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Original Research Article

Assessment of copper and zinc in liver diseases

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ABSTRACT

Introduction: The liver is a primary storage site for a variety of metabolites. It plays a role in wide variety of metabolic, toxic, excretory, circulatory and defence functions inside the body. Damage to the organ may not evidently affect its activity since the liver has considerable functional reserve. Liver disease is a common term for any damage that reduces the functioning of the liver. Chronic liver disease is identified by gradual destruction of liver cells resulting in fibrosis. It is affected by different conditions including viral hepatitis, excessive alcoholism, genetic, autoimmune and NAFLD.

Materials and Methods: The present study was carried out in Govt. Medical College, Jalaun at Department of Biochemistry. The diagnosis of Liver disease was done by ultrasonographic examination of liver. This study comprised a total of 50 patients, 25 of whom were healthy controls and 25 of whom were Liver Disease patients. After overnight fasting 8-12 hours (under aseptic condition) blood sample (8ml) was drawn from antecubital vein of each subject using a plain vial and was analyzed for serum Cu, Zn & liver profile parameters (serum bilirubin, serum SGOT, serum SGPT and serum ALP done by colorimetric method and calmagnite method, diazo method, IFCC method and assessed by kinetic method respectively.

Results: The present study's findings, indicates that the level of serum copper in liver disease patient was $127.38 \pm 28.81 \mu\text{g/dl}$, which is significantly higher than that of $86.54 \pm 15.88 \mu\text{g/dl}$ found in healthy controls ($p < 0.001$). Also, serum copper is strongly linked with biochemical parameters of liver enzyme (SGOT & SGPT).

Likewise, the mean value of serum zinc in liver disease were $58.08 \pm 13.11 \mu\text{g/dl}$, which is significantly lower than that of $69.88 \pm 6.67 \mu\text{g/dl}$ found in healthy subjects. Further, serum zinc has shown a significant weakly linked with serum SGPT.

Therefore, during routine assessments of individuals with liver disease, serum trace elements (Cu and Zn) can be highly effective indicators for detecting the severity of liver damage.

Conclusion: Thus, based on the findings of our current investigation, zinc and copper supplementation, as well as a reduction in copper intake, may help to enhance patient survival and preventing the development of hepatitis B to liver cirrhosis.

Considering findings of the study, it is recommended that serum trace element concentrations be corrected on a regular basis to help with various problems of liver cirrhosis and maybe to slow the progression of liver disease.

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1. Introduction

A variety of functions are performed by the liver, including metabolism, immune responses, and the production of

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complex compounds. In addition to its role in metabolism, the liver also transports and distributes trace elements.¹ A multitude of causes contribute to their development, including infection, autoimmune, metabolic, vascular, medicines, carcinogens, and other unidentified factors. The progression of liver disease usually results in cirrhosis and ultimately, fatal liver failure.

A deficiency or excess of trace elements has a significant impact on many biological systems. In some studies, trace elements which includes Zn & Cu additionally have been proven to have crucial defensive or stimulating results at the path of Liver Disease.^{2,3}

There are several enzymes and redox processes in which copper is involved. In the rapidly progressive reaction, ceruloplasmin serves as a copper transporter in the body.⁴ Increased iron absorption and phospholipid synthesis are achieved because of its effects on hemoglobin synthesis. Nonetheless, it is toxic in excessive quantities and can damage cellular structures.⁵ As a result of the elevated copper level in the liver, the liver parenchyma was thought to be subject to lipid peroxidation, resulting in abnormal cell membranes, decreased fluidity, enzyme inactivation, and ion permeability impairments.⁶

2. Materials and Methods

The study will be conducted in the Department of Biochemistry, Rajkiya Medical College, Jalaun (Orai). The study group consisted of 25 liver disease patients and 25 controls with informed consent was taken in the study. After an overnight fasting 8-12hrs, blood sample (8 ml) was obtained from all subjects & dispensed into plain vials under proper aseptic conditions. After centrifugation 3000 RPM for 5 min, serum sample was used for analysis of serum copper, serum zinc and serum liver profile by different methods.

