ESSENTIAL MINERAL ASSESSMENT IN CIRRHOTIC LIVER DISEASE PATIENTS

Vijay Laxmi Gupta[*]
Sunil Gupta[**]
Sunita Gajawat[***]
Suchitra Sharma[****]

ABSTRACT

This study aimed to assess the level of essential minerals (Cu, Zn, Fe and Se) in patients of cirrhotic liver disease. The study included 100 patients with liver cirrhotic disease of age between 20 to 60 years old and 50 healthy controls. 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. The results showed that the mean serum level of copper and iron were found significantly higher in patients as compared to healthy controls while the mean serum level of Zinc and selenium were significantly lower in patients than controls. The levels of these essential minerals were also correlated with the occurrence of disease, with more severe cases having lower level of Zn & Se. These findings suggest that some essential minerals may play an important role in the pathogenesis of liver cirrhosis and may serve as potential biomarkers for disease severity.

***Keywords:** Liver Cirrhosis, Trace Minerals, Copper, Iron, Zinc and Selenium.*

Introduction

Liver cirrhosis is a chronic liver disease that can lead liver failure and other serious health problems. It is a significant global health concern (1) and major cause of death in United states (2,3). 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" (4). 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 explaination 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 (5). Among these etiologies, alcoholism in the west, HBV infection in the orient and viral hepatitis in India are the most common causes of cirrhosis.(6)

Clinical feature of cirrhosis derive from morphological alteration and loss of hepatocellular mass, may lead to jaundice, edema, co-agulopathy, variety of metabolic abnormalities, Ascites and hepatic encephalopathy and also affect the nutrition (7). To prevent this mechanism our cells possesses antioxidant such as copper-zinc superoxide dismutase (Cu-Zn SOD), glutathione peroxidase (GSH-Px) &

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[*]   Assistant Professor, Department of Zoology, S. S. Jain Subodh P. G. Mahila Mahavidyalaya, Jaipur, Rajasthan, India.

[**]   Associate Professor, Department of Biochemistry, RUHS College of Medical Sciences, Jaipur, Rajasthan, India.

[***]   Assistant Professor, Department of Zoology, S. S. Jain Subodh P. G. Mahila Mahavidyalaya, Jaipur, Rajasthan, India.

[****]   Assistant Professor, Department of Zoology, S. S. Jain Subodh P. G. Mahila Mahavidyalaya, Jaipur, Rajasthan, India.

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 (8).

On theoretical ground some minerals 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 minerals (Cu, Zn, Fe and Se) in patients of liver cirrhosis as compared to control subjects and also to assess the levels of trace minerals with occurence 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 cubical vein and the copper, selenium, iron and zinc levels in the serum of each subgroup were measured with the help of an Atomic Absorption Spectrophoto meter. The statistical analysis was performed using Z-test and Pearson's correlation coefficient. The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

Results

In present study the out of total 150 study patients the maximum number of cases 41(41%) were in age group of 40-49 years, followed by 36(36%) in more than 50 years age group, 23(23%) cases in 30-39 age group were present. It was observed that maximum number of cases was in age group 40-49. This is consistent with the average age of diagnosis of liver cirrhosis. The Mean age for case was 46.45 $\pm$7.00 and for control was 44.86 $\pm$5.93. (Table-1)

Table 1: Distribution according to Age & Sex of Case & Control Group Subjects

Age group (In yrs.)	Case			Control		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**
30-39	11 (11.00)	12 (12.00)	23 (23.00)	9 (18.00)	6 (12.00)	15 (30.00)
40-49	20 (20.00)	21 (21.00)	41 (41.00)	15 (30.00)	8 (16.00)	23 (46.00)
50+	28 (28.00)	8 (8.00)	36 (36.00)	10 (20.00)	2 (4.00)	12 (24.00)
Total	59 (59.00)	41 (41.00)	100 (100.00)	34 (68.00)	16 (32.00)	50 (100.00)

