"CORRELATION OF SERUM ZINC LEVELS WITH STAGES OF HEPATIC ENCEPHALOPATHY IN CHRONIC ALCOHOLIC LIVER DISEASE"

BY

DR.PREM CHANDAR REDDY SANGAM

DISSERTATION SUBMITTED TO
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IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF MEDICINE (M.D.)

UNDER THE GUIDANCE OF

DR. RAVEESHA A, M.B.B.S, MD (MEDICINE)

PROFESSOR & HEAD OF UNIT
DEPARTMENT OF GENERAL MEDICINE
SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA ,KOLAR 563 103

SRI DEVARAJ URS MEDICAL COLLEGE
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DATE:
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SIGNATURE OF THE CANDIDATE
DR PREM CHANDAR REDDY SANGAM
Postgraduate
Department of General Medicine
Sri Devaraj Urs Medical College, &
Research Center, Tamaka, Kolar

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

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DR. VIDYASAGAR CR
Professor & HOD
Department of General Surgery,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:
Place: Kolar

DR. PRABHAKAR K
Principal,
Sri Devaraj Urs Medical College
Tamaka, Kolar.

Date:
Place: Kolar

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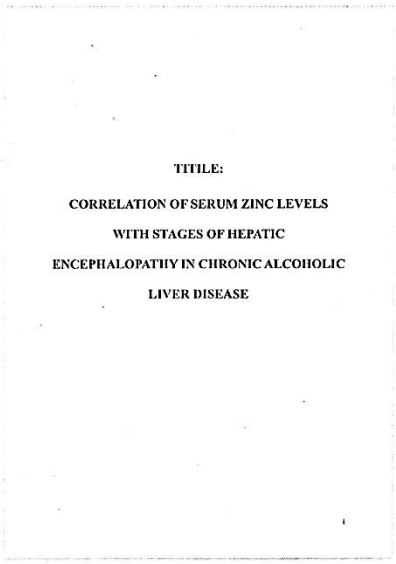

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Date: Signature of candidate

Place: Kolar **DR PREM CHANDAR REDDY SANGAM**

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ABBREVIATIONS

Glossary	Abbreviations
HE	Hepatic Encephalopathy
ALD	Alcoholic Liver Disease
Zn	Zinc
ROS	Reactive Oxygen Species
WHC	West-Haven Criteria
CPC	Child-Pugh Classification

ABSTRACT

Introduction: This study investigates the relationship between serum zinc levels and stages of hepatic encephalopathy in chronic alcoholic liver disease, aiming to understand zinc's role in disease progression and potential therapeutic implications.

Material and methods: This study will include adult patients diagnosed as chronic alcoholic liver disease with hepatic encephalopathy, presenting to the General Medicine department at R L Jalappa Hospital and Research centre(RLJH). Participants will be male patients consuming 60-80 grams of alcohol/day for 10 years or longer and females consuming 20-40 grams of alcohol/day over 10 years or longer.

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INTRODUCTION

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ALD is still a major global health issue. Since micronutrients frequently function as components or coenzymes of numerous biochemical enzymes involved in oxidative stress, cell division, and the inflammatory response, disruption of micronutrients has been widely recognized to be a prevalent feature in individuals with ALD. Before the implementation of a customized intervention in clinical practice, it is necessary to map the way these micronutrients work and their metabolic rhythm[2].

Overview of Hepatic Encephalopathy

Liver failure may result in reversible disorders of reduced brain function, such as hepatic encephalopathy (HE)/ portosystemic encephalopathy (PSE)[3]. HE perhaps evidence brain atrophy, cerebral edema, reversible metabolic encephalopathy/any integretion of these diseases. Liver failure is closely linked to these factors, such as reduced ammonia metabolism. Poor survival and a high chance of recurrence are linked to HE unless the underlying liver condition is effectively managed. HE lowers the standard of living and increases the chance of severe episodes, even in mild forms. HE arises as acute or chronic liver disease worsens, with the most harmful

consequences being variceal hemorrhage . Pathophysiological manifestations include lowgrade cerebral edema, inflammation, oxidative/nitrosative stressdisturbances in the brain's oscillatory networks. Diagnostic methods and severity grading for moderate forms of HE is ongoing. Current medical treatment consists of lactulose and rifaximin, with new therapies being developed based on a better understanding of the pathophysiology [3].

Definition and Classification

HE is a brain malfunction triggered by portal-systemic blood shunting and/or liver failure, resulting in changes in motor function, consciousness, personality, and thought processes. It is a serious repercussion of acute or chronic liver failure, leading to neuropsychiatric,neurological issues. Chronic liver failure can cause hyperammonemia, intracranial hypertension, and edematous brain. HE negatively impacts neurotransmission, immunological response, mitochondrial function, cerebral blood flow, NMDA(N-methyl-D-Asparate) receptor function, glutamine metabolism, lactic acid accumulation, astrocyte morphology, L-tryptophan metabolism, and cerebral bioenergetics. The manifestation range of HE is extremely diverse, varying from minor neuropsychological abnormalities to coma [4].

The definition of "HE" as of now "brain dysfunction caused by liver insufficiency and/or portosystemic shunting (PSS)". This definition is problematic in several ways. First off, since the liver is normal, it is inaccurate to call persons with PSS who do not have liver disease.It is obvious that patients with PSS have different prognoses, pathophysiologies, and therapy options than those with advanced liver disease. Furthermore, because liver disease is absent, newborns with urea cycle disorders (UCDs) who experience neurological dysfunction brought on by hyperammonaemia are not diagnosed with HE. All three conditions liver disease, PSS,UCDs share the trait of brain dysfunction brought on by hyperammonemia [5].

“WEST HAVEN CRITERIA”[5]

GRADE-1

- Trivial lack of awareness.
- Euphoria or anxiety.
- shortened attention span; impaired performance of addition or subtraction.

GRADE-2

- Lethargy or apathy.
- Minimal disorientation for time or place.
- Subtle personality change.
- Inappropriate behaviour.

GRADE-3

- Somnolence to semi-stupor,but responsive to verbal stimuli.
- Confusion.
- Gross disorientation.

GRADE-4

- Coma.

Chronic Alcoholic Liver Disease

Alcoholrelated liver disease (ARLD), sometimes referred to as chronic alcoholic liver disease, is a common and avoidable condition that develops when excessive alcohol use damages the liver. Alcohol is broken down by the liver, but when too much alcohol is drunk, the liver may suffer significant harm.

Epidemiology and Global Burden:

Chronic Alcoholic Liver Disease (ALD) enormous global contributing factor of liver-related death., responsible for nearly 1.7 million deaths annually, with alcohol accounting for about 50% of liver cirrhosis cases. The burden is highest in regions with excessive alcohol consumption, such as Eastern Europe and Central Asia, and disproportionately affects low-income populations.

Incidence and mortality:

Alcoholrelated liver disease (ALD) is a major illness primarily induced by political policies restricting alcohol access. ALD is responsible for over 5.9% of all deaths, 3.3 million annually, from alcohol-related illnesses and injuries in violent and traffic accidents. Alcohol use is linked to 139 million years of disability-adjusted life, with working-age people being disproportionately affected. The prevalence of ALD and alcohol use is highest in the WHO European Region, but there is a significant variance in alcohol intake and involved morbidity and mortality worldwide. Between 1990 and 2014, the WHO European Region saw a decline in alcohol consumption, but concurrent rises in consumption in the eastern and southeast regions were closely linked to a rise in liver cirrhosis-related deaths.

Liver transplantation:

As liver transplantation is the only treatment aimed at cure available patients with End stage liver disease or other liver disease which also associated with risk factors and postoperative complications[6].In many countries, patients must desist from alcohol for six months before surgery, which makes transplantation for chronic liver cell failure and hepatocellular carcinoma typically unsuitable treatment.

Risk factors:

As reported by seitz, H.K et al ,ALD is associated with alcohol intake; 90% of long-term heavy drinkers acquire AFL(Alcoholic fatty liver). But only 10% to 20% go on to acquire progressive ALD(Alcoholic liver disease). Both sex and heredity are important factors since women are more prone to drinking and acquire ALD more quickly and less frequently than men. This could be caused by several factors, including decreased body water content, decreased stomach alcohol metabolism, and alcohol-mediated elevations in serum estrogens. An increased chance of developing ALD is also linked to other underlying liver illnesses, including non-alcoholic steatohepatitis, α1-antitrypsin deficiency, hereditary hemochromatosis, and infection with the hepatitis C and B viruses. Drinking alcohol also raises the risk of HCC in MASH, HBV,

and HCV infections. People who are overweight or obese are more defenseless to alcohol's deleterious effects on the liver [7].

Impact of Alcohol on Liver Function:

Alcohol profoundly affects liver function. Indeed, liver represents the major site for the metabolism of alcohol. Chronic alcohol consumption can result in a spectrum of liver diseases. It starts from simple steatosis, also referred to as fatty liver. However, it can cause alcoholic hepatitis, fibrosis, cirrhosis, or even hepatocellular carcinoma. The two main enzymes are the ethanol-oxidizing microsomal system and alcohol dehydrogenase in the liver which breaks down alcohol to produce acetaldehyde, a hazardous byproduct of alcohol metabolism that damages the liver. Metabolic pathways are overwhelmed with increased levels of alcohol, causing oxidative stress, lipid peroxidation, and producing reactive oxygen species (ROS). These effects result directly in hepatocyte injury and enhance inflammation [8].

Hepatic Encephalopathy(HE) in Alcoholic Liver Disease

HE is typified by recurring episodes and a poor quality of life. HE is a familiar symptom of acute on chronic liver failure (ACLF), which primarily affects people with chronic liver disorders. HE is a common side effect of ALD; this results directly from the failure of the liver to detoxify ammonia and other neurotoxins due to alcohol-related damage. Chronic alcohol intake induces liver dysfunction, including steatosis, hepatitis, and cirrhosis that impairs ammonia metabolism by the urea cycle. It is the elevated ammonia concentration that contributes to neurotoxicity, leading to HE, which is characterized by cognitive impairment, altered mental status, and motor dysfunction. Alcohol further worsens the condition with zinc deficiency, oxidative stress, and inflammation, impeding ammonia detoxification. However, to treat HE efficiently in patients suffering from ALD, underlying liver disorders have to be addressed coupled with correcting nutritional deficiencies coupled with decreasing ammonia levels in the patient[9].

Clinical Manifestations and Stages

ALD causes HE, which manifests as a range of neuropsychiatric disorders divided into four severity-based stages. This describes the signs, symptoms, and course of the illness, describing the long-term effects of Chronic ALD on the body[10]. Patients in Stage 1 frequently report mild disorientation or exhilaration along with minor changes such as reduced concentration, attentiveness, and sleep patterns. Patients in stage 2 will report as increased sluggishness, confusion, personality changes, and the onset of asterixis (flapping tremor). In Stage 3, neurological symptoms including stiffness and clonus become apparent, along with extreme bewilderment, noticeable somnolence, and an inability to carry out daily chores. The most severe stage, stage 4, is characterized by a deep coma, a substantial risk of multiorgan failure, and an inability to respond to stimuli. Dehydration, high protein consumption, gastrointestinal bleeding, infections, and other conditions can all accelerate the development of HE by exacerbating hyperammonemia and neurotoxicity. To avoid lasting brain damage and enhance results, early detection and treatment are crucial[11].

Role of Micronutrients in Liver Disease

Patients with liver cirrhosis often suffer from malnutrition. Several analyses have highlighted that it is allied with decreased quality of life and increased rates of disease and mortality. Additionally, it may adversely affect liver transplant outcomes. The prevalence of malnutrition is determined by the severity of the condition:

Importance of Trace Elements in Liver Function

Maintaining the equilibrium of essential trace elements depends on the liver. By attaching itself to the plasma proteins, most of the trace elements leave the body through the portal circulation after being taken up by the jejunum or duodenum. The tissues or organs that need these trace elements receive them. To transport or distribute various trace elements, like zinc (Zn), iron (Fe), copper

(Cu), and selenium (Se) liver is largely accountable for starting the creation of the proteins attached to these elements. Because the liver produces bile, additionally, it contributes to trace metal excretion, including those of magnesium (Mg) and copper (Cu)[12]. The maintenance of vital activities depends on trace elements, and metabolic diseases result from excess or lack. Liver disease's prevalence and severity are indicated by the metabolism of different nutrients, and the presence and progression of the disease are significantly correlated with the metabolism of trace elements. Additionally, the body's metalloprotein concentration and serum trace element concentration are correlated, and liver disease is largely caused by imbalances in these two variables. The vital trace elements magnesium, manganese, copper, and zinc play a part in liver cirrhosis[13]. Certain disorders can be prevented or improved by trace metals like iron (Fe), copper (Cu), and zinc (Zn). Trace element transport ,metabolic pathways are regulated by the liver, which also affects the elements' bioavailability, tissue distribution, and ultimately toxicity. Bile production is another way that the liver contributes to the excretion of trace substances.

Zinc: Immune system function, protein synthesis, and liver enzyme functioning all depend on zinc. It aids in the production of antioxidants like superoxide dismutase (SOD) and helps the urea cycle, which detoxifies ammonia. Because zinc deficiency impairs immunological responses and increases oxidative stress, it can worsen liver dysfunction, which is frequently observed in liver illnesses such as cirrhosis and hepatitis. More than 300 enzymatic systems are linked to zinc. Zinc has several functions, including anti-inflammatory, anti-apoptotic, membrane, and cytoskeletal stabilizing, and is a crucial co-factor in DNA synthesis.

Copper: Copper is essential for enzymes involved in collagen formation, antioxidant defense, and iron metabolism. It also aids in producing ceruloplasmin, a protein controlling iron metabolism. Excess or lack of copper can cause liver dysfunction, leading to Wilson's disease. Reactive copper can stimulate Kupffer cells, contributing to liver injury. Magnesium is crucial for hydrogen exchange, oxidative phosphorylation, renal potassium, protein synthesis, and enzyme activation.

