IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 2 Ser.3 (February. 2023), PP 67-72
www.iosrjournals.org

Serum Zinc Level in Decompensated Liver Disease - A hospital based cross sectional study in Manipur

Dr Hajishmon Alikkanakath[1], Dr Kshetrimayum Birendra Singh[2], Dr Sarath Chandran K R[3], Dr Shyma O K[3], Dr Tenzin Gyaltsen[3], Dr Muhammed Nazeeb[3], Dr P Kireeti[3] Dr Gido pertin[3]

[1]*(Former Resident, Department of General Medicine, Regional Institute of Medical Sciences, Imphal, India)*
[2]*(Professor, Department of General Medicine, Regional Institute of Medical Sciences, Imphal, India)*
[3]*(Junior Resident, Department of General Medicine, Regional Institute of Medical Sciences, Imphal, India)*

Abstract:
Background*: Chronic diseases like liver cirrhosis and its complication are a major health problem particularly in developing countries. Burden of cirrhotic patients is ever increasing and most of the patients are admitted to hospital with complication of cirrhosis.In India most, common cause of cirrhosis are alcohol abuse and viral hepatitis.Hepatic encephalopathy (HE) in patient with liver failure is associated with poor prognosis and higher mortality.Zinc has a protective role against fibrosis by preventing the cellular damage by oxidative stress and hypozincemia seems to accelerate the manifestation of cirrhosis. We carried out this study tofind serum zinc levels in decompensated liver disease patients and to establish its correlation with hepatic encephalopathy.*
Materials and Methods*: The approval from the Institutional Research Ethics Board, RIMS, Imphal was taken. In this cross-sectional study, cases of decompensated liver disease above 18 years age, admitted in Medicine wardsbetweenSeptember 2019 and August 2021 giving consent were included.The diagnosis was based on history and detailed clinical examination.Serum zinc level detection by Quantichrom TM Zinc Assay Kit (DIZN-250).Data were collected in a pre-tested proformaand analyzed using SPSS 21 version. Descriptive statistics like mean, Standard Deviation and percentage were used. Chi-square test, t test was used for inferential statistics. P-value < 0.05 was taken as significant.*
Results*: All patient in decompensated chronic liver disease with complication of hepatic encephalopathy identified having low serum zinc level.Low serum zinc level is significantly associated with higher grade of hepatic encephalopathy, significantly more in higher class of child- Pugh classification and isassociated with low level of serum albumin and higher level of serum bilirubin. (p<0.001).*
Conclusion:*Low serum zinc level is an indirect precipitating factor in hepatic encephalopathy.Advice regarding proper diet which contain zinc and short-term zinc supplement may be useful in prevention and treatment of hepatic encephalopathy.*
Key Words*: Zinc; Cirrhosis; Hepatic encephalopathy; Albumin; Bilirubin, Alcohol*

Date of Submission: 22-01-2023 Date of Acceptance: 05-02-2023

I. Introduction

Chronic diseases like liver cirrhosis are a major health problem particularly in developing countries, 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[1,2]. Cirrhosis is a slowly progressing disease in which healthy liver tissue is replaced with scar tissue, eventually preventing the liver from functioning properly[2]. In India most, common cause of cirrhosis are alcohol abuse and viral hepatitis. Chronic HBV is an important global health problem, with more than 350 million people affected world-wide. Its prevalence in India is quite high and about 100,000 Indians die from HBV complication annually[3].Hepatic encephalopathy (HE) is life threatening complication that can occur in acute or chronic liver failure. About 30% patients of cirrhosis die due to hepatic coma.In subjects suffering from acute/chronic liver failure, HE is a poor prognostic indicator, with projected one and three-year survival rates of 42% and 23%, respectively, without liver transplantation.[4]

Zinc (Zn) is second most abundant trace element in the body and is associated with more than 300 enzymatic functions. Zinc act as antioxidant, anti-apoptotic, and anti- inflammatory agent and also has a protective role against fibrosis by preventing the cellular damage by oxidative stress. So hypozincemia seems to accelerate the manifestation of cirrhosis.The main protein involved in zinc metabolism, homeostasis and its release are called metallothionein. The reduced synthesis of this protein may decrease the availability of zinc.

