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Evaluating the Association of Serum Zinc Levels with Hepatic Encephalopathy in Decompensated Chronic Liver Disease Patients in Teritiary Care Center

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Abstract: ***Hepatic Encephalopathy is the term used to describe the complex and variable reversible changes in neuropsychiatric status in patient with chronic liver disease. It is defining feature of the fulminant hepatic failure. Zinc is a trace element which is an important cofactor of urea cycle enzymes like ornithine transcarboxylase, and others like glutamine synthetase which are essential for conversion of ammonia to urea. This study presents a remarkable insight of association of zinc levels with hepatic encephalopathy which helps as marker of investigation and helps in management and future therapeutic approaches.***

Keywords: Hepatic Encephalopathy (HE), Decompensated Chronic Liver Disease (DCLD)

1. Introduction

- HE is the term used to describe the complex and variable reversible changes in neuropsychiatric status in patient with chronic liver disease. It is defining feature of fulminant hepatic failure.
- Prevalence is 50 - 70% in patients with cirrhosis.
- Zinc is a trace element which is an important cofactor of urea cycle enzymes like ornithine transcarboxylase, and others like glutamine synthetase which are essential for conversion of ammonia to urea.
- **Study Design**: Cross sectional study
- **Sample Size:** 50 patients
- **Sampling Method:** Convenience sampling
- **Duration of Study:** From August 2022 to July 2023.

Inclusion Criteria: All patients of Decompensated Chronic Liver Disease and Patients with Hepatic encephalopathy.

Exclusion Criteria:
1) Altered sensorium due to trauma
2) Metabolic encephalopathy
3) Acute alcohol intoxication
4) Alcohol withdrawal
5) Known psychiatric illness

Statistical Analysis: SPSS (Statistical Package for Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis. Descriptive statistics of the explanatory and outcome variables were calculated.

Data Collection

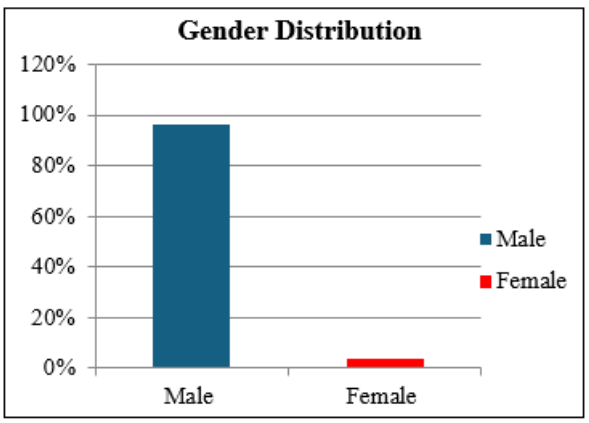
All patients with Decompensated chronic liver disease admitted in medical wards and medical ICU of Narayana medical college, Nellore during period of August 2022 - July 2023 are studied.

- Hepatic encephalopathy is diagnosed with the help of clinical history and neuropsychometric tests i. e., number connection tests.
- Serum zinc levels were assessed in all patients, and levels were correlated with stage of hepatic encephalopathy.

2. Observation and Results

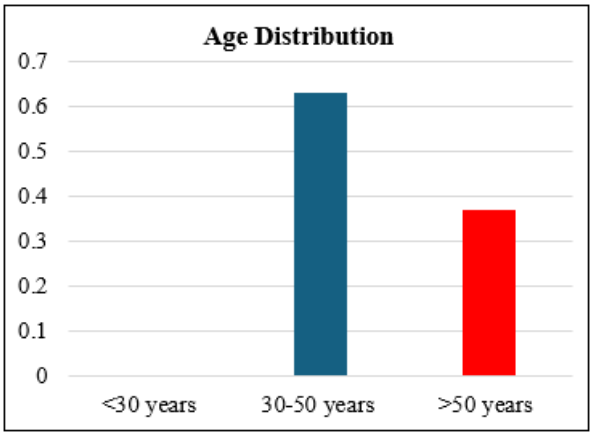
Gender Distribution

	Total	Percentage
Male	48	96%
Female	2	4%



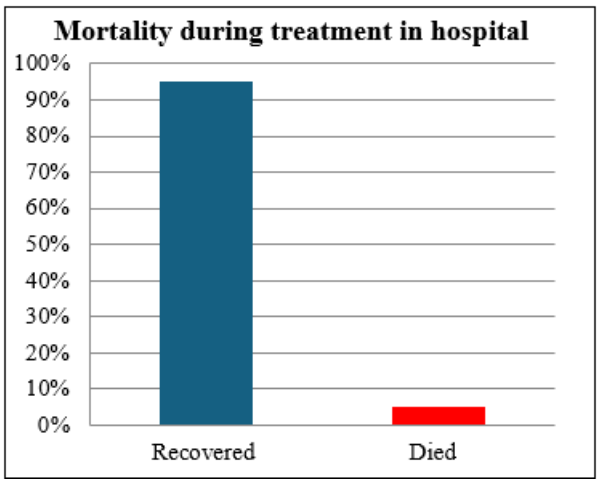
Age Distribution

Age Group	Total	Percentage
<30 years	0	0
30 - 50 years	32	64%
>50 years	18	36%



Mortality During Treatment in Hospital

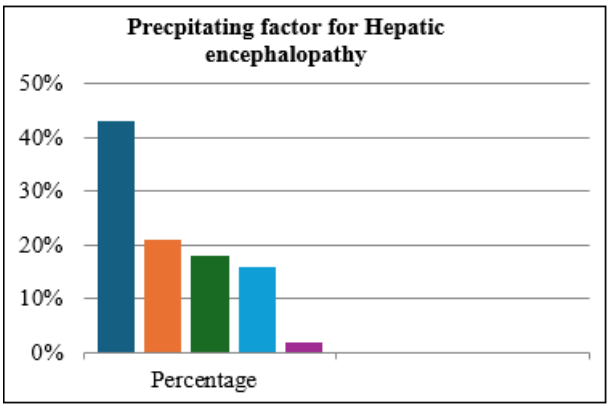
	Total	Percentage
Recovered	48	96%
Died	2	4%



