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A PROSPECTIVE STUDY OF SERUM MAGNESIUM IN LIVER DISEASE

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Abstract

Introduction: The liver is a multifaceted organ crucial for metabolic processes and various biochemical activities, including metabolic regulation, excretion, secretion, storage, and detoxification. Liver cirrhosis represents the last stage of liver fibrosis, marked by developing regenerative nodules surrounded by fibrous septa due to persistent hepatic injury. While alcoholism and hepatitis B or C infections are prominent causative factors, diverse elements such as advanced age (age >50 years), obesity, insulin resistance/type 2 diabetes, gastrointestinal disorders, hypertension, and hyperlipidemia collectively contribute to its pathogenesis.

Materials and methods: This is a cross-sectional observational study. The study was conducted in the Department of General Medicine, World College of Medical Sciences and Research Hospital, Jhajjar, Haryana from May 2023 to April 2024. 110 patients of liver disease admitted in wards and emergencies under the Department of General Medicine, after fulfilling all inclusion and exclusion criteria were included. Basic investigation including complete blood count (CBC), renal function test (RFT), liver function test (LFT), serological test, and estimation of serum magnesium levels were carried out in all the patients included in the study.

Results: All of the enrolled 110 patients were diagnosed with liver disease. The age of the study population varied from 16 years to 76 years of age with mean age of 46.9. Graph-1 and Graph-2 shows the distribution of total bilirubin and serum magnesium in different age group. The normal value of total bilirubin ranges between 0.2 to 1.0 mg%, the values of total bilirubin in our study population ranged from 0.7 to 26 mg %, with a mean of 6.457. The normal value of serum magnesium ranges between 1.9 to 2.9 mg%, the values of serum magnesium in our study population ranged from 0.9 to 2.7 mg %, with a mean of 1.73 mg %, showing the low level of serum magnesium in most of the liver disease populations in our study. Further, we observed the possibility of link between the total bilirubin levels and the serum magnesium levels in all the patients with liver diseases, and it was noted that there is no correlation between the total bilirubin levels and serum magnesium levels, a non-significant.

Conclusion: In our study conducted, patients with liver diseases presented with ascites, lower limb oedema, icterus, and some with hepatic encephalopathy. Majority of them are chronic liver disease, almost all of them had lower serum magnesium levels. The correlation between the level of serum magnesium and the total bilirubin levels of the patients in our study is observed and it showed negative correlation between level of total bilirubin and magnesium, a non-significant relationship.

Key Words: liver, hepatic encephalopathy, bilirubin, magnesium, hypertension, and hyperlipidemia.

INTRODUCTION

The liver is a multifaceted organ crucial for metabolic processes and various biochemical activities, including metabolic regulation, excretion, secretion, storage, and detoxification. Liver cirrhosis represents the last stage of liver fibrosis, marked by developing regenerative nodules surrounded by fibrous septa due to persistent hepatic injury.[1] While alcoholism and hepatitis B or C infections are prominent causative factors, diverse elements such as advanced age (age >50 years), obesity, insulin resistance/type 2 diabetes, gastrointestinal disorders, hypertension, and hyperlipidemia collectively contribute to its pathogenesis. This pathological condition poses a significant global health challenge, capable of inducing portal hypertension, leading to the development of gastroesophageal varices and intestinal edema, thereby compromising the liver's physiological function.[2]

Magnesium stands as the second most plentiful intracellular ion and holds the fourth position among cations within the human body. A mere 0.3% of the total body magnesium resides in serum, highlighting its predominantly intracellular distribution. Magnesium exhibits a broad presence across various cellular compartments, including the nucleus, cytoplasm, mitochondria, and endoplasmic reticulum.[3] Its significance extends to numerous cellular processes, encompassing DNA replication and repair, ion transportation, intermediary metabolism, cell proliferation, and signal transduction. Functionally, magnesium forms complexes with ATP, serving as a vital cofactor in approximately 300 enzymatic reactions of various metabolisms. It is essential for a healthy immune system, acting on various processes like antibody production, immune cell interaction, destruction of infected cells and responses mediated by T-helper and B-cells.

