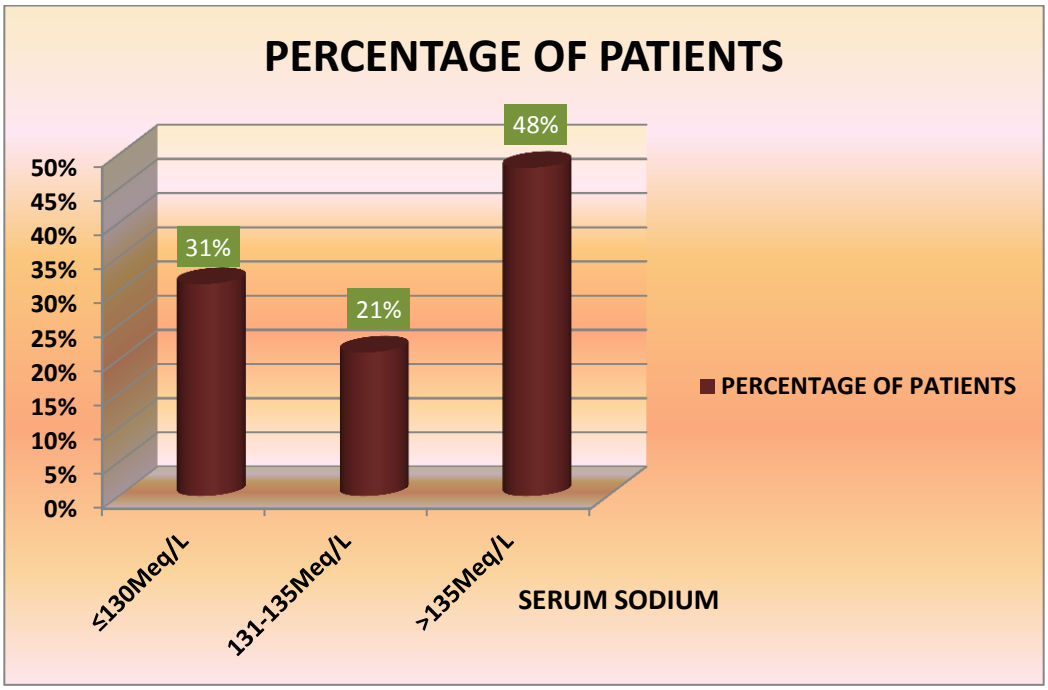

Figure 24:Bar diagram showing distribution of patients according to serum sodium concentration in Meq/L.

Among the 100 patients , 31 patients had serum sodium≤ 130Meq/L. 21 patients had mild hyponatremia with serum sodium concentration between 131-135 Meq/L. Remaining 48 patients had normal serum sodium concentration >135Meq/L.

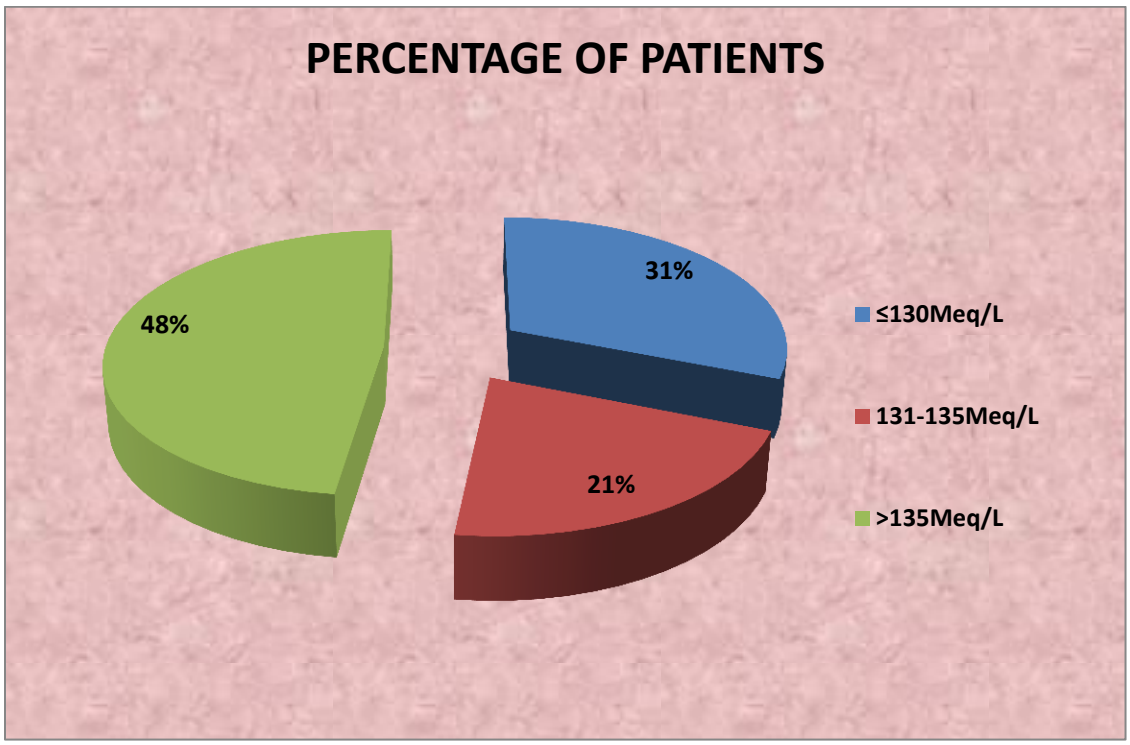

Figure 25: Pie chart showing distribution of serum sodium

Table 11:CHARACTERISTICS OF PATIENTS BASED ON SERUM SODIUM

S.NO	PARAMETER	Na^+≤130Meq/L (N=31)	Na^+ 131-135Meq/L (N=21)	Na^+≥136Meq/L (N=48)
1.	Age(mean ± SD)(years)	45.47±10.28	45.75±11.93	44.09 ±9.64
2.	Sex: M F	 27(87%) 4(13%)	 20(95%) 1(5%)	 46(96%) 2(4%)
3.	Cause of cirrhosis Alcohol Hepatitis B Hepatitis C	 30 1 -	 20 1 -	 46 0 2
4.	MELD * (MEAN±SD)	27.45±9.24	24.76±6.86	18.38±5.46
5.	Child-Pugh @ score (MEAN±SD)	11.29±1.49	10.76±1.48	9.63±1.65
	Class A# Class B Class C	0 3 28	0 3 18	4 13 31

*-p value<0.001, @ p value<0.001,# p value-0.049

The patients were divided into three categories based on serum sodium to compare patients belonging to each category. The mean age of the patients with serum sodium≤130Meq/L,131-135 Meq/L and ≥136Meq/L were 45.47±10.28, 45.75±11.93 and 44.09±9.64 respectively. The age of the patients was comparable in all the 3 categories and did not show any statistical significance.

Frequency of gender among these 3 groups was studied and did not show any significant correlation with serum sodium with a p value of 0.299.

