

Study of Serum Zinc and Magnesium Levels in Patients of Liver Cirrhosis

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ABSTRACT

The role of serum zinc and magnesium in liver cirrhosis is still a matter of investigation. In the present case control study, serum zinc and magnesium levels were monitored in 100 diagnosed cases of liver cirrhosis patients and 100 age and sex matched healthy controls. The serum zinc and magnesium levels were significantly ($p < 0.001$) low in liver cirrhosis patients as compared to healthy controls. Our findings showed that serum zinc and magnesium could be used as a valuable sensitive indicator of liver diseases, like liver cirrhosis. The correction of serum zinc and magnesium concentrations might have a beneficial effect on progression of liver cirrhosis. It would be recommendable to analysis of serum zinc and serum magnesium as a routine analysis.

Key words: Magnesium, Liver Cirrhosis, Hypomagnesaemia, Zinc, Hypozinceamia.

INTRODUCTION

Liver cirrhosis is a worldwide health problem. It is the end stage of liver fibrosis characterized by nodule formation¹. Most commonly causes of liver cirrhosis are alcoholism and hepatitis B or C. Epidemiology of liver cirrhosis varies between gender, geographical distribution and ethnic groups². Zinc is essential for the synthesis of many coenzymes that mediate biogenic amine synthesis and metabolism^{3, 4}. It is highly concentrated in the synaptic vesicles of glutanatergic neurons, which are located mainly in the forebrain that interconnects most of cerebral cortices and limbic structures⁴. Reduced serum and hepatic zinc levels correlated with reduced liver ornithine transcarbonylase activity and increased plasma ammonia level^{5, 6}. Some alterations of patients with cirrhosis may be associated with zinc deficiency: wound healing, lack of appetite, alopecia, hypogeusia, gonadal growth retardation⁷ added it is also associated with hepatic encephalopathy^{8, 9}.

Magnesium is an essential component of human body and other mammals, 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. Magnesium is associated with more than 300 enzymatic reactions involving energy metabolism and protein and nucleic acid synthesis^{10, 11}. Magnesium also involved in immunoglobulin synthesis, immune cell adherence, antibody-dependent cytotoxicity, GM lymphocyte binding, T helper B-cell adherence and additional responses¹². Only 0.3% of total body magnesium exists in serum^{13, 14}. In spite of all these knowledge regarding importance of zinc and magnesium in human body, very little is known about zinc and magnesium metabolism in diseased states, in comparison to the extensive studies of calcium, sodium and potassium etc. The data that are available from such studies are not conclusive to draw definite relation between serum zinc and magnesium with liver cirrhosis.

Hence, the present study was undertaken to determine the serum zinc and serum magnesium levels in liver cirrhosis patients and assessment of these micronutrients that would be beneficial in liver cirrhosis patients to avoid significant derangements in the health status.

MATERIALS AND METHODS

The study was carried out in the Department of Biochemistry, Gandhi Medical College and associated Hamidia Hospital, Bhopal (M.P) during July 2010 to April 2012. Total 200 subjects were selected and divided into two groups. Group I included 100 diagnosed cases with liver cirrhosis. They were recruited for the study after taking their due written consent. The diagnosis of liver cirrhosis was established by detailed history of all such patients, positive findings on clinical examination, relevant biochemical tests and histopathological examination of the liver tissues. The subjects were in the age group of 25 to 65 years male and female. Group II included 100 healthy control subjects. The age limits of this group were also 25 to 65 years in both male and female.

Fasting blood samples were collected from both controls and patients for a series of laboratory investigation using standard protocols.

The study was approved by the Institutional Ethical Committee, for biomedical research.

Exclusion Criteria

Hypertension, chronic diarrhea, alcoholism, use of diuretics, reduced renal function and past history of severe liver disorders were exclusion criteria.

Estimation of Serum Zinc by Colorimetric Method

Serum zinc was estimated by colorimetric method of Akita Abe.*et al.*¹⁵. Zn⁺⁺ reacts with NITRO-PAPS at room temperature and form a colored complex which intensity is proportional to the zinc concentration present in the sample. The method

does not require sample deproteinization either sample blank.

Zinc + NITRO-PAP → Purple colored complex

Estimation of Serum Magnesium by Xylidyl Blue Spectrophotometric Method

Serum magnesium was estimated by method of Kramer, B. Tisdall *et al* [16]. Serum magnesium ions react with Xylidyl Blue in an alkaline solution to produce a red complex that is measured spectrophotometrically. The intensity of colored produced is directly proportional to magnesium concentration. Calcium interference is virtually eliminated by use of EGTA and a surfactant system is included to remove protein interference.

Magnesium + Xylidyl Blue $\xrightarrow{\text{Alkaline Medium}}$ Red colored complex

Statistical Analysis

All the data were analyzed by using the SPSS version 10.0. Values presented are Means \pm standard deviation (SD). To test the significance between the study group and the con-trol groups were analyzed by a student's t- test. The p-value (p <0.05) was considered significant.

RESULTS AND DISCUSSION

Table-1 Shows the age and gender distribution in liver cirrhosis patients and healthy control. Among 100 liver cirrhosis patients, 60 were males and 40 were females. Among 100 healthy controls 67 were males and 33 were females.

