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SERUM ZINC LEVEL IN DECOMPENSATED LIVER DISEASE AND ITS CORRELATION WITH STAGE OF HEPATIC ENCEPHALOPATHY

Dr.Mir Mohd Mujtaba Ali Baquri* Junior Resident, S.Nijalingappa Medical College and HSK HOSPITAL, Bagalkot. *Corresponding Author

Dr.S.A.Kora Professor and Head of the Department, Department of General Medicine, S.Nijalingappa Medical College and HSK Hospital, Bagalkot.

ABSTRACT

Background: Chronic liver disease is one of the major health problems in India. With Zinc involved in Urea cycle for conversion of Ammonia to Urea, Zinc is key component in development of Hepatic encephalopathy

Objectives: To assess the serum Zinc levels in decompensated chronic liver disease (DCLD) patients with various stage of hepatic encephalopathy (HE) and determine the role of Zinc deficiency in precipitation of hepatic encephalopathy.

Materials and Methods: This was a prospective cross sectional study, conducted on 45 cases of decompensated liver disease, who met the inclusion and exclusion criteria of the study. This study was done in S.Nijalingappa Medical College,Bagalkot, Karnataka during the period of September 2021 to January 2022

Results: There was significant decrease in Serum Zinc levels in Decompensated chronic liver disease and more decrease was with higher stages of HE

Conclusion: This study concludes that there is significant decrease in Serum Zinc in DCLD and further decreased levels were found in higher stages of HE, indicating Serum Zinc plays an important role in progression of HE

KEYWORDS : Serum Zinc, Decompensated Liver Disease, Hepatic Encephalopathy

1.INTRODUCTION:

Chronic disease like liver cirrhosis and its complications are a major health problem particularly in India.

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the end result of the fibro genesis that occurs with chronic liver injury.[1] Diffuse fibrosis cause distortion of architecture with regenerative nodule formation, which results in decreased liver cell mass and reduced blood flow to the liver.[1,2]

In India, most common cause of cirrhosis is alcohol abuse and viral hepatitis. Reversible fibrosis with ongoing injury in course of time leads to decompensated condition, which is associated with one or more complications like ascites, jaundice, Hepatic encephalopathy and upper gastrointestinal (UGI) bleed.

About 30% patients of cirrhosis die due to hepatic coma.[3] Hepatic encephalopathy is precipitated by gut derived neurotoxin such as ammonia.

Zinc (Zn) is second most abundant trace element in the body. Zn is associated with more than 300 enzymatic functions.[4] It is an important co–factor in urea cycle, has a great role in conversion of ammonia to urea. Zn is an important part of natural defence mechanism involving of reactive oxygen species, it also act as an antioxidant, anti apoptotic agent, and anti-inflammatory agent. So hypozincemia seems to accelerate the manifestations of cirrhosis of liver.

2.OBJECTIVES:

To assess the serum Zinc levels in decompensated chronic liver disease (DCLD) patients with various stage of hepatic encephalopathy (HE) and determine the role of Zinc deficiency in precipitation of hepatic encephalopathy.

3.Methodology:

3.1 Study design:

Prospective cross sectional study

3.2 Source of study population:

Inpatients/outpatients of General Medicine in HSK Hospital, Bagalkot.

3.3Inclusion criteria:

- Age > 20 years
- Ascites
- Bleeding from any site including melaena
- Jaundice
- Pedal edema
- Altered sensorium

3.4 Exclusion criteria:

- Age < 20 years
- Metabolic causes of encephalopathy
- Psychiatric disorders.

