ORIGINAL ARTICLE

Serum Zinc Level in Decompensated Liver Disease and its Correlation with Stage of Hepatic Encephalopathy

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Abstract

Background and Study Aims: This cross-sectional study was done to assess the serum Zinc levels in decompensate chronic liver disease (DCLD) patients with various stage of hepatic encephalopathy (HE) and determine the role of Zinc deficiency in precipitation of hepatic encephalopathy.

Patients and Methods: This prospective cross-sectional study was conducted at Rajiv Gandhi Government General Hospital and Madras Medical College Chennai. We enrolled 75 adult diagnosed cases of DCLD. All cases were further evaluated for serum Zinc levels and all divided according to class of liver cirrhosis and stage of hepatic encephalopathy. The data was analyzed with SPSS soft ware version 22.

Results: Ninety six percent patients of liver cirrhosis were male (72/75) while 4% were female (3/75), 30-50 year of age group (63%) was predominantly affected. All DCLD patients (75/75) with HE had low serum Zinc level. There was statistically significant association between low serum zinc level and grade of HE (p-value 0.001) or class of liver cirrhosis (p-value 0.001). Our study also showed statistically significant association between low serum zinc level and hypoalbumenia (p-value 0.029)

Conclusion: All patients in DCLD particularly with hypoalbumenia and in hepatic encephalopathy should be evaluated for hypozincemia. As our study has concluded, hypozincemia in associated with cirrhosis and higher incidence of encephalopathy. Further study is indicated to establish role of correcting hypozincemia to prevent worsening of cirrhosis and development of encephalopathy.

Introduction

Chronic disease like liver cirrhosis and its complications are a major health problem particularly in developing countries like India, where large population are living with poverty, poor hygienic environment. Burden of cirrhotic patients is ever increasing and most of the patients are admitted to hospital with complication of cirrhosis.

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 B.[1,2]

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

Hepatic encephalopathy (HE) is life threatening complication that can be occur in acute or chronic liver failure. About 30% patients of cirrhosis die due to hepatic coma.[3] HE in patient with liver failure is associated with poor prognosis and higher mortality. In cirrhotic patient HE develops due to one or more precipitating factors or due to fulminate liver failure or it could be a result of prolonged portocaval shunting.

Hepatic encephalopathy is probably precipitated by gut derived neurotoxin such as ammonia. Other key factors are astrocytes dysfunction, disturbed neurotransmitter regulation and oxidative stress in astrocytes.

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 conversation 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, considering which we have done this study to establish correlation between hypozincemia and hepatic encephalopathy. Aim of this study to assess the serum Zinc levels in decompensate chronic liver disease (DCLD) patients with various stage of hepatic encephalopathy (HE) and determine the role of Zinc deficiency in precipitation of hepatic encephalopathy.

Material and Methods

This prospective observational study was conducted during April 2014 to September 2014 in Institute of Internal Medicine at Madras Medical College, Chennai (India). After obtaining a fully informed written consent, the 75 patients were enrolled into

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Table 1: Aetiology of cirrhosis

Aetiology	Frequency	Percent
Alcohol	68	90.7
HBV	3	4
Alcohol and HBV	3	4
Wilson	1	1.3

Table 2: Common presenting complaints in DCLD patients with HE

Presenting feature	Patients
Fever	28
Abdominal pain	42
Vomiting	12
Diarrhoea	7
Constipation	41
Ascites	61
Bleeding	34
Pedal oedema	49
Disorientation	41
Confusion	14
Coma	4

Table 3: Precipitating factors in hepatic encephalopathy

Precipitating factor	Patients
Infection	28
UGI Bleeding	34
Constipation	41
Diarrhoea	7
Hyponatremia	29
Hypokalemia	13
Hyperkalemia	9
Diuretics	21

Table 4: Patient according WHC grading

HE grade	Frequency	Percent (%)
MHE	10	13.3
Grade I	26	34.7
Grade II	24	32.0
Grade III	11	14.7
Grade IV	4	5.3

the study. In patients more than 20 years age who attended aforesaid hospital with signs and symptoms suggestive of decompensate chronic liver disease were enrolled in this study. Those patients having other metabolic causes of encephalopathy, altered sensorium due to head injury and stroke, psychiatric disorders, alcohol withdrawal state, acute alcohol intoxication and hemodynamically unstable were excluded from the study. A diagnosis of decompensate chronic liver disease and hepatic encephalopathy was made clinically.

