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Assessment of correlation of serum Mg level with hepatic encephalopathy in cirrhotic patients

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Abstract

Hepatic encephalopathy (HE) is a neurometabolic syndromecharacterized by impaired brain function in patientswith decompensated cirrhosis.[1-3] The pathogenesisof HE is not completely understood and several proposedpathways are implicated in the initiation and exacerbationof this syndromeMagnesium is an essential component ofhuman body and other mammals, whose role in livercirrhosis and its complications is still a matter ofresearch. There are contrary reports about theirserum concentrations in patients with liver cirrhosis.Magnesium is associated with more than 300enzymatic reactions involving energy metabolismand protein and nucleic acid synthesis **Aim:** To assess the correlation of serum Mg level with hepatic encephalopathy in cirrhotic patients **Objectives:**To study the serum electrolyte levels in hepatic encephalopathy in cirrhotic patientsTo assess the correlation of serum Mg level with hepatic encephalopathy in cirrhotic patients) **resulta** The mean Serum Sodium, Potassium, Calcium, Chloride, Bicarbonate and Magnesium levels of the patients were 134.6 ± 3.64.0±0.8, 8.8±1.3, 95.6±8.9, 22.3±5.7 and 1.2±0.2mEq/L, respectively.(Table No. 10) No correlation w **. Correlation is significant at the 0.01 level (2-tailed). Correlation is significant at the 0.05 level (2-tailed). In our study we came to a conclusion that deficiency in the serum magnesium levels is associated with cirrhosis in alcoholic patients **conclusions** In our study we came to a conclusion that deficiency in the serum magnesium levels is associated with cirrhosis in alcoholic patients

Keywords: Serum Magnesium, Hepatic Encephalopathy, Liver Cirrhosis

INTRODUCTION

Hepatic encephalopathy (HE) is a neurometabolic syndromecharacterized by impaired brain function in patientswith decompensated cirrhosis.[1-3] The pathogenesisof HE is not completely understood and several proposedpathways are implicated in the initiation and exacerbationof this syndrome.[3-5]

HE may be clinically apparent in as many as one third of cirrhotic patients and, if rigorously tested, up to two thirds have some degree of mild or subclinical HE.[6]

Ammonia plays a central role in HE asit crosses the blood brain barrier causing neurological insultmediated by a decrease in excitatory neurotransmission.[7] Multiple precipitating factors for HE has beenrecognized and if controlled, may alter the disease acuity

and improve mental status.[8] The most common precipitatingfactors for HE includes dehydration, acute kidney injury,non-adherence to medications (particularlynon-absorbable disaccharides), constipation and infections.[9-11]

Magnesium is essential for many intracellular processes andstructures in the human body, such as muscle contractionand relaxation, neuronal signal transduction, and conduction ofthe action potential in the myocardium [12]. Most of the body'smagnesium is intracellular and less than 1% of the total is foundin serum. Therefore, significant magnesium deficiency mightbe present even though the serum magnesium level is withinnormal limits. Magnesiumdeficiency has been associated with several systemic conditions,including metabolic syndrome, cerebrovascular diseases,malignancies, bacterial and fungal infections, osteoporosis, andliver cirrhosis [13-16].Several studies demonstrated a higher prevalence of magnesiumdeficiency in patients with liver cirrhosis comparedto the general population [17-20]. Suggested pathogenesisincludes decreased magnesium intake, fat malabsorption,diuretic use, renal tubular acidosis, and increased serum levelsof growth hormone and glucagon[20].Patients with alcoholic liver cirrhosis were found to havedecreased muscle mass and strength as well as lower magnesiumand potassium content in muscle tissue as compared toan age-matched control group[21,22]. Magnesium levels werefound to decrease as the severity of liver disease progressed(according to CHILD score) [21], and treatment with spironolactoneincreased muscle strength and electrolytes [21, 23].