Selenium: To maintain good health, selenium (Se) is essential. The expression of several selenoproteins is part of the cellular biochemistry of selenium. Glutathione peroxidase (GSH-Px), an antioxidant enzyme, contains selenium in its active site. Selenium is linked to albumin as selenomethionine and integrated into selenoprotein P as selenocysteine in plasma. Since the liver is primarily in charge of the synthesis and secretion of these selenoproteins, it stands the primary organ engaged in the human body's metabolism and selenium homeostasis[14].

Manganese: An essential enzyme in the metabolism of urea, arginase, contains manganese as a structural component. Many of the enzymes in the Krebs cycle, especially those involved in the decarboxylation pathway, are activated by manganese.

Magnesium: Magnesium is a necessary element for the human body and other mammals. Because of its functions in the body, its significance in liver cirrhosis and associated complications is currently being studied. Magnesium is involved in numerous enzymatic processes that include the production of proteins and nucleic acids as well as energy consumption[15].

Iron: Iron is essential for oxygen-carrying proteins like myoglobin and hemoglobin. On the other hand, too much iron might be harmful. An essential organ for maintaining iron homeostasis is the liver. Along with its involvement in iron storage,liver also makes the hormone that controls iron metabolism and the iron carrier protein transferrin and hepcidin in plasma. Reduced hepcidin synthesis due to liver injury results in increased absorption of iron[16].

Zinc as a Vital Micronutrient

Protein synthesis, enzyme activity, immunological function, and other physiological activities all depend on zinc, an important micronutrient. Maintaining healthy liver function, bolstering antioxidant defense, and aiding ammonia detoxification in liver disorders all depend on it.

Biological Roles of Zinc in the Human Body

More than 300 enzymatic systems are linked to zinc, a crucial essential metal. It is a vital component in the urea cycle and plays a crucial role in the transformation of ammonia to urea. Zinc contains qualities connected to DNA synthesis, anti-inflammatory, and anti-apoptotic. It also boosts the body's natural defenses opposed to reactive oxygen radicals. Consequently, it seems that the pathophysiology of HE is influenced by low zinc levels. The primary plasma carrier of zinc is albumin, and the quantity of zinc carried by the blood is dependent on both serum albumin availability and zinc levels. Zinc secretion in the urine is also increased by overuse of diuretics. Zinc loss through the gastrointestinal tract (GI) is also increased by frequent stool washing and lactulose. Most of the zinc in the body is bound; it may be tightly linked to α2-globulin or loosely attached to albumin. Patients with CLD have significantly lower albumin levels, and those with low serum albumin concentrations are also more likely to have zinc deficiencies. Loss of appetite is another factor contributing to low zinc levels in CLD patients, and low albumin levels are one of the main causes. The connection between liver cirrhosis with HE and serum zinc levels is less well-established in India. Thus, this study sought to ascertain people's serum zinc levels suffering from decompensated liver disease (DCLD), or cirrhosis of the liver, as well as how it related to, HE grades and patient outcomes [17].

Mechanisms Linking Zinc and HE

Zinc is crucial in the pathogenesis of HE through the mechanisms involving detoxification of ammonia and neuroinflammation. The support for urea cycle enzymes by zinc, particularly carbamoyl phosphate synthetase, will detoxify ammonia within the liver. Moreover, glutamine synthetase is improved by zinc activity which would help in converting ammonia into glutamine in the brain and muscles. Zinc deficiency impairs these detoxification processes, hence increasing ammonia levels, which subsequently contribute to neurotoxicity. Furthermore, zinc contributes to

the reduction of oxidative stress and inflammation in the liver and brain, which are also important in the HE[18].

Zinc Deficiency in Chronic Liver Disease

Zinc (Zn) deficiency is linked to chronic liver disorders. An important trace element with beneficial anti-inflammatory, apoptotic, and antioxidant properties is zinc (Zn). It has a role in cell division and activation, RNA transcription, and DNA synthesis. Numerous zinc proteins and enzymes, including essential zinc transcription factors, depend on it. Many forms of liver illness, such as viral and ALD, are characterized by zinc deficiency or altered metabolism. Zinc deficiency and altered metabolism are caused by several causes, including stimulation of hepatic metallothionein, increased excretion in the urine, activation of particular zinc transporters, and decreased food intake. Zinc deficiency in liver illness may manifest as skin lesions, reduced immune function, altered mental status, or inadequate liver regeneration or wound healing. Zinc supplementation demonstrated to suppress or reduce experimental ALD through a variety of pathways, such as stabilizing gut-barrier function, lowering endotoxemia, reducing the creation of proinflammatory cytokines, lowering oxidative stress, and reducing apoptotic hepatocyte death.

Mainly, the liver is essential for preserving systemic zinc homeostasis. As a result, the development of chronic liver illnesses such fatty liver, liver cirrhosis, or chronic hepatitis impairs zinc metabolism, which in effect leads to zinc shortage. Zinc deficiency causes a number of metabolic diseases, as insulin resistance and liver steatosis, and HE. However, metabolic conditions such hypoalbuminemia in liver cirrhosis patients are often the cause of zinc deficiency. The possible ways that zinc deficiency results in a range of metabolic problems in chronic liver disease have been uncovered by recent studies. In both real patients with CLD and experimental models, zinc supplementation has demonstrated positive benefits on these metabolic anomalies. The pathophysiology of metabolic issues brought on by the benefits of zinc therapy for patients

with CLD and zinc deficiency are compiled. Furthermore, we draw attention to how Zn interacts with additional vitamins, amino acids, hormones, or trace minerals in these patients[12].

Impact of Zinc on Ammonia Metabolism

Zinc plays a pivotal role in ammonia metabolism, especially with diseases of the liver: cirrhosis and HE where hyperammonemia typically arises. The liver, mainly through the urea cycle, detoxifies ammonia but in liver dysfunction, mechanisms are impaired. Hyperammonemia is thus significantly exacerbated by zinc deficiency. It is commonly found to occur in liver disease. Enzymes involved in the urea cycle require zinc as a cofactor, including carbamoyl phosphate synthetase, whose deficiency decreases the efficiency of this pathway and leads to the accumulation of ammonia. Furthermore, zinc activates glutamine synthetase, an enzyme that, in the muscle and brain, catalyzes the conversion of ammonia and glutamate into glutamine as an alternative route of detoxification when liver function is impaired. Low zinc levels also enhance ammonia production in the intestine through alterations in microbial activity and intestinal enzyme function. Zinc supplementation clinically Affirmed to lower serum ammonia levels enhance neurocognitive performance in patients with HE, and reduce HE episodes. Additionally, zinc has antioxidant and anti-inflammatory effects that minimize liver damage and oxidative stress, which can decrease ammonia production. Given its importance in ammonia detoxification and metabolic support, zinc supplementation is an effective supplemental treatment in the treatment of hyperammonemia and complications associated with liver diseases [19].

Significance of the Study

This study examines the relationship between serum zinc levels and progression of HE in patients with chronic ALD, hence detailing strong clinical and research implications. HE is an aggressive complication of ALD arising as a result of impaired ammonia metabolism leading to neuropsychiatric disturbances. Zinc is an important cofactor for most enzymes that participate in

the detoxification process of ammonia and has been entangled in the pathogenesis of HE. Understanding how zinc levels correlate with HE stages may serve as an insight into the role played by micronutrient deficiencies in advancing disease. This should facilitate the development of early diagnostic tools and target therapeutic interventions, such as zinc supplementation, to abate HE severity. In addition, this research adds value to personalized medicine approaches addressing the imbalances associated with ALD patients. As these findings bridge the gap between the status of micronutrients and HE management, they may promote patient outcomes with a better quality of care in a whole different setting.

AIMS & OBJECTIVES

OBJECTIVES

AIM AND OBJECTIVES

- To assess the serum zinc levels in chronic alcoholic liver disease(ALD) with Hepatic encephalopathy(HE)
- To correlate serum zinc levels with stages of alcoholic Hepatic encephalopathy(HE).

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Chronic Alcoholic Liver Disease Overview

Modern categories for jaundice, hepatitis, and liver failure are also presented. The liver's function is an important organ that governs the function of digestion, metabolism, lack of hemocoagulation, and detoxification. It has a wide range of diseases and is frequently associated with the pathology of other organs. Doctors frequently encounter liver illnesses, and physicians must comprehend the pathophysiology of this organ. The prevalence of liver illnesses is rising, particularly among working-age people. Acute and chronic liver disease may result in consequences, including liver failure. Chronic ALD refers to a group of liver illnesses caused by long-term and severe alcohol consumption [20]. ALD is a significant global health issue causing significant morbidity and mortality. It has various stages, including alcoholic steatosis, characterized by excessive fat accumulation, and alcoholic hepatitis, characterized by inflammation and liver tissue damage. Unchecked, it can lead to fibrosis, a form of connective tissue in the liver, and eventually cirrhosis, an irreversible condition with intense scarring and permanent liver function loss. The progression and severity of ALD are influenced by various factors [21].

These include the duration and amount of alcohol intake, the differences between genders, with females being at greater risk of liver damage at lower alcohol levels, and genetic predisposition. Malnutrition, particularly of essential vitamins and minerals, contributes to the susceptibility of the patient. The liver, being the main site for alcohol metabolism, is uniquely susceptible to damage due to the toxic by-products of this process. Alcohol metabolism produces harmful intermediates such as acetaldehyde and ROS, which disrupt hepatic cellular and molecular integrity[22]. Chronic alcohol exposure impairs the regeneration ability of the liver, compromises its structural framework, and disrupts immune homeostasis. This creates a vicious cycle of injury, inflammation, and repair that progressively damages liver tissue, causing considerable structural and functional decline.

Alcohol-Induced Liver Damage

Alcohol metabolism continues to be at the core of this process, producing toxic intermediates such as acetaldehyde and ROS. Acetaldehyde is considered the major metabolite of alcohol and is very reactive and capable of binding with proteins and forming acetaldehyde-protein adducts. These adducts interfere with normal cellular functions, decrease enzymatic activity, and activate inflammatory pathways that result in damage to the liver[23]. Alcohol-induced liver injury (ALD) is a complex condition characterized by oxidative stress, mitochondrial dysfunction, and cell death. The injury is primarily mediated by inflammation cytokines, TNF-α, which recruits neutrophils and macrophages to the liver, releasing more inflammatory mediators and ROS. This leads to tissue scarring, fibrosis,cirrhosis. The complexity of ALD is attributed to interplay of metabolic, inflammatory, and oxidative stress pathways in its development.

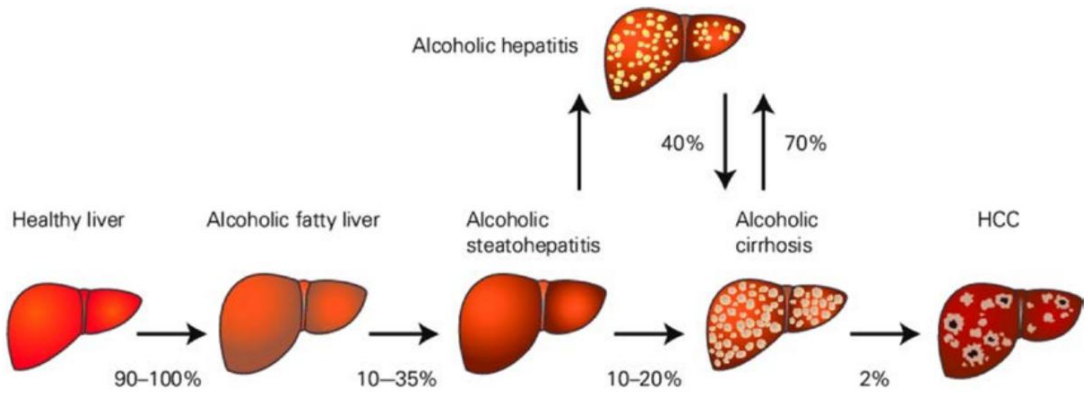


Figure 1: The progression of liver disease caused by alcohol [24]

The metabolism of zinc helps in maintaining cellular balance, and its dysregulation is commonly seen as an illness progresses. Though a low tissue concentration, zinc seems to promote malignancy and aggression in cancer cells. Zinc transport is managed through zinc transporters, viz., SLC30 ZnT for excretion and SLC39 ZIP for influx. The primary mediators of storage are metallothioneins (MTs). This review aims to summarize the body of knowledge on cellular zinc signaling and identify putative molecular pathways that connect zinc metabolism with the development of disease, specifically cancer. A summary of zinc ion clinical trials is provided, and

promising directions for further research are presented by targeted treatments like small molecules and monoclonal antibodies. Zinc (Zn) is an important trace element that possesses anti-oxidative, anti-inflammatory, and apoptotic properties[25].

The chronic liver conditions of hepatitis, cirrhosis, and fatty liver will cause a problem in zinc metabolism leading to deficiency. Such deficiency leads to metabolic alterations such as insulin resistance, hepatic steatosis, and hypoxia. On the other hand, the disease condition in subjects with liver cirrhosis can lead to Zn insufficiency. The administration of Zn has been reported to correct these abnormalities both in the laboratory model and the chronic liver disease human. The paper also discusses interactions of Zn with other trace elements, vitamins, amino acids, and regulators in these people.

Hepatic Encephalopathy (HE)

HE is a neurologic condition disorder triggered by advanced liver dysfunction, mainly due to the build up of ammonia in the bloodstream. HE is categorized into covert HE, where symptoms are mild and overt HE, with severe symptoms such as confusion and coma. The West Haven measures are used to assess degree of criticality of HE. Ammonia-induced astrocyte swelling, neurotransmitter imbalance, and systemic inflammation are thought to cause the pathophysiology involved in HE. This leads to cognitive and neurological symptoms, indicating that HE in liver disease is complex.

The brain's trip through liver disease development, organ transplantation, and post-transplant outcomes. It emphasizes the HE brains' susceptibility to perioperative variables and post-LT circumstances, which may explain persistent neurological damage[26]. HE is an illness of the brain that can arise with both acute and long-term liver disease. HE is normally reversible; however, it can cause long-term neurological issues in up to 47% percent of transplant recipients. According to research, those who have a history of HE, especially overt HE, continue to experience severe consequences even after liver donation. These long-term neurological problems have a substantial

influence on people's standards of life and increase the cost burden of ongoing liver damage on healthcare systems.