1. Cu and Zn serum levels were estimated with method of Colorimetric.
2. The Diazo technique was used to calculate total and direct bilirubin.
3. Serum glutamic pyruvic transaminase (SGPT/ALT) & Serum glutamic-oxaloacetic transaminase (SGOT/AST) were estimated by IFCC method.
4. Serum ALP was estimated by Kinetic method.

2.1. Inclusion criteria

1. Newly diagnosed cases of liver disease patients.
2. Individual aged 30-60 years.

2.2. Exclusion criteria

1. Malignancy
2. Diabetes mellitus
3. Pregnancy

4. Drugs affecting levels of trace elements e.g. corticosteroids, digoxin thiazide, diuretics & others.

2.3. Statistical analysis

The statistical analysis performed using SPSS. The results are shown as mean \pm SD (Standard Deviation) and median (range). The data was analyzed using the student's t-test. The p value of <0.001 was denoted as statistically significant.

2.4. Study design

Hospital based observational and case-control study.

3. Results and Discussions

The mean levels of serum Total bilirubin (8.10 ± 3.02 mg/dl), direct bilirubin (3.86 ± 1.88 mg/dl), indirect bilirubin (5.40 ± 2.88 mg/dl), SGOT (108.22 ± 34.50 IU/L), SGPT (124.64 ± 32.68 IU/L) and ALP (132.77 ± 19.58 U/L) of liver disease shows when compared to the mean of serum total bilirubin, there is a statistically significant difference total bilirubin (0.72 ± 0.12)mg/dl, direct bilirubin (0.20 ± 0.09 mg/dl), indirect bilirubin (0.52 ± 0.12)mg/dl, SGOT (28.15 ± 5.50 IU/L), SGPT (32.60 ± 6.20 IU/L) and ALP (82.50 ± 21.50 IU/L) in controls ($p < 0.001$ for all).

Trace elements, particularly those with antioxidant system, such as Zn, and those with redox properties, like Cu. For hepatic disorders, a variety of biochemical measures are frequently monitored, including TB, DB, INB, SGOT, SGPT & ALP.⁷ Infectious, metabolic, autoimmune, genetic, and drug-induced etiologies all have a role in chronic liver illnesses.

In present study, we included various measured parameters and found that the serum total bilirubin, serum direct bilirubin and serum indirect bilirubin was 8.10 ± 3.02 mg/dl, 3.86 ± 1.88 mg/dl and 5.40 ± 2.88 mg/dl respectively in liver disease patients, which is found to be statistically higher than the mean values of their respective controls (0.72 ± 0.12)mg/dl, (0.20 ± 0.09)mg/dl and (0.52 ± 0.12)mg/dl ($p < 0.001$).

Also, we found that the serum levels of SGOT, SGPT and ALP was 108.22 ± 34.50 IU/L, 124.64 ± 32.68 IU/L and 132.77 ± 19.58 U/L in Liver Diseases patients 28.15 ± 5.50 IU/L, 32.60 ± 6.20 IU/L and 82.50 ± 21.50 U/L were in the healthy controls respectively. This signifies increased in the SGOT, SGPT and ALP in Liver Diseases cases as comparison to individuals ($p < 0.001$).