Magnesium is an essential component ofhuman body and other mammals, whose role in livercirrhosis and its complications is still a matter ofresearch. There are contrary reports about theirserum concentrations in patients with liver cirrhosis.Magnesium is associated with more than 300
enzymatic reactions involving energy metabolismand protein and nucleic acid synthesis[24,25].Magnesium also involved in immunoglobulinsynthesis, immune cell adherence, antibodydependentcytolysis, GM lymphocyte binding, Thelper B-cell adherence and additional responses[26].Only 0.3% of total body magnesium exists inserum[27-29].
In spite of all this knowledge regardingimportance of magnesium in human body,very little is known about magnesiummetabolism in diseased states, in comparison to theextensive studies of calcium, sodium and potassiumetc. Hence, the present study is planned to assess the correlation of serum Mg level with hepatic encephalopathy in cirrhotic patients

AIM & OBJECTIVES

Aim: To assess the correlation of serum Mg level with hepatic encephalopathy in cirrhotic patients

Objectives:

1. To study the serum electrolyte levels in hepatic encephalopathy in cirrhotic patients
2. To assess the correlation of serum Mg level with hepatic encephalopathy in cirrhotic patients

MATERIAL AND METHODS

Study design: Cross sectional analytical

Study population: Patients diagnosed with liver cirrhosis with hepatic encephalopathy visiting**Noor hospital**

Study period:2 years

Sample size:20

Ethical clearance: The study will be initiated after approval of Institutional Ethical committee.

Selection criteria: Patients diagnosed with liver cirrhosis with hepatic encephalopathy visiting**Noor hospital** will be subjected to the following inclusion and exclusion criteria.

Inclusion criteria:

1. Patients diagnosed with liver cirrhosis with hepatic encephalopathy visiting **NOOR HOSPITAL**
2. Patients of age 18 years or above of either gender.
3. Patients/Patients legally acceptable representative willing to give written informed consent to participate in the study.

Exclusion criteria:

1. Patients with active cancer.
2. Special populationssuch as pregnant women.
3. Individuals with mental retardation, dementia.
4. Current treatment with magnesium supplements.
5. Renal failure patients

Patients who will satisfy the above inclusion and exclusion criteria will be included in the study. Written informed consent will be taken from all patients.

Study procedure:

After taking consent, patient's demographic data will be collected. Data for the following variables will be collected:
The following information regarding the patients will be collected:

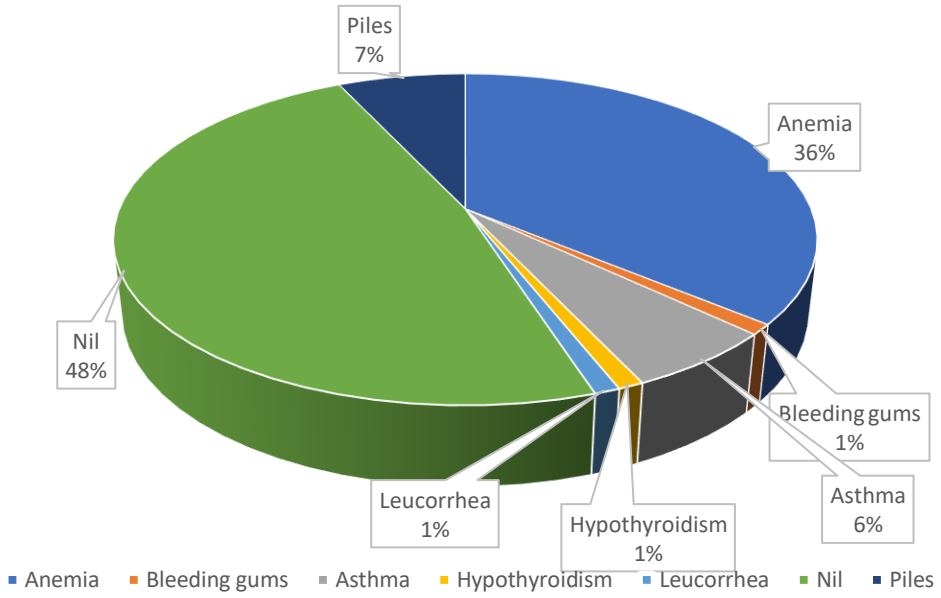
S. No.	Variable	Method of measurement	Measurement scale	Descriptive statistics
1.	Age	Interview	Ratio	Mean, S.D.
2.	Gender	Interview	Nominal	Frequency, Proportion
3.	Occupation	Interview	Nominal	Frequency, Proportion
4.	Comorbidities	Examination	Ratio	Mean, S.D.
5.	Causes of liver cirrhosis	Record	Nominal	Frequency, Proportion
6.	Serum Electrolytes	Investigation	Ratio	Mean, S.D.
7.	Liver function test	Investigation	Ratio	Mean, S.D.
8.	Glasgow coma scale	Examination	Ordinal	Frequency, Proportion