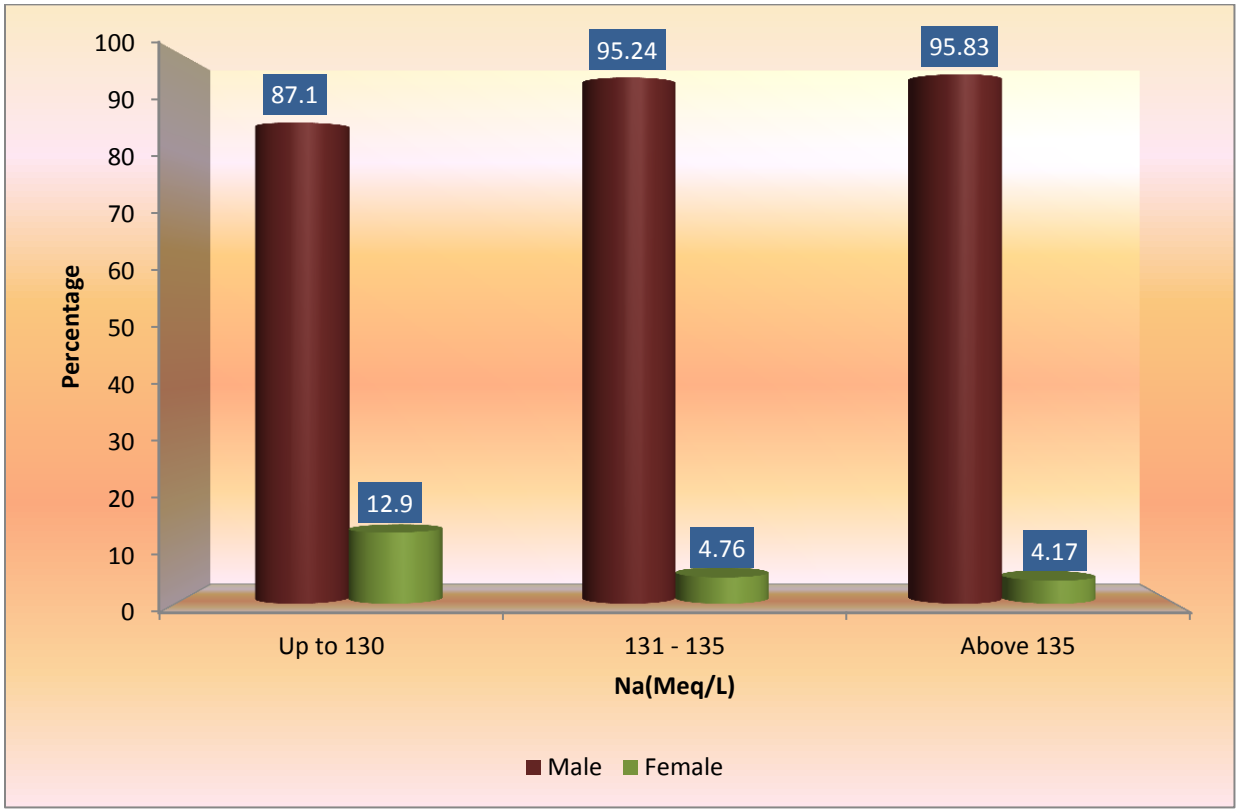

Figure 26: Bar diagram showing gender distribution according to serum sodium.

The etiology of cirrhosis was studied in the 3 groups and did not show any correlation with serum sodium .

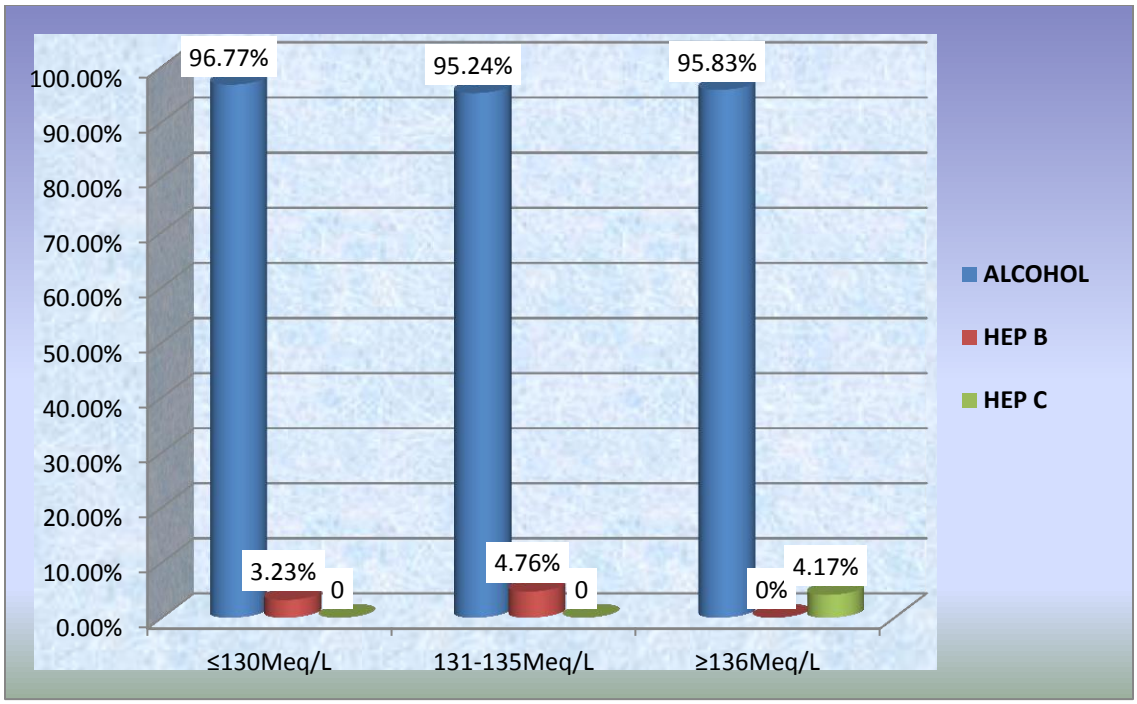

Figure 27: Bar diagram showing cause of cirrhosis according to serum sodium

Thus age, sex and etiology did not show any correlation with serum sodium and degree of hyponatremia.

The mean MELD score in patients with serum sodium ≤130Meq/L, 131-135 Meq/L and ≥136Meq/L was 27.45±9.24, 24.76±6.86 and 18.38±5.46 respectively. The association was found to have high statistical significance and p value <0.001. Patients with severe hyponatremia had higher mean MELD score compared to patients with normal sodium.

Table 12: Mean MELD score in various categories

SERUM SODIUM IN MEQ/L	MEAN MELD SCORE
≤130	27.45±9.24
131-135	24.76±6.86
≥136	18.38±5.46

P VALUE- <0.001

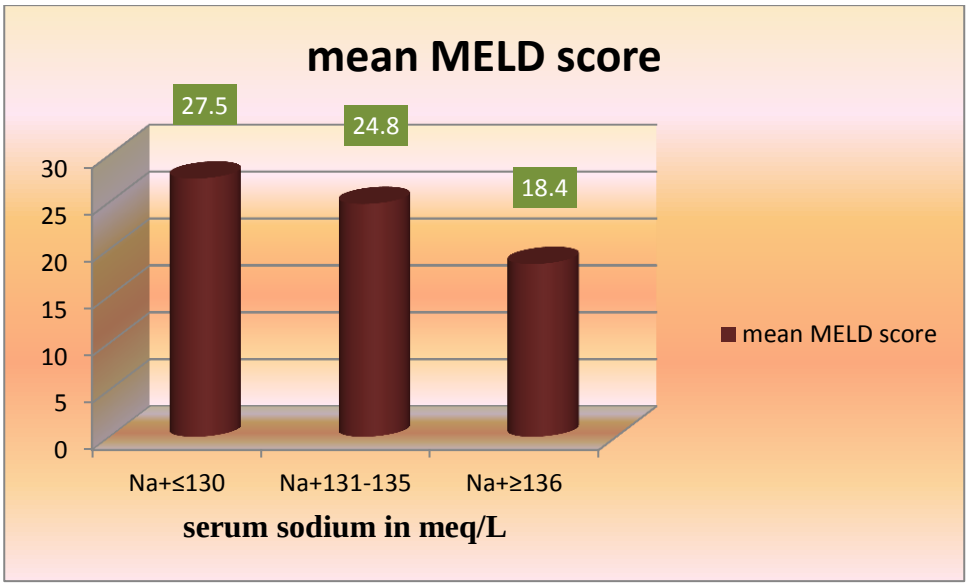

Figure 28:Bardiagram showing mean MELDscore according to serum sodium

Patients in each category were assessed for disease severity using Child Pugh score with severe disease having higher scores. The mean Child Pugh score in patients with serum sodium ≤130Meq/L, 131-135 Meq/L and ≥136Meq/L was 11.29±1.49, 10.76±1.48 and 9.67±.65 respectively. Patients with lower sodium levels had more severe disease as indicated by higher CPS scores.

90.32 % with serum sodium ≤130meq/L belonged to class C as compared to 85.71% in patients with sodium between 131-135 and 64.58% in patients with sodium >135 meq/L. The analysis showed significant statistical correlation with p value of 0.049. 8.33% of patients with sodium >135Meq/L belonged to child-pugh class A whereas no patient with serum sodium≤ 130 Meq/L belonged to child pugh class A. Only 9.68% of patients with sodium≤ 130Meq/L belonged to classB whereas 14.29% of the second category and 27.08% with serum sodium >135Meq/L belonged to class B.

