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ORIGINAL ARTICLE

STUDY OF SERUM MAGNESIUM IN LIVER DISEASES

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ABSTRACT: Magnesium is one of the four inorganic ions present in human body and most abundant intracellular ions next only to potassium.[1] Derangement of magnesium metabolism can occur in various disorders.[2,3] Acute liver diseases are associated with raised serum magnesium levels, this rise parallels with serum bilirubin levels.[3,4] With onset recovery from acute process the levels gradually returns to normal.[4,5] Low level serum magnesium are found in Cirrhosis of liver and in alcoholic liver diseases.[6] **AIM:** To study the levels of serum magnesium in acute and chronic liver diseases, to see any correlation between serum magnesium and serum bilirubin in acute liver disorder, and to see any variation in serum magnesium levels in acute liver disorder during acute phase and recovery phase. **SUBJECTS AND METHODS:** Study involved 50 patients with acute and chronic liver disorder like acute viral hepatitis and cirrhosis of liver in different medical wards of JJM. Medical college Hospital, Davangere over a period of one year. Detail clinical and biochemical investigations were carried out. Samples were tested for routine haemogram, liver function test, serum magnesium estimation, serological and other necessary test. **RESULTS:** All 50 cases were divided into two groups. In group "A' 25 cases (24 cases were viral hepatitis and one toxic hepatitis) and in group "B" 25 cases(21 cases of cirrhosis of liver and 4 alcoholic hepatitis). Out of 50 cases 35 were male and 15 were female. Maximum number of cases in group A were between 20-39 years and in group B were between 30-39 years. Frequent symptoms in group A observed were yellowish discolouration of sclera and passing of high colour urine. Symptoms in group B observed was abdominal distension. Frequent signs in group A observed were jaundice and hepatomegaly, and signs in group B observed were ascites and abdominal distension. In group A patients serum magnesium value ranged from 2.47 to 3.6mg% with mean value of 3.10mg% and mean levels of serum magnesium obtained during recovery phase was 2.70mg%. In group B patients mean serum magnesium was 1.74mg%. Control group magnesium levels ranged from 1.90 to 3.1mg% with mean of 2.48mg% (±0.21mg%). **CONCLUSION:** Acute liver disorder is associated with raised serum magnesium levels. This rise parallels with serum bilirubin level. Lower levels of serum magnesium are found in cirrhosis of liver and in alcoholic liver disease.

KEYWORDS: Acute viral hepatitis, Cirrhosis of liver, Serum Magnesium, Serum bilirubin.

INTRODUCTION: Role of magnesium as cofactor in enzyme coenzyme system in different metabolic reaction of the body is well documented.[1,2] It is necessary for the stability of DNA, RNA and the binding of mRNA to the ribosomes.[1,3] With ATP magnesium forms a substrate and is involved in all the reaction in which ATP takes part like glucose utilisation, protein, fat, nuclic acid metabolism, and nucleotide synthesise.[2,4]

It is also concerned with the membrane associated ATP dependent sodium and potassium pump system. It plays an important part in the homeostasis of the cell.[4,5,6]

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Many Indian workers also studied the effects of liver disorders on magnesium metabolism.[1.2.7] Laha and Vaishya studied the levels of magnesium in patients with cirrhosis and found low values in almost 90% of patient. Kadarnath, Misra, Fatima and others found generally higher values in acute liver diseases like viral hepatitis.[8] These were attributed to hepatocellular injury, liver cell necrosis and release of intracellular magnesium into the circulation.[8.9] Low levels were observed in cirrhosis by most workers. Various factors including secondary hyperaldosteronism and the alcohol per se were attributed to hypomagnesemia.[8.9.10]

With these backgrounds our study was undertaken to evaluate the levels of serum magnesium in acute and chronic liver disorders, correlation between serum magnesium and serum bilirubin levels in acute liver diseases, also to see variation in the serum magnesium levels in the acute liver diseases during acute phase of the illness and during recovery phase.[11]

SUBJECTS AND METHODS: This study included 50 patients with acute and chronic liver disorders. This included acute viral hepatitis, chronic liver diseases like cirrhosis of liver admitted in various medical wards of JJM Medical College, Davangere for a period of one year.