3.5 Sample size:

Sample size estimation was done using openepi software version 2.3.1

At 95% confidence level,
According to the study conducted by Soomro Aa[5]

Proportion of liver disease patients with low zinc levels was found in 69%=p
At 20% relative precision
Sample size estimated is 45

Formula used:

$[DEFF^*Np(1-p)]/[(d^2/Z^2\ 1-\alpha/2*(N-1)+p*(1-p)]$

3.6 Data collection :

1. Informed consent was taken for participation in the study
2. A questionnaire was used to collect history of jaundice ,bleeding including black stools,ascites

3.7 Investigations:

- Liver Function Test
- PT-INR
- Renal Function Test
- CBC
- Serum Zinc

Hepatic encephalopathy patients were clinically graded according West Hevan classification (WHC).[3] All patients also classified by Modified Child's classification4 and severity of liver cirrhosis were assessed by Modified Child–Pugh score.[4,6]

Normal serum Zinc level is 80-120mcg/dL

RESULTS:

Table 1: Mean Age of cases

Age	
Mean	44.53
Std. Deviation	9.29
Minimum	20.00
Maximum	62.00

The mean age of cases is 44.53±9.29 years. The highest age of the case being 62 years and minimum age of the case being 20 years (Table 1)

In our study 38 were males(84.4%) and 7 were females(15.6%) (Figure 1)

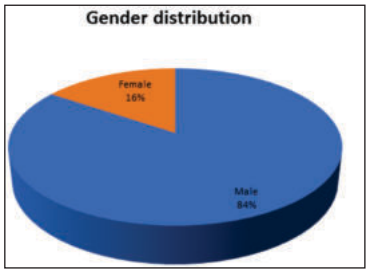

Fig 1: Genderwise distribution of participants

Table 2: Etiology of cirrhosis

Presenting features	No of cases	Percent
HBsAg Positive	7	15.6
Alcoholic	38	84.4

In our study etiologies of cirrhosis are Alcoholism in 38 cases(84.4%) and Hepatitis in 7 cases(15.6%) (Table 2)

In our study, number of cases in Stage 1 HE were 28 (62.2%); in Stage 2 HE were 10 (22.2%); and in Stage 3 were 7 (15.6%) (Figure 2)

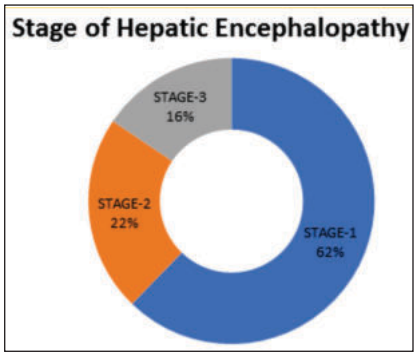

Fig 2: Distribution of case by stages of HE

In our study, the mean Serum Zinc in Child Pugh B category wqs 60.58±27.28 mcg/dL and in Child Pugh C Category was 50.07±24.00. The variation is statistically insignificant. (P>0.05) (Figure 3)

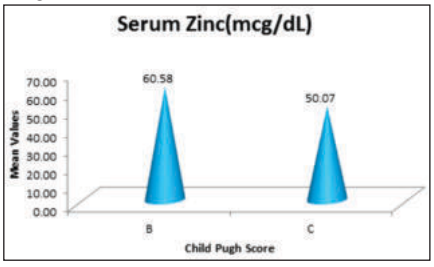

Fig 3: Distribution of Serum Zinc in Decompensated Liver Disease

The number of cases in Stage 1 HE were 28 with mean Serum Zinc 66.10±19.98 mcg/dL; in stage 2 HE were 10 with mean Serum Zinc being 42.60±7.06; in stage 3 HE being 7 with mean Serum Zinc being 14.61±5.38. The variation of serum Zinc with stages of Hepatic encephalopathy being statistically significant (P<0.05) (Figure 4)

