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Research Article

The Correlation Between the Serum Zinc Level in Decompensated Liver Disease and the Stage of Hepatic Encephalopathy - A Cross Sectional Study Conducted in North Karnataka, India

Vinayakar Baddi[1] and Umakant Boke[2]*

[1]*Resident, Department of General Medicine, S.N. Medical College, Bagalkot, India*

[2]*Associate Professor, Department of General Medicine, S.N. Medical College, Bagalkot, India*

***Corresponding Author:** Umakant Boke, Associate Professor, Department of General Medicine, S.N. Medical College and HSK Hospital, Bagalkot, India.

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Abstract

Introduction: Hypozincemia appears to hasten the liver cirrhosis symptoms, which is why we conducted this study to determine a link between hypozincemia and hepatic encephalopathy. In light of this, the current investigation was carried out to evaluate the serum zinc levels in patients with decompensated chronic liver disease (DCLD) and varying degrees of hepatic encephalopathy (HE).

Materials and Methods: This cross-sectional study was conducted in 85 patients with Decompensated Chronic Liver Disease presents with Hepatic encephalopathy. Patients with hepatic encephalopathy were clinically categorised using the West Hevan classification (WHC). All patients were also given a Modified Child's classification ranking, and the Child-Pugh score was used to determine the severity of liver cirrhosis. Serum Zinc and albumin levels were assessed using standard methods.

Results: Alcohol misuse was the most frequent aetiology in our sample (84.4%), followed by viral. the middle-aged male population in our study was predominately affected. All patients with decompensated chronic liver disease who were admitted for our research had HE. Patients with higher grades of HE were more likely to have low serum zinc levels. Low blood albumin levels were more frequently linked to lower serum Zn levels in our study.

Conclusion: In conclusion, we discovered that it is important to test for hypozincemia in all patients with decompensated chronic liver disease, especially those who had hypoalbuminemia and hepatic encephalopathy (HE).

Keywords: *Decompensated Liver Disease; Hepatic Encephalopathy; Serum Zinc; Serum Albumin*

Abbreviations

HE: Hepatic Encephalopathy; DCLD: Decompensated Chronic Liver Disease

Introduction

Every day, millions of individuals around the world suffer from liver disease. The cost of healthcare has long been a concern in developing nations like India. In India, where a huge population lives in poverty, in an unhygienic environment, and without access to education, chronic diseases like liver cirrhosis and its complications are a serious health concern.

Anatomically, cirrhosis is described as a diffuse process accompanied by fibrosis and nodule formation. As a result of persistent liver injury, fibrogenesis leads to this condition.[1] restricted liver cell mass and restricted blood flow to the liver are the outcomes of diffuse fibrosis, which causes architecture distortion and regenerative nodule development [1,2]. The most frequent causes of cirrhosis in India are viral hepatitis and alcohol addiction. A decompensate condition (DCLD) that is linked with one or more complications such ascites, jaundice, hepatic encephalopathy, and UGI bleed develops over time in reversible fibrosis with continuous damage.

A potentially fatal side effect of acute or chronic liver failure is hepatic encephalopathy (HE). Hepatic coma kills 30% of cirrhosis patients [3]. HE is a sign of poor prognosis in patients with cirrhosis who are experiencing liver failure. HE can occur as a result of persistent portal systemic shunting, fulminate liver failure, one or more triggering factors, or both. Hepatic encephalopathy likely brought on by a poison from the intestines like ammonia. The malfunctioning of the astrocytes, abnormal neurotransmitter modulation, and astrocyte-developed oxidative stress are additional important aspects.

Mineral concentrations in individuals with chronic hepatic illness have been thoroughly studied over the past few years [4]. In actuality, the liver is in charge of controlling the transit of trace elements (TE), as well as their bioavailability, distribution in tissue, and ensuing toxicity. Blood levels for copper in primary biliary cirrhosis, iron in primary or secondary hemochromatosis, and magnesium, manganese, chromium, selenium, and zinc in various kinds of chronic liver illness were shown to be abnormal [5]. Changes in these trace elements were primarily caused by starvation in cases of hepatic illness [6].