Zn supplementation was found to be beneficial in improving some features of liver cirrhosis, such as testicular atrophy, loss of body hair, night blindness, poor wound healing, poor appetite, decreased taste and smell acuity, susceptibility to infections, enhanced sensitivity to drugs, and decreased neurocognitive performances[5].This study was carried out to determine the serum zinc levels in decompensated liver disease patients and to establish its correlation with hepatic encephalopathy.

II. Material And Methods

This study was carried out on patients admitted in the Department of General Medicine at Regional Institute of Medical Science, Imphal (RIMS), Manipurfrom September 2019 to August 2021. A total 300 adult subjects (both male and females) of aged ≥ 18, years were for in this study.

Study Design: Cross sectional study

Study Location: RIMS is a 1074 bedded tertiary care teaching hospital.The hospital normally provides services to more than 2.4 lakh out-door patients and admits over 31 thousand patients in a year.

Study Duration: November 2014 to November 2015.

Sample size:124.

Sample size calculation: Sample size using the formula $N=Z^2PQ/L^2$, with prevalence of zinc deficiency in decompensated liver disease as 27.5%[6] at 95% confidence level andabsolute allowable error as 8% was calculated as 124.

Subjects & selection method: By consecutive sampling patients(> 18 years) admitted with decompensated Chronic Liver Disease (DCLD) in medicine wards, RIMS, Imphal were included in the study.

Inclusion criteria:

1. Patient diagnosed with Decompensated Chronic Liver Disease (DCLD)
2. DCLD due to all etiologies
3. Age >18 years.

Exclusion criteria:

1. All other causes of encephalopathy other than hepatic encephalopathy
2. Patients not willing to participate in the study.

Procedure methodology

Afterexplaining about the purpose and procedure of the study and obtaining written informed consent of patients,a detailed clinical history of subjects was taken regarding present and past illness.Detailed clinical examination for signs of liver failure was done.

Grading of hepatic encephalopathy was done by1. Clinical history, 2. PHES (Psychometric hepatic encephalopathy score),3. Asterixis, 4. WHC (West Hevan classification) and 5. GCS (Glasgow Coma Score). All patients were also classified by Child-Turcotte-Pugh score.

For each patient, following investigations were done- 1. Serum zinc level, 2. Complete blood counts, 3. Liver function test, 4. Renal function test, 5.PT/INR, 6.USG abdomen. Serum zinc level was detected by Quantichrom TM Zinc Assay Kit (DIZN-250). Hypozincemia was diagnosed when serum zinc level was less than 12mmol /L (70 microgram /dL).

Participant's confidentiality was maintained and assured that they could withdraw from the project at any time. Study was approved by Institutional Research Ethics Board, RIMS, Imphal.

Statistical analysis

Data were collected in a pre-tested proforma and analyzed using SPSS 21 version. Descriptive statistics like mean, Standard Deviation and percentage were used. Chi-square test, t test was used for inferential statistics. P-value < 0.05 was taken as significant.

III. Results

Of the total 124 decompensated liver disease patient studied 14 (11.3%) were in 30-39 age group, 65(52.4%) in 40-49 age group, 44 (35.5%) in 50-59 age group and 1(0.8%) in above 60 years age group. Majority (91.1%) of caseswere males (n=113).Most of them weremanual labourers by occupation (52.4%) followed by drivers(14.5%), farmers(7.3%) and businessman (4%).Majority of patients belonged to Hindu community followed by Christian and Muslim community with respective percentages of 66.2%, 30.6% and 3.2%.

Of the 124 patients of decompensated liver disease studied, 114 patients (91.9%) were due to alcoholism, 6(4.8%) were due to NASH., 4 (3.2%) patients came as both HCV and HBV positive. One patient among alcohol related cirrhosis was HCV positive. 87.7% patients consumed alcohol more than 10 years duration in alcohol related decompensated liver disease.There were no patient of Wilson disease and Hemochromatosis among these 124 patients.