Patients with liver cirrhosis usually have low body magnesium levels. Since our understanding of the mechanisms involved in magnesium homeostasis has improved, it has been shown that both serum and cellular magnesium levels are significantly lower in cirrhosis patients.[4]

According to a recent 2021 study published in the journal of hepatology, it was found that both patients and mice that had non-alcoholic steatohepatitis also had high amounts of cyclin M4 (CNNM4) protein. This protein has a job of transporting magnesium out of the liver. It is the

responsible party behind the imbalance of magnesium levels that can lead to liver disease development. Furthermore, magnesium supplementation can improve liver function in certain liver diseases.[5] This study comprehensively reviews the changes in magnesium concentrations associated with liver diseases.

AIMS

To study the levels of serum magnesium in acute and chronic liver diseases and to see any correlation between serum magnesium and serum bilirubin in acute and chronic liver disease.

MATERIALS AND METHODS

This is a cross-sectional observational study. The study was conducted in the Department of General Medicine, World College of Medical Sciences and Research Hospital, Jhajjar, Haryana from May 2023 to April 2024.

Study Group: 110 patients of liver disease admitted in wards and emergencies under the Department of General Medicine, after fulfilling all inclusion and exclusion criteria were included.
Sample Size: To achieve the objective of this study, input for statistical sample size calculation was taken from the study by Prakash Gurudevarahalli Made Gowda et al. (2015).

Minimum required sample size with ‘pedal oedema’ taking as factor and p value is 72 % for 12 % error and for 95 % confidence level, by using “Open Epi version-2” software we got sample size 109, marginally we have taken the sample size of 110.

Inclusion Criteria:

Diagnosed cases of acute and chronic liver diseases.

Exclusion Criteria:

1. Cases of hepatocellular Carcinoma,

2. Current treatment with magnesium supplements

3. Patients not willing for participation in the study.

Method of data collection:

We collected data from 110 patients with confirmed cases of liver diseases who were admitted in Department of General Medicine, World College of Medical Sciences and Research Hospital, Jhajjar, Haryana from May 2023 to April 2024. Basic investigation including complete blood count (CBC), renal function test (RFT), liver function test (LFT), serological test, and estimation of serum magnesium levels were carried out in all the patients included in the study.

Statistical Analysis:

Data were entered in Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) software version.19, percentages and proportions were used for qualitative data and mean and standard deviation for quantitative data. Chi-square test for proportions and student's t test was used for quantitative data. $P < 0.05$ is considered as statistically significant.

RESULTS

All of the enrolled 110 patients were diagnosed with liver disease. The age of the study population varied from 16 years to 76 years of age with mean age of 46.9. Graph-1 and Graph-2 shows the distribution of total bilirubin and serum magnesium in different age group. The normal value of total bilirubin ranges between 0.2 to 1.0 mg%, the values of total bilirubin in our study population ranged from 0.7 to 26 mg %, with a mean of 6.457.

The normal value of serum magnesium ranges between 1.9 to 2.9 mg%, the values of serum magnesium in our study population ranged from 0.9 to 2.7 mg %, with a mean of 1.73 mg %, showing the low level of serum magnesium in most of the liver disease populations in our study.

Further, we observed the possibility of link between the total bilirubin levels and the serum magnesium levels in all the patients with liver diseases, and it was noted that there is no correlation between the total bilirubin levels and serum magnesium levels, a non-significant.

S.No	Age group	N	Percentage
1	16-24	5	4.54
2	24-32	10	9.09
3	32-40	25	22.72
4	40-48	36	32.72
5	48-56	15	13.63
6	56-64	7	6.36
7	64-72	5	4.54
8	More than 72	7	6.36