The second-most abundant trace element in the body is zinc, which is a necessary trace element. More than 300 enzyme systems contain Zinc [7]. It is a crucial co-factor in the urea cycle and plays a significant part in the conversion of ammonia to urea. Zinc works as an anti-inflammatory, antioxidant, anti-apoptotic, and co-factor for DNA synthesis in addition to increasing the body's natural defence against reactive oxygen radicals. Therefore, hypozincemia appears to hasten the liver cirrhosis symptoms, which is why we conducted this study to determine a link between hypozincemia and hepatic encephalopathy. In light of this, the current investigation was carried out to evaluate the serum zinc levels in patients with decompensated chronic liver disease (DCLD) and varying degrees of hepatic encephalopathy (HE).

Methodology

After receiving approval from the institutional ethical committee, a cross-sectional study was conducted in department of General Medicine of a tertiary care centre. The study included both the gender aged more than 20 years that diagnosed as Decompensated Chronic Liver Disease presents with Hepatic encephalopathy. Individuals with metabolic encephalopathy, impaired sensorium as a result of head injury and stroke, individuals with psychiatric illnesses, acute alcohol intoxication, and alcohol withdrawal condition were all excluded from the study.

The sample size was calculated using Open Epi software version 2.3.2. According to the study conducted by Meena., *et al*. [8], the proportion of patients with grade III and IV HE with low zinc levels (< 30 mg/dl) was 68.2%, considering this as p, at 95% confidence level, 80% power of the study and 10% absolute precision, the calculated sample size was 82 inflated to 85 in our study. Formula used was n = [DEFF*Np(1-p)]/[(d2/Z2 1-α/2*(N-1)+p*(1-p)].

Clinical testing revealed hepatic encephalopathy and decompensated chronic liver disease. Physical indications of liver failure, such as icterus, pallor, spider nevi, palm erythema, and clubbing, ascetic, and pitting oedema, were thoroughly examined. Patients with hepatic encephalopathy were clinically categorised using the West Hevan classification (WHC) [9]. All patients were also given a Modified Child's classification ranking, and the Child-Pugh score was used to determine the severity of liver cirrhosis [10,11]. They underwent the necessary lab tests, such as complete blood counts, liver function tests, renal function tests, and coagulation profiles (PT/INR). All patients were

then instructed to check their serum zinc levels after fasting, but those with cirrhosis who weren't in stable condition were admitted and had their serum zinc levels checked the next morning using a 2cc venous blood sample. Microsoft Excel was utilised to enter all data, and SPSS version 21.0 was employed for statistical analysis. One-way ANOVA was used to analyse serum zinc levels between WHC and CPC grades and categorical results were shown as frequencies and percentages. A p-value of 0.05 or lower was deemed significant.

Results

The present study was conducted in 85 patients with Decompensated Chronic Liver Disease presents with Hepatic encephalopathy. Patients ranged in age from 29 to 83 years old with mean 47.37 ± 17.7 years.

Table 1 shows the baseline characteristics of study participants. We found that majority of the patients were aged between 41 to 50 years (43.5%) and were males (92.9%). Majority of the patients were alcoholics (83.5%) and were alcoholic since 5 to 10 years (81.2%).

Baseline characteristics		Frequency	Percentage
Age	< 30 years	1	1.2%
	31 to 40 years	32	37.6%
	41 to 50 years	37	43.5%
	> 50 years	15	17.6%
Gender	Males	79	92.9%
	Females	6	7.1%
Etiology	Alcohol	71	83.5%
	HBV	7	8.2%
	Alcohol and HBV	6	7.1%
	Wilson disease	1	1.2%
Duration of alcohol intake	Non-alcoholic	7	8.2%
	5 to 10 years	69	81.2%
	≥10 years	9	10.6%

Table 1: *Baseline characteristics of study participants.*

Table 2 shows that the classification of patients according to West-Hevan classification and Child-Pugh classification. We had majority of patients with Grade I (32.9%) followed by grade II (30.6%). With respect to Child-Pugh classification, class C was more common (54.1%) followed by class B (31.8%).

Severity		Frequency	Percentage
West Hevan classification	MHE	12	14.1%
	Grade I	28	32.9%
	Grade II	26	30.6%
	Grade III	13	15.3%
	Grade IV	6	7.1%
Child-Pugh classification	Class A	12	14.1%
	Class B	27	31.8%
	Class C	46	54.1%

Table 2: *Distribution of patients according to WHC and CPC.*

Findings of serum zinc levels are presented in table 3. In the present study, we found that the mean serum zinc was decreasing with increasing WHC grades and CPC classes and this was statistically significant when one-way ANOVA was applied ($p < 0.05$).