RESULTS

In the present study, 100 patients were included. All the patients were males.The mean Age of patients was 45.8 ± 13.3 years.

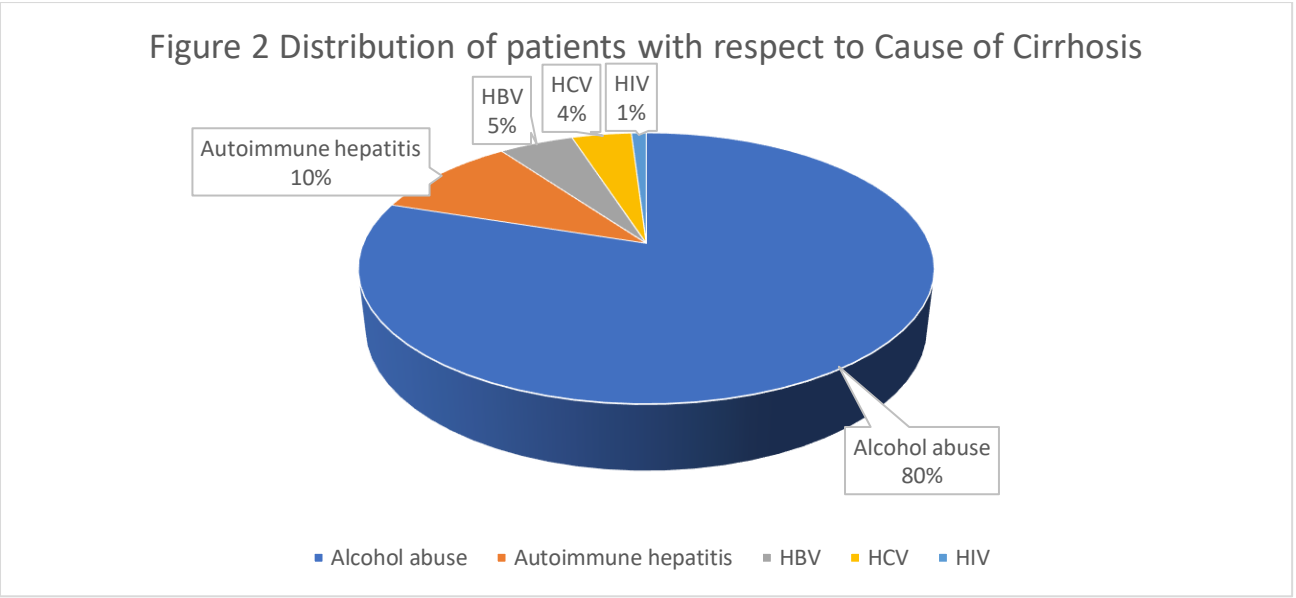
Table 1 Distribution of patients with respect to Comorbidities			
		Frequency	Percent
Comorbidity	Anemia	36	36
	Bleeding gums	1	1.0
	Asthma	6	6.0
	Hypothyroidism	1	1.0
	Leucorrhea	1	1.0
	Nil	48	48.0
	Piles	7	7.0
	Total	100	100.0