Table 1: Age Distribution

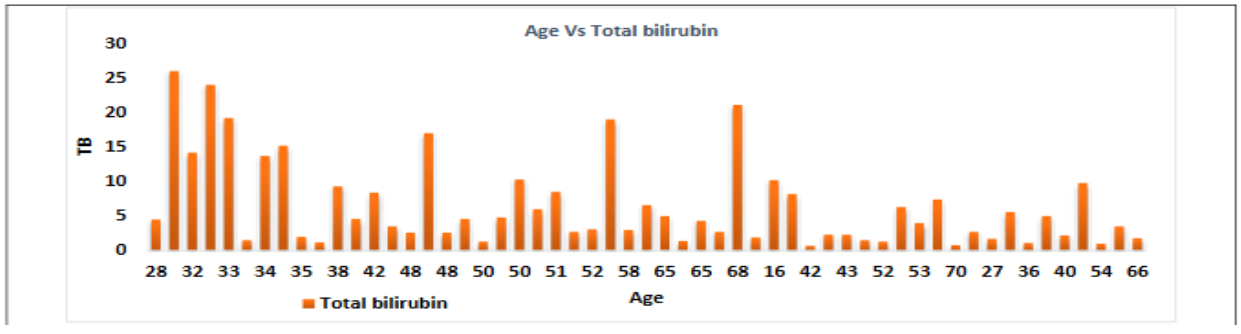

Figure 1: Comparison of Age of the Patient with Total Billirubin

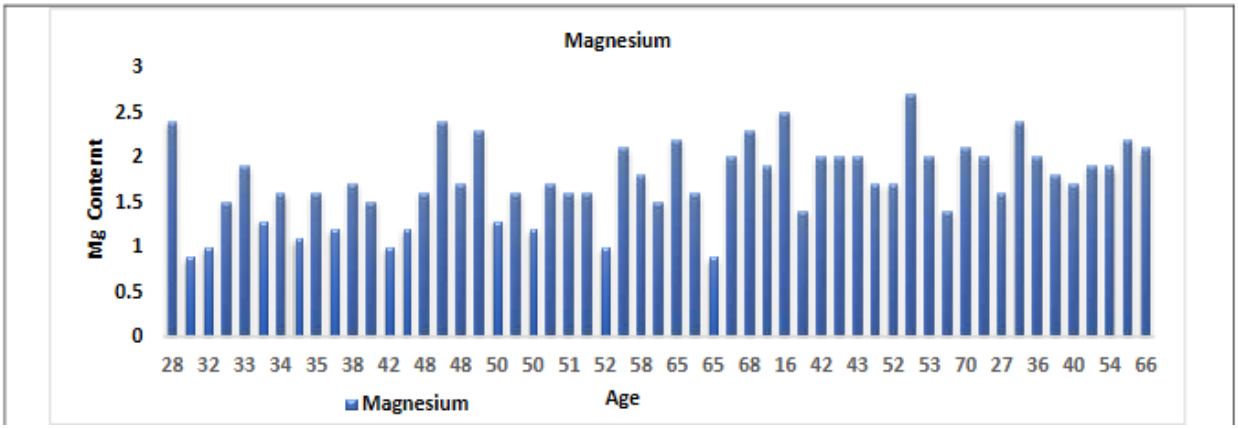

Figure 2: Comparison of Age of the Patient with Serum Magnesium

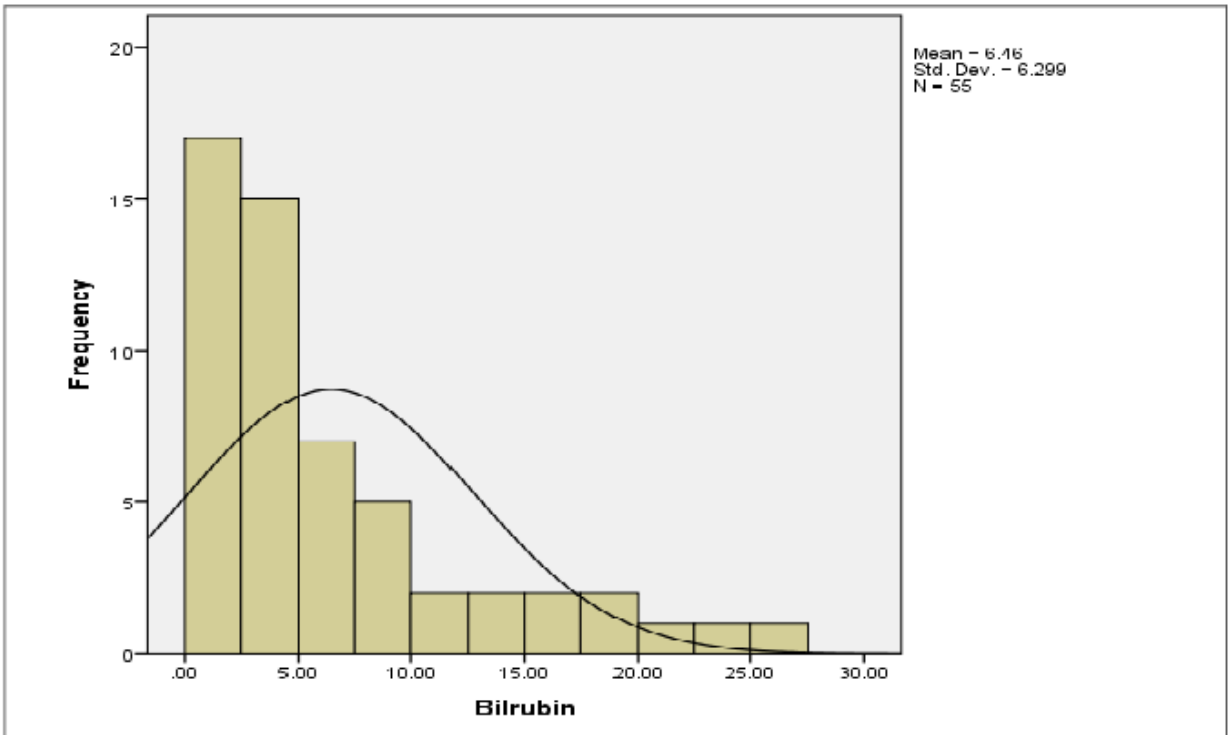

Figure 3: Bilirubin Levels Observed in the Study Group

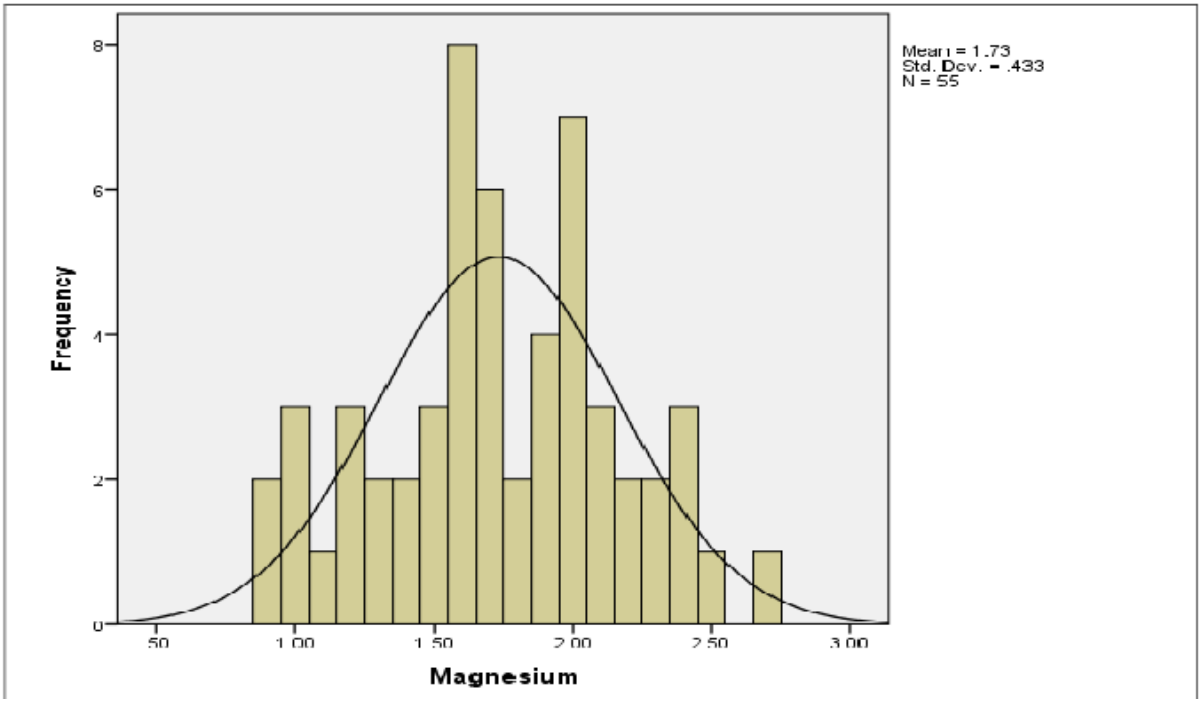

Figure 4: Serum Magnesium Levels Observed in the Study Population

Correlations			
		Magnesium	**Billirubin**
Magnesium	Pearson's correlation	1	0.091
	Sig. (1-tailed)		.255
	N	110	110
Bilirubin	Pearson's correlation	-.091	1
	Sig. (1-tailed)	.255	
	N	110	110

Table 2: Correlation between the level of serum magnesium and total bilirubin in liver disease patients

DISCUSSION

It was observed in our study, that there was magnesium deficiency in almost all of the liver disease patients. Magnesium is directly linked to liver function status. Liver diseases will have a remarkable effect on the body magnesium content, and magnesium levels in turn determine these disease processes. Serum zinc, magnesium, and selenium levels were significantly decreased with advancement of liver disease as compared to early stage of liver cirrhosis and showed a significant negative correlation with Child-Pugh score. Trace element abnormalities may reflect the condition of liver dysfunction. Liver dysfunction may alter the metabolism of trace elements. Some study showed that micronutrients status in liver cirrhosis correlates well with severity of liver cirrhosis.[6]