Patients presenting with acute onset of jaundice with or without prodormal symptoms who had predominantly raised conjugated hyperbilirubinemia and patients mainly with distension of abdomen or swelling of limbs with history of chronic liver diseases were taken up for this study. Relevent clinical information was collected from each patient that included presenting complaints, food habits, socio economic status, drug history, alcohol abuse, bleeding tendency, hematemesis, malena, history of blood transfusion within recent time. Clinical examination included general physical and systemic examination with special emphasis on icterus, anemia, odema, clubbing, white nails, signs of liver cell failure, present of organamegaly. Basic investigation including complete hemogram and renal function test were done in all the cases. X ray chest and upper GI endoscopy were undertaken whenever found relevant. Written informed consent was taken from patient or guardian. The institutional ethics committee approved the study.

Complete liver function test (LFT), prothrombin time (PT), ultrasonography, serological test, and estimation of serum magnesium levels were carried out in all the patients included in the study. In patients with acute hepatocellular diseases two estimations were done one at the time of admission before any treatment was instituted and second at the time of recovery by using Titan yellow method.[12.13.14] 25 normal healthy adults serum magnesium estimation was carried out and was taken as control group and this mean control was used for comparison.

Patients were followed up for complete clinical and biochemical recovery. Standard care treatment was given for acute symptoms whenever required.

RESULT: In the present study, 50 patients were studied with acute and chronic liver disease, admitted to JJM Medical College Davangere. Analysing the data following groups were made to divide the patients.

Group A: Acute hepatocellular disease - Viral hepatitis (24 patients), Toxic hepatitis (1 patient).

Group B: Chronic liver disease - Cirrhosis of liver (21 patients), Alcohol hepatitis (4 patients).

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AGE AND SEX INCIDENCE/DISTRIBUTION:

Age group	Acute			Chronic			Total	Percentage
	M	F	T	M	F	T		(%)
10 - 19	2	1	3	1	1	2	5	10
20- 29	4	3	7	3	1	4	11	22
30- 39	4	3	7	11	1	12	19	38
40- 49	2	2	4	2	0	2	6	12
50- 59	1	2	3	3	1	4	7	14
60- 69	1	0	1	1	0	1	2	4
Above 70	0	0	0	0	0	0	0	0
Total	**14**	**11**	**25**	**21**	**4**	**25**	**50**	**100**

Table 1: Shows age and sex incidence of all the cases studied

Out of the 50 cases, 35 cases were males and 15 females. The cases were belonged to the age group between 18-69 years. The maximum number of cases in groups "A" were found in the age group of 20-39 years (56%). Most of the cases in group "B" belonged to the age group of 30-39 year (48%). Youngest patient was 18 years old and eldest was 63 years.

PRESENTING SYMPTOMS:

Symptoms	No. of cases	Percentage (%)
Constitutional Symptoms	12	48
Anorexia	16	64
Yellow discoloration of the Sclera	25	100
Vomiting	10	40

Table 2: Showing frequency of Symptoms in Group "A" patients

All patients in group "A" with acute hepatocellular disease presented with yellowish discoloration of sclera and passing of high coloured urine. Also constitutional symptoms in the form of headache, bodyache, malaise, and joint pain were present in 48% of cases. Vomiting was seen in 40% of cases. No patients had any bleeding tendency. One patient was on anti-tubercular drugs and on Phenobarbitone.

Symptoms	No. of cases	Percentage (%)
Abdominal Distension	25	100
Anorexia	20	80
Weight loss	14	56
Yellow discoloration of the Sclerae	6	24

Table 3: Showing frequency of Symptoms in Group "B" patients.