Figure 1 Distribution of patients with respect to Comorbidities



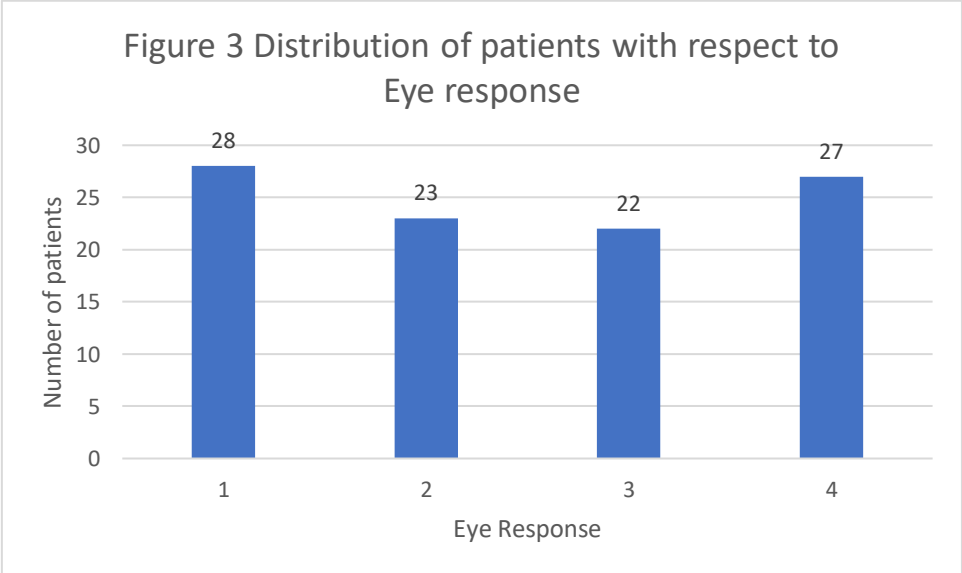
52 patients suffered from comorbidities. Most of the patients were suffering from anemia (36), followed by piles (7) and asthma (6).

Table 2 Distribution of patients with respect to Cause of Cirrhosis			
		Frequency	Percent
Cause of Cirrhosis	Alcohol abuse	80	80.0
	Autoimmune hepatitis	10	10.0
	HBV	5	5.0
	HCV	4	4.0
	HIV	1	1.0
	Total	100	100.0



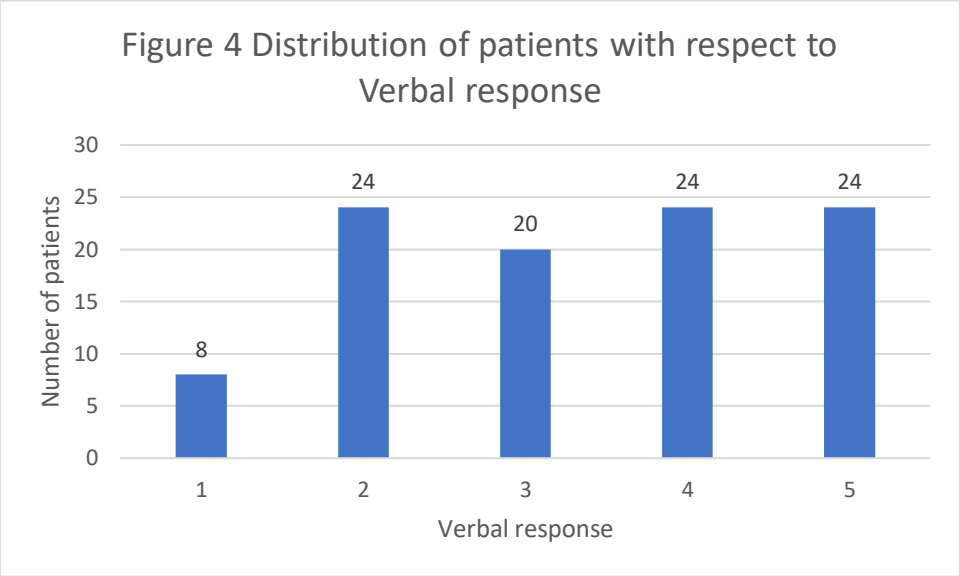
The most common cause of Cirrhosis was Alcohol abuse (80%) followed by Autoimmune hepatitis (10%) and HBV infection (5%).