A thorough physical examination was done for signs of liver failure like icterus, pallor, spider nevi, palmer erythema, and clubbing, ascetic and pitting oedema. Hepatic encephalopathy patients were clinically graded according West Hevan classification (WHC).[3] All patients also classified by Modified Child's classification[4] and severity of liver cirrhosis were assessed by Child–Pugh score.[4,5] The informed consent was taken from every patient or from there attendant after detail explanation of procedure regarding the study, and all such manoeuvres was performed under medical ethics and through the cooperation of whole research team. They were subjected to appropriate laboratory investigations including complete blood count and liver function tests, renal function test, coagulation profile (PT/INR). All patients were then advised for fasting serum zinc level whereas the cirrhotic patients who were not vitally stable were admitted and then their serum zinc level was assessed by taking 2cc venous blood sample on coming morning. The normal range of serum zinc level is 11-19 mmol/ L and the value < 11 mmol/L was considered as low (6). The serum zinc status was reviewed and labelled as "low" when the serum level was below the normal range (6). The data was analyzed by SPSS software version -22. P-value ≤0.05 was considered significant.

Table 5: Serum zinc level in various WHC grade

HE Grade	Patients	Serum Zinc Level (mcg/dl)					Total
		60-69	50-59	40-49	30-39	≤30	
MHE	Count	7 (70)	2 (20)	0	1 (10)	0	10
Grade I	Count	1 (3.8)	8 (30.8)	16 (61.5)	0	1 (3.8)	26
Grade II	Count	0	2 (8.3)	9 (37.5)	12 (50)	1 (4.2)	24
Grade III	Count	0	0	0	9 (81.8)	2 (18.2)	11
Grade IV	Count	0	0	0	2 (50)	2 (50)	4
Total	Count	8 (10.7)	12 (16)	25 (33.3)	24 (32)	6 (8)	75 (100)

Results

Ninety six percent patients of liver cirrhosis were male (72/75) while 4% were female (3/75). In our study were common causes of cirrhosis is Alcohol (91%) followed by viral (8%), Wilson (1%) shown in (Table 1). 87% patients consumed alcohol for more than 10 year duration in Alcohol related DCLD. In our study most common presenting complaint was abdominal distension, pedal oedema. Other Common symptoms have been depicted in (Table 2). It was found that hepatic encephalopathy was more common in middle age group between 30-50 year age (63%). There was 5% mortality in hepatic encephalopathy during the course of treatment. In our study common precipitating factors of HE were constipation and upper gastrointestinal bleeding (Table 3). In our study maximum patients were in grade-I and grade-II HE (35% and 32%) as (Table 4). All DCLD patients had Zn deficiency and low serum zinc level was significantly associated with higher grade of HE. In our study there was statistically significantly association between low serum zinc level and grades of hepatic encephalopathy (p-value 0.001) (Table 5 Figure 1). This study showed low serum Zn level has statistically significant association with higher modified child-Pugh class (p-value 0.001) (Table 6 Figure 2). In our study we found there was statistically significant association between hypoalbuminemia and low level of serum Zn (p-value 0.029) (Table 7 Figure 3).

Discussion

Hepatic encephalopathy is one of the most serious complications in DCLD.[7] In industrialised countries most common aetiology in cirrhosis is viral hepatitis followed by alcohol.[8] In our study most common aetiology was alcohol abuse (90% cases) followed by viral hepatitis.[9] Like other previous studies in our study also Male population[10] middle age group[11] were predominantly affected. In our study 63% cases were middle age between 30 to 50 year age group. Majority of DCLD patients presenting with HE have clear precipitating factors. Most common factors were constipation, infection and UGI bleeding.[12] UGI bleeding is most common factor according to Sheila Sherlock.[1] Serum zinc level was significantly low in DCLD in our study. Kar K et al.[13] Marcus R et al[14] also had similar result. In our study all DCLD patients admitted with HE. More ever patients with higher grade of HE had low 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 and higher

Table 6: Comparison of serum zinc level with child pugh class

CP Class	Patients	Serum Zinc Level (mcg/dl)					Total
		60-69	50-59	40-49	30-39	≤30	
Class A	Count	6 (66.7)	2 (22.2)	1 (11.1)	0	0	9
Class B	Count	2 (8.3)	6 (25)	10 (41.7)	6 (25)	0	24
Class C	Count	0	4 (9.5)	14 (33.3)	18 (42.9)	6 (14.3)	42
Total	Count	8 (10.7)	12 (16)	25 (33.3)	24 (32)	6 (8)	75 (100)