Mean age = 46.45 $\pm$ 7.00   Mean age = 44.72 $\pm$ 5.93

Table 2: Mean $\pm$ SD of Various Trace Elements of Case & Control Group Subjects

Parameters	Mean $\pm$ SD		P-value
	Case	**Control**	
Cu	133.73 $\pm$ 17.30	107.40 $\pm$ 9.03	< .001
Zn	68.90 $\pm$ 14.45	110.03 $\pm$ 11.20	< .001
Fe	156.13 $\pm$ 19.35	118.20 $\pm$ 14.32	< .001
Se	7.72 $\pm$ 2.27	12.45 $\pm$ 1.99	< .001

The serum levels of Copper was found to be higher in case group as compared to control group (133.73 + 17.30 vs 107.40 + 9.03,P< .001), and this is highly statistically significant.

The serum levels of Zinc was found to be lower in case group as compared to control group (68.90 + 14.45 vs 110.03 + 11.20, < .001), and this is also highly statistically significant.

The mean serum Iron levels was higher in case group as compared to control group (156.13+ 19.35 vs 118.20 + 14.32, P< .001), and this is also highly significant statistically. The mean serum level of Selenium was lower in case group as compared to control group (7.72 + 2.27 vs 12.45 + 1.99, P< .001) which was also statistically significant. (Table 2 & Fig -1)
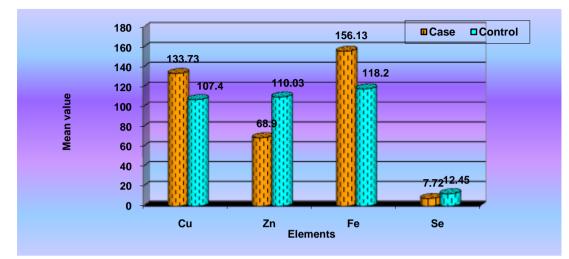
Figure 1: Graph showing mean of Various trace Elements of Case & Control Group Subjects

Discussion

The importance of trace minerals or 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 recognized 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 (9, 10). 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 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). The same finding was reported by Takashi Himoto et al 2018, Vijaylaxmi et al 2015, their results indicate that zinc concentration is associated with viral hepatitis, decreasing with the development of cirrhosis and low function of liver (11,12). Similarly the study done by Loguercio, et al in 2001, 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 (13). Alteration of Zn homeostasis in liver cirrhosis is supported by a large body of experimental and clinical evidence.

In our study the serum copper content was found significantly increased in patients with liver cirrhosis in comparison to the control group (Table 2, Figure 1).The same finding was reported by Vijaylaxmi et al in 2015.Their results indicate that the copper level of the patients with liver cirrhosis and hepatocellular carcinoma were significantly higher than in patients with chronic hepatitis and controls (12). Similarly one study was carried out by Dario et al in 2006.They revealed that the content of copper leveling plasma was significantly higher in Liver Cirrhosis patients compared to healthy controls (14).

Similarly, the mean value of iron in table no-2(Fig-1) summarized that the liver cirrhotic patients has increased serum iron concentration than the normal subjects. Hence the difference between the two samples mean statistically differ significantly i.e. P<0.001.The same findings were reported by Sandra et al in 2016 (15).

The mean serum level of Selenium was also found lower in case group as compared to control group which was statistically significant. Similar results were obtained by Ashwin et al in 2020 in patients with alcoholic hepatitis (16) and Vijaylaxmi et al 2015 in liver cirrhosis patients (12).

Conclusion

In conclusion, this study showed that the levels of serum trace minerals (Cu, Zn, Fe, and Se) were significantly altered in patients with liver cirrhosis compared to control subjects. The levels of trace minerals were also correlated with the severity of the disease. These findings suggest that serum trace elements may play an important role in the pathogenesis of liver cirrhosis and may serve as potential biomarkers for disease severity. Further studies are needed to confirm these findings and to explore the potential therapeutic role of trace elements in the management of liver cirrhosis.