Table 3 Distribution of patients with respect to Eye response			
		Frequency	Percent
Eye response	1	28	28.0
	2	23	23.0
	3	22	22.0
	4	27	27.0
	Total	100	100.0



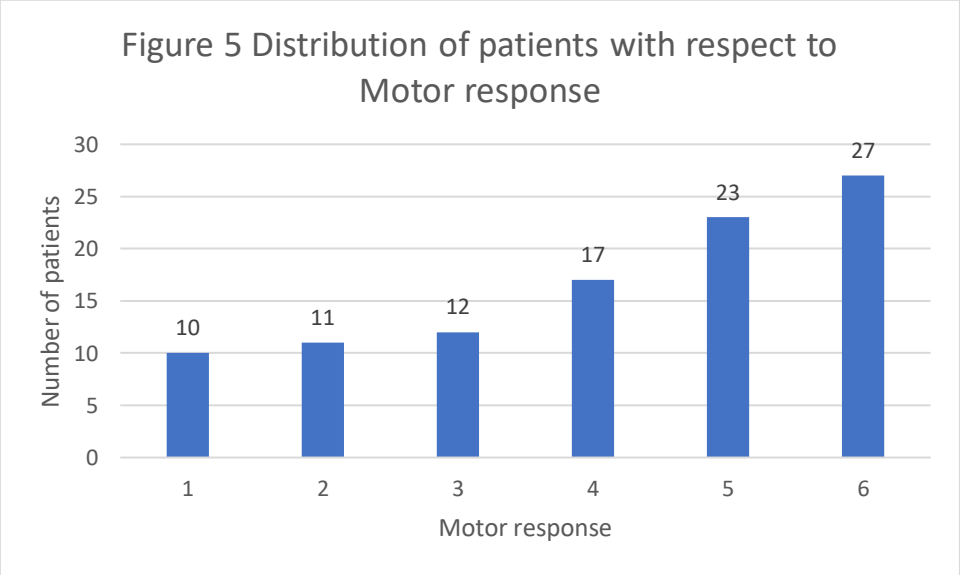
The most common eye response of the patients was 1 (28%) followed by 4 (27%).

Table 4 Distribution of patients with respect to Verbal response			
		Frequency	Percent
Verbal response	1	8	8.0
	2	24	24.0
	3	20	20.0
	4	24	24.0
	5	24	24.0
	Total	100	99.0



The most verbal response of the patients was 2, 4 and 5 (24% each).

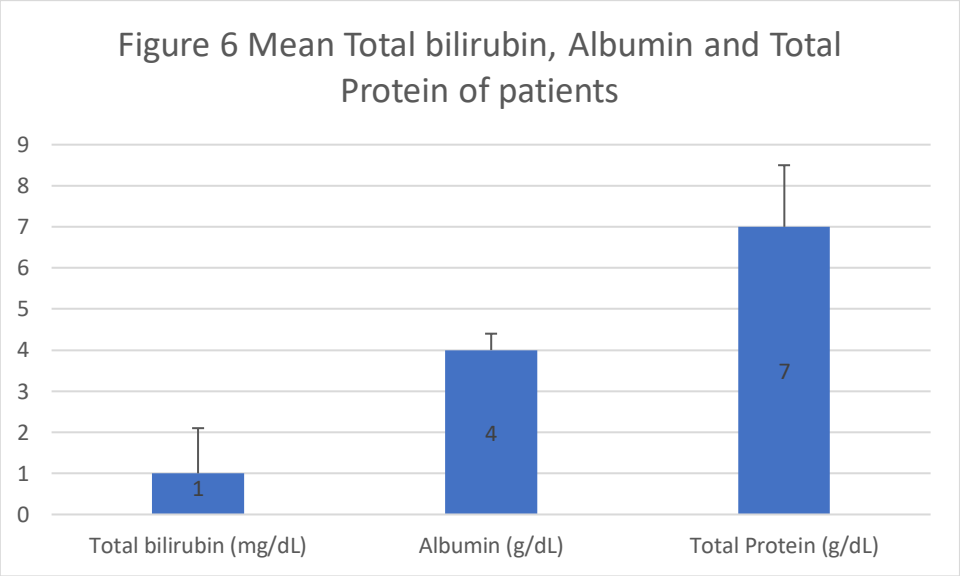
Table 5 Distribution of patients with respect to Motor response			
		Frequency	Percent
Motor response	1	10	10.0
	2	11	11.0
	3	12	12.0
	4	17	17.0
	5	23	23.0
	6	27	27.0
	Total	100	100.0