Definition and Classification of HE

HE is a catastrophic and possibly reversible neuropsychiatric illness that develops as a result of advanced liver disease when the liver's detoxifying function is significantly impaired. It appears as a Array of neurological and cognitive disturbances, from subtle alterations in mental status to deep coma. HE can be categorized broadly into two types they are covert HE and overt HE. Covert HE is considered to be a milder type, where there is minimal impairment in cognitive functions and these cannot be detected at times by routine clinical examination but are detected through neuropsychological testing.

In contrast, overt HE has more pronounced and easily observable clinical symptoms, such as confusion, disorientation, altered motor skills, and, in severe cases, stupor or coma. To assess the severity of HE, the West Haven classification system is widely used. This grading system ranges from Grade 0, indicating normal cognition with no clinical symptoms, to Grade IV, which signifies coma. Intermediate grades involve a sequence of manifestations, ranging from lethargy and disorientation to somnolence, often with localized neurological defects. Thus, the classification of HE is the basis of treatment planning as well as monitoring the progress of the disease.

Pathogenesis of HE

The pathophysiology of HE is complex,highly falec and is based on the toxic effects of ammonia and other neurotoxins that accumulate due to failure of the liver. Ammonia, primarily produced in the gastrointestinal tract during protein metabolism, is normally the urea cycle that detoxifies the liver. In advanced liver disease, the failing liver fails to adequately metabolize ammonia, causing its systemic accumulation. High concentrations of ammonia exhibit toxic effects on astrocytes, the

star-shaped glial cells in the brain and spine that help neurons operate properly. Astrocytes have tried to detoxify ammonia by converting it into glutamine.

The ammonia theory of pathophysiology and related high blood pressure forms the foundation of most contemporary therapeutic approaches. These findings on the activation of the adaptive route for ammonia removal in the form of glutamine will be utilized to further investigate medicines that improve ammonia clearance. The antagonist's action towards the neurosteroid site and the GABA receptor complex is highlighted as a potential cause of reduced GABA-ergic amplitude[27]. Over-accumulation of glutamine in astrocytes leads to osmotic stress, cellular swelling, and cerebral edema, compromising neuronal signaling. Imbalances in neurotransmitter concentrations are the primary contributors to hepatitis C. Increased GABAergic inhibition and changes in glutamatergic excitatory pathways disrupt neural transmission, leading to cognitive and motor dysfunction. Systemic inflammation and pro-inflammatory cytokines worsen the disorder by disrupting the blood-brain barrier(BBB), allowing neurotoxic mediators to penetrate the brain, and causing neuroinflammation and oxidative stress.

Zinc in Human Physiology

Zinc is an imperative trace element that plays a significant role in many biological functions necessary for maintaining health. As a cofactor, it participates in the activity of over 300 enzymes that mediate essential cellular functions including DNA synthesis, protein synthesis, and cell division. Its role in membrane stability, antioxidant defense, and immune modulation makes zinc an important protective agent against oxidative damage, promoting wound healing. Its contribution to maintaining the structural and functional integrity of many tissues underlines its physiological importance. Zinc is associated with apoptosis and regulation of gene expression and is important for growth, development, and immune responses. Deficiency in zinc compromises all these vital functions, impairing immunity, increasing oxidative stress, slowing down tissue repair, and heightening susceptibility to infections and chronic diseases. The role of zinc in maintaining health

becomes even more pronounced in states of increased metabolic demand, such as injury, inflammation, or chronic illness [19].

Zinc and the Liver

Zinc is essential for the maintenance of the morphological and functional integrity of the liver because this trace element is significantly required by the liver for numerous enzymatic and metabolic activities. These include detoxification of harmful metabolites, regulation of activity of various hepatic enzymes, and maintenance of immune homeostasis. Its deficiency is among the most commonly found conditions for chronic liver diseases, especially conditions such as ALD and cirrhosis. This deficiency results from several factors, which include a decreased intake of the diet, intestinal malabsorption, and excessive urinary loss. The presence of hypoalbuminemia hallmark sign of chronic liver dysfunction-this also worsens the severity of zinc deficiency.

Zinc is bound with albumin during transport within the bloodstream. Therefore, without sufficient zinc, the status of liver health is critically affected. It impairs the liver's antioxidant defense mechanism, hence increasing susceptibility to inflammation and oxidative damage in the hepatocytes. Zinc also has other functions in liver regeneration, where it facilitates cell proliferation and repair. Impairment of zinc leads to the deterioration of these processes, hence exacerbating the liver injury and prolonging the disease. In addition, low levels of zinc often enhance inflammation and complications such as HE, where zinc is significant in the detoxification of ammonia[28]. This would require keeping adequate zinc levels that can preserve liver function, helping minimize the adverse effects associated with chronic liver diseases.

Zinc Deficiency and Liver Disease

Zinc deficiency is a significant factor in chronic liver diseases, particularly ALD, as it increases the severity of liver damage and disease progression. Chronic alcohol consumption negatively impacts zinc metabolism, leading to impaired absorption, increased urinary excretion, and lower

dietary intake of zinc-containing foods. Zinc is crucial in the liver's antioxidant defense mechanisms, combating oxidative stress and enhancing enzyme activity. A zinc deficiency weakens these defense mechanisms, increasing oxidative stress, lipid peroxidation, and damage to hepatocytes. Zinc also controls inflammation by blocking the release of pro-inflammatory cytokines, which contribute to liver injury and fibrosis in ALD [29]. Zinc is pivotal for the proper functioning of the mitochondria and cellular regeneration in the liver. Mitochondrial instability caused by zinc deficiency worsens cellular damage, and its absence impairs the regenerative potential of the liver. Low zinc levels also promote systemic inflammation and complications such as HE, where ammonia detoxification via the urea cycle requires zinc. In sum, it not only reflects but actively contributes to the progression of liver dysfunction in ALD by intensifying oxidative stress, inflammation, and impaired regeneration. Zinc deficiency supplementation has been shown promising in addressing this deficiency to help improve liver function as well as clinical outcomes among patients with ALD.

Zinc Deficiency in Chronic Alcoholism

Chronic alcoholism has a very notable effect on zinc metabolism, leading to the development of zinc deficiency, which in turn worsens liver dysfunction. Alcohol intake affects zinc absorption in the gastrointestinal tract, thereby reducing its bioavailability for vital metabolic processes. Chronic alcohol consumption leads to an impaired absorption of zinc, mainly through the gastrointestinal mucosa, where alcohol interferes with normal cellular functions, thus reducing zinc uptake. Furthermore, alcohol causes an increase in urinary excretion of zinc, which depletes the body of zinc even further [30].

Zinc depletion becomes more severe by poor intake of diet from alcohol abusers, as such diets do not have sufficient quantity of zinc-containing food for a considerable amount of zinc intake, and zinc level lowers further. Alcohol causes a condition of systemic inflammation in the body, which influences the redistribution of zinc. In response to inflammation, the body sequesters zinc in the

liver and other tissues, reducing its availability for essential metabolic and cellular functions in peripheral tissues. The combined effects of impaired absorption, increased excretion, inadequate dietary intake, and altered zinc distribution contribute to a state of zinc deficiency, which can have profound implications for liver health and function in alcoholics[20].

Role of Zinc in HE

At a Jharkhand tertiary care facility, 150 patients with liver cirrhosis and HE participated in the study. The patients were categorized into various WHC grades during HE and CPC courses of cirrhosis after being assessed through polls, clinical examinations, and history taking. Morning serum zinc levels, imaging studies, and routine blood investigations were conducted. According to the findings, the majority of HE patients were zinc deficient, and there was a substantial connection between low zinc in the blood and HE WHC levels. There were notable variations in serum zinc levels across the various cirrhosis classes. In patients who passed away, the mean serum zinc level was noticeably lower. Serum zinc alongside albumin levels were found to be strongly positively correlated.

Zinc and Neurological Functions

Häussinger et al. (2021)[11] explored the mechanisms of zinc supplementation to improve communication between synapses and rebalance neurotransmitter functions, thus calming neurological symptoms caused by HE. Zinc is a trace element that plays a very influential role in the proper functioning of the brain and nervous system. It is an integral part of the modulation of neurotransmitter systems, particularly by corresponding with N-methyl-D-aspartate (NMDA)/gamma-aminobutyric acid (GABA) receptors. NMDA receptors are involved in excitatory neurotransmission and synaptic plasticity, while GABA receptors are implicated in inhibitory signaling, thus controlling neuronal excitability and a balance between excitation and

inhibition. Zinc is known to be a modulator of both these systems, maintaining normal neuronal function and performance in cognition.

This delicate balance is disrupted by zinc deficiency, bringing about dysfunctional synaptic signaling. The host is, as a result, made more prone to neurotoxicity and cognitive impairment. In HE, zinc deficiency exacerbates neurological dysfunction by augmenting damage caused by ammonia. Ammonia, a potent neurotoxin accumulated due to liver dysfunction, disrupts astrocyte function and disturbs the balance of neurotransmitters, thus causing cognitive and motor dysfunction. The neurotoxic effect in patients suffering from pre-existing zinc deficiency will be enhanced as the zinc serves as an intermediary to safeguard neurons, maintaining them in an active state of detoxification.

Zinc and HE

According to Kumar et al. (2024),[1] there is an inverse connection between zinc levels in the blood and the level of severity of HE. An absence of zinc is commonly observed in people with a liver condition. The progression and aggravation of HE have been directly correlated with zinc. Different authors in their studies, evaluated zinc concentration together with the HE grading to document a correlation where decreased zinc serum levels relate with high grading of encephalopathy. The authors found that lower zinc levels are correlated with greater cognitive impairment and more severe stages of the condition. Such findings have indicated that zinc can be used as a sensor to assess the course of HE in individuals with a liver condition. Zinc's role in detoxification within the liver explains its implication in HE. The liver is primarily concerned with metabolizing ammonia, that is, the major neurotoxin in HE.

Zinc is involved in the stimulation of the urea cycle and ammonia detoxification. The failure of these processes leads to increased levels of ammonia and neurotoxic effects, which are typical for HE. On the other hand, zinc supplementation was found to stimulate ammonia detoxification through its conversion into urea and its enhanced excretion, leading to a decrease in blood

ammonia levels. It is believed that this reduction in ammonia levels contributes to the cognitive improvements of HE patients. Chander et al. (2023) have demonstrated that zinc supplementation reduces ammonia levels and, more importantly, also leads to improved clinical outcomes such as cognitive functions of patients with HE. As such, zinc supplementation has become a well-established potential therapeutic intervention in the management of HE, particularly among those who are documented to have low serum zinc levels. Zinc restoration might, therefore, reduce some of the cognitive impairments and neurological dysfunctions characteristic of this debilitating disease. Hence, zinc has great importance in preventing and curing HE, because it is an essential factor to maintain liver function as well as protecting the brain from ammonia-induced damage.

Literature Review on Serum Zinc in ALD and HE

Zinc deficiency is highly pervasive among patients suffering from both ALD and HE and significantly contributes to the pathogenesis and severity of such diseases. In ALD, zinc deficiency contributes to liver damage, impaired regeneration, and detoxification, while in HE, the impairment of ammonia detoxification and neurotransmitter systems plays a crucial role in the exacerbation of neurotoxicity. Promising evidence has emerged that zinc supplementation can improve the cognitive outcome and functionality of the liver in both diseases. The mechanisms of action and how to use zinc as an intervention in ALD and HE better need to be established.

Literature Review on Serum Zinc in Chronic Alcoholic Liver Disease

Zinc deficiency is the commonly reported and documented condition of chronic ALD, especially in advanced disease states. Some investigations have established a highly significant decrease in serum zinc concentrations in ALD, which correlates directly with the grade of liver dysfunction[31] reported that of all subjects with advanced chronic liver disease, 73% were deficient in zinc and the degree of deficiency was significantly correlated with high MELD(The Model foe End stage Liver Disease) scores and higher hepatic venous pressure gradients indicators of the extent of liver cirrhosis and portal hypertension. The association of reduced zinc concentration with the intensity

of liver disease indicates an essential role of zinc in ensuring proper hepatic function as well as preventing liver dysfunction. This depletion of zinc in ALD is believed to be secondary to a multifactorial etiology, including reduced intake, impaired intestinal absorption, as well as an increased excretion in the urine characteristic of patients with chronic liver disease. This, in turn, worsens liver damage by disrupting antioxidant liver functions and disorganizing protein synthesis mechanisms in addition to inhibiting cellular regeneration processes. Zinc also significantly regulates the inflammatory process. Its deficiency may thus lead to chronic inflammation associated with ALD. Zinc deficiency is thus not only a marker of liver damage but also potentially a contributibg to the progression of ALD.

Zinc Level and HE Stage Correlation:

Hiwarkar et al. (2023)[17] stated that the serum zinc level was profoundlylower in patients with higher grades of HE according to the West Haven classification system. Many researchers have attempted to establish the link between zinc deficiency and the severity of HE, a complication that manifests in most advanced liver diseases. These results suggest a clear inverse relationship between zinc levels and HE severity, with lower zinc levels correlating to more severe neuropsychiatric manifestations. Similarly, Kumar et al. (2024)[1] found that the survival outcomes of patients with HE and lower serum zinc levels were poorer, which would indicate the potential clinical significance of monitoring zinc levels in HE patients.

Such a correlation might be due to the involvement of zinc in ammonia detoxification. Being a metal ion involved in the process of ammonia transformation into less toxic compounds, the deficiency of this metal could worsen the build up of ammonia in the blood and explain some of the typical characteristics of neurological impairment in HE. Another possible explanation might be zinc's role in blood-brain barrier integrity maintenance and the modulation of neurotransmitter function. This evidence would highlight the possible role of zinc as a biomarker in terms of the severity and prognosis of patients suffering from HE.

Zinc Repletion Effects on HE:

The possible benefits of zinc supplementation therapy on patients with HE have gained greater interest. Clinical studies have proved that zinc supplementation can lead to remarkable improvements in clinical outcomes, primarily through the diminishment of neurological symptoms linked with HE.

