

CORRELATION BETWEEN TRACE METALS (COPPER, ZINC IRON, SELENIUM) LEVELS AND THE SEVERITY OF LIVER CIRRHOSIS

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ABSTRACT:

Background: Liver cirrhosis is a major cause of death and in India its most common cause is viral hepatitis. The triad of parenchymal necrosis, regeneration and scarring is always present regardless of individual clinical manifestations. Trace elements act protective against oxygen free radicals in the development of liver cirrhosis. **Material & Methods:** 100 patients of liver cirrhotic diseases of age between 20 to 60 years and fifty healthy controls were taken for this present case control study. Written informed consent by the subjects and ethical approval was appropriately sought before the study. After taking detailed history the blood samples were collected after 12 hours of fasting for the estimation of serum copper, selenium, iron and zinc levels with the help of an Atomic Absorption Spectrophotometer.

Results: The study results showed that levels of Zn, albumin in the serum of patients with child-pugh class C were significantly lower than those with child-pugh class A&B. In contrast we did not observe statistically significant difference in the levels of Cu, Fe and Se in three groups. **Conclusion:** We concluded from the present study that Serum Zinc may consider as associate marker to assess severity of liver cirrhosis.

Key words: liver cirrhosis, trace elements, Child-Pugh classification.

INTRODUCTION:

The liver is the largest organ of the body, weighing 1–1.5 kg and representing 1.5–2.5% of the lean body mass. The majority of cells in the liver are hepatocytes, which constitute two-thirds of the mass of the liver and perform vital role in maintaining homeostasis and health. Liver cirrhosis is a major cause of death in the United States (1). The definition of cirrhosis remains morphological, described by a working party for the World Health Organization as: “a diffuse

process characterized by fibrosis and the conversion of normal liver architectures into structurally abnormal nodules” (2). The triad of parenchymal necrosis, regeneration and scarring is always present regardless of individual clinical manifestations. Cirrhosis is the terminal phase of irreversible liver disease. It may have a range of explanation such as viral hepatitis (hepatitis B virus, hepatitis C virus), alcohol consumption (alcoholic liver disease), metabolic disorder,

cholestasis (Primary sclerosing cholangitis), autoimmune events (autoimmune hepatitis), Non-alcoholic steato-hepatitis, toxic substances, drugs, infections, congenital diseases, it does not heal in general and chronically progresses (3). Among these etiologies, alcoholism in the west, HBV infection in the orient and viral hepatitis in India are the most common causes of cirrhosis. (4)

Clinical feature of cirrhosis derive from morphological alteration and loss of hepatocellular mass, may lead to jaundice, edema, coagulopathy, variety of metabolic abnormalities, Ascites and hepatic encephalopathy and also affect the nutrition (5). To prevent this mechanism our cells possesses antioxidant such as copper-zinc superoxide dismutase (Cu-Zn SOD), glutathione peroxidase (GSH-Px) & catalase are present in the cell. All these antioxidant are designed to prevent the occurrence of free radical injury under normal condition. These antioxidants contain trace elements such as selenium, copper, zinc and iron (6).

On theoretical ground trace element may be protective against oxygen free radicals in the development of liver cirrhosis. So the present study has been designed to study the levels of serum trace elements (Cu, Zn, Fe and Se) in patients of liver cirrhosis as compared to control subjects and also to assess the levels of trace elements with severity of diseases.

MATERIALS & METHODS

The present study was conducted in the Department of Biochemistry, SMS Medical College and Hospital, Jaipur on 100 patients of liver cirrhotic diseases of age between 20 to 60 years admitted in medical wards, under Department of Medicine and Gastroenterology

wards, under Department of Gastroenterology, SMS Medical College and Hospital, Jaipur. Fifty healthy controls were taken. Control subjects were selected from general population of Jaipur. Written informed consent by the subjects and ethical approval was appropriately sought before the study. Patient with hepatocellular carcinoma, renal failure, any chronic disease and on drugs affecting levels of trace metals eg. Corticosteroids, digoxin, thiazide diuretics etc were excluded from the study. After taking detailed history the blood samples were collected after 12 hours of fasting. The peripheral venous blood samples were taken at 8 AM. 10 ml of blood was drawn from the cubital vein and the copper, selenium, iron and zinc levels in the serum of each subgroup were measured with the help of an Atomic Absorption Spectrophotometer. The statistical analysis was performed using Z-test and Pearson's correlation coefficient. Atomic Absorption Spectrophotometer ECIL AAS-4141(AAS) is a pc based instrument for absorption and emission analysis. It is used for quantitative element analysis mainly like copper, zinc, iron, lead etc. by measuring the absorbance of a sample atomized in a flame. The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22. The severity of cirrhosis is commonly classified with the child-pugh score:

Designation	A	B	C
Bilirubin	<2.0	2-3	>3.0
Albumin	>3.5	3-3.5	<3.0
Ascites	None	Easily Controlled	Poorly Controlled
Neurological Disorder	None	Minimal	Advance
Nutrition	Excellent	Good	Wasting

RESULTS

In present study the out of total 150 study patients the study results showed that levels of Zn, albumin in the serum of patients with child-pugh class C were significantly lower than those with child-pugh class A&B. In contrast we did not observe statistically significant difference in the levels of Cu, Fe and Se in three groups. The means \pm SD between serum levels of trace elements and stages of liver cirrhosis is shown in table 1.