Most common presenting complaint (Figure 1) was altered sleep pattern (89.5%) and icterus (87.1%), followed by ascites (81.5%), pedal oedema (65.3%), pallor (61.3%), constipation (55.6%), disorientation (55.6%) and UGI bleeding (46.8%).

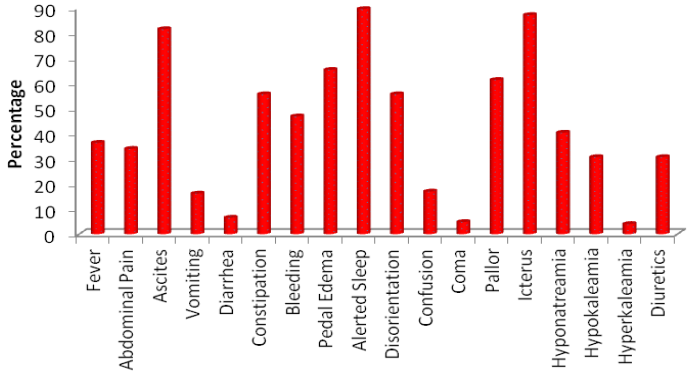

Figure 1: Distribution of clinical features

3 patients (10.5%) had minimal hepatic encephalopathy (MHE) while 46(37.1%) had grade 1, 39(31.5%) had grade 2, and 20 (16.1%) were found to have grade 3 HE. Only 6 patients (4.8%) had grade 4 hepatic encephalopathy. The most common precipitating factor for HE was constipation in 69 patients (55.6%) followed by UGI bleed in 58 patients (46.7%) and hyponatremia in 50 patients (40.3%). The other precipitating factors in decreasing order of incidence were infection (36.3%) diuretic intake (30.6%), hypokalemia (30.6%), diarrhea (6.4%), and hyperkalemia (4%). As shown in table 1 majority of the cases were included in class C(71.8%).

Table 1: Child-Pugh distribution of the cases

CP Class	No. of Patients n (%)
Class A	8 (6.5)
Class B	27 (21.8)
Class C	89 (71.8)

Table 2: Distribution of serum zinc level in study population

Serum Zinc (microgram/dl)	No. of Patients n (%)
60-69	11 (8.9)
50-59	22 (17.7)
40-49	43 (34.7)
30-39	37 (29.8)
<30	11 (8.9)

11 patients (8.9%) had serum zinc level within 60-69microgram/dl, 22 (17.7%) patients had zinc level within 50-59 microgram/dl while 43(34.7%) were within 40-49 microgram/dl,37(29.8%) patients had serum zinc level within 30-39 microgram/dl but only 11(8.9%) patients had level below 30 microgram/dl

Majority of patients (63.7%) had serum bilirubin between 2-5mg/dl. 26.6% of patient's serum bilirubin came above 5mg/dl andin only 9.7% bilirubin came below 2mg/dl.Most of the patients (54.8%) had serum albumin level below 2.8 gram/dl while 34.7% patients had serum albumin level within the range of 2.8-3.5gram/dl.Distribution of other biochemical parameters are shown in table 3.

Table 3: Distribution of other biochemical parameters

Investigation	No of patients n (%)
Serum Creatinine (mg/dL)	
<1.4	96 (77.4)
1.4-2.0	22 (17.7)
>2	6 (4.8)
Serum Sodium (mEq/L)	
>135	75 (60.5)
120-135	46 (37.1)
<120	3 (2.4)
SerumPotassium(mEq/L)	
>3.5	61 (49.2)
3-3.5	19 (15.3)
2.5-3.0	27 (21.8)
<2.5	12 (9.7)
>5.5	5 (4.0)
Hemoglobin (g/dL)	
>10	2 (1.6)
8-10	58 (46.8)
<8	64 (51.6)
Platelet Count (per microliter)	
>150000	3 (2.4)
50000-150000	101 (81.5)
<50000	20 (16.1)
INR	
<1.5	26 (21.0)
1.5-2	71 (57.3)
>2	27 (21.8)

