Original Article

Serum zinc levels and the prevalence of zinc deficiency in patients with liver cirrhosis

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Objective: To measure the serum zinc levels in liver cirrhosis patients and determine the frequency of zinc deficiency in Pakistani population.

Methodology: In this study, a total of 220 patients with liver cirrhosis were recruited. Serum zinc level was measured by atomic absorption spectrophotometer. Data analysis was carried out by SPSS 20.

Results: Out of 220 patients, there were 112 males (50.9%) and 108 females (49.1%). Mean age was 55.1±11.1 years. Patients according to Child Pugh classification, 62(28.2%) were in class A, 85 (38.6%) in class B and 73 (33.2%) in class C. Zinc deficiency was found in 136(61.8%) patients.

Conclusion: It is concluded that serum zinc concentration was low in 61.8% patients of liver cirrhosis. (Rawal Med J 202;46:37-40).

Keywords: Serum levels of zinc, zinc deficiency, Child-Pugh score, liver cirrhosis.

INTRODUCTION

Cirrhosis is the advance form of fibrosis and chronic liver disease which occurs due to necro-inflammation and fibrinogenesis resulting in disruption of hepatic vascular microenvironment.[1] Cirrhosis and chronic liver disease results in death rates in the United States, of 10 per 100,000 population.[2] In Pakistan, cirrhosis developing due to chronic hepatitis C virus and hepatitis B infections results about 84% cases develop chronic liver disease.[3] Amino acids treatment may improve the metabolic and nutritional anomalies.[4]

From few decades, there is an advancement in the pathophysiology of liver and role of trace elements.[5] The liver regulates the metabolic pathways and transportation of trace elements including their bioavailability, tissue distribution and toxicity.[6] Trace elements impart many enzymatic reactions by inhibiting or activating them, including competition with other elements and metallo-proteins for binding sites. Changes in trace elements physiology has consequence on liver pathology.[7]

Zinc is considered as an essential element which has many biological activities like anti-oxidant, anti-inflammatory and apoptotic activities. It has key functions in cellular metabolism, gene expression, differentiation and development of immunity.[8] Liver is associated with zinc homeostasis and deficiency of zinc has been documented in liver cirrhosis.[9] Multiple factors contribute in zinc deficiency due to alteration of zinc metabolism or due to liver associated diseases.[10] Its deficiency can alter the reduction mechanism of reactive oxygen species that can disturb cell function, propagation and existence.[11] Various cirrhosis features including deficient immunity, multiple infections, loss of hair, diarrhea, and mental disorders are suggestive of zinc deficiency.[12-14] Anti-oxidant property of zinc causes regulation of metallo-proteins to curtail the collagen production in hepatocytes.[15] This study aimed to determine the serum zinc levels and explore the impact of zinc in liver cirrhosis patients with the severity of disease on the basis of Child Pugh score.

METHODOLOGY

The diagnosed liver cirrhosis patients (duration of disease more than six months) with age ranges from 20 to 80 years of both sexes were included in the study. Those with renal failure (serum creatinine >1.3mg/dl, hepatocellular carcinoma (biphasic CT scan abdomen), diuretic therapy (medical history), diabetes mellitus (HbAIc >6.5%) and individuals on zinc therapy or on hormonal drugs (from available record) and the pregnant women were excluded

from the study. Ethical approval was obtained from Shalamar Hospital and University of Health Sciences, Lahore, Pakistan.

Patient's demographic information including name, age, and gender were recorded. A 5.0 ml blood sample from each subject and determination of serum zinc levels was done by using polarized flame atomic absorption spectrophotometer (Hitachi Z 2000). Standard curve was generated by using commercially available zinc standard (1000 (µg/dl)) to report the concentration of patients zinc levels.

Statistical Analysis: Data analysis was performed by using SPPS version 20.0. The data stratification for age, gender and Child Pugh classification was done to determine the modifier's effect. After stratification, the Chi-square test was applied to check the correlation. $p \leq 0.05$ was considered as statistically significant.

RESULTS

Out of 220 patients, males were 112 (50.9%) and females were 108 (49.1%). The age ranged between 20-80 years (mean 55.1±11.1). Most patients belonged to Child Pugh class B and C. The reduced serum zinc level was found in 136 (61.8%) patients (Table 1).

Table 1. Frequency of different variables in cirrhotic patients.