Table No.-1: Mean + SD of trace elements according to Ch PU class

Element	Mean \pm Sd		
	A	B	C
Zn	74.88 \pm 11.36	68.66 \pm 14.77	52.16 \pm 6.02
Cu	132.04 \pm 16.51	136.73 \pm 15.09	132.31 \pm 22.52
Fe	152.77 \pm 20.97	159.95 \pm 15.72	158.71 \pm 19.56
Se	8.37 \pm 2.08	7.11 \pm 2.08	7.08 \pm 2.62

A v/s B = < .001 HS

A v/s B = >.05 NS

A v/s B = >.05 NS

A v/s C = < .001 HS

A v/s C = >.05 NS

A v/s C = >.05 NS

B v/s C = < .001 HS

B v/s C = >.05 NS

B v/s C = >.05 NS

DISCUSSION

The importance of trace elements in the process of maintaining life is well known. Trace elements are uniquely required for growth and maintenance of life and health. At present, it is

recognize that 14 trace elements including copper, zinc, iron and selenium are essential for human body. Lack or an inadequate supply of such nutrients produces a functional impairment or can result in disease. The clinical significance and evaluation of trace elements such as Copper, Iron, Selenium and Zinc in regard to different diseases including liver cirrhosis remain conflicting as well as controversial and many questions still remain unanswered (7). Mechanisms linked on ethanol metabolism, especially oxidative stress, redox potentials and acetaldehyde, participate in the emergence of liver damage. Trace elements play an important role in oxidative stress and redox potentials. A possible role of zinc, copper, iron and selenium in pathogenesis of liver cirrhosis and its complications is still subject of research. This present study, though probably first of its kind in Indian population, is an attempt forward in series of previous studies done internationally to study the levels of trace elements in the patients of liver cirrhosis and also to see that if there is any association between levels of trace elements and severity of disease which is measured by child-Pugh score. We took initiative to study levels of trace elements in Indian cirrhotic population and analyze it's with the severity of diseases.

In our research the serum levels of zinc were significantly lower in patients with liver cirrhosis in comparison to controls (Table 2, fig.1) and also serum levels of zinc were lower in patients with liver cirrhosis. The same finding was reported by Loguercio, et al in 2001, their results indicate that zinc concentration is associated with viral hepatitis, decreasing with the development of cirrhosis and low function of liver (8). In contrast to this, the study done by Lin et al in 2006, the mean zinc level in the serum of

patients with hepatic cirrhosis was significantly lower than that of the control group. Moreover they found markedly elevated cu: Zn Ratio in patients with hepatic cirrhosis or hepatocellular carcinoma. Their finding implies that the level of some trace elements, such as selenium, iron, copper, and zinc and cu: Zn ratio might serve as biomarkers for the increased severity of viral hepatic damage (9). Alteration of Zn homeostasis in liver cirrhosis is supported by a large body of experimental and clinical evidence. Hypozincemia in cirrhosis is also seen by Celik et al in 2002, in this study they observed that the mean value of serum and ascites zinc level was significantly lower in cirrhotic patients than healthy controls (10).

Alteration of Zn homeostasis in liver cirrhosis is supported by a large body of experimental and clinical evidence. Nangliya et al in 2015 demonstrated that the levels of zinc were significantly lower in patients with liver cirrhosis in comparison to controls ($p<0.001$). They also observed that there was a decrease in serum zinc concentration in patients with more severe clinical state of liver cirrhosis (stage C) according to Child-Pugh classification (11). Hypozincemia in cirrhosis is also demonstrated by kar et al in 2014, in this study they observed that the mean value of serum and ascites zinc level was significantly lower in cirrhotic patients than healthy controls (12).

Similarly one cross-sectional analytic study was carried out by Mohammed somi et al in 2007 in 60 continuous patients with liver cirrhosis referred to hepatology clinic, Tabriz University of Medical Sciences. They observed that serum levels of Zn, Albumin and Zn/Cu ratio in patients with Child-Pugh class B were significantly lower than those with Child-Pugh class A. (13).

CONCLUSION

We concluded from the present study that Serum Zinc may consider as associate marker to assess severity of liver cirrhosis. The copper and selenium levels were found higher and serum zinc and iron levels were found lower in cirrhosis patients and this difference of mean levels of trace elements in liver cirrhosis patients to the control were highly significant. Since this study provide a snapshot on the trace elements hence elaborative multicentric studies with larger sample size are necessary for the overall generalization of results.

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