The main prospective of our study was to compare the levels of Cu & Zn in patients of chronic liver diseases to healthy controls. The serum concentration of copper between the cases and controls was 127.38 ± 28.81 µg/dl and 86.54 ± 15.88 µg/dl. It has been evident that raised levels of serum copper was observed in liver disease patients as compared to their controls and their statistically, the

Table 1: Mean and SD of cases & controls, serum copper and serum zinc levels were compared

Trace elements	Patients Mean \pm SD n= 25	Control Mean \pm SD n= 25	p value
Copper ($\mu\text{g}/\text{dl}$)	127.38 \pm 28.81	86.54 \pm 15.88	<0.001
Zinc ($\mu\text{g}/\text{dl}$)	58.08 \pm 13.11	69.88 \pm 6.67	<0.001

The data were expressed as mean \pm SD. The data was analyzed using the student's t- test.* indicates p<0.001 and statistically significant

Table 2: Comparison of various measured parameters between chronic liver disease patients and healthy controls

Parameters measured	Patients (n= 25)	Controls (n= 25)	p value
Total bilirubin (mg/dl)	8.10 \pm 3.02	0.72 \pm 0.12	<0.001
Direct bilirubin (mg/dl)	3.86 \pm 1.88	0.20 \pm 0.09	<0.001
Indirect bilirubin (mg/dl)	5.40 \pm 2.88	0.52 \pm 0.12	<0.001
SGOT (IU/L)	108.22 \pm 34.50	28.15 \pm 5.50	<0.001
SGPT (IU/L)	124.64 \pm 32.68	32.60 \pm 6.20	<0.001
ALP (IU/L)	132.77 \pm 19.58	82.50 \pm 21.50	<0.001

The data were expressed as mean \pm SD. The data was analyzed using the student's t- test.* indicates p<0.001 and statistically significant.

relationship is shown to be significant (p<0.001).

There was an elevated level of serum copper in liver disease cases than healthy controls. This is because copper is a cofactor in collagen production, which prevents fibrosis in chronic liver disease.⁸ In accordance with our findings, serum copper levels significantly increased as liver disease progressed.⁹ Copper levels increase markedly with liver disease severity compared to early stages of cirrhosis.¹⁰ As indicated copper levels may be increased due to increased intestinal uptake. Copper reserves may also be released due to less liver excretion and tissue breakdown.¹¹

The another parameter of our study, a serum zinc has shown the mean values of serum Zn levels of 58.08 \pm 13.11 $\mu\text{g}/\text{dl}$ in patients of Liver Diseases and in controls were 69.88 \pm 6.67 $\mu\text{g}/\text{dl}$ and signifies statistically lower levels as compared their healthy subjects (p<0.001). Nevertheless, other studies determined that patients levels of zinc were slightly reduced as compared to healthy controls. They suggested that Zn supplementation could reduce inflammation and contribute to faster illness resolution in cirrhotic due to lower serum Zn levels.¹²

Additionally, serum Zn levels found in cases were lower compared to controls, which was also reported in studies who noted the same thing. Furthermore, when liver cells are damaged or inflamed, they take up more Zn to synthesize Zn-related enzymes, nucleic acids, proteins, and enzymes that are related to nucleic acids. The liver becomes increasingly damaged, resulting in a decrease in Zn consumption and absorption due to reduced appetite, poor high portal vein flow, and decreased gastrointestinal and intestinal function. Consequently, because of the diffusion characteristic of blood Zn, there is less association with Zn and it is rapidly excreted through renal excretion.

4. Conclusions

Moreover, we found that of all liver disease patients, the majority of patients (40%) falls into the 50-60 years age

group, and males were affected more than females.

We understand from the current study that the serum copper concentration in Liver Disease patients is significantly higher than that of normal healthy individuals, while serum zinc concentrations in Liver Disease patients are significantly lower than that of controls.

Increasing Cu levels may result in liver dysfunction and altered trace element metabolism in liver disease. So, patients with chronic liver disease need less Cu in their diet or through therapeutic means, while cirrhosis severity increases when Zn levels are low.

In order to avoid Zn deficiency and use it as a sensitive marker of liver cirrhosis, Zn supplementation should be included among the micronutrients given special attention in cirrhotic therapy.

Individuals with liver disease should be screened for serum Cu & Zn levels in order to determine whether a treatment strategy can be developed to slow the progression of their disease.

5. Source of Funding

None.

6. Conflict of Interest

None.

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