

## Frequency of Low Zinc Levels in Cirrhotic patients with Hepatic Encephalopathy

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### ABSTRACT

**Aim:** To determine the frequency of low serum zinc levels in cirrhotic patients with hepatic encephalopathy.

**Study design:** Cross-sectional survey

**Place and duration:** Department of Gastroenterology, Medical Unit-3. Services Hospital Lahore, Pakistan. Study was carried out over a period of six months from Feb 2013 to Aug 2013

**Methods:** A total of 114 cases were included in this study. Serum zinc level was done in all patients. The outcome variable of this study was low serum zinc levels.

**Results:** Mean age of the patients was  $47.8 \pm 7.5$  years. Regarding gender distribution, 79 patients (69.3%) were male while 35 patients (30.7%) were female. Distribution of grades of hepatic encephalopathy was as follows: 18 patients (15.8%) of grade-I, 32 patients (28.1%) of grade-II, 47 patients (41.2%) of grade-III and 17 patients (14.9%) of grade-IV. Low serum zinc levels in cirrhotic patients with hepatic encephalopathy was found in 82 patients (71.9%).

**Conclusion:** In conclusion, the lower level of serum zinc level in patients of liver cirrhosis with hepatic encephalopathy identified. Therefore, a routine biochemical assessment of zinc status in patients with liver cirrhosis is an important step in the management protocol and to reduce progression of the disease.

**Keywords:** Serum zinc levels, Cirrhosis, hepatic Encephalopathy

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### INTRODUCTION

Cirrhosis is a consequence of chronic liver disease characterized by replacement of liver tissue by fibrous scar leading to progressive loss of liver function. Majority of patients remain asymptomatic until the advanced stage called decompensated cirrhosis, characterized by ascites, spontaneous bacterial peritonitis, hepatic coma or variceal bleeding from portal hypertension<sup>1</sup>.

Liver diseases affect millions of people worldwide each day. However, in the developing countries where cost of health care has always been an issue, long lasting diseases such as liver cirrhosis and its complications are a major health problem and pose a big challenge to the health economy<sup>2</sup>.

About 30% of patients with cirrhosis die due to hepatic coma (hepatic encephalopathy). Cirrhosis of liver is a common cause of mortality amongst Pakistani population and a frequent cause of admission in our hospitals.

Hepatic encephalopathy is characterized by personality changes, intellectual impairment and a depressed level of consciousness. An

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important prerequisite for the syndrome is diversion of portal blood into the systemic circulation through portosystemic collateral vessels. Hepatic encephalopathy may develop in patients without cirrhosis who have undergone portocaval shunt surgery. The development of hepatic encephalopathy is explained, to some extent, by the effect of neurotoxic substances, which occur in patients with cirrhosis and portal hypertension<sup>3</sup>.

Hepatic encephalopathy is associated with a poor prognosis<sup>4</sup>. In a study of Stamoulis et al published by Digestive Diseases and Science in 2007 the prevalence of low serum zinc level in cirrhotic patients was 65.3%<sup>5</sup>. Zinc is essential for the synthesis of coenzymes that mediate biogenic amine synthesis and metabolism<sup>6</sup>.

The serum zinc was low in 69% patients. According to Child-Pugh classification, 72% zinc deficient cirrhotic subjects were in class C, 16% in class B and 12% in class A<sup>1</sup>. The Recommended Dietary Allowance (RDA) is 8mg/day for women and 11 mg/day for men. Red meats, especially beef, lamb and liver have some of the highest concentration zinc in food<sup>7</sup>.

Disorders of protein metabolism in liver cirrhosis can affect prognosis or cause complication, so more improvement in disorders of nitrogen metabolism in liver cirrhosis occurred

after administration of branched-chain amino acid with zinc<sup>8</sup>.

No local data is available regarding the frequency of low serum zinc levels in cirrhotic patients with hepatic encephalopathy. Therefore, this study is designed to determine the frequency of low serum zinc levels in cirrhotic patients who will be in hepatic encephalopathy, in our population. This study will signify the magnitude of low zinc in hepatic encephalopathy in our patients. If the results of this study will eventful, then to incorporate its addition in future local treatment protocol of hepatic encephalopathy will be suggested.

## MATERIAL AND METHODS

Study was carried out over a period of six months from 21-02-2013 to 20-08-2013 at Department of Gastroenterology, Medical Unit-3, Services Hospital, Lahore. One hundred and fourteen patients were enrolled in the study. Inclusion criteria included both gender of patients between 18-60 years of age having coarse echotexture of liver on abdominal ultrasound and having any grade of encephalopathy in the presence of coarse echo texture of liver on abdominal ultrasound and elevated serum ammonia levels.

Patients with cerebrovascular accident, hypoglycemia, or not willing to give consent for enrollment were excluded from the study.

A total number of 114 patients who had coarse echo texture of liver on abdominal ultrasound and above normal serum ammonia levels and in any grade of encephalopathy were selected from Medical emergency, Department, Services Hospital, Lahore. Patient's bio-data was recorded and informed written consent was taken. Serum zinc levels were done in all the selected patients.