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All the patients in group ' B' presented mainly with abdominal distension, poor appetite, poor general health, discomfort in the abdomen, pedal odema, and oliguria. 6 patients (24%) presented with yellow discoloration of the sclerae and passing of high coloured urine. 14 patients (56%) had breathlessness and some of these had orthopnoea due to gross ascites. 6 patients(24%) were chronic alcoholic. One patient gave history of hematemesis for which he was treated accordingly.

PRESENTING SIGNS:

Signs	No. of cases	Percentage (%)
Jaundice	25	100
Hepatomegaly	25	100
Hepatosplenomegaly	1	4
Swelling of limbs	1	4

Table 4: Showing Signs in Group "A" patients with Acute liver disease.

Most of them had jaundice and hepatomegaly (100%). One patient who had congestive failure due to rheumatic heart disease had pedal odema and ascites as well. None of the patients had signs of hepatocellular failure.

Signs	No. of cases	Percentage (%)
Abdominal distension	25	100
Anemia	24	96
Jaundice	12	48
Clubbing	11	44
Pedal odema	18	72
Ascites	25	100
Hepatomegaly	11	44
Spleenomegaly	11	44
Hepatosplenomegaly	7	28

Table 5: Showing Signs in Group "B" patients with Chronic liver disease.

In group B patients, the commonest finding present in all the patients are abdominal distension and ascites (100%). Majority were anemic (96%), 18 patients (72%) had pedal odema. 11 patients (44%) had clubbing in absence of any other disease.

INVESTIGATION:

Sl. No.	Cases No.	Age	Sex	Serum Bilirubin (mg%)	Serum Magnesium (mg%)
1	1	18	M	11.0	3.60
2	2	26	M	4.3	2.95

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3	3	39	M	6.6	3.20
4	4	35	M	3.2	2.68
5	5	19	F	4.1	2.60
6	6	37	M	3.8	2.47
7	7	38	M	8.0	3.50
8	8	29	F	4.6	2.56
9	9	36	F	11.6	2.72
10	10	27	F	15.0	3.56
11	11	38	F	7.8	3.42
12	12	19	M	8.2	3.32
13	13	37	F	6.0	3.10
14	14	28	M	8.2	3.26
15	15	29	M	6.0	3.00
16	16	42	M	6.8	3.16
17	17	28	F	7.4	3.12
18	18	43	M	7.8	3.20
19	19	28	M	9.2	3.54
20	20	43	F	1.8	3.56
21	21	45	F	4.8	3.24
22	22	58	M	6.8	3.10
23	23	54	F	7.2	3.20
24	24	52	F	3.4	2.74
25	25	61	M	8.0	3.42
MEAN					3.10

Table 6: Showing levels of Serum Bilirubin and Serum Magnesium in group “A” patients

(P-Less than 0.001 statistically significant).

Serum magnesium values ranged from 2.47 to 3.6mg% with a mean value of 3.10mg%.

Sl. No.	Case No.	Age	Sex	Active phase		Recovery phase	
				S.Bil mg%	S.Mg mg%	S.Bil mg%	S.Mg mg%
1	1	19	M	11.0	3.60	6.0	3.20
2	2	26	M	4.3	2.95	2.0	2.54
3	5	19	F	4.1	2.60	3.2	2.48
4	7	38	M	3.8	3.50	1.8	2.68
5	8	29	F	4.6	2.56	2.8	2.43
6	9	36	F	11.6	2.75	5.6	2.50
7	10	27	F	15.0	3.56	6.0	3.16
8	12	19	M	8.2	3.32	3.2	3.10

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9	14	28	M	8.2	3.26	3.5	2.76
10	15	29	M	6.0	3.00	2.4	2.58
11	16	42	M	6.8	3.16	1.6	2.92
12	18	43	M	7.8	3.20	3.2	3.00
13	19	28	M	9.2	3.54	4.0	2.64
14	22	58	M	6.8	3.10	3.2	2.86
15	25	61	M	8.0	3.42	3.2	2.98
MEAN					3.10		2.70

Table 7: Showing the Serum Bilirubin and Serum Magnesium profile in Acute phase of Hepatitis and during Recovery

(P-Less than0.01 statistically significant).