Table 4 shows serum zinc levels and its correlation with stages of Hepatic Encephalopathy, Child Pugh Class, Serum Albumin and Serum Bilirubin.Out of 124 decompensated liver disease patients enrolled in the study, all had zinc deficiency, The study also showed statistically significant association between low zinc values and higher grades of hepatic encephalopathy (p- value <o.oo1). There was a statistically significant association between low serum zinc level with higher Child-Pugh score with a (p-value<0.001). Low levels of serum albumin were statistically was associated with low levels of serum zinc level (p-value <0.001).Statistically significant relationship was seen between higher level of serum bilirubin with low levels of serum zinc levels (p value <0.001)

IV. Discussion

Hepatic encephalopathy, a challenging complication of advanced liver disease, occurs in approximately 30-45% patients with decompensated liver disease and 10-50% of patients with trans-jugular intrahepatic porto- systemic shunt, while minimal hepatic encephalopathy affects approximately 20-60% of patients with liver disease. HE in patient with liver failure is associated with poor prognosis and higher mortality. The study was conducted to document the serum zinc level in decompensated liver disease and its correlation with various grade of hepatic encephalopathy. In this study 124 patients with decompensated liver disease were taken up after fulfilling the inclusion and exclusioncriteria.

Maximum affected population were middle age between 30-50 age group (63.7%) followed by above 50 years (36.2%). The incidence of HE was more in 40–49-year age group followed by 50-59 years age group and 30-39 years age group. The findingswere similar to the study conducted by Alam et al[7] and Meena RK et al[8]. Similar to their study, there was male preponderance across all age group, with male contributing 91.1% of study population. As the RIMS hospital, where the present study was conducted is situated at the heart of the Hindu dominated area, majority of patient belonged to Hindu community followed by Christian and Muslim community. Most of the patients enrolled in the study were manual labourers by occupation.

The most common cause of decompensated liver disease was found to be alcohol (91.9%) followed by NASH (4.8%) and viral hepatitis (Hepatitis B and C). The finding was similar to that observed by Meena RK et al[7] and Khalid et al.[9] Alcohol was the most prevalent etiological factor both in the male and female population, but in male population viral hepatitis being the second most common etiological factor while in female it was NASH.

Mode of presentation of patient with chronic liver disease was an important consideration taken in our study. In this study, the most common presenting symptoms was altered sleep pattern (89.5%), jaundice (87.1%), abdominal distention (81.5%), disorientation (55.6%) and constipation (55.6%).Icterus was the most common presenting sign in the study group with 87.1% patients with sign followed by ascites (81.5%), pedal edema (65.3%) and pallor(61.3%).These are contradictory to that observed by Kabir et al[10]where all

patients included in the study presented with jaundice and ascites but this finding was in concordance with the observation of Meena RK et al.[8]

Table no 4: Serum zinc levels and its correlation with stages of Hepatic Encephalopathy, Child Pugh Class, Serum Albumin and Serum Bilirubin.