Micronutrients supplementation in liver cirrhotic patients may prevent progression of disease and development of complications. In acute and chronic liver diseases, patients show magnesium deficiency that results from reduced dietary intake, increased urinary excretion, lower plasma albumin concentrations, and hormone inactivation.[7]

Conversely, magnesium deficiency aggravates acute and chronic liver diseases and can cause liver carcinoma progression, due to mitochondrial function, defective PKC translocation, inflammatory responses, oxidative stress, and metabolic disorders. Alcohol consumption is associated with a reduction in liver Mg2+ content.16 Acute alcohol administration affects the Na+/Mg2+ exchanger as follows.[8]

It affects G protein signalling, leading to greater cAMP generation within hepatocytes, which activates the PKC pathway and disrupts PKCε translocation to the cell membrane, resulting in greater magnesium extrusion via the Na+/Mg2+ exchanger. Biochemical analysis also indicates that Mg2+ loss by hepatocytes is the result of decrease in cellular ATP concentrations, which is consistent with magnesium deficiency being characterized by markedly lower Mg2+ content in the mitochondria and cytoplasm, the two main cellular compartments containing both Mg2+ and ATP.22 Chronic alcohol administration results in an impairment of the function of both Na+-dependent and Na+-independent Mg2+ transporters (by ~75 %).[9]