Table-2 Shows serum zinc level ($\mu\text{g}/\text{dl}$) in liver cirrhosis patients and healthy control. It describes the serum zinc levels significantly (p<0.001) decrease in liver cirrhosis patients.

Table 1: Age and gender distribution in liver cirrhosis patients and healthy controls

Age in years	(Liver cirrhosis patients) n=100			(Healthy controls) n=100		
	No of cases	Male	Female	No of cases	Male	Female
25-35	11	05	05	10	07	05
36-45	17	10	08	20	10	08
46-55	45	30	15	40	35	10
56-65	27	15	12	30	15	10

Table-3 Shows serum magnesium level (mg/dl) in liver cirrhosis patients and healthy control. It describes the serum magnesium level significantly ($p < 0.001$) decrease in liver cirrhosis patients.

Table-4 & Table-5 Shows Serum zinc and serum magnesium levels in male and female liver cirrhosis patients and healthy controls. It describe the serum zinc and serum magnesium levels both more significantly ($p < 0.001$) decreased in male liver cirrhosis patients as compare to female liver cirrhosis

Table 2: Serum zinc level ($\mu\text{g/dl}$) in liver cirrhosis patients and healthy controls

	Range	Mean \pm SD	P-value	Significant
Liver cirrhosis patients	30.08-57.13	46.38 \pm 8.59	<0.001	HS
Healthy Controls	58.09 - 112.7	67.34 \pm 10.58		

*(<0.001 = HS)

Table 3: Serum magnesium level (mg/dl) in liver cirrhosis patients and healthy controls

	Range	Mean \pm SD	P-value	Significant
Liver cirrhosis patients	0.68-1.03	0.85 \pm 0.17	<0.001	HS
Healthy Controls	0.99-1.92	1.36 \pm 0.40		

*(<0.001 = HS)

Table 4: Serum zinc and magnesium level in male liver cirrhosis patients and healthy controls

	Male		P-value
	Liver cirrhosis patients (Mean \pm SD)	Healthy controls (Mean \pm SD)	
Serum Zn level	44.28 \pm 7.56	63.31 \pm 8.48	<0.001
Serum Mg level	0.88 \pm 0.16	1.32 \pm 0.40	<0.001

*(<0.001 = HS)

Table 5: Serum zinc and magnesium levels in female liver cirrhosis patients and healthy controls

	Female		P-value
	Liver cirrhosis patients (Mean \pm SD)	Healthy controls (Mean \pm SD)	
Serum Zn level	47.38 \pm 9.39	65.24 \pm 7.58	<0.001
Serum Mg level	0.90 \pm 0.14	1.34 \pm 0.34	<0.001

*(<0.001 = HS)

The liver is important for the regulation of zinc homeostasis, while zinc is necessary for proper liver function. Decreased zinc level has been implicated in both acute and chronic liver disease states. Trace elements concentrations in plasma are reported to be a good indicator for diagnosis and prognosis of many diseases¹⁷. Previous many studies already reported decrease in zinc level (Hypo zincemia) in liver cirrhotic patients. The study of Pramoolsinsap *et al.*, reported that serum zinc levels were significantly decreased in patients with chronic active hepatitis, liver cirrhosis, and hepatocellular carcinoma¹⁸. Lin *et al.*, showed that the zinc concentration in the serum of Chinese patients with hepatic cirrhosis was significantly less than as compare to control¹⁹. A study with adult patients with cirrhosis found an association between zinc deficiency and the increase in the severity of cirrhosis^{20, 21}.

Decrease in serum magnesium level also found in Miller's research²² as well as in study of Sullivan *et al.*,²³ in liver cirrhosis patients. The study of Rocchi²⁴ and Suzuki²⁵ also reported the same findings. The factors that might cause hypomagnesaemia in patients with liver cirrhosis include 1. Poor absorption of magnesium in distal jejunum 2. Administration of magnesiuric diuretics (furosemide) and 3. Decreased plasma level of albumin^{26, 27}. This finding is in conformity with the values reported by Wallach *et al.*,²⁸ , who reported the serum magnesium concentration significantly decrease in patients with liver cirrhosis in comparison to the control groups.

Many studies prove that mg deficiency associated with alcoholic fatty liver disease because the connection of hypomagnesaemia with alcoholism has been known for long time^{29,30}. Several mechanism associated with alcoholism contributed to magnesium deficiency, including urinary Mg wastage, malnutrition, gastrointestinal losses, phosphate deficiency, acidosis, vitamin D deficiency and free fatty acidemia associated with alcohol withdrawal²⁹. We found that, decreased Mg levels not only in patients with alcoholic disease but also in non alcoholic disease suggests that alcoholism can not be the only cause of hypomagnesaemia in patients with fatty liver and that in the latter patients also other factors participate in pathogenesis of hypomagnesaemia. Koivisto *et al.*,³¹ described hypomagnesaemia in patients with cirrhosis.

CONCLUSION

In conclusion, our study showed that lower zinc and magnesium concentrations associated with an increase in cirrhosis severity. Therefore, zinc and magnesium should be included among the micronutrients that are given particular consideration in the management of cirrhosis in order to prevent zinc and magnesium deficiency and could be used as a sensitive indicator of liver cirrhosis. A routine assessment of zinc and magnesium in liver cirrhosis patients may be effective in management protocol and to reduce progression of the disease and avoid significant derangements in the health status.

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