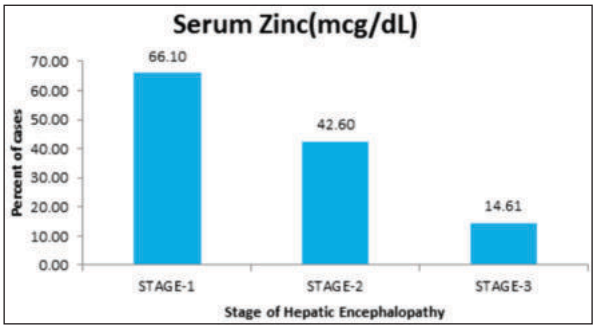

Fig 4:Distribution of Serum Zinc by stages of HE

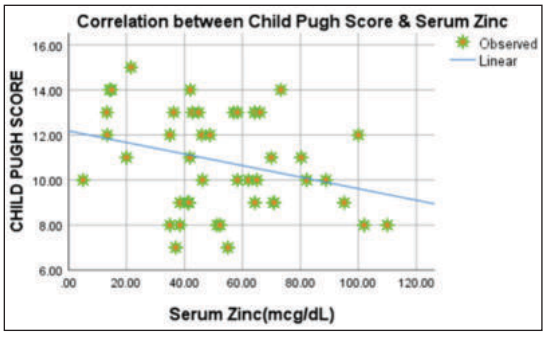

Fig 5: Correlation between Child Pugh Score and Serum Zinc

As observed, the serum Zinc has inverse correlation between Child Pugh Score and Serum Zinc.

That is, as Child Pugh increases, serum Zinc levels decrease (Figure 5)

DISCUSSION:

Hepatic encephalopathy is one of the most serious complications in DCLD.[7] In our study most common aetiology was alcohol abuse (84.4%ases) followed by viral hepatitis. Majority of DCLD patients presenting with HE have clear precipitating factors. Most common factors are constipation, infection and UGI bleeding.[8]

Serum zinc level was significantly low in DCLD in our study. Kar K et al.[9] Marcus R et al[10] also had similar result.

Patients with higher grade of HE had lower serum zinc level. Zinc is important co-factor for many enzymes. Zn has key role in physiological detoxification of ammonia via urea cycle in liver and as a co factor in ornithine Transcarbamylase (OTC) so low zinc level associated with decreased OTC activity

Low plasma Zn impairs nitrogen cycle in muscle and increase glutamine in blood. As result in advanced grade HE, significantly more drop in plasma Zinc is found. Short term oral Zinc supplement is very useful as an adjunct treatment in DCLD patient with hepatic encephalopathy.[10] Study done in Egypt by Mohsen Maher et al.[11] had similar results.

West Haven staging of HE:

Grade 0 - Minimal hepatic encephalopathy; lack of detectable changes in personality or behavior; minimal changes in memory, concentration, intellectual function, and coordination; asterixis is absent.

Grade 1 – Rrversal of sleep pattern, inattention.

Grade 2 - Lethargy or apathy; disorientation; inappropriate behavior; slurred speech; obvious asterixis;

Grade 3 - Somnolent but can be aroused; unable to perform mental tasks; disorientation about time and place; marked confusion;

Grade 4 - Coma with or without response to painful stimuli

Modified Child Pugh Score:

Factor	1 point	2 points	3 points
Total bilirubin (μmol/L)	<34	34-50	>50
Serum albumin (g/L)	>35	28-35	<28
PT INR	<1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

	Class A	Class B	Class C
Total points	5-6	7-9	10-15
1-year survival	100%	80%	45%

Figure 6:Child Pugh Scoring system

Class A- Compensated Liver failure
Class B- Early decompensated liver failure
Class C- Late decompensated liver failure

CONCLUSION:

DCLD and HE are one of the major diseases affecting India
DCLD patients had hypozincemia and there was inverse correlation between stage of HE and serum Zinc.

As Zinc is required for proper functioning of Urea cycle and hypozincemia being found in higher stages of HE, it is imperative to start all cases of DCLD on Zinc supplements to halt the progression of HE.

List of abbreviations:

- DCLD- Decompensated Chronic Liver Disease
- HE- Hepatic Encephalopathy
- Zn- Zinc
- UGI- Upper Gastrointestinal
- OTC- Ornithine Transcarbamoylase

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