Chander et al. (2023) concluded that the clinical response was enhanced after zinc supplementation, characterized by decreased levels of serum ammonia and improvement of cognitive function. Restoring zinc levels may help decrease the neurotoxic effects of ammonia build-up, a primary pathogenetic mechanism of HE, and may alleviate some components of this pathology. Zn supplementation appears to improve the biochemical markers of liver functions and the neuropsychiatric symptoms of HE, proposing thus a potential adjunctive treatment modality for managing this demanding condition. However, evidence is still somewhat inconsistent because of differences in study protocols, including varying dosages, routes of administration, and duration of treatment, that have led to divergent results across studies.

Li et al., (2022)[32] emphasized the need for more standardized treatment regimens to establish optimal zinc supplementation strategies. More research data is needed to identify the optimal zinc dose and preparation, the type of patient, and the treatment duration that would confer long-term clinical benefit. It is also true that developing these issues may be more difficult; however, results obtained thus far indicate that the use of zinc repletion could have a significant position in the treatment of HE as well as potentially enhance patients' quality of life with advanced liver disease.

Gaps in Current Research and Justification for the Study

Knowledge gaps in the literature:

Despite the growing number of researches on the involvement of zinc in liver disease and its potential influence in HE, significant gaps continue to exist in the explanation of the complex

mechanisms that connect the deficiency of zinc to severity exacerbation in HE. While many investigations have shown that zinc is necessary to safeguard liver function and brain protection, particularly in ammonia detoxification, the cellular processes connecting zinc shortage to cognitive impairment in HE is not yet well established. Most of the existing literature on the topic only emphasizes the general benefits of zinc in liver diseases and its supplementation to reduce symptoms.

However, there is a poor investigation of how zinc deficiency is specifically associated with various stages of HE and whether it directly alters the neurological deterioration observed among patients with advanced liver disease. Furthermore, although various studies have indicated the possible medical application of zinc supplementation in improving cognition in, HE, the evidence so far remains inconclusive and inconsistent. Differences in study designs, patient populations, and zinc dosages administered are some reasons why there is no clear consensus on its efficacy. Therefore, although the theoretical and preliminary data are promising, there is still a big gap in understanding how zinc supplementation may prevent or treat HE, and extended research is needed to ascertain the beneficial significance of zinc treatment.

Key Findings from Literature

The literature review demonstrated that zinc deficiency is a typical and crucial component in the pathophysiology of ALD and its neurological manifestation, HE. This is because zinc has important functions in preserving the homeostasis of the liver organ and brain activity, more significantly through its antioxidant properties, anti-inflammatory effects, and metabolic regulatory function. Chronic alcohol abuse disrupts zinc metabolism through inhibition of intestinal absorption, enhancement of urinary zinc excretion, and contributing to malnutrition. These mechanisms have resulted in systemic zinc deficiency that has been very strongly associated with the disease's progression in ALD. Zinc deficiency worsens oxidative stress, which is the central mechanism driving hepatocyte injury, through a reduction in antioxidant enzyme activity

such as superoxide dismutase. It also enhances inflammation by not modulating the production of pro-inflammatory cytokines which include tumor necrosis factor-alpha(TNF-α), which enhances further liver injury, fibrosis, and cirrhosis.

In HE, zinc deficiency exacerbates neurological impairment through the inhibition of ammonia detoxification, which is the major pathogenic mechanism of HE. Zinc is an relevant contributing element in the urea cycle enzymes that convert ammonia into urea, and this process is severely impaired in advanced liver disease. Inadequate zinc levels disrupt this process and cause elevated systemic ammonia that crosses the blood-brain barrier and causes neurotoxicity. Zinc deficiency also compromises the function of astrocytes, exacerbates cerebral oxidative stress, and disrupts neurotransmitter homeostasis, thus causing cognitive and motor dysfunction. Besides this, many studies have reported an inverse correlation of serum zinc concentration with the grade of HE. Thus, decreased levels of zinc have been reported with increasing grades of encephalopathy and poorer clinical course. Therefore, the above facts bring into sharp focus the requirement of zinc replacement therapy in the management plan for ALD and HE.

MATERIALS & METHODS

MATERIALS AND METHODS

Source of data: The study was conducted in the department of General Medicine at RLJH(R L jalappa hospital) – A teaching hospital of SDUMC(Sri Devaraj Urs Medical college), A Constituent college of SDUAHER(Sri Devaraj Urs Academy of Higher Education and Research) Tamaka,kolar,karnataka.

Study design: A Prospective Study

Study period: 18 months(May 2023 to October 2024)

Method of collection of data: All adult patients of chronic alcoholic liver disease with hepatic encephalopathy presenting to the department of general medicine to be included in this study.

Inclusion criteria:

1. Patients equal or more than 21 years

2. Patients with chronic ALD(Alcoholic Liver Disease) with HE(Hepatic Encephalopathy)

3. Patients who consumed alcohol of 60-80 grams/day for 10 years or longer in men and 20-40 grams /day for 10 years or longer in women in HE(Hepatic encephalopathy)

Exclusion criteria:

1. Patients less than 21 years

2. Adults with any of the following will be excluded from the study:

- Ongoing anticoagulation therapy.
- Liver cyst, pancreatitis, inherited bleeding disorder, orthotopic liver transplantation.
- Altered sensorium due to head injury and stroke.
- Psychiatric disorders.
- Alcohol withdrawl state.

Sample Size

The Estimated Sample Size is 41. It was estimated by using the proportion of low serum zinc less than 60mcg/dl in subjects with HE was 89.3% from the study by Rajesh Kumar Meena et al[33]. Using the formula,

$$\textbf{Sample Size} = \frac{\mathbf{Z1-\alpha\ /2\ 2\ P\ (1-P)}}{\boldsymbol{D2}}$$

- Z1-α /2 = is standard normal variate (at 5% type 1 error (P < 0.05) it is 1.96 and at 1% type 1 error (P < 0.01) it is 2.58). As in the majority of studies, P values are considered significant below 0.05 hence 1.96 is used in the formula.
- P= Expected proportion in population based on previous studies or pilot studies
- D= Absolute error or precision; P = 89.3% or 0.893; Q = 10.7% or 0.107; D = 10% or 0.10

Using the above values at 95% Confidence level a sample size of 37 subjects will be included in the study. Considering 10% Nonresponse a sample size of 37 + 3.7 ≈ 41 subjects will be included in the study.

Statistical Analysis

Descriptive Statistics: Descriptive statistics outline the key points of the serum zinc levels and stages of HE in chronic ALD patients. Key measures include the mean, median, standard deviation, and range of serum zinc levels. Frequency distributions highlight the prevalence of HE stages. These statistics help summarize the data, identify trends, and reveal potential relationships between serum zinc levels and disease severity, forming a basis for further correlation analysis.

Correlation: The correlation between serum zinc levels and stages of HE in chronic ALD underline the potential contribution of zinc deficiency in disease progression. Studies suggest that lower serum zinc levels are attributed to more advanced stages of HE, likely due to impaired ammonia metabolism and increased oxidative stress. Assessing this correlation aids in

understanding HE pathophysiology and could guide therapeutic strategies to improve patient outcomes.

Regression: Regression analysis can be used to assess the interaction between serum zinc levels with Serum Albumin, Serum Sodium, and the stages of HE in chronic ALD. By treating serum zinc levels as the independent variable and Serum Albumin, Serum Sodium, and HE stages as the dependent variable, regression models help quantify ramification of zinc on disease progression.

Chi-square: The Chi-square test can be employed to scrutinize correlation among serum zinc levels and the stages of HE in patients with chronic ALD. This statistical method evaluates the association between categorical variables, such as different HE stages, and zinc deficiency prevalence. A significant Chi-square result would indicate a non-random association, suggesting that serum zinc levels may vary meaningfully across the stages of HE.

RESULTS

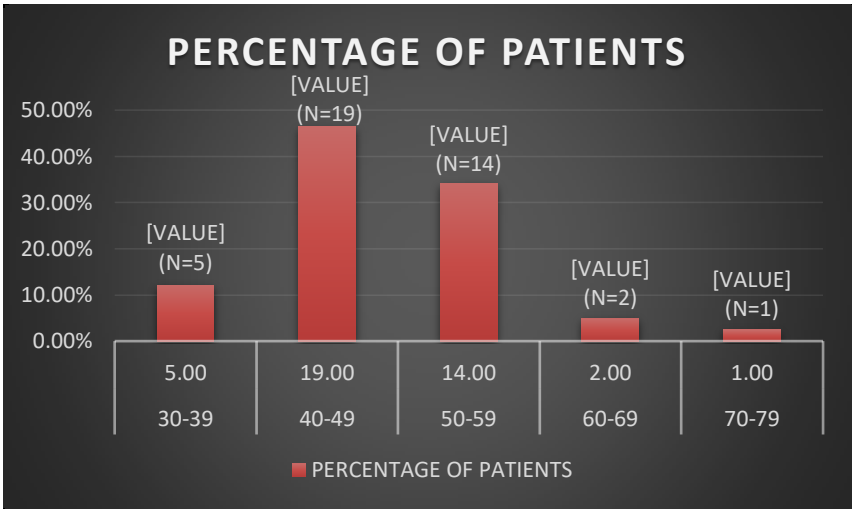
RESULT

Table 1 presents the age-wise distribution of 41 patients in the study with The majority of cases 46.34%(N=19) fall within the 40-49 age group, indicating a higher prevalence of the condition in middle-aged individuals. This is followed by 34.1%(N=14) of cases in the 50-59 age group, suggesting continued vulnerability in older middle-aged individuals. The younger age group accounts for 12.1%(N=5) of cases, while the older age groups, 60-69 and 70-79 years, constitute only 4.87% (N=2) and 2.43%(N=1) of patients respectively. This trend highlights that the condition predominantly affects individuals in their 40s and 50s, with decreasing prevalence in older age groups.The study population comprised 100 % male patients.

Table 1: Percentage of patients based on Age

Age	No of Patients(N=41)	% of patients
30-39	5	12.1%
40-49	19	46.34%
50-59	14	34.1%
60-69	2	4.87%
70-79	1	2.43%

Figure 2: Percentage of Patients



Presenting clinical Features

Table 2 summarizes the presenting features among the patients. Ascites is the most prevalent symptom, observed in all patients, highlighting its strong association with the condition. Constipation and disorientation are next common, each equally affecting 56% (N=23) of patients, followed closely by abdominal pain at 51.2%(N=21). Pedal edema is present in 34.1%(N=14) of cases, while fever occurs in 26.8%(N=11). Less common symptoms include bleeding and confusion, each reported in 12%(N=5) of patients, and vomiting, seen in only 7%(N=3). These findings suggest that ascites is a universal feature, with gastrointestinal and neurological symptoms varying in frequency among the patients.

Table 2: Presenting clinical Features of the Patients

PRESENTING CLINICAL FEATURE	**PATIENT N (%)**
ASCITES	41 (100%)
CONSTIPATION	23 (56 %)
DISORIENTATION	23 (56 %)
ABDOMINAL PAIN	21 (51.2 %)
PEDAL EDEMA	14 (34.1%)
FEVER	11(26.8 %)
BLEEDING	5 (12 %)
CONFUSION	5 (12 %)
VOMITING	3 (7 %)

