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Research Article

PREVALENCE OF HYPOMAGNESEMIA IN CIRRHOSIS OF LIVER AND ITS ASSOCIATION WITH SEVERITYOF THE DISEASE

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ABSTRACT

Objectives: The objectives of the study are as follows: (1) To study the prevalence of hypomagnesemia in liver cirrhosis patients. (2) To evaluate association between hypomagnesemia and severity of liver disease.

Methods: It was a cross-sectional study for 1 year. Seventy-one liver cirrhosis patients attending medicine OPD and those admitted in ward, ICU at Government Medical College, Kozhikode. Informed consent was taken from 71 liver cirrhosis patients. Samples for serum magnesium, total bilirubin, and albumin were collected from cases in blood collection tube without anticoagulant and centrifuged to get serum. Estimation of magnesium was done using colorimetric end point method. Estimation of total bilirubin was done using Diazo method and that of serum albumin with Bromocresol Green dye method. SPSS (Version 22.0) was used for analysis.

Results: Among the study patients, hypomagnesemia was prevalent in majority (71.8%) of cases. The mean magnesium levels between different grades of liver cirrhosis were statistically significant at p=0.001. Levels of serum magnesium were significantly decreased with advancement of liver cirrhosis.

Conclusion: Hypomagnesemia is prevalent in liver cirrhosis patients. Serum magnesium decreases significantly with severity of liver cirrhosis. A routine assessment of serummagnesium in liver cirrhosis patients may be effective in management protocol ofliver cirrhosis.

Keywords: Liver cirrhosis, Hypomagnesemia, Hyperbilirubinemia, Prevalence, Serum albumin, Diazo method.

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INTRODUCTION

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end stage liver disease [1]. Globally, cirrhosis is the leading cause of liver-related death [2,3].

Decompensation in patients with compensated cirrhosis is usually characterized by the first occurrence of ascites, oesophageal variceal bleeding, hepatic encephalopathy, and, in some individuals, increased bilirubin concentration [4]. As cirrhosis progresses, decompensation occurs with clinical signs of portal hypertension. Once decompensation sets in, 10-year survival is only about 20% [5].

Magnesium deficiency is a common problem in hospital inpatients, with a prevalence of about 10% [6]. Higher intakes of magnesium may be associated with a decreased risk of mortality due to liver disease particularly among alcohol drinkers and those with hepatic steatosis [7].

In conclusion, this review demonstrates the importance of links between magnesium and liver disease and implies that novel therapeutic approaches giving importance to magnesium may be used to improve liver function in the future.

METHODS

The study was conducted after the approval of the Institutional Ethics Committee (IECNO: GMCKKD/RP2017/EC/186). After getting written informed consent, detailed history and demographic data were obtained from all subjects. It was a cross-sectional study conducted at Medicine OPD, ward, and ICU at Government Medical College, Kozhikode for the duration of 1 year.

Sample size

Calculated with the formula "4pq"/d2. From the study [8], p was taken as 92, d as 7% of p and q is 100-p. Substituting these values, sample size obtained is 71.

Inclusion criteria

Cases: Patients with cirrhosis of both sexes in age group above 18 years attending medicine outpatient unit, admitted in medicine ward, and ICU of Government Medical College Kozhikode were included in the study.

Exclusion criteria

Cases: Patients with chronic diarrhoea, malignant disease, use of diuretics, reduced renal function, and patient not willing to participate in the study were excluded from the study.

Sampling procedure

Seventy-one liver cirrhosis patients of both sexes in the age group above 18 years were selected from both inpatient and outpatient unit. To assess severity of disease, patients were further segregated according to Child-Pugh-Turcotte classification. No specific sampling technique was employed.

Child-Pugh–Turcotte classification [9]

Parameter	1 point	2 points	3 points
Total bilirubin (μmol/L) mg/dL	<34 <2	34–50 2–3	>50 >3
Serum albumin (g/L)	>35	28–35	<28
INR	<1.7	1.71–2.30	>2.30
Ascites	None	Mild (or controlled by diuretics)	Moderate to severe (or refractory to diuretics)
Hepatic encephalopathy	None	Grade I–II (or absent with medication)	Grade III–IV (or recurrent)

Child-Pugh-Turcotte

Class	Class A	Class B	Class C
Total points	56	79	1015

Method of data collection and outcome measurement

After obtaining consent, 71 liver cirrhosis patients attending medicine outpatient unit, admitted in ward, and ICU at Kozhikode Medical College were evaluated for serum magnesium.

Following general parameters were considered:

1. Informed consent was taken from all cases
2. Detailed history was taken about duration of the illness and other significant medical illness
3. Samples for serum magnesium were collected from cases in blood collection tube without anticoagulant and centrifuged to get serum. Estimation was done using colorimetric end point method in COBAS c-311
4. Samples for total bilirubin and albumin were collected from cases in blood collection tube without anticoagulant and centrifuged to get serum. Estimation was done using ERBA EM 360
5. Values of PT or INR was obtained from case record.