The most common Motor response of the patients was 6 (27%) followed by 5 (23%) and 4 (17%). The mean Glasgow coma scale of the patients was 9.9 ± 1.8

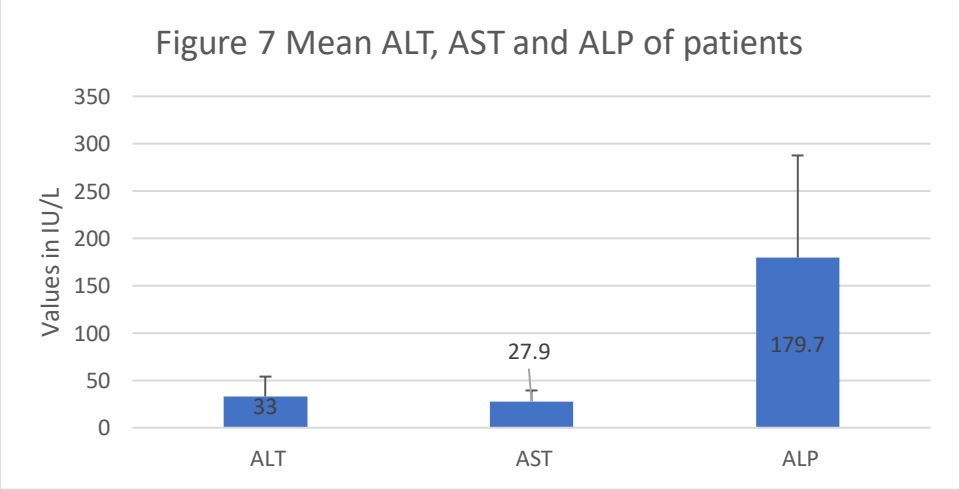
Table 6 Mean Total bilirubin, Albumin and Total Protein of patients

	Mean	Std. Deviation
Total bilirubin (mg/dL)	1.0	1.1
Albumin (g/dL)	4.0	0.4
Total Protein (g/dL)	7.0	1.5



The mean Total bilirubin, Albumin and Total Protein of the patients was 1.0 ± 1.1mg/dL, 4.0 ± 0.4g/dL and 7 ± 1.5g/dL, respectively.

Table 7 Mean ALT, AST and ALP of patients		
	Mean	Std. Deviation
ALT (IU/L)	33.0	21.0
AST (IU/L)	27.9	11.5
ALP (IU/L)	179.7	107.9



The mean ALT, AST and ALP of the patients was 33.0 ± 21 mg/dL, 27.9 ± 11.5 g/dL and 179.7 ± 107.9IU/L, respectively.

Table 8 Mean S. Urea, S. Creatinine and S. Uric acid of patients		
	Mean	Std. Deviation
S. Urea (mg/dL)	43.4	12.1
S. Creatinine (mg/dL)	1.5	0.3
S. Uric acid (mg/dL)	5.6	0.9

The mean S. Urea, S. Creatinine and S. Uric acid of the patients was 43.4 ± 12.1 mg/dL, 1.5 ± 0.3mg/dL and 5.6 ± 0.9 mg/dL, respectively.

Table 9 Mean S. Electrolytesof patients		
	Mean	Std. Deviation
Serum Sodium (mEq/L)	134.6	3.6
Serum Potassium (mEq/L)	4.0	0.8
Serum Calcium (mEq/L)	8.8	1.3
Serum Chloride (mEq/L)	95.6	8.9
Serum Bicarbonate (mEq/L)	22.3	5.7
Serum Magnesium (mEq/L)	1.2	0.2

The mean Serum Sodium, Potassium, Calcium, Chloride, Bicarbonate and Magnesium levels of the patients were 134.6 ± 3.6
4.0±0.8, 8.8±1.3, 95.6±8.9, 22.3±5.7 and 1.2±0.2mEq/L, respectively.