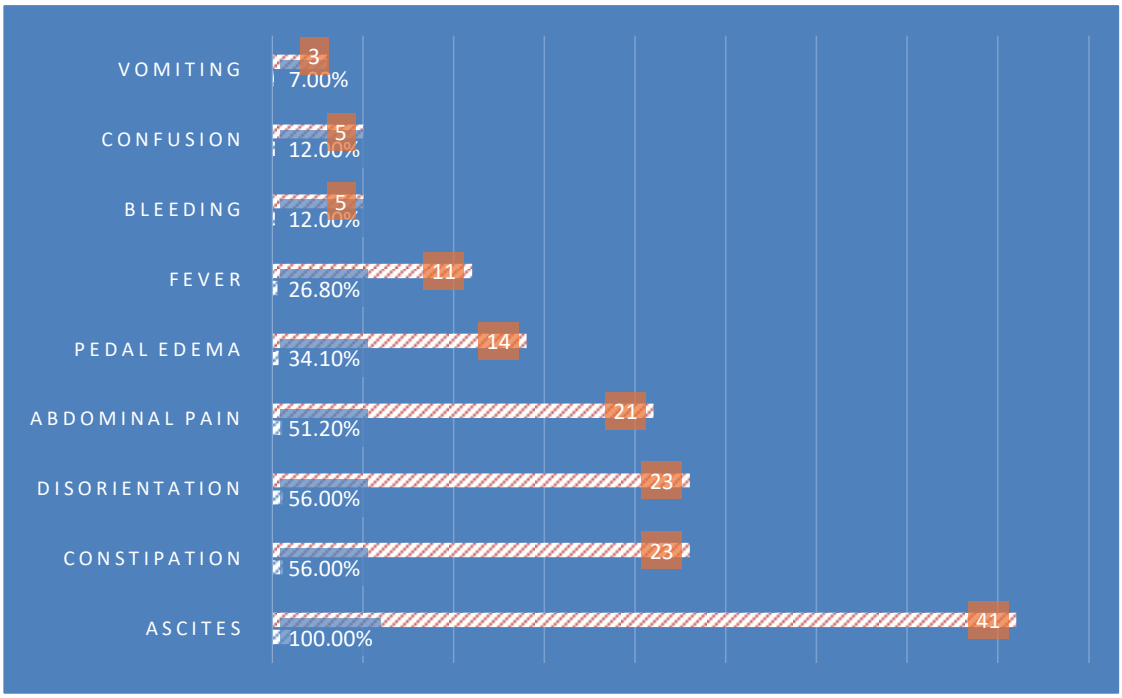


Figure 3: Percentage of Presenting clinical Features

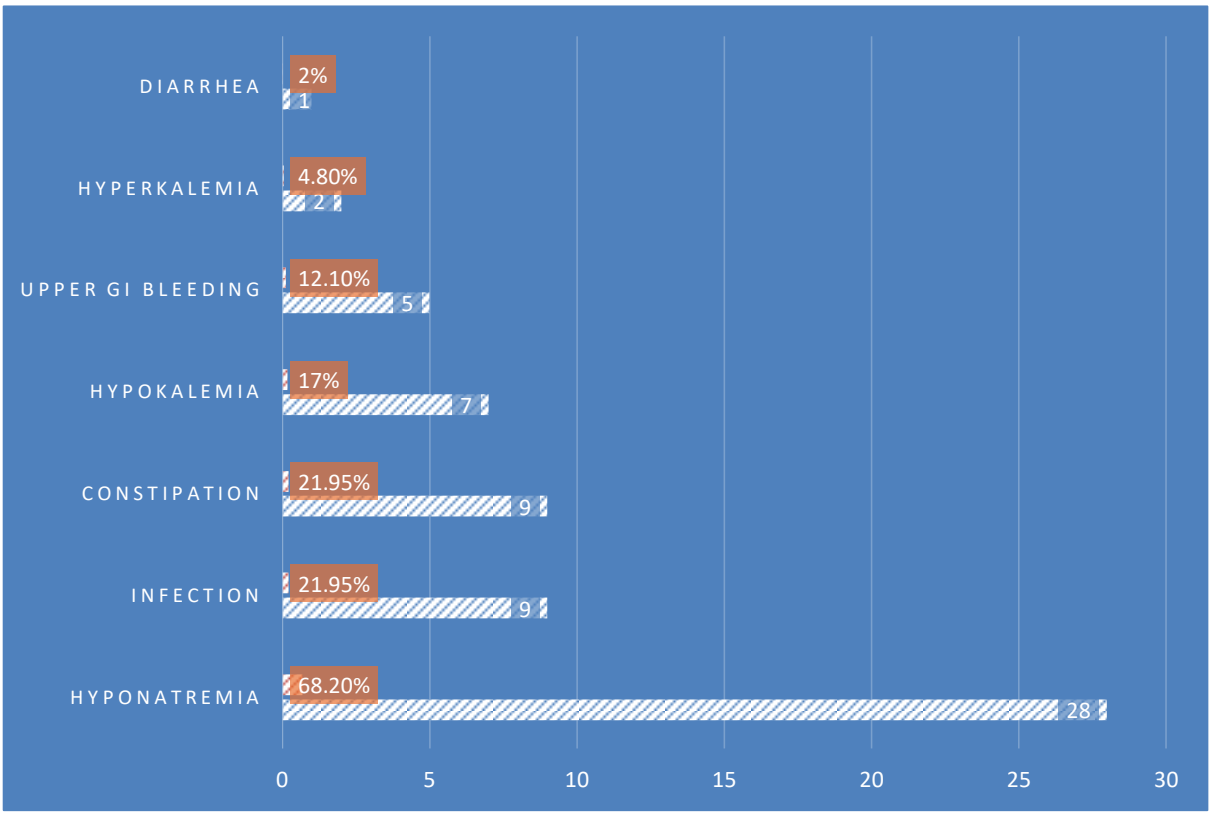
Precipitating Factor

Table 3 highlights the precipitating factors in patients. Hyponatremia is the most common factor, affecting 28(68.2%) patients, indicating its significant role in disease progression. Infection and constipation each contribute to 9(21.95%) cases, followed by hypokalemia in 7(17 %)patients. Less frequent factors include upper GI bleeding in 5(12.1%) cases, hyperkalemia in 2(4.8 %) cases, and diarrhoea in 1(2 %)case, emphasizing electrolyte imbalances as key contributors.

Table 3: precipitating Factor

Precipitating Factor	Patients N (%)
Hyponatremia	28(68.2%)
Infection	9(21.95%)
Constipation	9(21.95%)
Hypokalemia	7(17%)
Upper GI Bleeding	5(12.1%)
Hyperkalemia	2(4.8%)
Diarrhoea	1(2%)

Figure 4: Percentage of Precipitating Factor



Descriptive Statistics

Table 4 provides descriptive statistics for the study variables among 41 patients. The age distribution shows a mean of 2.66 with a range of 3, indicating most patients belong to middle age groups. Gender is uniform, with all participants being male, reflected by a mean of 1.00. Symptoms like fever with a mean of 1.68, abdominal pain at 1.54, vomiting at 1.95, and diarrhoea at 1.98 are present with varying frequencies, reflecting moderate variability. Constipation has a lower mean of 1.37, suggesting a less frequent occurrence. Abdominal distension is uniformly present with a mean of 1.00. Indicators like icterus at 1.05, pedal edema at 1.07, and fetor hepaticus at 1.85 show variability, indicating their differential presence among patients. Clinical parameters, including WHC(West Haven Criteria) with a mean of 2.54, CPC(Child-Pugh Score) at 2.61, SZ(Serum Zinc) at 4.05, and SA(Serum Albumin) at 2.00, highlight varying disease severity, with SZ reflecting higher mean values. Overall, the table emphasizes the heterogeneity in clinical features and severity of HE(Hepatic Encephalopathy) in the patient cohort,symptoms like

abdominal distension,vomiting and diarrhoea were commonly seen across patients,while findings such as icterus and pedal edema were less frequent.This indicates variability in clinical presentation and differing degrees of hepatic dysfunction.

Table 4: Descriptive Statistics

	N	Range	Minimum	Maximum	Sum	Mean	Std. Error	Std. Deviation
Age	41	3	1	4	109	2.66	.108	.693
Sex	41	0	1	1	41	1.00	0.000	0.000
Fever	41	1	1	2	69	1.68	.074	.471
Abdominal pain	41	1	1	2	63	1.54	.079	.505
Vomiting	41	1	1	2	80	1.95	.034	.218
Diarrhoea	41	1	1	2	81	1.98	.024	.156
Constipation	41	1	1	2	56	1.37	.076	.488
Abdominal distension	41	0	1	1	41	1.00	0.000	0.000
Icterus	41	1	1	2	43	1.05	.034	.218
Pedal edema	41	1	1	2	44	1.07	.041	.264
Clubbing	41	1	1	2	71	1.73	.070	.449
Fetor hepaticus	41	1	1	2	76	1.85	.056	.358
WHC	41	4	1	5	104	2.54	.153	.977
CPC	41	4	1	5	107	2.61	.110	.703
SZ(serum zinc)	41	4	2	6	166	4.05	.144	.921
SA(serum albumin)	41	2	1	3	82	2.00	.078	.500
SS(serum sodium)	41	1	2	3	101	2.46	.079	.505

Correlation

Table 5 presents the Pearson correlation coefficients between WHC(West Haven Criteria), CPC Child-Pugh Score), SZ(serum zinc), SA(serum albumin), and SS(serum sodium). WHC shows a strong positive correlation with SZ at 0.720 and a moderate correlation with CPC at 0.531 and SS at 0.446, all statistically significant. CPC exhibits a moderate positive correlation with SZ at 0.339, significant at the 0.05 level, but weaker correlations with SA and SS. SZ correlates moderately with WHC but has weaker associations with SA and SS. SA and SS show weak correlations with all other variables. These findings indicate WHC and SZ as key interrelated parameters in disease severity assessment.Serum Zinc showed a substantial role than serum albumin and serum sodium in correlating with West Haven Criteria(WHC).

Table 5: Pearson Correlation

	WHC	**CPC**	**SZ**	**SA**	**SS**
WHC	1	.531**	.720**	.307	.446**
CPC	.531**	1	.339*	.142	.241
SZ	.720**	.339*	1	.217	.165
SA	.307	.142	.217	1	.297
SS	.446**	.241	.165	.297	1

** P value ≤ 0.01

Regression

Table 6 shows the regression analysis with an R-value of 0.744, indicating a strong positive interrelation between the independent(like serum zinc ,serum albumin,serum sodium) and dependent (like WHC)variables. The R Square of 0.553 suggests that 55.3% of the variability in the dependent variable is explained by the model. The Adjusted R Square of 0.503 accounts for model complexity, ensuring reliability.Our regression model shows that serum zinc,CPC score and albumin together can explain more than half of the variation in WHC.Among these ,serum zinc has strong association compare to others.

Table 6: Regression Analysis

R	R Square	Adjusted R Square	Std. Error of the Estimate
.744[a]	.553	.503	.649

Chi-Square Test

Table 7 presents the Chi-Square test results comparing serum zinc levels and the West-Haven Criteria (WHC) grading of HE. The table shows that the highest number of patients with minimal HE are in the 40-49 age group with 13 cases in Grade 1. The 30-39 age group exhibits a spread across higher grades, with 5 patients in Grade 3 and 1 case in Grade 4. The 50-59 age group shows a variety of grades, with the majority in Grade 1. There is only one patient in the less than 30 age group, indicating a lower incidence of advanced encephalopathy in younger patients which also suggests lower serum zinc levels are affliated with advanced liver disease as classified by WHC.

Table 7: Chi-Square Test in comparison of Serum Zinc and WHC

		WHC-(WEST HAVEN CRITERIA)					Total
		MHE	Grade 1	Grade 2	Grade 3	Grade 4	
SZ(SERUM ZINC)	60-70	3	0	0	0	0	3
	50-59	1	4	1	0	0	6
	40-49	0	13	6	0	0	19
	30-39	1	0	5	5	1	12
	<30	0	0	0	1	0	1
Total		5	17	12	6	1	41

Table 8 presents the Chi-Square test results comparing serum zinc levels with the Child-Pugh Classification (CPC) of liver disease severity. Patients in the 40-49 serum zinc range are predominantly in Class C, with 14 cases, highlighting its association with advanced liver disease. The 30-39 range also has a notable presence in Class C, with 8 cases, indicating moderate severity. The 50-59 range is evenly distributed, with most in Class B. The 60-70 range is primarily in Class A, reflecting better liver function. The data suggests lower serum zinc levels are attributed to advanced liver disease as classified by CPC.

Table 8: Chi-Square Test in Comparison of Serum Zinc and CPC

		CPC(CHILD-PUGH SCORE)			
		Class A	**Class B**	**Class C**	**Total**
SZ(SERUM ZINC)	**60-70**	2	1	0	3
	50-59	0	4	2	6
	40-49	0	5	14	19
	30-39	0	4	8	12
	<30	0	0	1	1
Total		2	14	25	41

Table 9 presents the Chi-Square test results comparing clinical symptoms with the WHC grading of HE. Fever is present in 13 patients, with the majority in Grade 1 and Grade 2, indicating a higher frequency in the early stages. Abdominal pain is observed in 19 patients, distributed across all grades, but more prevalent in Grades 2 and 3. Vomiting and diarrhoea are rare, seen in only 2 and 1 patients, respectively, suggesting a minimal role in grading severity. Constipation is a common symptom, present in 26 patients, predominantly in higher grades, highlighting its association with disease progression. Abdominal distension is universal, affecting all 41 patients, making it a key symptom across all grades. Icterus and pedal edema are also frequent, seen in 39 and 38 patients, respectively, predominantly in advanced grades. Clubbing is present in 11 patients, with most in higher grades, reflecting its relevance in severe cases. Fetor hepaticus is less common, noted in only 6 patients, primarily in advanced grades. These results suggest that symptoms like abdominal distension, icterus, pedal edema, and constipation are prominent across grades, while vomiting, diarrhea, and fetor hepaticus are rare and associated with advanced stages of HE.

Table 9: Chi-Square Test in Comparison of Clinical Symptoms and WHC

		WHC(WEST HAVEN CRITERIA)					Total
		MHE	Grade 1	Grade 2	Grade 3	Grade 4	
Fever	Yes	2	6	4	0	1	13
	No	3	11	8	6	0	28
Abdominal pain	Yes	3	6	8	2	0	19
	No	2	11	4	4	1	22
Vomiting	Yes	1	0	1	0	0	2
	No	4	17	11	6	1	39
Diarrhoea	Yes	0	0	1	0	0	1
	No	5	17	11	6	1	40
Constipation	Yes	2	8	9	6	1	26
	No	3	9	3	0	0	15
Abdominal distension	Yes	5	17	12	6	1	41
Icterus	Yes	3	17	12	6	1	39
	No	2	0	0	0	0	2
Pedal oedema	Yes	3	16	12	6	1	38
	No	2	1	0	0	0	3
Clubbing	Yes	2	1	5	2	1	11
	No	3	16	7	4	0	30
Fetor hepaticus	Yes	0	0	3	2	1	6
	No	5	17	9	4	0	35

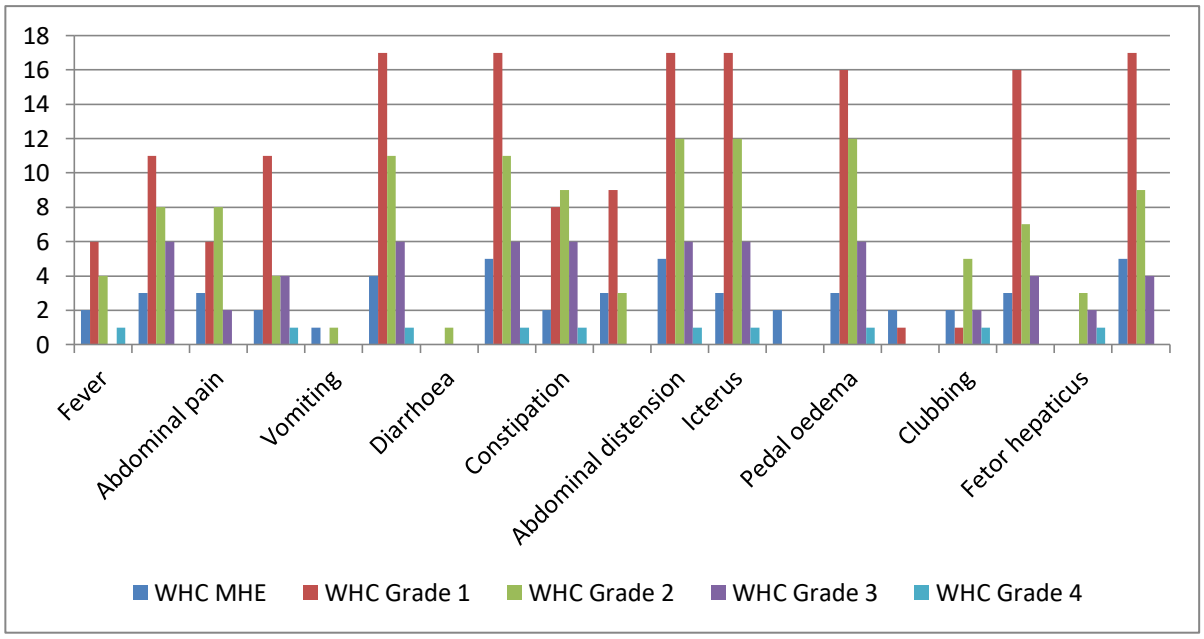


Figure 5: Comparison of Clinical Symptoms and WHC

Table 10 presents the Chi-Square test results comparing clinical symptoms with the CPC of liver disease severity. Fever is observed in 13 patients, with the majority in Class C, suggesting its association with advanced liver disease. Abdominal pain is reported by 19 patients, predominantly in Class C, further supporting its link to more severe cases. Vomiting and diarrhea are rare, with only 2 and 1 cases, respectively, indicating minimal correlation with disease severity. Constipation is a common symptom, affecting 26 patients, mostly in Class B and C, highlighting its relevance in advanced liver disease stages. Abdominal distension is universal across all CPC classes, reflecting its consistent association with liver disease. Icterus and pedal edema are prevalent in 39 and 38 patients, respectively, and are most frequent in Class C, underscoring their role as markers of severity. Clubbing is present in 11 patients, more frequent in Class C, indicating its relevance in advanced cases. Fetor hepaticus is less common, observed in only 6 patients, all in Class C, pointing to its association with severe liver disease. Overall, symptoms like abdominal distension, icterus, pedal edema, and constipation are strongly linked to disease severity, while vomiting and diarrhea are less significant.