The following laboratory parameters were analyzed

1. Serum magnesium: Colorimetric end point method
2. Total bilirubin: Diazo method, end point
3. Serum albumin: BCG dye method, end point.

Statistical analysis

Statistical analysis was done using SPSS for Windows Version 22.0. Descriptive analysis of all the explanatory and outcome parameters was done using frequency and proportions for categorical variables, whereas mean and SD for continuous variables.

Kruskal–Wallis test followed by Mann–Whitney *Post hoc* analysis was used to compare the mean magnesium levels (in mg/dl) based on different Child-Pugh-Turcotte grades. Mann–Whitney test was used to compare the mean age (in years) among liver cirrhosis patients having hypomagnesemia and those with normal magnesium levels. Chi-square test was used to compare the gender distribution among liver cirrhosis patients having hypomagnesemia and those with normal magnesium levels. The level of significance was set at $p<0.05$.

RESULTS AND OBSERVATIONS

As per Table 1, the mean age of the study patients was 54.41±7.75 with a majority of the cases that were distributed in the age group of 51 (49.3%), followed by 41 with very few cases distributed in the extremes, that is, years, n=1 (1.4%). Among the study patients, males were more predominant, n=44 (62%) as compared to females, n=27 (38%).

As per Table 2, normal level of magnesium in a healthy adult is 1.60 magnesium levels lesser than this value will be considered as hypomagnesemia. Among the study patients, hypomagnesemia was prevalent in 51 cases (71.8%) and remaining cases presented with normal levels in 20 cases (28.2%).

As per Table 3, the mean age distribution between the hypomagnesemia and those with normal magnesium levels among the study patients was estimated, which showed that the mean age in hypomagnesemia patients was 54.00±7.60 and in patients with normal magnesium levels, it was 55.45±8.21. However, no significant difference was observed for mean age difference between hypomagnesemia and those with normal magnesium levels among the study patients (p=0.65).

With respect to gender distribution among the study patients exhibiting hypomagnesemia and those with normal magnesium levels, males were predominant in both groups, n=32 (62.7%) in hypomagnesemia and n=12 (60%) in patients with normal magnesium levels as compared to the female counter parts with n=19 (37.3%) and n=8 (40%) distributed in those groups, respectively. However, no significant difference was observed for gender distribution between study patients exhibiting hypomagnesemia and those with normal magnesium levels (p=0.83).

According to Table 4, Grade A showed a mean magnesium level of 1.540±0.282, Grade B showed 1.423±0.23, and Grade C showed a mean magnesium level of 1.186±0.298. The mean magnesium levels between different grades of liver cirrhosis was statistically significant at p=0.001. Grade C showed significantly least mean magnesium levels as compared to Grade A and Grade B. Moreover, Grade B showed lesser mean magnesium levels as compared to Grade A. Serum magnesium levels were significantly decreased with advancement of liver disease (From Child A to C).

As per Table 5, the test results showed that alcohol was a predominant cause of liver cirrhosis among 51–60 years (48.7%), as compared to viral hepatitis and NASH which was predominantly in 51–60 years (57.1% and 43.5%, respectively).

DISCUSSION

Liver cirrhosis is the final pathological result of various chronic liver diseases and fibrosis is the precursor of cirrhosis [10]. This cross-

Table 1: Age and gender distribution of study participants

Variable	Category	n	%
Age	≤40 years	4	5.6
	41–50 years	20	28.2
	51–60 years	35	49.3
	61–70 years	11	15.5
	>70 years	1	1.4
		Mean	**SD**
	Mean and SD	54.41	7.75
	Range	38–75	

Table 2: Prevalence of hypomagnesemia among study patients

Variable	Category	n	%
Hypomagnesemia	Hypomagnesemia	51	71.8
	Normal	20	28.2

Table 3: Distribution of age and gender among liver cirrhosis patients having hypomagnesemia

Variable	Category	Hypomagnesemia		Normal		p-value
		Mean	SD	Mean	z	
Age	Mean and SD	54.00	7.60	55.45	8.21	0.65*
	Range	38–70		45–75		
		n	%	n	%	
Gender	Males	32	62.7	12	60.0	0.83**
	Females	19	37.3	8	40.0	

Significant of p-value 0.04*

Table 4: Comparison of mean difference in magnesium levels b/w different Child-Pugh-Turcotte grades

(I) Child-Pugh-Turcotte Grade	(J) Child-Pugh-Turcotte Grades	Mean different (I-J)	95% CI of the different		p-value
			Lower	Upper	
Grade A	Grade B	0.118	−0.071	0.306	0.04*
Grade A	Grade C	0.355	0.164	0.545	0.001*
Grade B	Grade C	0.237	0.046	0.427	0.005*

Significant of p-value 0.04*

Table 5: Comparison of age and gender distribution based on different etiology of liver cirrhosis