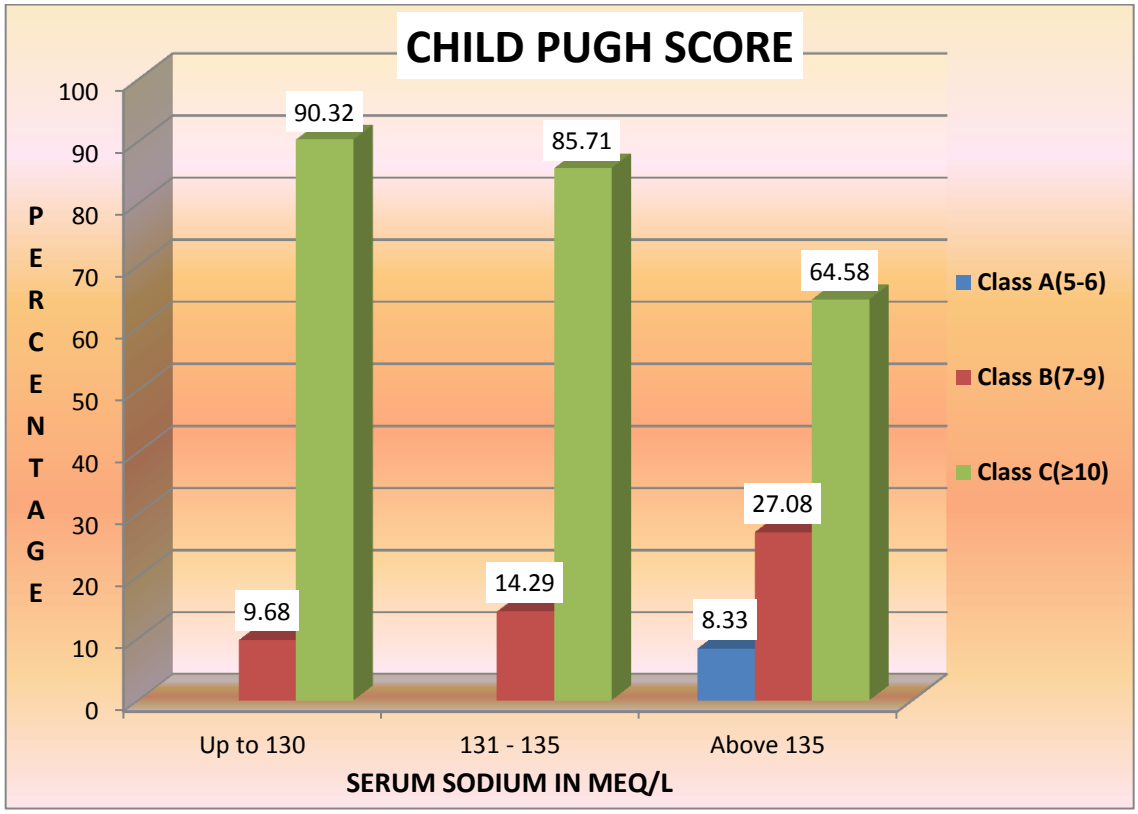

Figure 29: Bar diagram showing subclassification of patients into child pugh severity class.

Table 13: FREQUENCY OF COMPLICATIONS IN STUDY PATIENTS

S.NO	COMPLICATION	FREQUENCY(%)
1	Ascites	95
2	Portal hypertension(PHT)	98
3	Hepatic encephalopathy(HE)	33
4	Variceal bleeding	28
5	Coagulopathy	17
6	Hepatorenal syndrome(HRS)	9

Among the 100 patients studied 95(95%) had ascites, 98(98%) had portal hypertension, 33(33%) patients developed hepatic encephalopathy. Variceal bleeding was present in 28(28%) patients and coagulopathy was present in 17(17%) persons. 9 patients(9%) developed hepatorenal syndrome.

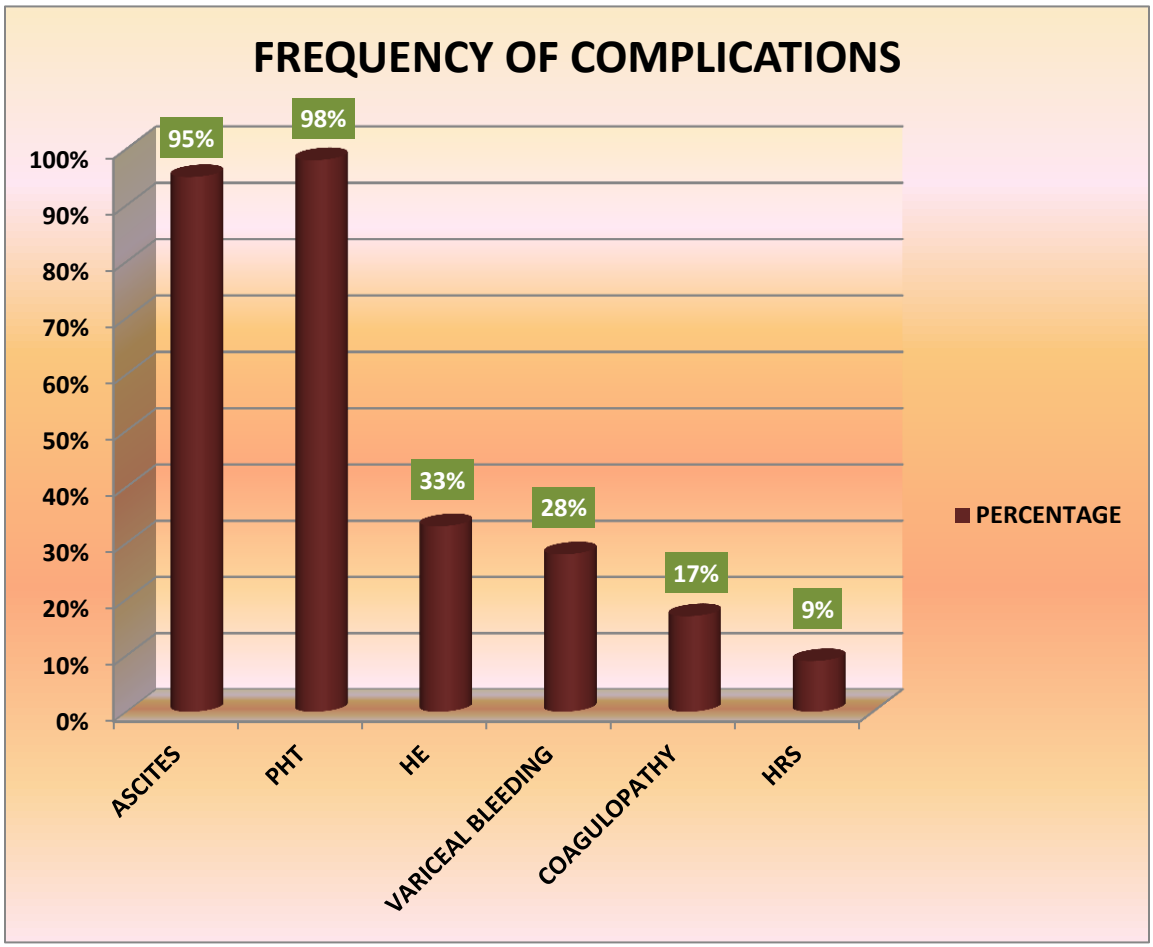

Figure 30:

Bar diagram showing frequency of various complications in 100 patients

Table 14: FREQUENCY OF COMPLICATIONS ACCORDING TO SERUM SODIUM

S. NO	COMPLICATIONS	$Na^+ \leq 130$ meq/L (n=31)	Na^+ 131-135 Meq/L (n=21)	$Na^+ \geq 136$ Meq/L (n=48)	Chi square	P value
1	Ascites	31 (100%)	21 (100%)	43 (89.58%)	5.7	0.058
2	Portal hypertension	31 (100%)	21 (100%)	46 (95.83%)	2.21	0.331
3	Hepatic encephalopathy(HE)	20 (64.52%)	10 (47.62%)	3 (6.25%)	31.49	<0.001
4	Variceal bleeding	11 (35.48%)	10 (47.62%)	7 (14.58%)	9.16	0.06
5	Coagulopathy	10 (32.26%)	2 (9.52%)	5 (10.42%)	7.42	0.024
6	Hepatorenal syndrome(HRS)	7 (22.58%)	2 (9.52%)	0	11.14	0.003

There was a no significant difference in between these 3 groups of sodium levels in the frequency of ascites and portal hypertension. The p values were not significant. There was no significant correlation between sodium level and variceal bleeding (p value 0.06).