Table 10: Chi-Square Test in Comparison of Clinical Symptoms and CPC

		CHILD PUGH CLASS			
		Class A	**Class B**	**Class C**	**Total**
Fever	Yes	1	3	9	13
	No	1	11	16	28
Abdominal pain	Yes	2	4	13	19
	No	0	11	11	22
Vomiting	Yes	1	0	1	2
	No	1	15	23	39
Diarrhoea	Yes	0	0	1	1
	No	2	14	24	40
Constipation	Yes	0	10	16	26
	No	2	4	9	15
Abdominal distension	Yes	2	15	24	41
Icterus	Yes	2	13	24	39
	No	0	2	0	2
Pedal edema	Yes	1	13	24	38
	No	1	2	0	3
Clubbing	Yes	0	5	6	11
	No	2	10	18	30
Fetor hepaticus	Yes	0	0	6	6
	No	2	15	18	35

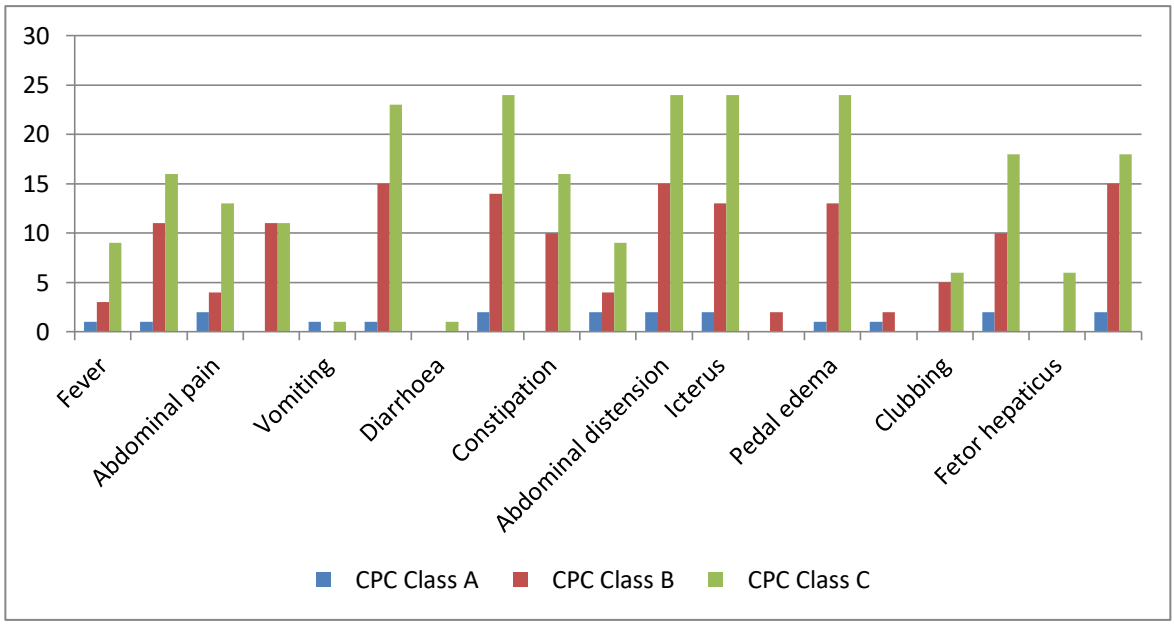


Figure 6: Comparison of Clinical Symptoms and CPC

DISCUSSION

DISCUSSION

Association of serum zinc(SZ) levels with HE(Hepatic Encephalopathy) in chronic ALD: Zinc is an important cofactor for the proper functioning of certain enzymes that play crucial roles in the detoxification of ammonia, a fundamental mechanism in the pathogenesis of HE. The zinc deficiency impairs the functioning of certain enzymes such as ornithine transcarbamylase involved in ammonia metabolism, thus aggravating hyperammonemia. This deficiency is common in chronic liver disease, especially because of cut back on diet, malabsorption, and enhanced urinary elimination of zinc, all of which significantly contribute to the progression of HE[34].

Lower serum zinc values are positively associated with higher grades of HE. Patients with a more advanced phase of HE reveal significantly lower values of serum zinc compared to those exhibiting minimal HE. There is an apparent role of zinc in modulating the severity of HE, thus monitoring serum levels of zinc allows for the appraisal of disease progression in patients [1].

Zinc treatment has been evidenced to improve neurologic outcomes even in mild-moderate levels of HE, thus pointing to its possible therapeutic use in the management. Direct hepatotoxic effects of alcohol also compromise hepatic zinc stores leading to aggravated deficiencies of chronic ALD. Serum levels are lowest in the most advanced Class C patients of Child-Pugh liver disease. Zinc therapy benefits the patient in treating HE through its ammonia-detoxifying ability and reducing oxidative stress in the hepatocytes [35].

The pathogenesis and management of HE in chronic ALD can be associated with the role of zinc, according to evidence. Serum zinc level monitoring would thus be an effective biomarker of disease progression. Zinc supplementation as an adjunctive therapy also promises improved patient outcomes and mitigation of the severity of HE.

This study is in accordance with the study conducted by Tapper,E.B et al which showed a higher prevalence of the condition in individuals aged 40-59, aligning with findings that chronic

liver diseases and HE are more common in middle-aged populations due to prolonged exposure to risk factors such as alcohol consumption and metabolic stress[36]. The decreasing prevalence in older groups may reflect survival bias or reduced exposure to cumulative risk factors [37].

This study supports the observations made by Meena et al reveal that ascites is a universal presenting feature among patients, consistent with its well-established association with HE and chronic liver disease. Gastrointestinal symptoms like constipation 56% and abdominal pain 51.2% are frequent, reflecting impaired gut motility and systemic inflammation commonly linked to chronic liver conditions[38]. Neurological symptoms such as disorientation 56% and confusion 12% underline the neurotoxic effects of elevated ammonia levels, a hallmark of HE[39]. Peripheral manifestations like pedal edema 34.1% further emphasize systemic fluid dysregulation in these patients.

Hyponatremia is the predominant precipitating factor in 68% of cases, reinforcing its critical role in exacerbating HE through cerebral edema and neurotransmitter imbalances[40]. Infections and constipation, each contributing to 22% of cases, are significant triggers due to their impact on systemic inflammation and ammonia accumulation. Electrolyte imbalances, such as hypokalemia and hyperkalemia, along with upper GI bleeding and diarrhoea, represent additional contributors to disease progression, highlighting the multifactorial nature of HE.These findings stress the importance of addressing underlying precipitating factors for effective management of the condition this findings are in accordance with the study done by Roger F.Butterworth[41]

Ascites are the most prevalent presenting feature, observed in all patients, which is consistent with previous studies that identify ascites as a key symptom of HE and advanced liver disease [40]. Constipation and disorientation, each present in 56% of patients, are also commonly observed in liver cirrhosis due to impaired gastrointestinal motility and altered neurological function. Abdominal pain was reported in 51.2%, pedal edema in 34.1%, and fever in 26.8%, demonstrating the variability in symptoms among individuals with chronic liver disease. Less

common symptoms, such as bleeding and confusion, were seen in only 12% of patients, and vomiting was observed in 7%, indicating the varied clinical presentations of the condition.

Hyponatremia was the most common precipitating factor, affecting 28 patients at 68.3%, which is in line with findings from other studies that highlight electrolyte imbalances, particularly hyponatremia, as a major trigger for HE [42]. Infection and constipation, each seen in 9 patients at 22%, were also significant contributing factors, as they are well-documented precipitating conditions in individuals with liver disease. Hypokalemia, upper gastrointestinal bleeding, and hyperkalemia were observed in fewer patients, emphasizing the role of electrolyte disturbances in the disease progression and the importance of addressing these factors in clinical management.

The descriptive statistics highlight the clinical and demographic variability among the 41 patients with HE. The age distribution, with a mean of 2.66, reflects a predominance of middle-aged individuals, consistent with prior studies identifying this demographic as more susceptible to HE due to prolonged exposure to liver disease risk factors [43]. Key clinical symptoms include abdominal distension, uniformly present in all patients, along with icterus and pedal edema, observed in 95% and 93%, respectively. Constipation, present in 63% of patients, emerges as a significant symptom associated with disease progression, paralleling evidence that links gastrointestinal disturbances with advanced liver disease[44]. Less frequent symptoms like vomiting (5%) and diarrhoea (2%) suggest a limited role in disease severity.

The correlation analysis showed strong and significant interdependency between WHC and Serum Zinc(SZ) at 0.720. Other correlations were revealed between WHC and CPC, though only at 0.531, as well as WHC and Serum Sodium(SS) at 0.446. It reflects that CPC, in its partial dependency on disease dynamics, was seen to moderately correlate with SZ at 0.339. However, weaker correlations of SA(Serum albumin) with other variables point to their limited individual significance in this regard. Findings point to the critical interplay of WHC(west haven criteria) and SZ (serum zinc)in assessing the results of the disease.

Findings in this study are accordance with study done by Meena RK et al[45] as regression analysis supports these findings with an R-value of 0.744, implying that the independent and dependent variables have a strong positive relationship. The R Square value of 0.553 indicates that the model explained 55.3% of the variability in the dependent variable. The Adjusted R Square of 0.503 guards against overfitting by adjusting for complexity within the model. These results indicate the predictive value of the model, which points out the necessity of considering WHC and SZ as key indicators in clinical assessments of HE.

The results of the Chi-Square test demonstrate a substantial relationship among serum zinc levels and the WHC grading of HE. Most of the patients with minimal HE fall in the category of 40-49 years, with high concentration in Grade 1, meaning that the severity of the disease is low in this age range. The 30-39 age group has a greater spread in higher grades, and Grade 3 and Grade 4 have significant presence, which means younger patients in this group might have advanced stages of encephalopathy. It appears that increasing age is associated with lower probability of advanced HE, and younger patients show a broader spectrum of grades.

Analysis of serum zinc levels in correlation with the CPC of liver disease further supports a correlation between the lack of zinc and the worsening liver disease. In the age range of 40-49 years, which exhibited the most low serum zinc, individuals are almost all classified in Class C or the most severely deranged state. Similarly, moderate distribution is displayed in the Class C range within the 30-39 bracket, further illustrating that lower levels of serum zinc are attributed to more severe cases of liver disease. On the other hand, the 60-70 years age group has the highest likelihood of falling in Class A mainly because of greater zinc levels as observed in healthier liver functions. The results reveal that serum zinc levels may, therefore, form an important clinical biomarker to the severity and clinical progression of liver disease in which similar findings were reported by Rajesh K Meena et al[33]

The study done by Meena RK et al[33] concurs with findings of in this study where Chi-Square test show an affinity between clinical symptoms and the degree of HE that is usually graded using the WHC. The overall presence of abdominal distension, icterus, and pedal edema was seen in most patients with each grade, but frequencies increased with more severe stages, hence raising their importance as cardinal signs of progression. Constipation was most common in higher grades, and hence, it was highly relevant in advanced HE. In contrast, symptoms like vomiting and diarrhea were rare and appeared mostly in less severe stages, suggesting that they may have minimal impact on the grading of the condition. This presence of fever and abdominal pain was more frequent in the early grades and further supports the idea that gastrointestinal and systemic symptoms vary with disease severity.

Comparison between clinical symptoms and CPC also disclosed a unique association; results revealed more prevalence in conditions like fever, abdominal pain, and constipation among those belonging to advanced classification (Class C) with severity in their disease state. Abdominal distension and icterus were uniformly present in all CPC classes. Pedal edema was mainly seen in Class C. Clubbing and fetor hepaticus, indicative of severe liver disease, was also more frequent in patients of Class C. These findings are therefore supportive of the notion that clinical symptoms like abdominal distension, icterus, and pedal edema are important markers for liver disease severity, whereas vomiting and diarrhoea are less important in indicating the progression of the disease.

SUMMARY

SUMMARY

The study explores interconnection among serum zinc levels and stages of HE in chronic ALD in 41 male patients, with most patients being 40-49 years old, accounting for 46.34 percent of the patient base. The major symptoms were ascites, with 100 percent presentation, and constipation and disorientation each being presented with 56 percent. This observation reported there was a profound reduction in serum zinc with the increasing severity of Hepatic Encephalopathy(HE). This was significantly correlated with the West Haven Criteria with a correlation coefficient of 0.720 and moderately correlated with the child pugh class (CPC), with a correlation coefficient of 0.531. The results of the regression analysis unveiled that serum zinc accounted for 55.3 percent of the variation in the severity of Hepatic Encephalopathy (HE), indicating a model fit value of 0.553. Lower levels of zinc were associated with impaired ammonia detoxification and enhanced oxidative stress, which worsened neuropsychiatric symptoms. Notably, the most severe stages of Hepatic Encephalopathy (HE) were associated with significantly lower zinc levels. These findings point to the monitoring of serum zinc levels as a biological marker and its supplementation as part of treatment strategies to deal with neurocognitive dysfunction and better outcomes in Hepatic Encephalopathy (HE).