Variable	Category	Alcohol		Hepatitis B		NASH		Autoimmune		p-value
		n	%	n	%	n	%	n	%	
Age	<40 years	4	10.3	0	0.0	0	0.0	0	0.0	0.63
	41–50 years	10	25.6	3	42.9	7	30.4	0	0.0	
	51–60 years	19	48.7	4	57.1	10	43.5	2	100.0	
	61–70 years	5	12.8	0	0.0	6	26.1	0	0.0	
	>70 years	1	2.6	0	0.0	0	0.0	0	0.0	
Sex	Males	38	97.4	5	71.4	1	4.3	0	0.0	<0.001*
	Females	1	2.6	2	28.6	22	95.7	2	100.0	

Significant of p-value 0.04*

sectional study was done to assess the prevalence of hypomagnesemia in liver cirrhosis patients and its association with the severity of the disease. Seventy-one clinically diagnosed patients of liver cirrhosis (male 62% and female 38%) were included in this study. The majority (49.3%) of the cases were distributed in the age group of 51–60 years, 28.2% in the age group of 41–50 years, and 15.5% in the age group of 61–70 years, with very few cases distributed in the extremes.

Das *et al.* conducted hospital-based study in Bareilly, India to analyze magnesium levels in serum in patients of cirrhosis of liver and to compare them with the serum magnesium levels of controls. The subject group included 50 diagnostic cases of alcohol induced liver cirrhosis (Group I) and 50 normal control group (Group II). Serum magnesium levels were measured by spectrophotometer at 530 nm in both the selected groups. Moreover, they found that serum magnesium levels in Group I were found to be significantly lowered ($p<0.0001$) than in Group II [11]. Gurudevarahalli *et al.* conducted a hospital based study on serum magnesium in liver disease and observed that lower levels of serum magnesium were found in cirrhosis of liver. In his study, out of 25 patients with chronic liver disease, 23 patients had shown a low serum magnesium [8]. Kar *et al.* from India conducted a hospital based study in Andhra Pradesh to assess alteration in the micronutrient homeostasis in compensated and decompensated liver cirrhosis. They analyzed magnesium levels in the serum of compensated (n=34) and decompensated (n=31) liver cirrhosis patients and compared with that of healthy control group (n=36) by *post hoc* ANOVA. Although a significant decrease in serum magnesium levels was found in cirrhosis patients overall (both Group I and 2) in comparison to the control subjects ($p<0.05$), no such difference was observed between the compensated and decompensated groups within the case population ($p>0.05$) [12].

Koivisto *et al.* from Finland conducted a study to evaluate the magnesium status in end-stage chronic cirrhotic patients and in healthy controls. They performed magnesium loading test in ten chronic cirrhotics listed for liver transplantation and in six healthy control patients. Uptake of magnesium is increased in cirrhotic patients compared to healthy controls. They found that uptake of magnesium was about 8% in healthy controls and 34% in cirrhotics ($p<0.01$) [13]. Rocchi *et al.* from Italy conducted a study to analyze zinc and magnesium status among 38 liver cirrhosis patients and compared with 54 healthy controls, matched for age and sex. Patients were further divided according to Child-Pugh-Turcotte classification. The plasma level of magnesium was found to be reduced. They showed that plasma and RBC magnesium levels remain almost unchanged from Child-Pugh-Turcotte A to C class, while a more apparent increase in urinary output seems linked to progression of the disease [14].

Arakawa *et al*. from Japan conducted a study on comparison of serum trace element concentrations (including magnesium) between patients with chronic hepatitis, liver cirrhosis or primary biliary cirrhosis, and normal adults and showed that the magnesium concentration decreased as the pathophysiological condition advanced from chronic hepatitis to liver cirrhosis [15]. Sullivan *et al*. conducted a study of serum trace elements concentrations (including magnesium) in a control group of adult males and in 11 groups of patients in various disease states. They found that cirrhotic patients had a low serum magnesium compared to controls [16].

CONCLUSION

Among the study patients, hypomagnesemia was prevalent in majority (71.8%) of cases. Mean magnesium levels between different grades of liver cirrhosis were statistically significant. Mean level difference of serum magnesium among the Child-Pugh-Turcotte groups was statistically significant. Males showed predominant cause as alcoholism (97.4%) and viral hepatitis (71.4%) for liver cirrhosis as compared to NASH (95.7%) and autoimmune disorders (100.0%) among females.

As magnesium level was found to be decreased in liver cirrhosis, it is advisable to screen the patients for serum magnesium. Further trials should be done in the future to know the effectiveness of magnesium supplementation in retarding the progression as well as preventing complications of liver cirrhosis.

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AUTHOR'S CONTRIBUTION

Dr. Veena G and Dr. Rebecca James have finalized the draft and guarantor, Dr. Rebecca James have prepared the conceptual framework, designing of draft, and data analysis, Dr. Veena G was involved in data collection and analysis, and Dr. Veena G and Dr. Rebecca James has done manuscript writing and data collection.

COMPETING INTERESTS

None declared.

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