There was significant difference between 3 groups in the occurrence of hepatic encephalopathy, coagulopathy and hepatorenal syndrome. The p values were 0.001, 0.024 and 0.003 repectively.

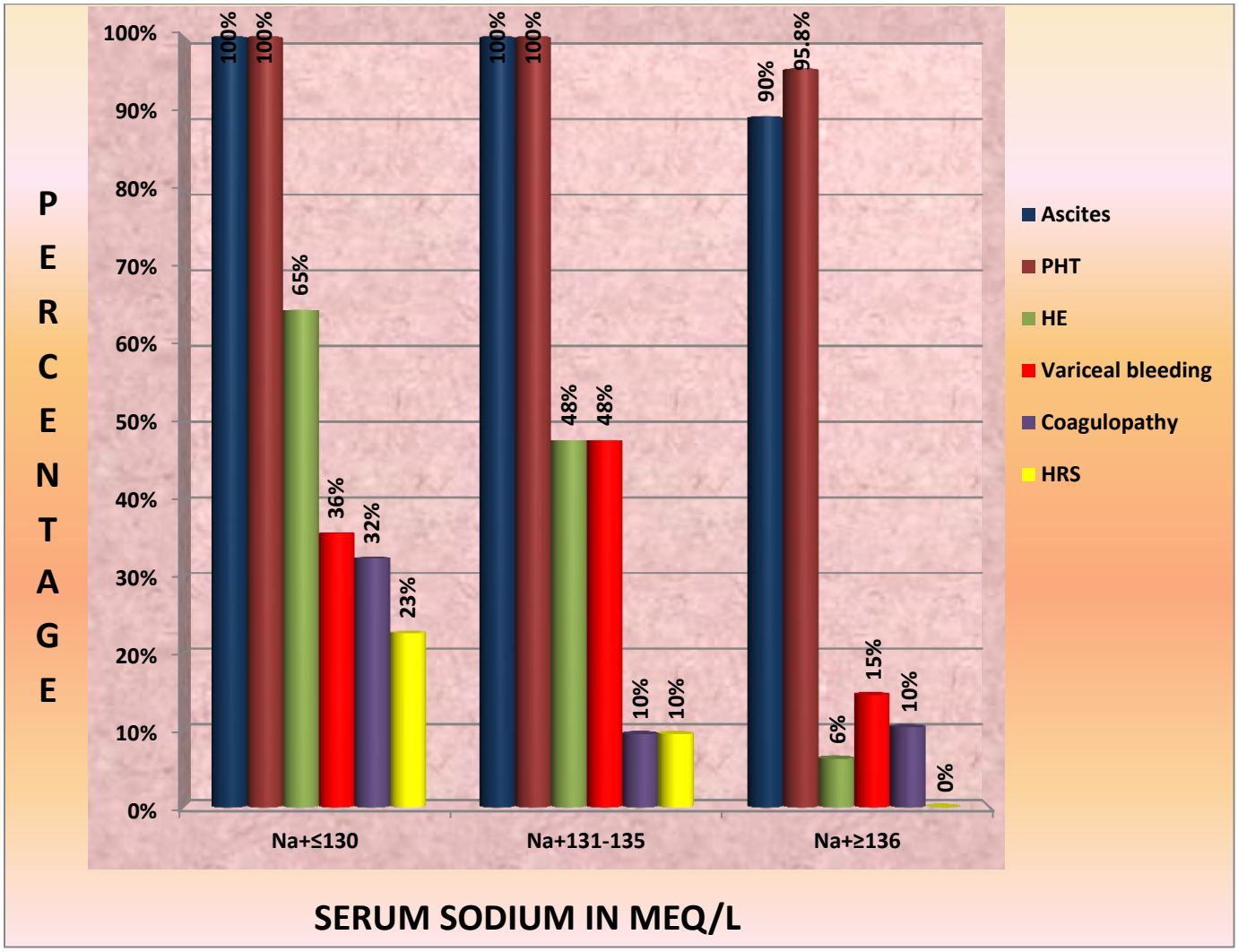

Figure 31: Bar diagram showing comparison of complications between various sodium levels

Patients with sodium less than 130 meq/L had more incidence of complications when compared to patients with higher sodium concentration.

Table 15: COMPARISON OF COMPLICATIONS ACCORDING TO SERUM SODIUM CONCENTRATION

COMPLICATIONS	**Sodium ≤130meq/L**		**Sodium 131-135meq/L**	
	Odds ratio (95%CI)	P value	Odds ratio (95%CI)	P value
ASCITES	14.8	0.0647	12.8	0.128
PHT	38.5	0.2553	33.5	0.350
HE	0.411	0.0001	0.232	0.001
Coagulopathy	0.234	0.0153	0.113	0.912
HRS	0.097	0.0004	0.03	0.030
Variceal Bleeding	0.295	0.0307	0.327	0.003

CI-confidence interval

Patients with serum sodium ≤ 130meq/L had increased risk of complications when compared to patients with serum sodium >135meq/L. There was increased risk of hepatic encephalopathy(p value-0.0001), coagulopathy(p value-0.0153), hepatorenal syndrome(p value-0.0004) and variceal bleeding(p value-0.037).

Ascites and portal hypertension were not associated with increased risk in patients with serum sodium≤ 130meq/L(p values were not significant).

Patients with serum sodium between 131-135meq/L when compared to patients with serum sodium>135 meq/L had increased risk of hepatic encephalopathy (p value 0.001), hepatorenal syndrome(p value 0.030) and variceal bleeding (p value 0.003). These patients did not have increased risk of ascites(p value-0.128), portal hypertension(p value-0.350) and coagulopathy(p value-0.912).

Table 16: OUTCOME OF PATIENTS UNDER STUDY

Total no of patients	**No of deaths**	**Patients on treatment**
100	9	91

Out of the 100 patients studied, 9 patients died.

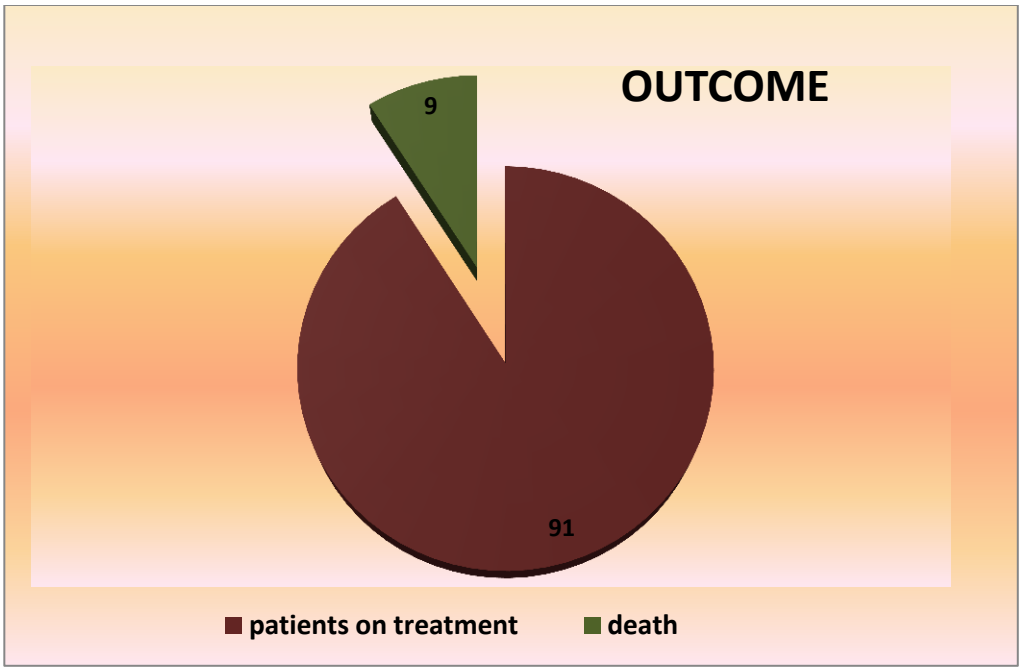

Figure 32: Pie chart showing mortality rate of patients studied

Table 17: MORTALITY ACCORDING TO SERUM SODIUM

SERUM SODIUM	≤130Meq/L	131-135 Meq/L	>135 Meq/L	P VALUE
MORTALITY	7(22.6%)	2(9.5%)	0	0.003

P value<0.05-statistically significant

7(22.6%) out of 31 patients with serum sodium died and 2(9.5%) out of 21 patients with serum sodium between 131-135meq/L died. No patient in the group with serum sodium> 135meq/L died. There was significant statistical correlation of mortality with serum sodium in these 3 groups.