Table 10 Correlation of parameters of LFT, RFT, serum electrolytes and Glasgow coma scale with each other.

		Total bilirubin	Albumin	Total protein	ALT	AST	ALP	S Urea	S Creatinine	S Uric Acid	S Sodium	S Potassium	S Calcium	S Chloride	S bicarbonate	S Magnesium	Glasgow coma scale
Total bilirubin	Pearson Correlation	1	.055	-.038	.172	.091	-.004	-.057	.135	.096	-.069	-.048	-.049	-..003	-.041	-.125	-.040
	Sig. (2-tailed)		.585	.710	.087	.370	.965	.574	.180	.342	.496	.637	.627	.979	.684	.216	.691
Albumin	Pearson Correlation	.055	1	-.170	.293**	.373**	.235*	.080	.144	-.145	.158	.122	-.012	-.033	.142	-.008	-.049
	Sig. (2-tailed)	.585		.092	.003	.000	.019	.431	.153	.150	.117	.225	.907	.747	.158	.940	.626
Total protein	Pearson Correlation	-.038	-.170	1	-.121	-.105	-.248*	.104	.053	-.086	.063	.082	.277**	-.062	.087	-.038	.074
	Sig. (2-tailed)	.710	.092		.231	.299	.013	.304	.600	.397	.534	.418	.005	.539	.390	.710	.464
ALT	Pearson Correlation	.172	.293**	-.121	1	.773**	.612**	.116	.225*	.111	-.022	.023	-.425**	.022	.059	.114	-.045
	Sig. (2-tailed)	.087	.003	.231		.000	.000	.251	.024	.271	.826	.818	.000	.828	.561	.258	.659
AST	Pearson Correlation	.091	.373**	-.105	.773**	1	.437**	.273**	.234*	-.105	.114	.219*	-.128	.067	.198*	.184	-.069
	Sig. (2-tailed)	.370	.000	.299	.000		.000	.006	.019	.299	.257	.028	.206	.510	.048	.066	.495
ALP	Pearson Correlation	-.004	.235*	-.248*	.612**	.437**	1	.074	.134	.135	-.005	.066	-.463**	.055	.268**	.073	-.067
	Sig. (2-tailed)	.965	.019	.013	.000	.000		.464	.185	.182	.963	.516	.000	.589	.007	.471	.510
S Urea	Pearson Correlation	-.057	.080	.104	.116	.273**	.074	1	.735**	-.011	.400**	.513**	.397**	.223*	.620**	.054	.162
	Sig. (2-tailed)	.574	.431	.304	.251	.006	.464		.000	.917	.000	.000	.000	.025	.000	.592	.108
S Creatinine	Pearson Correlation	.135	.144	.053	.225*	.234*	.134	.735**	1	.173	.328**	.292**	.149	.087	.325**	-.012	.066
	Sig. (2-tailed)	.180	.153	.600	.024	.019	.185	.000		.085	.001	.003	.138	.391	.001	.907	.514
SUricAcid	Pearson Correlation	.096	-.145	-.086	.111	-.105	.135	-.011	.173	1	-.095	-.083	-.220*	-.145	-.141	-.014	.105
	Sig. (2-tailed)	.342	.150	.397	.271	.299	.182	.917	.085		.347	.410	.028	.151	.160	.888	.299
S Sodium	Pearson Correlation	-.069	.158	.063	-.022	.114	-.005	.400**	.328**	-.095	1	.450**	.215*	.185	.394**	.066	-.075
	Sig. (2-tailed)	.496	.117	.534	.826	.257	.963	.000	.001	.347		.000	.032	.065	.000	.511	.456
S Potassium	Pearson Correlation	-.048	.122	.082	.023	.219*	.066	.513**	.292**	-.083	.450**	1	.326**	.315**	.527**	.092	.010
	Sig. (2-tailed)	.637	.225	.418	.818	.028	.516	.000	.003	.410	.000		.001	.001	.000	.365	.924
S Calcium	Pearson Correlation	-.049	-.012	.277**	-.425**	-.128	-.463**	.397**	.149	-.220*	.215*	.326**	1	.146	.331**	-.081	.030
	Sig. (2-tailed)	.627	.907	.005	.000	.206	.000	.000	.138	.028	.032	.001		.147	.001	.421	.768
SChloride	Pearson Correlation	-.003	-.033	-.062	.022	.067	.055	.223*	.087	-.145	.185	.315**	.146	1	.433**	.096	.126
	Sig. (2-tailed)	.979	.747	.539	.828	.510	.589	.025	.391	.151	.065	.001	.147		.000	.344	.212
