ORIGINAL ARTICLE

Serum Zinc Levels in Patients with Liver Cirrhosis and its Correlation with Severity of Disease

Punam Rani, Karanpreet Bhutani , Suvarna Prasad

Abstract

Background: Liver cirrhosis is a worldwide slowly progressing health problem. It is the end stage of liver fibrosis characterized by nodule formation in which healthy liver tissue is replaced with scar tissue, ultimately preventing the liver functioning. Liver plays an important role in regulating zinc homeostasis, while zinc is necessary for proper liver function.**Aim and objectives:** In view of the above facts, the present study was aimed to evaluate serum zinc levels in patients with liver cirrhosis and to establish any correlation between severity of the disease and serum zinc status. **Methods:** The present study was carried out in the Department of Biochemistry in collaboration with Department of Medicine, M.M Institute of Medical Sciences and Research, MMDU, Mullana, Ambala on 100 males divided into 2 groups. Group I included 50 diagnosed cases with liver cirrhosis, further divided according to severity of liver cirrhosis and Group II included 50 healthy control subjects. Estimation of Serum Zinc was carried out by Colorimetric Method. **Results:** The mean zinc levels were lower in the study group (64.47±21.01) compared to the control group (87.65±15.01) and the difference was statistically highly significant ($p<0.001$). Serum zinc levels were compared in the various stages of cirrhosis and it was found that with increasing severity of the disease, the fall in the level of the zinc was more. **Conclusion:** There was fall in the levels of Zinc in patients with liver cirrhosis. The zinc deficiency was more profound in patients with increasing severity of the disease. Low Zinc levels can be implicated in the development of liver cirrhosis. Therefore, zinc level is useful in the timely management of these patients and to prevent worsening of cirrhosis and development of hepatic encephalopathy.

Keywords

Zinc, Liver cirrhosis, Stages, Severity

Introduction

Zinc, an essential micro nutrient in the human body, is a component in over 300 enzyme & involves in regulation of enzyme activity.[1] Zinc metalloenzymes play a crucial role in physiological processes including antioxidant, anti-inflammatory and immune system as well as apoptosis.[2,3,4] With these facts an imbalance in Zinc homeostasis can result in serious health forms.[5] In developed countries, the elderly and people with chronic disease are more likely to develop Zinc deficiency.[5] There are variety of risk factors and diseases that cause chronic liver diseases (CLD). Importantly, there are three common risk factors for CLD which include excessive alcohol consumption, blood borne viruses, in particular Hepatitis B and C and obesity. [6,7,8] As cirrhosis is a leading cause of mortality and morbidity across the world. It is the 11th leading cause of death and 15th leading cause of morbidity accounting

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for 2.2% of deaths worldwide.[9] CLD caused 1.32 million deaths worldwide in 2017[10], approximately two -thirds among men and one- third among women. A multi-centric center study from India revealed that alcoholism was the commonest factor contributing about 34.3 %, while hepatitis B (33.3%) was predominant cause of chronic liver disease in general and non- cirrhotic chronic liver disease.

There is limited data on association of zinc with liver cirrhosis and its severity. Therefore, the present study was undertaken to evaluate zinc levels in liver cirrhosis patients so that timely zinc management can be done in patients with liver disease.

Material and Methods

The present study was carried out in the Department of Biochemistry in collaboration with Department of Medicine, M.M Institute of Medical Sciences and Research, MMDU, Mullana, Ambala. The present study was approved by ethical committee of this institute.

Total 100 male subjects were selected and divided into two groups. Group I included 50 diagnosed cases with liver cirrhosis. They were recruited for the study after taking their due written consent. The diagnosis of liver cirrhosis was established by detailed history of all such patients, positive findings on clinical examination, relevant biochemical tests and histopathological examination of the liver tissues. The subjects were in the age group of above 40 years. Group 1 was further divided according to severity of liver cirrhosis based on Child Pugh Scoring.[11] Group II included 50 healthy control subjects with comparable age group. Fasting blood samples were collected from all the subjects. Biochemical parameters viz SGOT, SGPT, ALP and Bilirubin were done on autoanalyzer.

Exclusion criteria

Female patients, Patients suffering from chronic kidney disease, non- alcoholic fatty liver disease, type 2 diabetes, pregnant women, gastrointestinal diseases like celiac disease, chronic diarrhea, viral hepatitis B or C and less than 40 years.

Estimation of Serum Zinc was done by Colorimetric Method of Akita Abe. *et. al.* [12]

In this procedure Zinc reacts with NITRO-PAPS at room temperature and form a purple colored complex whose intensity was measured at 540 nm which is proportional to the zinc concentration present in the sample.

Statistical Analysis

All the data were analyzed by using the SPSS version 20. Values were presented as Means ± standard deviation (SD). Significance between the study group and the control groups' was done by a student's t- test. The p-value ($p < 0.05$) was considered as significant. Correlation between the zinc levels and severity of disease was estimated using one- way ANOVA with post hoc Bonferroni Test.