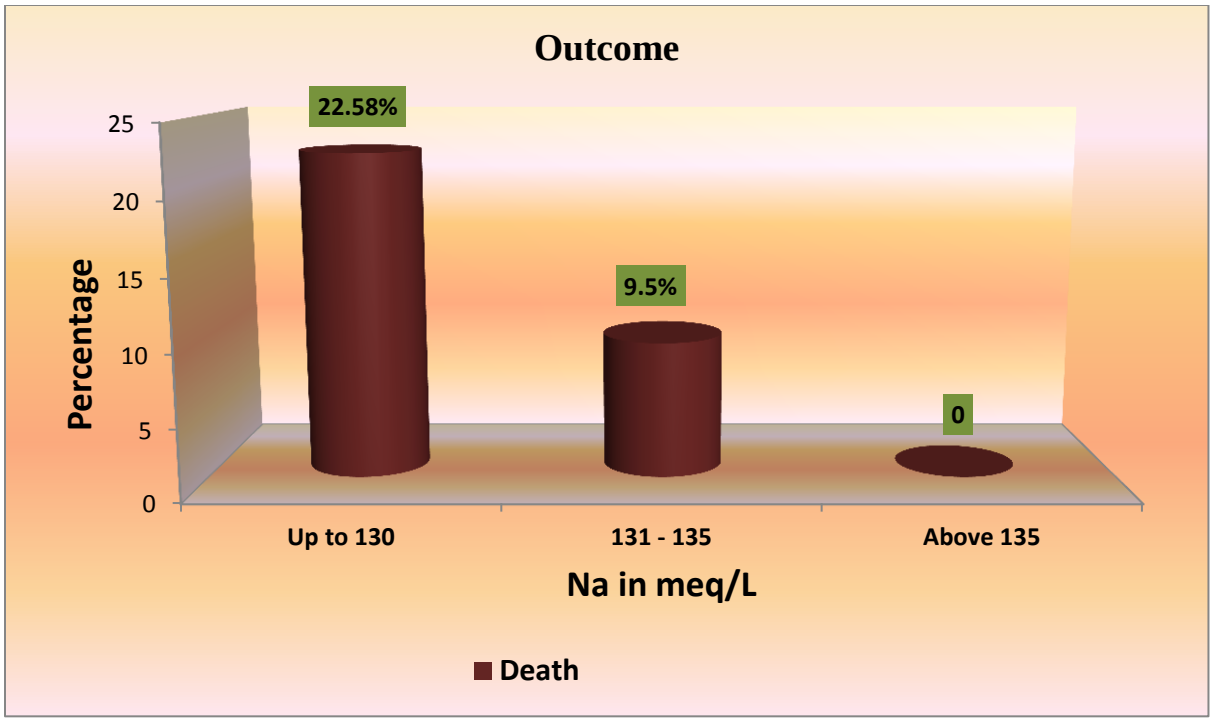

Figure 33: Bar diagram showing percentage of mortality according to serum sodium.

Patients with severe hyponatremia had increased mortality(22.6%) when compared to patients with mild hyponatremia(9.5%). There was no mortality in patients with sodium >135meq/L.

DISCUSSION

Hyponatremia is the most prevalent electrolyte imbalance in hospitalised patients. Dilutional hyponatremia(50) is common in patients with cirrhosis, it develops as a result of compensatory mechanisms that act to increase the effective circulatory volume. Therefore more severe form of the disease is associated with robust activation of compensatory mechanisms and the extent of hyponatremia can give as an idea about the severity of the underlying pathology. There has been recent interest in using sodium as a variable to prognosticate cirrhotic patients.

Our study was done to study the prevalence of hyponatremia and its association with various complications of the disease.

In our study the prevalence of hyponatremia as per definition ≤ 130 Meq/L was found to be 31%. The prevalence was 52% for serum sodium cut off value of 135Meq/L. 48 % patients had normal sodium levels. Several studies showed similar incidence of hyponatremia in patients with cirrhosis.

Table 18: STUDIES COMPARING PREVALENCE OF HYPONATREMIA

Studies	Prevalence of hyponatremia%		
	≤130	**131-135**	**≥136**
Present study (n=100)	31%(31/100)	21%(21/100)	48%(48/100)
Angeli P et al(51) (n=997)	21.6% (211/997)	27.8% (275/997)	50.6% (497/997)
Jong H Kim et al(52) (n=188)	27.1% (51/188)	20.8% (39/188)	52.1% (98/188)
Shaikh S (53) (n=217)	26.7% (58/217)	24.9% (54/217)	48.4% (105/217)
Borroni G et al (54) (n=156)	29.8% (57/156)		

Similar study was conducted by Angeli et al in 997 consecutive patients from 28 centers in 4 continents Europe, Asia, North and South America . The study was conducted for a period of 28 days. The prevalence of hyponatremia was found to be 21.6% and 27.8% in the categories of sodium ≤130 and 131-135Meq/L. The patients with lower sodium levels had more complications and more difficult to treat ascites, poorly responding to medical therapy.

Another study by Sheikh et al was a case control study consisting of 217 patients. The incidence of hyponatremia was 58/217(26.7%). 54(24.9%) patients had serum sodium between 131-135Meq/L. The remaining 48. 4% patients had normal serum sodium.

Yet another study conducted by Jong Hoon Kim et al conducted on 188 patients showed 27.1%, 20.8% and 52.1% patients with serum sodium≤130, 131-135 and ≥136 Meq/L respectively.

Table 19:COMPARISON OF PREVALENCE OF HEPATIC ENCEPHALOPATHY

Studies	Frequency of hepatic encephalopathy		
	≤130	131-135	≥136
Present study(n=100)	64.52%(20/31)	47.62%(10/21)	6.25%(3/48)
Angeli P et al (n=997)	38%	24%	15%
Kim JH et al (n=188)	23%	14%	24%
Shaikh S et al (n=217)	25.8%		

In our study the frequency of hepatic encephalopathy was 64.52% in pateints with hyponatremia and 47.62% and 6.25% in patients of other two categories. The frequency of encephalopathy in patients with hyponatremia in other studies varied from 23% to 38% respectively.

Qureshi(55) et al studied patients admitted to shifa hospital, Islamabad. He selected 202 patients with cirrhosis and hepatic encephalopathy and measured their sodium values. Patients were graded according to severity of encephalopathy. Patients with lower sodium had higher incidence of encephalopathy and higher grade of encephalopathy according to West Havens grading.

Guevera et al(56) did a prospective study on 61 patients for 1 year while monitoring their sodium levels every week. He looked for the development of encephalopathy and correlated with serum sodium values. He concluded that sodium could be used to predict onset of encephalopathy.

Hyponatremia acts as a further insult to the already damaged brain in cirrhosis due to various factors such as hyperammonemia, altered neurotransmitters. Both hyponatremia and hyperammonemia cause shift of extracellular water into astrocytes. This causes astrocyte swelling and reduction in osmolytes. This leads to brain dysfunction. Thus hyponatremia acts as an independent risk factor for hepatic encephalopathy. Studies by Guevera et al showed that patients with decreased serum sodium had decreased intracellular osmolytes in astrocytes, especially myoinositol. Patients who went in for hepatic encephalopathy had decreased myoinositol levels. This suggests us a new treatment strategy to treat hyponatremia in order to prevent hepatic encephalopathy.