The mean level of serum magnesium obtained was 2.70mg% during recovery phase. 15 patients turned up for follow up after a variable period from 2 to 6 weeks.

Sl. No.	Case No.	Age	Sex	S. Bil (mg%)	S. Total Proteins (gm%)	S.Alb (gm%)	Serum Magnesium (mg%)
1	1	18	M	0.8	5.9	3.2	2.60
2	2	35	M	0.6	6.9	4.1	1.70
3	3	25	M	1.0	6.9	4.1	1.82
4	4	37	M	1.0	6.0	3.7	1.74
5	5	39	M	2.0	6.0	3.2	2.50
6	6	27	M	0.8	6.0	4.2	1.90
7	7	34	M	2.0	7.3	4.9	1.60
8	8	32	M	0.4	6.3	4.0	1.64
9	9	36	M	0.6	6.6	4.0	1.54
10	10	19	F	0.4	6.3	3.8	1.56
11	11	37	M	0.5	7.2	4.9	1.75
12	12	38	M	0.6	6.9	4.0	1.62
13	13	28	M	0.9	6.0	3.6	1.14
14	14	35	M	0.8	6.6	4.0	1.83
15	15	33	M	2.4	6.6	4.0	1.60
16	16	37	M	1.0	6.0	3.3	1.64
17	17	34	F	1.6	6.0	3.1	1.73
18	18	46	M	3.8	6.0	3.1	1.62
19	19	48	M	7.7	6.2	4.0	1.72
20	20	55	M	4.0	6.2	3.2	1.76
21	21	52	F	4.6	7.2	5.4	1.56
22	22	57	M	0.6	7.4	4.2	1.92
23	23	58	M	0.8	6.8	3.8	1.62

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24	24	61	F	1.0	6.2	3.4	1.70
25	25	63	M	0.8	7.4	4.2	1.82
MEAN					6.5	3.89	1.74

Table 8 : Showing the Serum Bilirubin, Serum Proteins, Serum Albumin and Serum Magnesium in group "B" Patients

(P-Less than0.05 Statistical significant).

Mean serum total protein levels observed in these patients was 6.5 gm%, mean serum albumin 3.89gm%, and the mean serum magnesium 1.74mg%.

CONTROL GROUP: 25 healthy individuals were studied for the estimation of serum magnesium as control, consisting of 15 males and 10 females belonging to age of between 18-34 years. The magnesium levels ranged from 1.96 to 3.1 mgs% with a mean of 2.48 (±0.21mg%).

DISCUSSION: In this study the common cause of acute liver disease was viral hepatitis and the maximum cases were seen in the 3rd and 4th decade. The chronic disorder including cirrhosis was found in 4th decade and the alcoholic disorder affecting the liver in 3rd decade. The later sequele in the form of cirrhosis was found in the 4th and 5th decade. It was found that generally greater the levels of serum bilirubin, greater were the level of magnesium in the serum. The mean magnesium level noted was 3.10mg% which was higher than the control value 2.48mg%. This is in agreement with the findings of other workers including Chatterjee, Kadarnath, Misra, Fatima & others.[7.8] During the recovery period the mean level of serum magnesium found was 2.70mg% which was still higher as compared to control. But there was a significant decline as compared to the previous levels. This indicates that as the recovery from the acute hepatitis was in progress, the higher serum magnesium levels tended to gradually return to normal. Similar observations were made by Kadarnath (1969), Chatterjee (1976) and Misra & Fatima (1974) who observed reduction in the raised magnesium levels with onset of recovery.[7.8.15.16]

The value obtained by other workers are shown in the table 9. Wallach observed no significant change in magnesium levels in patients with viral hepatitis. Also he did not mention the relation between serum bilirubin and serum magnesium levels. Chatterjee, Kadarnath, Misra, Fatima & others observed that the levels of serum magnesium raised during acute viral hepatitis and these correlated with serum bilirubin.[7.8] Also the levels were observed to decline with improvement in the acute hepatitis process.[7.8.17]