Grade	Count	Serum Zinc Levels (md/dl)				
West Haven grade	Count	<30	30 - 39	40 - 49	50 - 59	60 - 69
Minimal HE	7	0	1	2	1	3
Grade 1	17	1	3	5	5	3
Grade 2	16	2	2	4	5	3
Grade 3	8	3	2	0	2	1
Grade 4	2	2	0	0	0	0

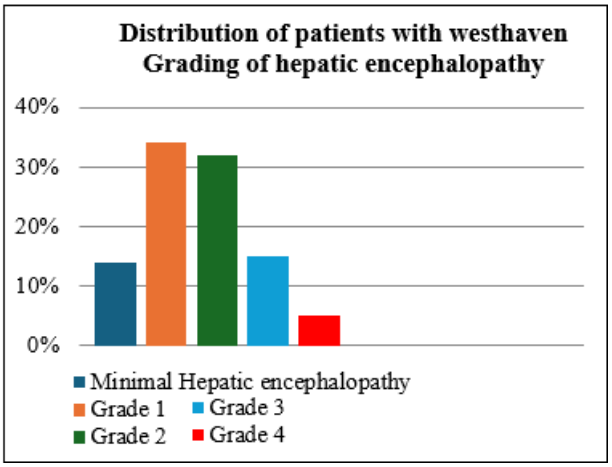
Precipitating Factor for Hepatic Encephalopathy

	Total	Percentage
Constipation	22	44%
Upper GI bleed	10	20%
Dyselectrolytemia	9	18%
Diuretics	8	16%
Infections	1	2%



Distribution of Patients with West Haven Grading of Hepatic Encephalopathy

	Total	Percentage
Minimal Hepatic encephalopathy	7	14%
Grade 1	17	34%
Grade 2	16	32%
Grade 3	8	16%
Grade 4	2	4%



3. Discussion

Hepatic encephalopathy is characterized at the neurophysiological level by disturbed corticocortical and corticomuscular coupling, and at the cellular level by primary gliopathy. A number of factors, occurring alone or in combination, have been implicated in development of HE. These include production of neurotoxins, altered permeability of Blood Brain Barrier, abnormal neurotransmission. The best described neurotoxin involved in HE is ammonia. Which is primarily produced in colon, where bacteria metabolize proteins and other nitrogen - based products into ammonia. Once produced, ammonia enters portal circulation and under normal conditions, it is metabolized and cleared by hepatocytes. In cirrhosis and portal hypertension, reduced hepatocyte function and portosystemic shunting contribute to increased circulating ammonia levels. Increased permeability of Blood Brain Barrier increases uptake and extraction of ammonia by cerebellum and basal ganglia. In brain ammonia is detoxified by astrocytes through a reaction catalyzed by glutamine synthetase, increased brain glutamine/glutamate ratio is associated with decreased myoinositol, reflecting compensation for glial edema. Swollen astrocytes predispose to neuronal dysfunction by impairing their regulatory activity

against the increase in protein tyrosine nitration and the formation of reactive oxygen and nitrogen oxide species including nitric oxide. If not counteracted, these reactions promote RNA oxidation, which prompts gene expression and the transcription of altered proteins. Cytokines or lipopolysaccharides could induce the formation of nitrogen oxide species and trigger zinc release from metallothionein, the principal zinc storage protein. A fluctuation in intracellular zinc levels modulates signal transduction, transcription factor activity, and gene expression, causing hepatic encephalopathy symptoms. Zinc is an important key element of many physiological mechanisms, important co - factor of many urea cycle enzymes like ornithine transcarbamylase, glutamine synthetase and with advanced class of cirrhosis and increasing HE class the zinc level in blood also decrease. Low serum and liver Zinc levels decrease the activity of ornithine transcarbamylase in liver. Due to disturbance in urea cycle leads to increase in ammonia levels in blood. Raised ammonia levels and low zinc levels are associated with HE and malnutrition, patients those had more severe HE also had more low plasma zinc levels. Raised ammonia levels and low zinc levels are associated with HE and malnutrition, patients those had more severe HE also had more low plasma zinc levels.

4. Conclusion

Hepatic encephalopathy is one of the life - threatening complications in Decompensated chronic liver disease patients. We have studied the correlation between serum zinc levels and their effect on various stages of hepatic encephalopathy. With this finding we conclude that, Low serum zinc levels is associated with severe hepatic encephalopathy, and with decreasing zinc levels, Hepatic encephalopathy grade progressed.

5. Future Scope

There are only a few reports on the association of zinc levels with hepatic encephalopathy. Hence, it is critical to forecast this complication as accurately as possible. Ongoing research and interdisciplinary collaboration will be instrumental in improving the management and prevention of Hepatic Encephalopathy.

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