Variables	Serum Zinc levels n(%)					Total	P Value
	60-69 microgram/ dl	50-59 microgram/ dl	40-49 microgram/ dl	30-39 microgram/ dl	<30 microgram/ dl		
HE GRADE							
MHE	11 (100%)	2 (9.1%)	0 (0%)	0 (0%)	0 (0%)	13 (10.5%)	<0.001**
grade 1	0 (0%)	13 (59.1%)	32 (74.4%)	1 (2.7%)	0 (0%)	46 (37.1%)	
grade 2	0 (0%)	7 (31.8%)	10 (23.3%)	20 (54.1%)	2 (18.2%)	39 (31.5%)	
grade3	0 (0%)	0 (0%)	1 (2.3%)	15 (40.5%)	4 (36.4%)	20 (16.1%)	
grade4	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	5 (45.5%)	6 (4.8%)	
CP CLASS							
class A	7 (63.6%)	1 (4.5%)	0 (0%)	0 (0%)	0 (0%)	8 (6.5%)	<0.001**
class B	3 (27.3%)	12 (54.5%)	9 (20.9%)	3 (8.1%)	0 (0%)	27 (21.8%)	
class C	1 (9.1%)	9 (40.9%)	34 (79.1%)	34 (91.9%)	11 (100%)	89 (71.8%)	
Serum Albumin (g/dL)							
>3.5	6(54.5%)	7(31.8%)	0(0%)	0(0%)	0(0%)	13(10.5%)	<0.001**
2.8-3.5	4(36.4%)	14(63.6%)	18(41.9%)	5(13.5%)	2(18.2%)	43(34.7%)	
<2.8	1(9.1%)	1(4.5%)	25(58.1%)	32(86.5%)	9(81.8%)	68(54.8%)	
Serum Bilirubin (mg/dL)							
<2	8 (72.7%)	1 (4.5%)	3 (7%)	0 (0%)	0 (0%)	12 (9.7%)	<0.001**
2-5	2 (18.2%)	17 (77.3%)	28 (65.1%)	23 (62.2%)	9 (81.8%)	79 (63.7%)	
>5	1 (9.1%)	4 (18.2%)	12 (27.9%)	14 (37.8%)	2 (18.2%)	33 (26.6%)	

The grading of hepatic encephalopathy was done using West-Heven classification. Maximum number of patients had grade 1 encephalopathy with 46 patients (37.1%) falling in this group. It was followed by grade 2 encephalopathy in39(31.5%) patients and grade 3 in 20(16.1%). The least number of patients were in grade 4 encephalopathy group (4.8%). This was contradictory to those noted by Alam et al[7] and Waheed A et al.[11]where, most of the patient in grade 2 encephalopathy, but finding similar to observation made by Meena at al[8]. The precipitating factors of hepatic encephalopathy were thoroughly evaluated. In the study population,the most common precipitating factor was constipation (55.6%) followed by UGI bleed (46.8%) hyponatremia (40.3%), infection (36.3%), and hypokalemia (30.6%). These findings are similar to the finding obtained in the studies done by Umar et al[12] and Alam et al[7]but contradictory to that observed by Kabir et al[10].

89(71.8%) patients of total 124 patients were in Child- Pugh class C followed by Child -Pugh B with a total number of 27 patients (21.8%). Rest of the patients was in Child-Pugh class A. This is in accordance with the finding observed by the Gad et al[13] in their study.

The study population further assessed for the serum zinc level in all patients of decompensated liver disease. All the patients had zinc deficiency (below 70 microgram/dl). For majority of patients serum zinc level was in between40-49 microgram/dl (34.7%) followed by in the range of 30-39microgram/dl (29.8%), range of 50-59 microgram/dl (17.7%) and 11% of patients both in the range of 60-69microgram/dl and below30 microgram/dl. This study also showed statistically significant association between low zinc values and higher grades of hepatic encephalopathy with a p value<o.oo1.This was similar to observation made by the Waheed A et al[10] and Meena RK et al[8].

Study showed statistically significant association between serum zinc level and serum bilirubin with a p value<0. 001 which was similar to observation made by Loomba V et al[13] and Katayama K et al.[14]

Serumzinc (>80%) is bound loosely with albumin and serum albumin obviously decreased in decompensated liver disease patients. Study showed statistically significant association between low levels of serum zinc level and low serum albumin level with a p value <o.oo1.Similar finding was also observed by Katayama K et al14 and Khalil KA et al[15]in their studies.

Further studies with higher sample size and extended period are needed to confirm this study in decompensated chronic liver disease patients with hepatic encephalopathy.

V. Conclusion

All patient in decompensated chronic liver disease with complication of hepatic encephalopathy were identified having low serum zinc level and low serum zinc level is significantly associated with higher grade of hepatic encephalopathy. Low serum zinc level is significantly more in higher class of child- Pugh classification. Moreover, it was also observed that low serum zinc level is associated with low level of serum albumin and higher level of serum bilirubin.