Table 20: COMPARISON OF PREVALENCE OF HEPATORENAL SYNDROME

Studies	Frequency of hepatorenal syndrome		
	≤130	**131-135**	**≥136**
Present study(n=100)	22.58%(7/31)	9.52%(2/21)	0
Angeli P et al (n=997)	17%	10%	6%
Kim JH et al (n=188)	3.9%	2.5%	3%

The incidence of hepatorenal syndrome was 22.58% in pateints with hyponatremia and 9.52% in patients with intermediate sodium levels and none of the patients with normal sodium had hepatorenal syndrome.

The prevalence of hepatorenal syndrome in patients with hyponatremia in other studies ranged from 3.9% to 17%. Patients with severe hyponatremia usually have more decreased effective circulatory volume and decreased renal perfusion leading to more number of cases of hepatorenal syndrome. Hepatorenal syndrome usually sets in only after the exhaustion of compensatory mechanisms and persistent renal retention of sodium. So it is logical to think that serum sodium starts falling earlier than when actual hepatorenal syndrome develops. Serum sodium can hence be used to reasonable extent to assess the risk of development of renal failure.

When patients were classified according to severity using child pugh score, among 31 patients with hyponatremia 90.3% belonged to child Pugh class C whereas among patients with sodium131-135meq/L 85.7% belonged to class C. among patients with normal sodium only 64.6% belonged to class C. This shows that in liver cirrhosis, the more severe the hyponatremia the more severe is the underlying disease.

Table 21: MORTALITY RATE ACCORDING TO SERUM SODIUM

Serum sodium(meq/L)	**No of deaths**
≤130	7(22.6%)
131-135	2(9.5%)
≥136	0

When comparing the mortality rate among 3 categories, 7 out of 31 with hyponatremia died, 2 out of 21 with sodium 131-135meq/L died but no deaths occurred in patients with normal sodium. In another study on patients with cirrhosis the mortality rate among patients with sodium ≤ 130 meq/L was found be 27%. Similar mortality rate was found in our study also. Patients in that study with sodium <125 meq/L showed even higher mortality rate of 48%. Thus serum sodium correlates with morbidity and mortality and can be used as a prognostic

factor in patients with cirrhosis. Hence our study suggests the importance of treating hyponatremia in cirrhosis. Improvement of hyponatremia reduces the need for very strict fluid restriction in patients. It also reduces the risk of complications.

CONCLUSION

Hyponatremia is very common in patients with cirrhosis, mostly as a result of dilutional hyponatremia. The severity of decrease in sodium levels is associated with increased risk of complications such as hepatic encephalopathy, hepatorenal syndrome and coagulopathy. Patients with severe hyponatremia are also associated with significantly higher rates of morbidity and mortality.

SUMMARY

- The present study was conducted on 100 patients diagnosed with cirrhosis in Government Mohan Kumaramangalam Medical College Hospital in salem from August 2014-August 2015.
- All cases were evaluated with detailed history and relevant investigations.
- Out of 100 patients 93 were males and 7 were females
- The prevalence of hyponatremia was found to be 31% and it increased to about 52% if a cut off value of 135meq/L was taken.
- Severity of hyponatremia was associated with increased severity of complications.
- Severe hyponatremia had increased correlation with hepatic encephalopathy, hepatorenal syndrome and coagulopathy.
- Ascites and portal hypertension was not significantly associated with serum sodium levels
- Mortality rate in this study was 9%
- Severe hyponatremia was associated with increased mortality
- Hence hyponatremia can be used to predict prognosis of a patient with cirrhosis.

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PROFORMA

Name: **Age/sex:**

Address:

O.PNo: **I.P No:**

D.O.A: **D.O.D:**

CHIEF COMPLAINTS:	**YES**	**NO**
Jaundice		
Abdominal distention		
Leg swelling		
Fever		
Bleeding		
Abdominal pain		
Altered sesorium		
Others		

PAST HISTORY:

PERSONAL HISTORY:

FAMILY HISTORY:

PERSONAL HISTORY:

Alcohol

Smoking

GENERAL PHYSICAL EXAMINATION:

Nourishment anemia

Jaundice cyanosis

Clubbing pedal edema

lymphadenopathy

Vitals: PR :

BP :

RR :

Temperature :

Weight : ( ) kg

Signs of liver cell failure

SYSTEMIC EXAMINATION:

1. Abdomen: ascites

Liver spleen

Bowel sounds

2. Respiratory system:

3. Cardiovascular System:S1 S2 murmurs

4. Central Nervous System:sensorium

asterixis

COMPLICATIONS:

Ascites

Hepatic encephalopathy

Hepatorenal syndrome

Coagulopathy

Bleeding varices

others

INVESTIGATIONS:

Complete blood count

Renal function tests

Electrolytes including serum sodium

Urine complete

Liver function tests

Prothrombin time,INR

USG Abdomen

Ascitic fluid analysis

Upper GI Endoscopy

MASTER CHART

S.NO	NAME	AGE/SEX	ASCITES	PHT	HE	COAG	HRS	UREA	Cr	VB	Na	TB/DB	TP/ALB	AST/ALT/ALP	PT/INR	MELD	CPS	CAUSE	OUTCOME
1	Sengottuvel	40/M	P	P	P	P	P	160	4.8	P	118	16/ 8.2	6.3/ 3	80/ 60/ 140	48/ 3.2	43	13	ALC	D
2	Shanmugam	43/M	P	P	A	A	A	32	1.3	A	136	5/ 3.8	5.3/ 2.8	74/ 68/ 158	15/0.9	15	9	ALC	OT
3	Raman	38/M	P	P	A	A	A	33	0.9	A	139	6.3/ 2.8	6.2/ 3.6	46/ 29/ 98	14/1	13	8	ALC	OT
4	Kangamuthu	55/M	P	P	P	A	A	40	0.7	A	132	10.2/ 5.6	7.4/ 2.8	36/ 68/ 158	23/1.2	17	10	ALC	OT
5	Venkatappan	30/M	P	P	P	A	A	26	0.8	A	120	8.9/ 4.3	8.6/ 3.9	69/ 82/ 177	24/1.8	21	10	ALC	OT
6	Rajendran	48/M	P	P	A	A	A	22	1.1	P	136	4.2/ 2.1	7.4/ 2.9	45/ 77/ 154	22/1.6	18	9	ALC	OT
7	Mani	48/M	P	P	A	P	P	49	3.2	A	122	18.4/ 11.6	5.2/ 2.0	90/ 70/ 126	74/4.0	44	13	ALC	OT
8	Suresh kumar	48/M	P	P	A	A	A	18	1.2	A	131	8.4/ 6.3	8.1/ 3.3	77/ 69/ 101	29/1.9	23	10	ALC	OT
9	Chella durai	36/M	P	P	P	A	A	17	0.5	A	110	11/ 5.5	9.5/ 2.6	59/ 49/ 188	27/1.3	18	11	ALC	D
10	Mohana sundaram	33/M	P	P	A	P	A	22	0.8	A	140	2.5/ 1.2	7.0/ 4.4	48/ 66/ 159	32/2.9	22	9	ALC	OT
11	Jayaraman	48/M	P	P	A	A	A	16	0.7	A	118	6.8/ 2.1	8.0/ 2.9	50/ 61/ 97	16/1.1	15	9	ALC	OT
12	Murugesh	53/M	P	P	A	A	A	25	0.9	A	134	7.0/ 3.2	5.9/ 2.9	46/ 33/ 131	19/1.5	18	9	ALC	OT
13	Chellapan	60/M	P	P	A	A	A	28	0.4	A	138	2.3/ 0.9	6.6/ 2.8	20/ 55/ 155	17/1.7	16	8	ALC	OT
14	Backiyalakshmi	55/F	P	P	P	A	A	35	0.8	A	120	7.6/ 1.6	8.4/ 3.7	44/ 66/ 147	19/0.9	14	9	ALC	OT
15	Kaliyappan	36/M	P	P	A	A	A	33	0.8	A	136	6.9/ 3.1	7.3/ 2.7	55/ 33/ 100	11/0.8	14	10	HEP C	OT
16	Paramasivam	35/M	A	P	A	A	A	28	0.9	A	139	1.9/ 1.2	5.3/ 3.1	77/ 29/ 92	18/1.2	11	6	ALC	OT
17	Ayyanar	38/M	P	P	A	A	A	26	1	A	120	8.8/ 1.8	8.0/ 4.0	66/ 39/ 88	22/1.8	21	9	ALC	OT
18	Veeran	58/M	P	P	A	A	A	30	1.1	A	138	9.3/ 5.8	8.0/ 2.9	104/ 98/ 199	32/2.6	26	12	ALC	OT
19	Kuppusamy	75/M	P	P	P	P	P	80	3.8	P	133	10/ 4.2	8.2/ 1.5	29/ 39/ 166	78/5	46	14	HEP B	D
20	Palaniyappan	69/M	P	P	A	A	A	18	0.8	A	136	3.2/ 2.3	7.2/ 3.0	44/ 66/ 161	27/1.5	15	9	ALC	OT
21	Rajamani	48/F	P	P	A	A	A	22	0.4	A	130	8.8 /2.7	7.3 /3.5	57/39/105	31/ 2.1	23	10	ALC	OT
22	Ramesh	46/M	P	P	P	A	A	20	0.3	A	116	9.7 /2.8	6.6/ 1.4	38/ 44/ 104	33/2.2	24	12	ALC	OT
23	Vadivel	40/M	P	P	P	A	P	86	3.8	P	110	12/ 5.7	5.9/ 2.6	44/ 55/ 178	36/ 2.4	38	13	ALC	OT
24	Perumal	49/M	A	A	P	A	A	21	0.6	A	138	2.4 /0.9	6.2/3.6	58/ 66/ 111	13/ 0..9	10	6	ALC	OT
25	Kandan	60/M	P	P	A	A	A	30	0.7	A	138	3.6 / 2.8	7.5/ 2.8	44/ 61/ 89	14/ 1	11	9	ALC	OT