References

1. Yuan-Bin Liu , Ming-Kai Chen. Epidemiology of liver cirrhosis and associated complications: Current knowledge and future directions World J Gastroenterol. 2022 Nov 7;28(41):5910-5930

2. Yoon Y-H, Yi H, Thomson PC. Alcohol-related and viral hepatitis C-related cirrhosis mortality among Hispanic subgroups in the United States, 2000-2004. Alcohol Clin Exp Res. 2011 Feb ;35(2):240–9.

3. Donghee Kim et al, Andrew A Li, Ryan B Perumpail, George Cholankeril, Stevan A Gonzalez, Won Kim, Aijaz Ahmed. Disparate trends in mortality of etiology specific chronic liver disease among hispanic subpopulations. Clin Gastroenterol Hepatol 2019 July;17(8):1607-1615.

4. Anthony PP, Ishak KG, Nayak NC, Poulsen HE, Scheuer PJ, Sobin LH. The morphology of cirrhosis. Recommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. J Clin Pathol. 1978 May ;31(5):395–414.

5. Arakawa Y, Moriyam M. Liver cirrhosis and metabolism (sugar, protein, fat and trace elements). Hepatol Res. 2004 Dec ;30:46–58.

6. Zandi M, Adib-Hajbagheri M, Memarian R, Nejhad A, Alavian S. Effects of a self-care program on quality of life of cirrhotic patients referring to Tehran Hepatitis Center. Health Qual Life Outcomes [Internet]. 2005 May 18;3(1):35.

7. Alberino F, Gatta A, Amodio P, Merkel C, Di Pascoli L, Boffo G, et al. Nutrition and survival in patients with liver cirrhosis. Nutrition. 2001 Jun;17(6):445–50.

8. Halliwell B. Antioxidants in Human Health and Disease. Annu Rev Nutr . 1996 Jul;16(1):33–50.

9. Bhattacharya PT, Misra SR, Hussain M. Nutritional Aspects of Essential Trace Elements in Oral Health and Disease: An Extensive Review. Scientifica (Cairo). 2016 Jun 28;2016:1–12.

10. Takashi Himoto , Tsutomu Masaki Current Trends of Essential Trace Elements in Patients with Chronic Liver Diseases Nutrients. 2020. 2020 Jul 14;12(7):2084.

11. Takashi Himoto , Tsutomu Masaki. Associations between Zinc Deficiency and Metabolic Abnormalities in Patients with Chronic Liver Disease. Nutrients 2018 Jan 14;10(1):88.

12. Vijaylaxmi Nangliya, Anjali Sharma, Dharamveer Yadav, Shyam Sunder, Sandeep Nijhawan, Sandhya Mishra. Study of trace elements in liver cirrhosis patients and their role in prognosis of disease Biol Trace Elem Res. 2015 May;165(1):35-40.

13. Loguercio C, De Girolamo V, Federico A, Feng SL, Crafa E, Cataldi V, et al. Relationship of Blood Trace Elements to Liver Damage, Nutritional Status, and Oxidative Stress in Chronic Nonalcoholic Liver Disease. Biol Trace Elem Res. 2001 Sep;81(3):245–54.

14. Dario Rahelic, Milan Kujundzic, Zeljko Romic, Kristina Brkic, Mladen Petrovecki. Serum concentration of zinc, copper, manganese and magnesium in patients with liver cirrhosis. Coll Antropol. 2006 Sep; 30(3):523-8.

15. Sandra Milic , Ivana Mikolasevic, Lidija Orlic , Edita Devcic, Nada Starcevic-Cizmarevic, Davor Stimac, Miljenko Kapovic, Smiljana Ristic The Role of Iron and Iron Overload in Chronic Liver Disease. Med Sci Monit. 2016. Jun 22;22:2144-51.

16. Ashwin Dhanda , Stephen Atkinson, Nikhil Vergis, Doyo Enki , Andrew Fisher , Robert Clough , Matthew Cramp , Mark Thursz. Trace element deficiency is highly prevalent and associated with infection and mortality in patients with alcoholic hepatitis. Aliment Pharmacol Ther. 2020 Aug;52(3):537-544.

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