LIMITATIONS

LIMITATIONS

- The study's findings are based on a limited number of patients (N=41), which may not provide sufficient statistical power to generalize results to broader populations.
- Conducted at a single institution, the study may lack geographical and demographic diversity, limiting its applicability to other settings.
- The research provides a snapshot of serum zinc levels and Hepatic Encephalopathy(HE) stages without tracking changes over time, missing longitudinal insights.
- Factors like nutritional status, concurrent infections, or other comorbidities influencing zinc levels were not included and comprehensively analysed.
- Further research is needed to evaluate the direct impact of zinc supplementation to assess its therapeutic efficacy and outcomes.

CONCLUSION

CONCLUSION

Serum zinc levels have played a essential role in the pathogenesis and progression of severity of Hepatic encephalopathy in chronic Alcoholic liver disease. Lower serum zinc levels have always been attributed to higher grades of HE. Thus, zinc deficiencies were most profound in the most advanced stages such Grades 3 and 4 of West haven criteria. It focuses on the use of zinc as a cofactor during ammonia detoxification and its deprivation worsens the condition of hyperammonemia which is a crucial mechanism in Hepatic Encephalopathy (HE) pathogenesis.Hyponatremia was observed in majority of patients around 68%, which needs recognition and further evaluation. The clinical presentation was characterized uniformly by abdominal distension, icterus, and pedal edema, increasing with the grade of severity which makes them potential markers of progression. The prevalence of constipation became highly significant as the grade progressed, and vomiting and diarrhea were not commonly found, less often being correlated with increasing grade. It also points to important precipitants, like hyponatremia, infections, and electrolyte imbalance, as more importantly correlated with the exacerbation of HE. All these features again underscored that this is indeed a multi-factorial disease process. Serum zinc monitoring may serve as a valid biomarker to measure HE grade and assess disease progression.

RECOMMENDATIONS

RECOMMENDATIONS

- Prospective research should include a larger and more diverse sample to strengthen the generalizability of findings.
- Conducting follow-up studies can help understand the progression of zinc deficiency and its impact on HE over time.
- Further, zinc supplementation is promising as an adjunctive therapy to reduce symptoms, improve neurological outcomes, and diminish the effects of oxidative stress, providing a pragmatic approach to managing Hepatic Encephalopathy (HE) in chronic alcoholic liver disease (ALD).Clinical trials to determine therapeutic efficiency of zinc supplementation in reducing Hepatic Encephalopathy (HE) severity should be prioritized.
- Future research should account for factors like diet, infections, and comorbidities to better understand their role in zinc deficiency and Hepatic Encephalopathy (HE).
- Exploring other biomarkers like alongside serum zinc levels can provide a more holistic understanding of disease severity and progression.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Kumar D, Prasad MK, Kumar S, Aziz T, Prasad ML, Sinha R, et al. Serum zinc level in liver cirrhosis with hepatic encephalopathy and its correlation with different stages of hepatic encephalopathy. J Family Med Prim Care. 2024 Sep;13(9):3979–87.

2. Wu J, Meng QH. Current understanding of the metabolism of micronutrients in chronic alcoholic liver disease. World J Gastroenterol. 2020 Aug 21;26(31):4567–78.

3. Weiss N, Jalan R, Thabut D. Understanding hepatic encephalopathy. Intensive Care Med. 2018 Feb 25;44(2):231–4.

4. Weissenborn K. Hepatic Encephalopathy: Definition, Clinical Grading and Diagnostic Principles. Drugs. 2019 Feb 31;79(S1):5–9.

5. Jalan R, Rose CF. Heretical thoughts into hepatic encephalopathy. J Hepatol. 2022 Aug;77(2):539–48.

6. Cervantes-Alvarez E, Vilatoba M, Limon-de la Rosa N, Mendez-Guerrero O, Kershenobich D, Torre A, et al. Liver transplantation is beneficial regardless of cirrhosis stage or acute-on-chronic liver failure grade: A single-center experience. World J Gastroenterol. 2022 Oct 21;28(40):5881–92.

7. Seitz HK, Bataller R, Cortez-Pinto H, Gao B, Gual A, Lackner C, et al. Alcoholic liver disease. Nat Rev Dis Primers. 2018 Aug 16;4(1):16.

8. Dubinkina VB, Tyakht A V., Odintsova VY, Yarygin KS, Kovarsky BA, Pavlenko A V., et al. Links of gut microbiota composition with alcohol dependence syndrome and alcoholic liver disease. Microbiome. 2017 Dec 17;5(1):141.

9. Peng Y, Wei Q, Liu Y, Wu Z, Zhang H, Wu H, et al. Prediction and Risk Factors for Prognosis of Cirrhotic Patients with Hepatic Encephalopathy. Gastroenterol Res Pract. 2021 Oct 18;2021:1–14.

10. Kibble H, Ryan JM, Shawcross DL. Hepatic encephalopathy. Medicine. 2023 Jun 1;51(6):440–4.

11. Häussinger D, Butz M, Schnitzler A, Görg B. Pathomechanisms in hepatic encephalopathy. Biol Chem. 2021 Aug 26;402(9):1087–102.

12. Himoto T, Masaki T. Current Trends of Essential Trace Elements in Patients with Chronic Liver Diseases. Nutrients. 2020 Jul 14;12(7):2084.

13. Asprouli E, Kalafati IP, Sakellari A, Karavoltsos S, Vlachogiannakos J, Revenas K, et al. Evaluation of Plasma Trace Elements in Different Stages of Nonalcoholic Fatty Liver Disease. Biol Trace Elem Res. 2019 Apr 16;188(2):326–33.

14. Nangliya V, Sharma A, Yadav D, Sunder S, Nijhawan S, Mishra S. Study of Trace Elements in Liver Cirrhosis Patients and Their Role in Prognosis of Disease. Biol Trace Elem Res. 2015 May 24;165(1):35–40.

15. Agarwal A. Correlation of Trace Elements in Patients of Chronic Liver Disease with Respect to Child- Turcotte- Pugh Scoring System. JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH. 2017;

16. Farhan Thajeel R, Al Baldawi DH, Najim WA. Trace Elements in Children with Chronic Liver Disease. J Clin Gastroenterol Hepatol. 2017;01(03).

17. Hiwarkar SR, Holay MP, Bhiwagade R, Patil P. Study of Serum Zinc Level in Liver Cirrhosis and its Correlation with Stages of Hepatic Encephalopathy. Indian Journal of Medical Specialities. 2023 Apr;14(2):93–6.

18. Soma N, Uchida Y, Kouyama JI, Naiki K, Usui N, Sato A, et al. Serum zinc levels as predictors of covert hepatic encephalopathy in patients with liver cirrhosis. J Gastroenterol. 2025 Jan 16;60(1):96–106.

19. Brus T V., Evgrafov VA. Pathophysiology of hepatic insufficiency. Pediatrician (St Petersburg). 2022 Aug 12;13(3):55–64.

20. Gao B, Bataller R. Alcoholic Liver Disease: Pathogenesis and New Therapeutic Targets. Gastroenterology. 2011 Nov;141(5):1572–85.

21. Arab JP, Roblero JP, Altamirano J, Bessone F, Chaves Araujo R, Higuera-De la Tijera F, et al. Alcohol-related liver disease: Clinical practice guidelines by the Latin American Association for the Study of the Liver (ALEH). Ann Hepatol. 2019 May;18(3):518–35.

22. Subramaniyan V, Lubau NSA, Mukerjee N, Kumarasamy V. Alcohol-induced liver injury in signalling pathways and curcumin's therapeutic potential. Toxicol Rep. 2023 Dec;11:355–67.

23. Avila MA, Dufour JF, Gerbes AL, Zoulim F, Bataller R, Burra P, et al. Recent advances in alcohol-related liver disease (ALD): summary of a Gut round table meeting. Gut. 2020 Apr;69(4):764–80.

24. Chen B, Yu P, Chan WN, Xie F, Zhang Y, Liang L, et al. Cellular zinc metabolism and zinc signaling: from biological functions to diseases and therapeutic targets. Signal Transduct Target Ther. 2024 Jan 3;9(1):6.

25. Ochoa-Sanchez R, Tamnanloo F, Rose CF. Hepatic Encephalopathy: From Metabolic to Neurodegenerative. Neurochem Res. 2021 Oct 15;46(10):2612–25.

26. Podymova SD. New approaches to the pathogenesis, clinic, and treatment of hepatic encephalopathy. Ter Arkh. 2021 Feb 15;93(2):236–42.

27. Ullah MI, Alameen AAM, Al-Oanzi ZH, Eltayeb LB, Atif M, Munir MU, et al. Biological Role of Zinc in Liver Cirrhosis: An Updated Review. Biomedicines. 2023 Apr 4;11(4):1094.

28. Halsted CH, Medici V. Alcohol: Metabolism and Health Effects. In: Encyclopedia of Food and Health. Elsevier; 2016. p. 82–7.

29. Hussain A, Jiang W, Wang X, Shahid S, Saba N, Ahmad M, et al. Mechanistic Impact of Zinc Deficiency in Human Development. Front Nutr. 2022 Mar 9;9.

30. Dominik N, Balcar L, Semmler G, Simbrunner B, Schwarz M, Hofer BS, et al. Prevalence and prognostic value of zinc and selenium deficiency in advanced chronic liver disease. Aliment Pharmacol Ther. 2024 Oct 29;60(7):876–87.

31. Li X, Wang L, He N, Zhang Y, Pang J, Wang H, et al. The relationship between zinc deficiency and infectious complications in patients with hepatitis B virus-related acute-on-chronic liver failure. Gastroenterol Rep (Oxf). 2022;10:goac066.

32. Katayama K. Zinc and protein metabolism in chronic liver diseases. Nutrition Research. 2020 Feb;74:1–9.

33. Meena RK, G. S, P. K, Mohamed I, Masiwal P, Ramadoss K. Constipation and upper gastrointestinal bleed: Leading precipitating factors of hepatic encephalopathy in Indian cirrhotic patients. Indian Journal of Medical Specialities. 2018 Oct 1;9(4):192–4.

34. Kamran U, Towey J, Khanna A, Chauhan A, Rajoriya N, Holt A. Nutrition in alcohol-related liver disease: Physiopathology and management. World J Gastroenterol. 2020 Jun 14;26(22):2916–30.

35. Tong X, Hussain H, Shamaladevi N, Norenberg M, Fadel A, El Hiba O, et al. Age and Sex in the Development of Hepatic Encephalopathy: Role of Alcohol. Biology (Basel). 2024 Mar 29;13(4):228.

36. Tapper EB, Aberasturi D, Zhao Z, Hsu C, Parikh ND. Outcomes after hepatic encephalopathy in population-based cohorts of patients with cirrhosis. Aliment Pharmacol Ther. 2020 Jun 3;51(12):1397–405.

37. Kronsten VT, Tranah TH, Pariante C, Shawcross DL. Gut-derived systemic inflammation as a driver of depression in chronic liver disease. J Hepatol. 2022 Mar;76(3):665–80.

38. Gallego-Durán R, Hadjihambi A, Ampuero J, Rose CF, Jalan R, Romero-Gómez M. Ammonia-induced stress response in liver disease progression and hepatic encephalopathy. Nat Rev Gastroenterol Hepatol. 2024 Nov 9;21(11):774–91.

39. Ciećko-Michalska I, Szczepanek M, Słowik A, Mach T. Pathogenesis of Hepatic Encephalopathy. Gastroenterol Res Pract. 2012;2012:1–7.

40. Ellul MA, Gholkar SA, Cross TJ. Hepatic encephalopathy due to liver cirrhosis. BMJ. 2015 Aug 11;h4187.

41. Butterworth RF. Hepatic encephalopathy. Alcohol Res Health. 2003;27(3):240–6.

42. Jiménez JV, Carrillo-Pérez DL, Rosado-Canto R, García-Juárez I, Torre A, Kershenobich D, et al. Electrolyte and Acid–Base Disturbances in End-Stage Liver Disease: A Physiopathological Approach. Dig Dis Sci. 2017 Aug 13;62(8):1855–71.

43. Bertolotti M. Nonalcoholic fatty liver disease and aging: Epidemiology to management. World J Gastroenterol. 2014;20(39):14185.

44. Kalaitzakis E. Gastrointestinal dysfunction in liver cirrhosis. World J Gastroenterol. 2014;20(40):14686.

45. Meena RK, G. S, P. K, Mohamed I, Masiwal P, Ramadoss K. Constipation and upper gastrointestinal bleed: Leading precipitating factors of hepatic encephalopathy in Indian cirrhotic patients. Indian Journal of Medical Specialities. 2018 Oct 1;9(4):192–4.

ANNEXURES

INFORMED CONSENT FORM

STUDY TITLE:-Correlation of serum zinc levels with stages of hepatic encephalopathy in chronic alcoholic liver disease.

Principal investigator: Dr.Sangam Prem chandar reddy

I, Mr/Mrs _____ ,have been explained in my own vernacular language that I/We will be included in "Correlation of serum zinc levels with stages of hepatic encephalopathy in chronic alcoholic liver disease"**,**hereby I/We give my valid written informed consent without any force or prejudice for recording the observations of haematological and clinical parameters . The nature and risks involved have been explained to me, to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I provide consent voluntarily to allow myself / my relative as a participant in this research. I hereby give consent to provide history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc to the doctor / institute etc. For academic and scientific purpose the operation / procedure, etc may be video graphed or photographed. All the data may be published or used for any academic purpose.