Low serum zinc level is an indirect precipitating factor in hepatic encephalopathy. Advice regarding proper diet which contain zinc and short-term zinc supplement may be useful in prevention and treatment of hepatic encephalopathy.

References

[1]. Sherlock S, Dooley J, Anna SFL, Andrew KB, Heathcote EJ, editors. Sherlock Diseases of Liver and Biliary System.12th ed. Black well science; 2011. p. 121-46.

[2]. Bruce R, Bacon. Cirrhosis and its complication. In; Kasper D L, Hauser SL, Jameson JL, Fauci A S, Longo D L, Loscalzo J, editors. Harrison's principles of internal medicine.18th ed. New York; McGraw-Hill; 2012. p. 2592-605.

[3]. Misra B, Panda c, Das H S, Nayak K.C, Singh S P. Study on awareness about hepatitis B viral infection in coastal eastern India. Int J Hep Annual 2009; 6(1):19-28.

[4]. Bustamante J, Rimola A, Ventura PJ, Navasa M, Cirera I, Reggiardo V, Rodés J. Prognostic significance of hepatic encephalopathy in patients with cirrhosis. Journal of hepatology. 1999 May 1;30(5):890-5.

[5]. Atia F, Sultana N, Ahmed S, Ferdousi S, Sultana R, Atiquzzaman. A study of serum zinc level in cirrhosis of liver.Bangladesh J Med Biochem 2012;5(2):44-7.

[6]. Zergani F J, Parsi A, Farhang M. The correlation of serum zinc concentration with liver cirrhosis events. Bali Med J 2017;6(3): 655-8.

[7]. Alam I, Razaullah HI, Humayun M, Taqweem MA, Nisar M. Spectrum of precipitating factors of hepatic encephalopathy in liver cirrhosis. Pak J Med Res. 2005;44(2):96-100

[8]. Meena R K, Sundarmurthy G, Pushpa S, Karthik P, Karthika R, Vivekanandan A. Serum zinc level in decompensated liver disease and its correlation with stage of hepatic encephalopathy. J Assoc of Physicians India 2019;67(1):30-2.

[9]. Khalid A, Afsar A, Arshad MM, Ghafoor A, Khalid S, Saleem S. Prevalence of Hepatic Encephalopathy and Its Precipitating Factors in CLD Cirrhotic Patients. International Neuropsychiatric Disease Journal. 2017 Sep 9:1-7

[10]. Kabir MA, Chowdhury J, Bari MA, Bodruddoza K, Saha AK, Alam SB. Detection of Precipitating Factors of Hepatic Encephalopathy in Chronic Liver Disease Patients in a Tertiary Hospital. Journal of Medicine. 2018;19(1):10-4.

[11]. Waheed A, Farhan S, Nadeem M A, Suleiman T. Frequency of Low Zinc Levels in Cirrhotic patients with Hepatic Encephalopathy. PJMHS 2015;9(3):834-7.

[12]. Qazi F, Khan SB, Umar A. Hepatic encephalopathy in chronic liver disease: predisposing factors in a developing country. Asian Journal of Medical Sciences. 2015;6(2):35.

[13]. Gad YZ. precipitating factors of hepatic encephalopathy: An experience at Mansoura Specialized Medical Hospital, Egypt. Annals of Tropical Medicine and Public Health. 2012 Jul 1;5(4):330.

[14]. Loomba V, Pawar G, Dhar KL, Setia MS. Serum zinc level in hepatic encephalopathy. Indian J 1995;14(2):51-3.

[15]. Katayama K, Kawaguchi T, Shiraishi K, Ito T, Suzuki K, Koreeda C, et al. The prevalence and implication of zinc deficiency in patient with chronic liver diseases. J Clin Med Res 2018;10(5):437-44.

[16]. Khalil K A, Attia F M, Fawzy A, Tabey A H, Haron H, Drwesh H. Study of Zinc Level in Egyptian Cirrhotic Patients with Different Stages of Liver Cirrhosis. Int J Med Res Prof 2018;4(6):40-7.