S.NO	NAME	AGE/SEX	ASCITES	PHT	HE	COAG	HRS	UREA	Cr	VB	Na	TB/DB	TP/ALB	AST/ALT/ALP	PT/INR	MELD	CPS	CAUSE	OUTCOME
26	Udhaya kumar	25/M	P	P	A	A	A	35	1.1	A	144	5.2/ 2.2	8.3/ 4.2	76/ 89/ 121	18/ 1.2	16	8	ALC	OT
27	Hazeeb	37/M	P	P	A	A	A	36	0.9	P	134	9.5 /4.6	8.3/ 2.2	88/ 29/ 131	33/ 2.1	23	11	ALC	OT
28	Kaliyan	62/M	P	P	A	A	A	31	1.2	A	138	4/2.2	8.8/ 1.9	73/ 89/ 99	21/1.9	21	11	ALC	OT
29	Madheswaran	65/M	P	P	A	P	A	28	0.8	A	140	3.2/2.1	6.4/ 2.1	67/ 58/ 98	45/3.2	24	12	ALC	OT
30	Rajappan	50/M	P	P	A	A	A	22	0.9	A	142	2/1.2	6.9/ 2.9	58/ 83/ 105	28/ 1.8	16	9	ALC	OT
31	Sadhasivam	62/M	P	P	P	A	A	26	1.2	P	132	13.8/7.8	6.0/2.0	66/88/299	39/2.3	27	14	ALC	D
32	Karunanithi	60/M	P	P	A	A	A	18	0.8	A	136	2.8/1	7.2/2.6	22/78/177	23/1.2	12	10	ALC	OT
33	Gunasekar	45/M	P	P	A	A	A	10	0.6	A	136	4.2/2.5	8.4/2.2	77/49/117	24/1.6	17	10	ALC	OT
34	Suresh	28/M	P	P	A	A	A	16	0.7	A	137	6/3.6	8.0/2.4	67/88/179	15/1.1	14	10	ALC	OT
35	Krishnamoorthy	80/M	P	P	P	P	A	15	0.8	A	116	10.3/8.2	8.8/2.1	79/58/121	46/3.4	31	14	ALC	D
36	Ganesan	52/M	P	P	P	A	A	28	0.9	P	114	10.5/3.5	5.8/2.8	72/59/99	27/1.9	23	11	ALC	OT
37	Elango	45/M	A	P	A	A	A	26	1	A	140	2.4/1.1	6.6/2.1	88/62/100	22/1.1	11	8	ALC	OT
38	Sakthivel	43/M	P	P	P	A	A	24	1.2	A	118	8.5/2.2	6.8/2.7	79/82/99	24/1.6	22	11	ALC	OT
39	Mohan	50/M	P	P	A	A	A	25	0.8	A	143	3.5/2.5	7.0/3.1	99/82/201	38/1.9	18	10	ALC	OT
40	Dhanasekar	30/M	P	P	P	A	A	18	0.8	P	116	14.6/4.8	7.2/3.6	112/108/23	42/2.6	27	11	ALC	OT
41	Murugesan	60/M	P	P	A	A	A	32	0.9	p	135	18.6/7.8	8.4/3.9	67/88/99	44/3.1	30	10	ALC	OT
42	Kandhasamy	59/M	P	P	A	A	A	36	0.7	A	129	15.5/5.6	8.4/3.7	90/69/171	37/2.8	28	10	ALC	OT
43	Raja	42/M	P	P	A	P	A	37	1.1	A	142	4.5/2.9	8.8/3.7	89/80/170	63/4.3	29	10	ALC	OT
44	Devendiran	40/M	p	P	P	A	A	38	1.2	P	131	18.5/7.4	7.8/1.9	99/88/94	28-Feb	27	11	ALC	OT
45	chinadurai	50/M	p	P	A	A	A	39	0.6	A	143	6.5/3.8	7.3/1.4	99/77/164	26/1.8	20	11	ALC	OT
46	Selvam	55/M	p	P	P	P	P	86	4.3	P	118	8.3/4.2	6.3/1.6	82/76/112	62/3.3	41	14	ALC	D
47	prakash	52/M	p	P	A	A	A	15	0.8	A	139	2.5/2.9	6.9/2.8	88/48/89	29/1.7	17	10	ALC	OT
48	Lakshmi	48/F	p	P	A	A	A	16	0.7	A	140	3.9/2.8	8.2/3.1	90/69/136	28-Feb	19	10	ALC	OT
49	Munusamy	28/M	p	P	A	A	A	35	0.9	A	139	3.9/2.7	5.6/1.5	60/73/177	24/1.4	15	10	ALC	OT
50	Raja	50/M	p	P	P	A	A	32	1	A	131	10.3/3.1	6.9/2.5	88/37/153	41/2.8	27	13	ALC	OT