_____

Name of Patient/Guardian (Relation with patient)

_____

(Signature of Patient / Attendant)

(Signature & Name of Research doctor)

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿ ನಮೂನೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ:-ದೀರ್ಘಕಾಲದ ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯಲ್ಲಿ ಸೀರಮ್ ಸತು ಮಟ್ಟಗಳ ಮಟ್ಟ ಮತ್ತು ಹೆಪಾಟಿಕ್ ಎನ್ಸೆಫಲೋಪತಿಯ ಹಂತಗಳ ನಡುವಿನ ಪರಸ್ಪರ ಸಂಬಂಧ.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ.ಸಂಗಮ್ ಪ್ರೇಮ್ ಚಂದ್ರ ರೆಡ್ಡಿ

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ _____, ನನ್ನ ಸ್ವಂತ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಿದ್ದೇನೆ, ನಾನು/ನಾವು "**ದೀರ್ಘಕಾಲದ ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯಲ್ಲಿ ಸೀರಮ್ ಸತು ಮಟ್ಟ ಮತ್ತು ಹೆಪಾಟಿಕ್ ಎನ್ಸೆಫಲೋಪತಿಯ ಹಂತಗಳ ನಡುವಿನ ಪರಸ್ಪರ ಸಂಬಂಧ**"ದಲ್ಲಿ ಸೇರಿಸಲ್ಪಡುತ್ತೇವೆ, ಇದರಿಂದಾಗಿ ನಾನು/ನಾವು ಹೆಮಟೊಲಾಜಿಕಲ್ ಮತ್ತು ಕ್ಲಿನಿಕಲ್ ನಿಯತಾಂಕಗಳ ಅವಲೋಕನಗಳನ್ನು ದಾಖಲಿಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನನ್ನ ಮಾನ್ಯ ಲಿಖಿತ ಮಾಹಿತಿಯುಕ್ತ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ. ಒಳಗೊಂಡಿರುವ ಸ್ವರೂಪ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನ್ನ ತೃಪ್ತಿಗೆ ವಿವರಿಸಲಾಗಿದೆ. ನಡೆಸಲಾಗುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶ ಸಿಕ್ಕಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ನನ್ನನ್ನು / ನನ್ನ ಸಂಬಂಧಿಯನ್ನು ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ನಾನು ಈ ಮೂಲಕ ವೈದ್ಯಕೀಯ ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗಳಿಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ವೈದ್ಯರು / ಸಂಸ್ಥೆಗೆ ಒದಗಿಸಲು ಸಮ್ಮತಿಸುತ್ತೇನೆ. ಶೈಕ್ಷಣಿಕ ಮತ್ತು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಗಳಿಗಾಗಿ ಕಾರ್ಯಾಚರಣೆ / ಕಾರ್ಯವಿಧಾನ ಇತ್ಯಾದಿಗಳನ್ನು ವೀಡಿಯೊಗ್ರಾಫ್ ಮಾಡಬಹುದು ಅಥವಾ ಛಾಯಾಚಿತ್ರ ಮಾಡಬಹುದು. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಬಹುದು.

_____

ರೋಗಿಯ ಹೆಸರು / ರಕ್ಷಕ (ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

_____

(ರೋಗಿಯ / ಪರಿಚಾರಕರ ಸಹಿ)

(ಸಂಶೋಧನಾ ವೈದ್ಯರ ಸಹಿ ಮತ್ತು ಹೆಸರು)

PATIENT INFORMATION SHEET

STUDY TITLE : Correlation of serum zinc levels with various stages of hepatic encephalopathy in chronic alcoholic liver disease.

Principal investigator: Dr Sangam prem chandar reddy

I Dr.SANGAM PREM CHANDAR REDDY , Post graduate student in Department of general medicine at Sri Devraj Urs Medical College, will be conducting a study titled**"**Correlation of serum zinc levels with various stages of hepatic encephalopathy in chronic alcoholic liver disease" . This study will be useful for further management of Hepatic Encephalopathy with Chronic Alcoholic Liver Disease in the near future. The funds needed for the serum Zinc levels and Necessary investigations will be done at my own expense .2 ml of blood will be drawn for estimation of serum zinc levels , from each of the participating patients in this study .This study will be done under the guidance of Dr.RAVEESHA A, HOU & Professor of Department of GENERAL MEDICINE .

All the data will be kept confidential and will be used only for purpose specified by the institution. You are free to provide consent for the participation of yourself in this study. You can also withdraw yourself from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution.In case of any clarifications are needed you are free to contact me on this mobile number - 9480456435

Name and Signature of the Principal Investigator

Date-

Patient or patient bystanders Signature

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ: ದೀರ್ಘಕಾಲದ ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯಲ್ಲಿ ಸೀರಮ್ ಸತು ಮಟ್ಟಗಳ ಪರಸ್ಪರ ಸಂಬಂಧ ಹೆಪಾಟಿಕ್ ಎನ್ಸೆಫಲೋಪತಿಯ ವಿವಿಧ ಹಂತಗಳೊಂದಿಗೆ.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಸಂಗಮ್ ಪ್ರೇಮ್ ಚಂದ್ರ ರೆಡ್ಡಿ

ಶ್ರೀ ದೇವರಾಜ್ ಅರಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜಿನಲ್ಲಿ ಜನರಲ್ ಮೆಡಿಸಿನ್ ವಿಭಾಗದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿಯಾಗಿರುವ **ಡಾ. ಸಂಗಮ್ ಪ್ರೇಮ್ ಚಂದ್ರ ರೆಡ್ಡಿ** ಅವರು "**ದೀರ್ಘಕಾಲದ ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯಲ್ಲಿ ಹೆಪಾಟಿಕ್ ಎನ್ಸೆಫಲೋಪತಿಯ ವಿವಿಧ ಹಂತಗಳೊಂದಿಗೆ ಸೀರಮ್ ಸತು ಮಟ್ಟಗಳ ಪರಸ್ಪರ ಸಂಬಂಧ**" ಎಂಬ ಶೀರ್ಷಿಕೆಯ ಅಧ್ಯಯನವನ್ನು ನಡೆಸಲಿದ್ದಾರೆ. ಈ ಅಧ್ಯಯನವು ಮುಂದಿನ ದಿನಗಳಲ್ಲಿ ದೀರ್ಘಕಾಲದ ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯೊಂದಿಗೆ ಹೆಪಾಟಿಕ್ ಎನ್ಸೆಫಲೋಪತಿಯ ಹೆಚ್ಚಿನ ನಿರ್ವಹಣೆಗೆ ಉಪಯುಕ್ತವಾಗಿರುತ್ತದೆ. ಸೀರಮ್ ಸತು ಮಟ್ಟಗಳು ಮತ್ತು ಅಗತ್ಯ ತನಿಖೆಗಳಿಗೆ ಅಗತ್ಯವಿರುವ ಹಣವನ್ನು ನನ್ನ ಸ್ವಂತ ಖರ್ಚಿನಲ್ಲಿ ಮಾಡಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವ ಪ್ರತಿಯೊಬ್ಬ ರೋಗಿಯಿಂದ ಸೀರಮ್ ಸತು ಮಟ್ಟವನ್ನು ಅಂದಾಜು ಮಾಡಲು 2 ಮಿಲಿ ರಕ್ತವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನವನ್ನು ಡಾ. ರವಿಶಾ ಎ, ಹೆಚ್.ಒ.ಯು ಮತ್ತು ಜನರಲ್ ಮೆಡಿಸಿನ್ ವಿಭಾಗದ ಪ್ರಾಧ್ಯಾಪಕರ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಾಡಲಾಗುತ್ತದೆ.

ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುವುದು ಮತ್ತು ಸಂಸ್ಥೆಯು ನಿರ್ದಿಷ್ಟಪಡಿಸಿದ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುವುದು. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಗೆ ನೀವು ಒಪ್ಪಿಗೆ ನೀಡಲು ಸ್ವತಂತ್ರರು. ಯಾವುದೇ ಕಾರಣಗಳನ್ನು ನೀಡದೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು. ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ನಿರಾಕರಣೆಯು ಈ ಸಂಸ್ಥೆಯಲ್ಲಿನ ಯಾವುದೇ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೈಕೆಗೆ ನಿಮ್ಮನ್ನು ಹಾನಿಗೊಳಿಸುವುದಿಲ್ಲ. ಯಾವುದೇ ಸ್ಪಷ್ಟೀಕರಣಗಳ ಅಗತ್ಯವಿದ್ದರೆ ನೀವು ಈ ಮೊಬೈಲ್ ಸಂಖ್ಯೆ - 9480456435 ನಲ್ಲಿ ನನ್ನನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ-

ರೋಗಿ ಅಥವಾ ರೋಗಿಯ ಪಕ್ಕದಲ್ಲಿರುವ ಪ್ರೇಕ್ಷಕರ ಸಹಿ

PROFORMA

STUDY TITLE: Correlation of serum zinc levels with stages of hepatic encephalopathy in chronic alcoholic liver disease

PARTICULARS OF THE PATIENT:

NAME	
AGE	
GENDER	
DATE OF ADMISSION	
OCCUPATION	
PRESENTING COMPLAINTS	
Risk factor : **1. ALCOHOLIC**	
Is the patient already a known case of CHRONIC ALCHOLIC LIVER DISEASE	
If Yes then details about treatment history	
PAST HISTORY	
COMORBIDITIES	
DURATION OF STAY IN HOSPITAL	
TIMES OF READMSSION FOR THE SAME COMPLAINTS	
WEST HAVEN CRITERIA(WHC)	

INVESTIGATIONS

1.SERUM ZINC LEVELS

2.LIVER FUNCTION TESTS

3.SERUM ELECTROLYTES AND RENAL FUNCTION TESTS

DATE	UREA (MG/DL)	CREAT (MG/DL)	SODIUM (MEQ/L)	POTASSIUM (MEQ/L)

4 . COMPLETE HEMOGRAM

DATE	HBGM %	RBC MIL/CU.MM	PCV %	MCV FL	WBC TH/CU.MM	PLATLETS TH/CU.MM

5.ULTRASOUND ABDOMEN AND PELVIS

6.COAGULATION PROFILE

MASTER CHART

S.NO	age	sex	fever	Abd pain	vomiting	diarrhea	constipation	Abd distension	icterus	Pedal edema	clubbing	Fetor hepaticus	WHC	CPC	Serum zinc	Serum albumin	Serum sodium
1	47	1	1	1	2	2	1	1	1	1	2	2	2	3	3	2	3
2	42	1	1	1	2	2	2	1	1	1	2	2	1	1	2	2	3
3	47	1	2	1	2	2	1	1	1	2	2	2	3	3	5	1	3
4	59	1	2	2	2	2	2	1	1	1	2	2	2	3	4	1	2
5	72	1	2	2	2	2	2	1	1	2	1	1	3	3	4	2	3
6	52	1	2	2	2	2	1	1	1	1	1	1	4	3	5	3	3
7	55	1	2	1	2	2	2	1	1	1	2	2	3	5	3	2	2
8	68	1	2	1	2	2	1	1	1	2	1	1	3	3	4	2	3
9	47	1	1	1	2	2	1	1	1	1	2	2	1	2	2	2	2
10	56	1	2	2	2	2	1	1	1	1	2	2	4	3	5	2	2
11	49	1	2	2	2	2	1	1	1	2	2	1	4	3	5	1	3

S.NO	age	sex	fever	Abd pain	vomiting	diarrhea	constipation	Abd distension	icterus	Pedal edema	clubbing	Fetor hepaticus	WHC	CPC	Serum zinc	Serum albumin	Serum sodium
12	52	1	2	1	2	2	1	1	1	1	2	2	4	3	5	3	3
13	48	1	2	2	2	2	1	1	1	2	2	2	2	2	4	2	3
14	40	1	1	1	2	2	2	1	1	2	2	2	2	3	4	2	2
15	50	1	1	2	2	2	1	1	1	2	1	2	3	2	5	2	3
16	47	1	1	1	2	2	2	1	1	2	2	2	2	3	4	2	2
17	55	1	2	2	2	2	1	1	1	1	2	2	2	3	4	2	3
18	51	1	2	1	1	2	2	1	1	2	2	2	1	1	2	1	3
19	43	1	2	1	2	2	1	1	1	1	2	2	3	2	5	2	2
20	50	1	2	1	2	2	1	1	1	1	2	2	2	2	4	2	3
21	43	1	2	2	2	2	2	1	1	2	2	2	2	2	4	2	3
22	55	1	2	1	2	2	1	1	1	2	2	2	3	3	4	2	3
23	42	1	2	2	2	2	1	1	1	2	2	2	2	2	3	2	3

S.NO	age	sex	fever	Abd pain	vomiting	diarrhea	constipation	Abd distension	icterus	Pedal edema	clubbing	Fetor hepaticus	WHC	CPC	Serum zinc	Serum albumin	Serum sodium
24	45	1	2	2	2	2	2	1	2	2	1	2	1	2	3	2	2
25	35	1	1	1	2	1	2	1	1	1	1	1	3	3	5	3	3
26	49	1	1	2	2	2	1	1	1	1	1	1	5	3	5	2	3
27	43	1	2	2	2	2	2	1	1	2	1	2	2	2	3	2	2
28	40	1	2	2	2	2	1	1	2	2	1	2	1	2	5	2	3
29	46	1	2	2	2	2	1	1	1	2	1	2	4	3	6	2	3
30	34	1	1	1	1	2	1	1	1	1	2	2	3	3	4	3	3
31	38	1	1	1	2	2	2	1	1	1	2	2	2	3	4	1	2
32	36	1	2	2	2	2	1	1	1	2	2	2	3	3	4	2	3
33	43	1	2	1	2	2	2	1	1	1	2	2	2	2	4	2	2
34	55	1	2	1	2	2	1	1	1	2	2	2	3	3	4	2	3
35	42	1	2	2	2	2	1	1	1	1	2	2	2	2	3	2	3

S.NO	age	sex	fever	Abd pain	vomiting	diarrhea	constipation	Abd distension	icterus	Pedal edema	clubbing	Fetor hepaticus	WHC	CPC	Serum zinc	Serum albumin	Serum sodium
36	52	1	2	1	2	2	1	1	1	2	2	2	4	3	5	3	3
37	48	1	2	2	2	2	2	1	1	2	2	2	2	2	4	2	2
38	39	1	1	1	2	2	2	1	1	2	2	2	2	3	4	2	3
39	50	1	1	2	2	2	2	1	1	2	1	2	3	2	5	2	3
40	55	1	1	1	2	2	2	1	1	2	2	2	2	3	4	2	2
41	61	1	2	2	2	2	2	1	1	2	2	2	2	3	4	2	3