Table 7: Comparison between serum Zn level and serum albumin level

Serum albumin (gm/l)	Patients	Serum zinc level (mcg/dl)					Total
		60-69	50-59	40-49	30-39	≤30	
3.5-5	Count	4 (40)	2 (20)	2 (20)	2 (20)	0	10
2.5-3.5	Count	4 (7.4)	9 (16.7)	21 (38.9)	15 (27.8)	5 (9.3)	54
≤2.5	Count	0	1 (9.1)	2 (18.2)	7 (63.6)	1 (9.1)	11
Total	Count	8 (10.7)	12 (16)	25 (33.3)	24 (32)	6 (8)	75 (100)

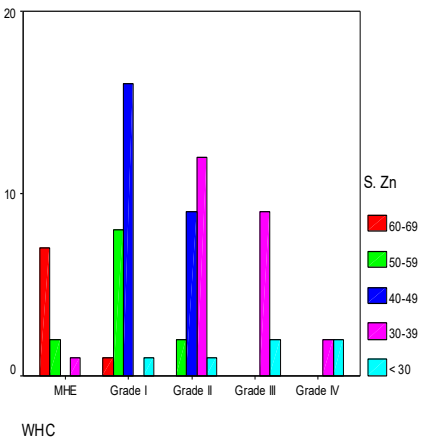

Fig. 1: Distribution of HE grade according serum Zn level. In our study statistically significantly association low zinc values and higher grades of hepatic encephalopathy (p-value 0.001)

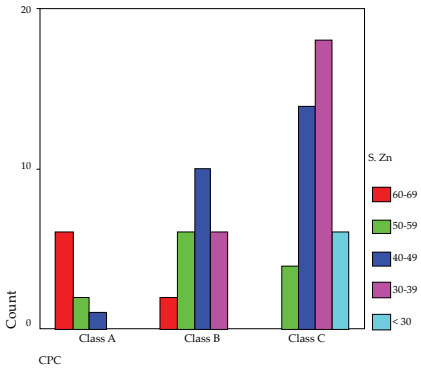

Fig. 2: Comparison of serum Zn level and Child Pugh score. In our study low serum Zn level have statistically significant association with higher child-Pugh score (p-value 0.001)

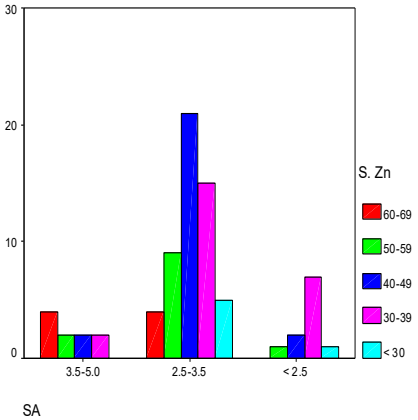

Fig. 3: Comparison between serum zinc and serum albumin level. In our study patients with low serum albumin statistically association with low level of serum Zn (p-value 0.029)

plasma concentration of ammonia. Low plasma Zn impairs nitrogen cycle in muscle and increase glutamine in blood. As result in advanced grade in HE significantly more drop in plasma Zinc. Short term oral Zinc supplement is very useful as an adjunct treatment in DCLD patient with hepatic encephalopathy.[14] Study done in Egypt by Mohsen Maher et al.[15] had similar results. In our study serum Zinc level was significantly low in higher class of cirrhosis and the correlation was statistically significant, similar conclusion was made by Soomro AA, et al. In DCLD patients other factors like malnutrition, poor oral intake and diuretic use is also related to low Zn level.

Serum Zinc is bound loosely with albumin in plasma and availability of serum albumin decides the amount of zinc transported in blood similar results seen Kar K et al[13] study also. In our study low serum albumin level was associated more lower serum Zn level. Hence this study also indicates that low serum Zn level may be contributed by significant hypoalbunemia. As conclusion we found that all patients in DCLD particularly with hypoalbumenia and in hepatic encephalopathy (HE) should be evaluated for hypozincemia. As our study has concluded, hypozincemia in associated with cirrhosis and higher incidence of encephalopathy. Further study is indicated to establish role of correcting hypozincemia to prevent worsening of cirrhosis and development of encephalopathy.

Conclusion

All patients in DCLD particularly with hypoalbumenia and in hepatic encephalopathy should be evaluated for hypozincemia. As our study has concluded, hypozincemia in associated with cirrhosis and higher incidence of encephalopathy. Further study is indicated to establish role of correcting hypozincemia to prevent worsening of cirrhosis and development of encephalopathy.

Abbreviations

CP Score: Child Pugh score; DCLD: Decompensate Chronic Liver Disease; HE: Hepatic Encephalopathy; HBV: Hepatitis B Virus; PT: Prothrombin Time; MHE: Minimal Hepatic Encephalopathy; UGI: Upper Gastrointestinal; WHC: West Hevan Classification

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