Worker	No. of Cases	Control Mg	Study Mg	Remarks
Wallach et al	5	2.00 ± 0.15 mEq/l	2.11 ± 0.22 mEq/l	Not Significant
Misra & Fatima	10	2.30 ± 0.08 mg%	5.34mg%	Raised
Chatterjee & Sarang[7]	8	1.83 ± 0.28 mEq/l	2.11 mEq/l	Raised
Misra & Sarang	68	1.82 ± 0.10mg%	2.26mg%	Raised

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Kadarnath et al [8]	16	2.5mg%	2.93mg%	Raised
Present Study	25	2.48 ± 0.21 mg%	3.10mg%	Raised

Table 9: COMPARING THE PRESENT STUDY WITH THAT OF OTHER WORKERS IN ACUTE LIVER DISEASE

The cause of raised serum magnesium could be possibly due to the leakage of magnesium ions from the acutely injured liver cells. As magnesium is present mainly intracellular and as it is present in major quantity in liver, acute hepatcellular injury leading to increase permeability and necrosis and rupture of the liver cells might have resulted in the leakage of the ions into the plasma.

Worker	No. of Cases	Control Mg	Study Mg	Remark
Misra & Fatima	15	2.30 ± 0.08 mg%	1.00 mg%	Lower
Misra & Sarang	53	1.82 ± 0.10 mg%	1.47 mg%	Lower
Kadarnath et al [8]	36	2.50 ± 0.30 mg%	1.87 mg%	Lower
Pin lim & Jacob[11]	10	2.00 ± 0.17 mEq/L	1.92 mEq/L	No significant change
Chatterjee & Sarang [3]	15	1.83 ± 0.28 mEq/L	1.61 mEq/L	Lower
Gupta et al	30	2.09 ± 0.22 mg%	1.80mg%	Lower
Present Study	25	2.48 ± 0.21mg%	1.74mg%	Lower

Table 10: COMPARING THE PRESENT STUDY WITH THAT OF OTHER WORKERS IN CHRONIC LIVER DISEASE

Out of 25 patients with chronic liver disease 23 patients had shown a low serum magnesium, 2 patients had shown a normal value. Various studies have indicated that there is hypomagnesemia in chronic liver disease. Flink (1954), Wallach (1963), Laha & Vaishya (1963), observed similar findings. Misra & Fatima (1974) reported hypomagnesemia in majority of cases of portal cirrhosis. Misra & Sarang studied 53 patients with cirrhosis and found significant hypomagnesemia. Gupta studied 30 patients and observed significant hypomagnesemia.

The aetiology of hypomagnesemia is believed to be multifactorial in cirrhosis. It is reported to be due to the decreased dietary intake and hypoalbuminaemia (Chatterjee),[7] Impaired absorption due to portal congestion and secondary hyperaldosteronism (Nath), Increased extracellular shift of magnesium (Misra & Fatima), Alcoholic Ingestion with associated tendency for vomiting and diarrhoea and increased renal excretion of magnesium as the result of direct effect of alcohol (Heaton et al).

CONCLUSION: Studies carried out in the past have indicated alterations in the level of serum magnesium in the liver disease.[3.8.10.11.17] Many workers found raised serum levels of magnesium in acute hepatocellular damage whereas some workers failed to find significant alterations.[7.8.16] In cirrhosis low levels of serum magnesium were observed by some workers whereas some workers found low levels only in alcoholic cirrhosis.[7.8.17] From the present study following conclusions were reached. Acute hepatocellular disease is associated with a raised serum magnesium levels. This raise parallels with serum bilirubin levels (P less than 0.001 statistically significant). With the onset of

recovery from the acute process the levels gradually return to normal. Lower levels of serum magnesium are found in cirrhosis of liver.

None of the patients had symtomatic hypo magnesemia in the present study. The serum levels are influenced by conditioning factors like anorexia, poor dietary intake, presence of vomiting and diarrhoea.

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