S.NO	NAME	AGE/SEX	ASCITES	PHT	HE	COAG	HRS	UREA	Cr	VB	Na	TB/DB	TP/ALB	AST/ALT/ALP	PT/INR	MELD	CPS	CAUSE	OUTCOME
51	Gunasekar	45/M	p	P	A	A	A	34	1.1	A	118	10.3/6.4	8.3/2.9	83/93/162	38/2.4	24	11	ALC	OT
52	Prakasam	61/M	p	P	A	A	A	36	0.7	P	142	11.6/6.4	7.9/2.4	63/79/141	36/2.5	27	11	ALC	OT
53	Karupannan	46/M	p	P	P	A	A	39	0.8	P	131	10.3/3.8	6.4/2.0	41/59/111	28/2.1	24	12	ALC	OT
54	Husain	40/M	p	P	P	A	A	15	0.7	A	133	9.3/6.8	7.3/2.7	83/99/166	26/1.8	21	12	ALC	OT
55	Venu	60/M	p	P	A	A	A	17	0.8	A	145	5.3/2.5	7.9/3.1	92/88/170	28/2	20	12	ALC	OT
56	Chinnaponu	45/F	p	P	P	A	A	16	0.8	A	118	11/6.3	8.3/3.0	99/77/132	16/0.8	15	10	HEP B	OT
57	Nagaraj	48/M	p	P	A	A	A	24	0.9	P	135	9.6/5.4	8.0/2.5	55/67/129	20/1.2	17	10	ALC	OT
58	Murugan	43/M	p	P	P	A	A	15	1	A	137	2.7/2	7.4/2.9	60/59/89	17/1.5	15	10	ALC	OT
59	Subramani	55/M	p	P	A	A	A	28	1	A	118	10.6/7.9	7.7/3.6	88/79/102	19/1.8	22	10	ALC	OT
60	Marudhamuthu	45/M	p	P	A	A	A	15	1.2	A	130	12.6/8.9	6.0/2.1	58/62/104	23/2.0	26	11	ALC	OT
61	Mohan	53/M	P	P	P	P	P	98	3.6	P	127	14.6/3.8	7.7/3.0	77/84/105	56/3.8	44	14	ALC	OT
62	Asaithambi	40/M	A	A	A	A	A	25	0.5	A	143	2.2/1.3	7.2/3.6	66/49/91	16/1.1	10	6	ALC	OT
63	Ponnusamy	58/M	A	P	A	A	A	26	0.9	A	139	1.8/.9	8.3/4.5	88/77/99	12/0.6	9	5	ALC	OT
64	Mohammad mustafa	45/M	P	P	P	P	A	28	0.5	A	117	10.4/3.8	6.1/3.1	81/93/164	50/3.7	30	12	ALC	OT
65	Srinivasan	32/M	P	P	A	A	A	27	0.4	A	136	5.8/2	6.7/2.5	51/63/79	18/0.9	13	10	ALC	OT
66	Karupannan	17/M	P	P	P	A	A	19	0.8	P	108	9.3/6.1	6.9/2.8	88/56/158	24/1.2	17	10	ALC	OT
67	Venkatesan	44/M	P	P	A	A	A	17	0.7	A	131	8.4/4.7	7.3/3.3	57/77/167	26/1.9	22	10	ALC	OT
68	Mohana	44/M	P	P	A	A	A	18	0.9	P	136	4.3/2.8	7.9/3.5	88/99/159	26/1.9	19	10	ALC	OT
69	Velusamy	47/M	P	P	A	A	A	39	0.4	A	138	1.6/0.5	7.2/3.8	47/79/153	28/2	16	7	ALC	OT
70	Karnanithi	60/M	P	P	P	A	A	25	0.8	A	131	12.6/4.6	7.3/4.1	67/79/127	18/0.9	16	9	ALC	OT
71	Krishnamoorthy	50/M	P	P	P	A	A	26	1 . 2	A	119	7.9/4.9	7.7/3.3	83/64/172	24/1.5	21	10	ALC	OT
72	Sivakumar	43/M	P	P	A	A	A	27	1.3	P	131	8.6/3.6	7.9/3.5	83/58/163	30/2.2	26	10	ALC	OT
73	Sokkalingam	61/M	P	P	A	A	A	28	1.1	P	139	9/5.5	8.3/3.0	77/99/105	27/1.9	23	10	ALC	OT
74	Thiyagarajan	57/M	P	P	P	A	A	37	1	A	132	8.3/3.5	6.4/2.9	58/64/98	29/1.6	20	10	ALC	OT
75	Madheswaran	55/M	P	P	P	A	A	36	0.8	A	117	9.8/3.2	6.3/2.0	89/48/88	31/1.8	22	12	ALC	OT

S.NO	NAME	AGE/SEX	ASCITES	PHT	HE	COAG	HRS	UREA	Cr	VB	Na	TB/DB	TP/ALB	AST/ALT/ALP	PT/INR	MELD	CPS	CAUSE	OUTCOME
76	Arun kumar	36/M	P	P	A	A	A	28	0.7	A	140	6.3/2.6	6.6/1.9	37/28/98	18/1.6	19	10	ALC	OT
77	Jagan	40/M	P	P	A	A	A	27	0.4	P	139	4.9/2.5	7.6/1.9	72/59/107	38/1.9	20	11	ALC	OT
78	Mahalingam	32/M	P	P	P	A	A	12	0.5	A	136	10.4/7.8	6.3/3.3	88/66/167	41/2.7	26	12	ALC	OT
79	Maarichetty	52/M	P	P	A	P	A	16	0.9	P	116	12.7/7.3	8.3/2..7	67/83/163	60/3.7	31	10	ALC	OT
80	Nali goundar	43/M	P	P	A	P	A	38	0.8	P	118	16.3/6.6	5.8/2.1	17/29/149	61/1.2	30	12	ALC	OT
81	Palani	44/M	P	P	A	A	A	19	0.8	A	136	11.3/5.7	6.7/2.0	84/93/163	48/2.6	26	12	ALC	OT
82	Santhappan	57/M	P	P	A	A	A	28	0.7	A	140	13.5/7.3	7.0/2.4	70/83/157	24/1.6	22	10	ALC	OT
83	Rajeswari	57/M	P	P	A	P	A	38	0.6	P	132	12.4/8.3	7.2/3.6	67/88/99	72/4.1	32	10	ALC	OT
84	venkatesan	59/M	P	P	A	P	A	27	1.1	A	142	5.7/3.5	8.4/3.3	80/104/194	68/3.4	28	11	ALC	OT
85	Kumar	52/M	P	P	A	A	A	28	0.5	P	139	4.2/2.9	7.3/3.2	52/49/173	42/2.8	23	11	ALC	OT
86	Selvam	39/M	P	P	A	P	A	15	1.1	A	118	13,4/7	6.7/2.5	33/72/138	39/2.5	27	12	ALC	OT
87	Unnamalai	30/M	P	P	A	A	A	16	1.3	A	138	10.6/4.4	5.8/2.1	22/63/89	20/1.4	22	10	ALC	OT
88	Sakthivel	38/M	P	P	A	A	A	21	1.2	A	136	7.6/3.6	6.2/2.8	37/49/93	18/1.6	21	9	HEP C	OT
89	Kesavan	45/M	P	P	P	A	P	90	4.2	A	131	10.6/4.3	6.9/2.3	49/62/168	17/1.6	34	11	ALC	OT
90	Aranganathan	51/M	P	P	A	A	A	38	0.6	P	138	8.8/2.2	4/2.1	39/82/182	28/1.8	21	11	ALC	OT
91	Selvagounder	50/M	P	P	A	A	A	22	0.9	A	133	10.6/5.8	8.5/2.8	54/79/170	36/2.1	24	10	ALC	OT
92	Krishnaraj	63/M	P	P	A	A	A	26	0.4	A	142	5.3/3.8	6.6/2.9	60/77/152	16/1.1	14	9	ALC	OT
93	ravi	55/M	P	P	A	A	A	31	0.7	A	132	12.4/6.8	7.7/3.0	47/49/99	23/1.6	21	9	ALC	OT
94	Prem kumar	49/M	P	P	A	A	A	38	0.9	A	141	4.3/3.5	7.9/1.9	84/69/105	21/1.3	15	10	ALC	OT
95	Venkatachalam	60/M	P	P	A	A	A	15	0.5	P	133	12.2/7.4	5.9/1.4	59/69/169	32/2.2	25	11	ALC	OT
96	Rajendran	46/M	P	P	A	P	A	19	1.2	A	136	11.6/4.8	7.2/2.9	77/44/181	59/3.3	31	11	ALC	OT
97	Varadharajan	57/M	P	P	P	P	P	80	3.6	P	125	14.4/3.8	8.4/3.9	31/49/89	60/4.0	44	12	ALC	D
98	Chandra	57/M	P	P	P	A	P	78	4.3	A	118	18.2/5.8	7.3/2.5	52/49/169	37/2.6	41	13	ALC	D
99	Muniyan	53/M	P	P	P	A	A	26	0.8	P	129	11.4/5.8	7.6/3.2	28/36/152	27/2.1	24	11	ALC	D
100	Muthugounder	62/M	P	P	A	A	A	39	0.9	A	138	8.2/6.5	8.3/2.9	46/37/133	25/1.9	22	10	ALC	OT

KEY TO MASTER CHART

PHT- PORTAL HYPERTENSION

HE- HEPATIC ENCEPHALOPATHY

HRS- HEPATORENAL SYNDROME

Na- SODIUM

TB- TOTAL BILIRUBIN

DB- DIRECT BILIRUBIN

TP-TOTAL PROTEIN

ALB- ALBUMIN

ALT- ALANINE TRNSAMINASE

AST- ASPARTATE TRANSAMINASE

ALK- ALKALINE PHOSPHATASE

PT- PROTHROMBIN TIME

INR- INTERNATIONAL NORMALISED RATIO

MELD- MODEL FOR ENDSTAGE LIVER DISEASE

CPS- CHILD PUGH SCORE

HEP B-HEPATITIS B

HEP C-HEPATITIS C

ALC- ALCOHOL

OT- ON TREATMENT

VB –VARICEAL BLEEDING

COAG- COAGULOPATHY

Cr –CREATININE

D- DEATH

A-ABSENT

P-PRESENT