The same defect in PKCε translocation is observed, and the magnesium deficiency is associated with a 17% decrease in cellular ATP concentration.23 Patients with liver cirrhosis usually have low body magnesium levels. Since our understanding of the mechanisms involved in magnesium homeostasis has improved, it has been shown that both serum and cellular magnesium levels are significantly lower in cirrhosis patients. In cirrhosis, a reduction in intracellular magnesium content has a negative impact on mitochondrial bioenergetics, which heavily depends on the appropriate intramitochondrial magnesium concentration. When mitochondrial function is impaired, oxidation in the hepatocytes is affected, which is associated with a 17 % reduction in ATP production and hepatocytes damage. The subsequent liver repair process leads to additional fibrosis and worsens the cirrhosis.[10]

CONCLUSION

In our study conducted, patients with liver diseases presented with ascites, lower limb oedema, icterus, and some with hepatic encephalopathy. Majority of them are chronic liver disease, almost all of them had lower serum magnesium levels. The importance of links between magnesium and liver function or disease, implies that novel therapeutic approaches targeting magnesium may be used to improve liver function in the future. Magnesium should be included in the micronutrients that are given in management of all liver diseases patients. The correlation between level of serum magnesium and the total bilirubin levels of all the patients in our study were also studied. Table-1 shows correlation between the level of serum magnesium and total

bilirubin in liver disease patients of our study, which reveals negative correlation between them, a non-significant relationship.

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