## RESULTS

A total of 114 patients were recruited in this study. Most of the patients were between 41-50 years of age while minimum patients were 20-30 years old. Mean age of the patients was  $47.8 \pm 7.5$  years (Table 1). Regarding gender distribution, 79 patients (69.3%) were male while 35 patients (30.7%) were female (Table 2).

Distribution of grades of hepatic encephalopathy was as follows: 18 patients (15.8%) of grade-I, 32 patients (28.1%) of grade-II, 47 patients (41.2%) of grade-III and 17 patients (14.9%) of grade-IV (Table 3).

Low serum zinc levels in cirrhotic patients with hepatic encephalopathy was found in 82 patients (71.9%) (Table 4). Stratification for different grades of hepatic encephalopathy presented in Table-5.

Table-1: Distribution of patients by age

Age (Year)	n	%age
20-30	12	10.5
31-40	37	32.5
41-50	40	35.0
51-60	25	22.0
Total	114	100.0
Mean $\pm$ SD	47.8 $\pm$ 7.5	

Table-2: Distribution of patients by sex

Sex	n	%age
Male	79	69.3
Female	35	30.7
Total	114	100.0

Table-3: Distribution of cases by grades of hepatic encephalopathy

Grade	n	%age
I	18	15.8
II	32	28.1
III	47	41.2
IV	17	14.9
Total	114	100.0

Table-4: Low serum zinc levels in cirrhotic patients with hepatic encephalopathy

Low Zinc Level	n	%age
Yes	82	71.9
No	32	28.1
Total	114	100.0

Table 5: Stratification for different grades of hepatic encephalopathy

Low serum zinc level	Grades of hepatic encephalopathy			
	I	II	III	IV
Yes	11	23	35	13
No	07	09	12	04
Total	18	32	47	17

## DISCUSSION

Hepatic encephalopathy is characterized at the neurophysiological level by disturbed corticocortical and corticomuscular coupling, and at the cellular level by primary gliopathy<sup>9</sup>. Ammonia is a key pathophysiological factor in hepatic encephalopathy<sup>10</sup>. In the brain, ammonia is detoxified by astrocytes through a reaction

catalyzed by glutamine synthetase; an increased brain glutamine/glutamate ratio is associated with decreased myoinositol, reflecting compensation for glial edema<sup>11</sup>. Swollen astrocytes predispose to neuronal dysfunction by impairing their regulatory activity against the increase in protein tyrosine nitration and the formation of reactive oxygen and nitrogen oxide species including nitric oxide. If not counteracted, these reactions promote RNA oxidation, which prompts gene expression and the transcription of altered proteins<sup>12</sup>.

Zinc, copper, manganese and magnesium are essential trace elements whose role in liver cirrhosis and its complications is still a matter of research. There are contrary reports about their serum concentrations in patients with liver cirrhosis.

Zinc is associated with more than 300 enzymatic systems<sup>13</sup>. Zinc augments the natural defense of reactive oxygen radicals by Zn-enzyme Cu-Zn superoxide dismutase. Zinc acts as an antioxidant, a membrane and cytoskeletal stabilizer, an anti-apoptotic agent, an important co-factor in DNA synthesis, an anti-inflammatory agent etc<sup>14</sup>.

Since zinc, copper, manganese and magnesium have a possible role in the pathogenesis of cirrhotic complications, the aim of this study was to investigate the serum concentrations of mentioned trace elements in patients with liver cirrhosis and compared them with concentrations in controls.

In present study the serum levels of zinc were significantly lower in majority of the patients of liver cirrhosis with encephalopathy (71.9%). The results confirm Kugelmans' study, who explained low zinc levels with low ingestion due to protein reluctance, increased loss in gastroenterological system due to diarrhea or intestinal malabsorption and increased urinary losses<sup>15</sup>.

The assumption is also based on the study carried by McClain<sup>16</sup> and Gill-Extremera et al<sup>17</sup>. Protein deficiency occurs frequently due to poor dietary intake. Our results confirm findings of decreased serum concentrations of zinc in patients with liver cirrhosis.

In Celik's study<sup>18</sup> the decrease in both serum and ascites zinc content was found in patients with liver cirrhosis. The interaction between zinc and copper in their intestinal absorption and their competition for binding sites on the carrier proteins and cellular uptake may be regulators of their homeostasis. Maybe this can explain inverse concentrations of zinc and

copper. Zinc binds on albumin, transferrin and metalloproteins in the cell, so relative concentrations of these proteins might regulate the serum concentration of zinc<sup>19</sup>.

As zinc is bound to albumin in the serum, it has been thought that the serum zinc concentration would decrease with advancing grades of hepatic fibrosis<sup>19</sup>. Yoshida et al [20] found that patients with decompensated liver cirrhosis have lower levels of zinc than patients with compensated cirrhosis. However, in study of Hatano et al<sup>19</sup> serum zinc levels did not differ significantly between grades of hepatic fibrosis.

## CONCLUSION

In conclusion, the lower level of serum zinc level in patients of liver cirrhosis with hepatic encephalopathy identified. Therefore, a routine biochemical assessment of zinc status in patients with liver cirrhosis is an important step in the management protocol and to reduce progression of the disease.

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