Variables	Groups	Number	Percentage
Age (years)	20-50	81	36.8%
	51-80	139	63.2%
Gender	Male	112	50.9%
	Female	108	49.1%
Zinc deficiency (µg/dl)	Yes	136	61.8%
	No	84	38.2%
Child Pugh Class	A	62	28.2%
	B	85	38.6%
	C	73	33.2%

Table 2. Descriptive analysis of quantitative variables.

Variables	Mean ± SD	Minimum	Maximum
Duration of disease (months)	49.6±30.1	6	150
Portal vein diameter (mm)	13.8±1.2	12.1	18
Spleen size (cm)	14.2±1.6	12.12	19
Serum total bilirubin (mg/dl)	2.2±2.97	0.10	28
Serum albumin (g/l)	2.56±0.59	0.58	4.0
Pro-thrombin time (seconds)	17.5±4.8	10	42
Serum zinc (µg/dl)	0.61±0.161	0.25	1.10

Table 3. Correlation of zinc deficiency with variables.

Variables	Groups	Zinc Deficiency		Total	*p*-value
		Yes	No		
Child Pugh class (Index score)	**A**	14	48	62	<0.001*
	B	62	23	85	
	C	60	13	73	
Age (years)	**20-50**	48	33	81	0.551
	51-80	88	51	139	
Gender	**Male**	66	46	112	0.369
	Female	70	38	108	

*p-value <0.05 is statistically significant.

The mean size of portal vein, mean spleen size, serum albumin, mean pro-thrombin time (PT) and mean serum zinc level are shown in Table 2. The deficiency of zinc was significantly associated with Child Pugh score ($p<0.05$) but no correlation was found between reduced zin with age and gender groups ($p>0.05$) (Table 3).

DISCUSSION

In this study, the reduced serum zinc was found in patients with wide range of age groups however, it was not significant ($p>0.05$). Though, the previous studies showed that zinc deficiency occur at any age.[16] This study also showed the reduced serum zinc in patients with the longer duration of liver cirrhosis and high bilirubin. A previous study showed higher bilirubin levels which are similar to the results of this study.[17]

As duration of liver fibrosis progresses the spleen increases in size mainly due to raised pressure of portal circulation. The mean spleen size in our study was 11.94±2.1 cm and these findings are similar to a study by Suzuki et al.[18] In our study, low albumin and zinc levels are comparable to a previous study which showed strong association between hypo-albuminemia and low serum zinc concentration.[19]

In present study, liver cirrhosis patients mainly presented with hepatic encephalopathy with reduced Zn levels. It has been documented that the incidence of hepatic encephalopathy increases with low serum zinc levels.[19] Out of 220 cirrhotic patients, 101 patients developed hepatic encephalopathy at any stage of their illness, similar to a previous study.[19] In current study, patients who

developed encephalopathy were mostly of Child Pugh Class C (n= 65), while 12 patients were of Child Class A and 25 patients were of Child Class B. Moreover, we found that serum zinc was remarkably low in patients with hepatic encephalopathy. A previous study showed that lower zinc level might be involved in hepatic encephalopathy.[20]

In our study, the frequency of zinc deficiency was found 61.8%. These results are in accordance to the previous studies which demonstrated the low zinc.[21] Some other studies described the higher frequency of zinc deficiency in cirrhotics from different populations.[22,23] The variable zinc deficiency is directly related to the grades of liver fibrosis. Furthermore, data was stratified according to Child-Pugh Class to document the severity of liver fibrosis. The serum zinc levels were significantly decreased in our study as disease progress from mild form of liver disease to severe fibrosis. In Child Class A the mean serum zinc was observed 74.6±17.0, while Child Class B score between 7-9 showed mean serum zinc level 60.6±8.9 and Child Class C with score >9 sows significantly reduced serum zinc with mean 41.1±10.1 (p=0.001). The difference in serum zinc concentration may be due to age of the patients, duration of disease, stage of disease, ethnicity, and dietary habits of the patients, cultural and genetic variations.[24]

The zinc deficiency in liver cirrhosis may occur due to several factors including poor intake of zinc, metabolic pathway dysregulation and decreased hepatic uptake, high pressure in portal-venous system, impaired intestinal Zn absorption and interleukin-6 dysfunction.[20]

CONCLUSION

The frequency of zinc deficiency was 61.8% in cirrhosis patients in our study. It may be associated with hepatic encephalopathy. Therefore, evaluation of zinc is an important step of management and their supplementation in cirrhotic patients.

ACKNOWLEDGMENTS

We are thankful to the patients who participated in this study.

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Conflict of Interest: None declared
Rec. Date: Dec 29, 2019 Revision Rec. Date: Jan 1, 2021 Accept Date: Jan 21, 2021

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