		Serum Zinc in mcg/dl (Mean ± S.D)	p-value
WHC grading	MHE	65.3 ± 13.54	< 0.001
	Grade I	58.98 ± 21.6	
	Grade II	45.38 ± 11.2	
	Grade III	36.8 ± 16.7	
	Grade IV	18.6 ± 7.91	
CPC	Class A	67.4 ± 19.3	0.03
	Class B	60.51 ± 21.3	
	Class C	51.1 ± 21.07	

Table 3: *Serum zinc levels according to WHC and CPC classes.*

Figure 1 shows the association of serum albumin with serum zinc levels in decompensated chronic liver disease patients. In the present study, we found that the majority of patients with low serum albumin (≤ 2.5 g/l) had serum zinc between 30 to 39 mcg/dl (57.1%) and this association was statistically significant when chi-square test was applied ($p = 0.002$).

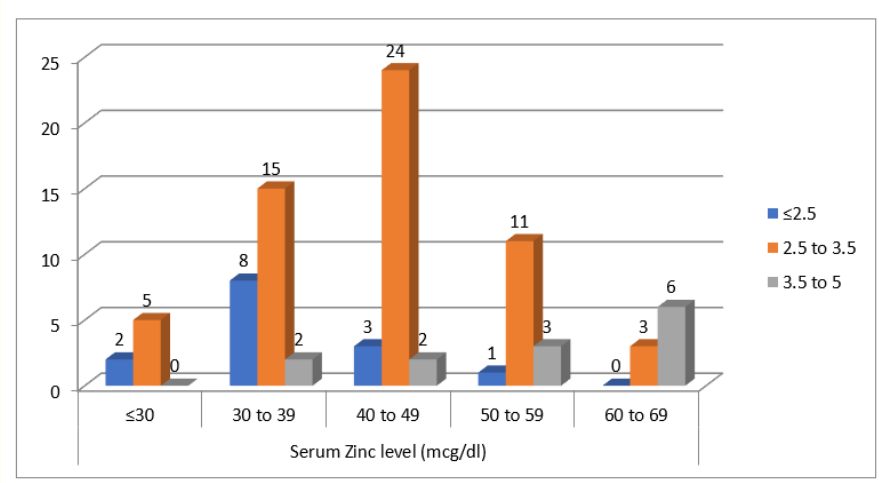

Figure 1: *Bar graph showing association between serum albumin and serum zinc.*

Discussion

One of the most dangerous side effects of DCLD is hepatic encephalopathy [12]. Alcohol misuse was the most frequent aetiology in our sample (84.4%), followed by viral. Similarly, studies by Meena RK., *et al.* [8] (90%) and Baquri., *et al.* [13] (84.4%) also reported alcohol as the main etiology.

Similar to earlier studies, the middle-aged male population [8,13-15] in our study was predominately affected. In our study, 82.1% of the cases were middle-aged people between the ages of 30 and 50, and 92.9% of them were men.

A crucial co-factor for many enzymes is zinc. In order to properly detoxify ammonia through the urea cycle in the liver and as a cofactor in ornithine transcarbamylase (OTC), zinc is essential. As a result, low zinc levels are linked to reduced OTC activity and increased plasma ammonia concentrations. Low plasma Zn affects the muscle nitrogen cycle and raises blood glutamine levels. Advanced HE grades cause a considerable decline in plasma zinc levels. When treating DCLD patients with hepatic encephalopathy, a short-term oral zinc supplement is extremely helpful [16].

All patients with decompensated chronic liver disease who were admitted for our research had HE. Patients with higher grades of HE were more likely to have low serum zinc levels. K. Kar., *et al*. [17] and Marcus R., *et al*. [16] results were comparable. Similar findings were found in a study conducted in Egypt by Mohsen Maher., *et al*. [18]. Similar findings were reached by Soomro AA., *et al*. [19] and our investigation found that upper class cirrhosis patients had considerably reduced serum zinc levels, with the connection being statistically significant.

Serum zinc is loosely linked to albumin in plasma, and the amount of serum albumin available determines the amount of zinc transported in blood. Low blood albumin levels were more frequently linked to lower serum Zn levels in our study. Similar findings were found in the Kar K., *et al*. [17] investigation. Therefore, this study also suggests that substantial hypoalbuminemia may be a factor in low serum Zn levels. Our results agreed with those of Meena., *et al*. [8] and Khali., *et al*. [20].

Conclusion

In conclusion, we discovered that it is important to test for hypozincemia in all patients with decompensated chronic liver disease, especially those who had hypoalbuminemia and hepatic encephalopathy (HE).

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