Results

The mean age of subjects in study group was 50.96 ±8.34 and in control group was 51.94 ±10.64. Both the groups were comparable with respect to age. The mean zinc levels were lower in the study group (64.47±21.01) compared to the control group (87.65±15.01) and the difference was statistically highly significant ($p<0.001$). (*Fig 1*) On comparing the zinc levels and other variables amongst various classes of Liver cirrhosis, the levels vary significantly with severity. (*Table 1*)

Discussion

Liver plays an important role in maintaining systemic Zinc homeostasis. Therefore, level of zinc can be altered by liver disease and in turn the Zinc deficiency may influence the liver functioning also. By inducing oxidative stress, the redox state is altered, which compromises functioning of oxidative -sensitive transcription factor, leading to disturbed cell function, proliferation and survival. [13] This also contributes to inflammation of the hepatic parenchyma and also to failure of eliciting the acute phase response as a shield against viruses and toxins. Two mechanisms proposed for Zinc malabsorption in liver cirrhosis include small bowel mucous damage and impaired pancreatic exocrine function. [14]

The mean age of subjects in study group was 50.96 ±8.34 and in control group was 51.94 ±10.64.The mean Zinc level in present study was 64.47+21.01 which was significantly lower than the Zinc level in control group (87.65+15.01) ($p<0.001$). Studies by Parmoolsinsap C *et*

Fig 1. Comparison of Mean Zinc Levels in Study Group and Control Group

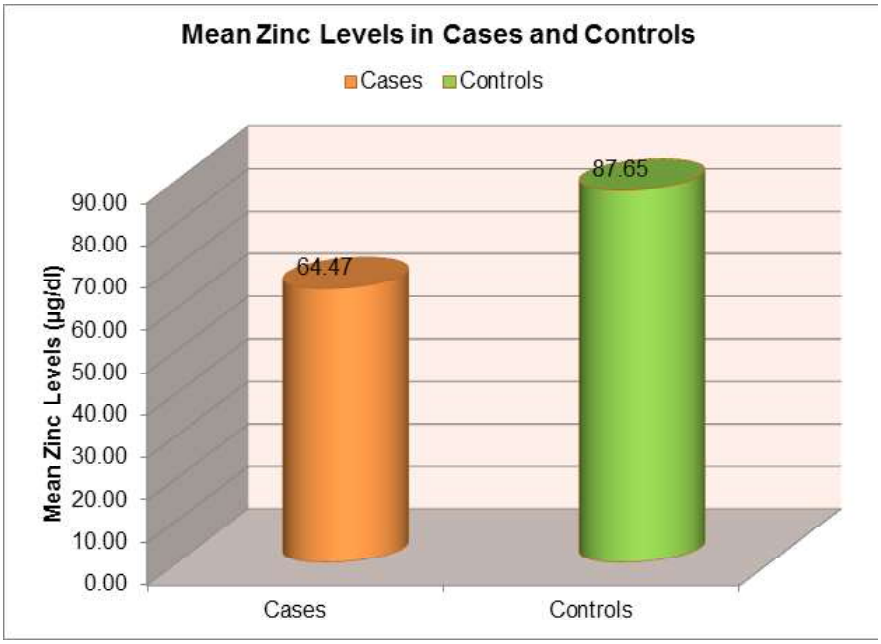

Table 1 Association of Various Variables with Classes of Liver Cirrhosis

Variables	Class A (n = 9)		Class B (n = 15)		Class C (n = 26)		A vs B	A vs C	B vs C
	Mean	± SD	Mean	± SD	Mean	± SD	P value	P value	P value
Zinc (µg/dl)	96.63	20.56	70.65	7.83	49.77	8.72	**<0.001****	**<0.001****	**<0.001****
SGOT (IU/L)	52.00	4.18	88.40	21.32	282.04	56.84	0.153	**<0.001****	**<0.001****
SGPT (IU/L)	51.67	7.98	100.73	21.99	278.54	48.83	**0.010***	**<0.001****	**<0.001****
ALP (IU/L)	109.67	10.43	147.00	20.98	192.96	38.56	**0.018***	**<0.001****	**<0.001****
Bilirubin (Total) (mg/dl)	1.24	0.25	2.38	0.20	5.97	5.09	1.000	**0.006***	**0.014***
Bilirubin (Direct) (mg/dl)	0.62	0.25	1.49	0.27	3.64	3.85	1.000	**0.023***	0.068
Ascites	Not seen		++			+++			

al [15] ,Poo JL *et. al.*[16] , Lin CC *et al* [17], D. Rahelic *et.al* [18] also showed similar findings in patients with liver cirrhosis. The low zinc levels can be attributed to reduced liver ornithine transcarboxylase activity and increased plasma ammonia level. The synthesis of proteins is reduced in Liver Cirrhosis. Metallothionein plays an important role in Zinc homeostasis and its release in a number of oxidants. The released Zinc then inhibits the activity of the enzymes involved in fibrogenesis (fibrosis) in the liver. The reduced synthesis of this protein, will decrease Zinc availability and cause its deficiency. Some alteration of patients with cirrhosis may be associated with zinc deficiency: wound healing, lack of appetite, alopecia, hypogeusia, gonadal growth retardation

and hepatic encephalopathy (by inducing alteration in urea metabolism). [19]

On further comparing Zinc levels in the various classes of cirrhosis, it was found that level of zinc decreased significantly with severity of the disease. This finding was comparable with the studies by Stamoulis *et.al* [20] and Poo JL *et al* [16] who found an association between zinc levels and the severity of cirrhosis.

Conclusion

There is fall in the levels of Zinc in patients with liver cirrhosis. The levels of zinc decrease significantly with severity of the disease. Therefore, zinc level should be evaluated in all patients with liver cirrhosis so as to manage these patients timely and prevent worsening of cirrhosis and development of hepatic encephalopathy.

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Conflicts of Interest
There are no conflicts of interest.

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