Sbicarbonate	Pearson Correlation	-.041	.142	.087	.059	.198*	.268**	.620**	.325**	-.141	.394**	.527**	.331**	.433**	1	.089	.067
	Sig. (2-tailed)	.684	.158	.390	.561	.048	.007	.000	.001	.160	.000	.000	.001	.000		.381	.507
SMagnesium	Pearson Correlation	-.125	-.008	-.038	.114	.184	.073	.054	-.012	-.014	.066	.092	-.081	.096	.089	1	-.057
	Sig. (2-tailed)	.216	.940	.710	.258	.066	.471	.592	.907	.888	.511	.365	.421	.344	.381		.573
Glasgow coma scale	Pearson Correlation	-.040	-.049	.074	-.045	-.069	-.067	.162	.066	.105	-.075	.010	.030	.126	.067	-.057	1
	Sig. (2-tailed)	.691	.626	.464	.659	.495	.510	.108	.514	.299	.456	.924	.768	.212	.507	.573	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Hepatic encephalopathy (HE) is a neurometabolic syndromecharacterized by impaired brain function in patientswith decompensated cirrhosis.[1-3] The pathogenesisof HE is not completely understood and several proposedpathways are implicated in the initiation and exacerbationof this syndrome.[3-5]HE may be clinically apparent in as many as one third of cirrhotic patients and, if rigorously tested, up to two thirds have some degree of mild or subclinical HE.[6] Ammonia plays a central role in HE asit crosses the blood brain barrier causing neurological insultmediated by a decrease in excitatory neurotransmission.[7] Multiple precipitating factors for HE has beenrecognized and if controlled, may alter the disease acuityand improve mental status[8](Table No. 1) In the present study, 100 patients were included. All the patients were males.The mean Age of patients was 45.8 ± 13.3 years.(Fig. no.1) 52 patients suffered from comorbidities. Most of the patients were suffering from anemia (36), followed by piles (7) and asthma (6).(Table No. 2) The most common cause of Cirrhosis was Alcohol abuse (80%) followed by Autoimmune hepatitis (10%) and HBV infection (5%).Fig. no.3)here our study is in accordance with the study done by Vilstrup H,etal The most common eye response of the patients was 1 (28%) followed by 4 (27%).again here our study is in acccordancw with the study done by Pantham Getal(Table No. 4) The most verbal response of the patients was 2, 4 and 5 (24% each).(Table No. 5) The most common Motor response of the patients was 6 (27%) followed by 5 (23%) and 4 (17%). The mean Glasgow coma scale of the patients was 9.9 ± 1.8(Fig. no.6) The mean Total bilirubin, Albumin and Total Protein of the patients was 1.0 ± 1.1mg/dL, 4.0 ± 0.4g/dL and 7 ± 1.5g/dL, respectively.(Fig. no.7) The mean ALT, AST and ALP of the patients was 33.0 ± 21 mg/dL, 27.9 ± 11.5 g/dL and 179.7 ± 107.9IU/L, respectively.(Fig. no. 8) The mean S. Urea, S. Creatinine and S. Uric acid of the patients was 43.4 ± 12.1 mg/dL, 1.5 ± 0.3mg/dL and 5.6 ± 0.9 mg/dL, respectively.(Fig. no. 9b) The mean Serum Sodium, Potassium, Calcium, Chloride, Bicarbonate and Magnesium levels of the patients were 134.6 ± 3.64.0±0.8, 8.8±1.3, 95.6±8.9, 22.3±5.7 and 1.2±0.2mEq/L, respectively.(Table No. 10) No correlation w **. Correlation is significant at the 0.01 level (2-tailed). Correlation is significant at the 0.05 level (2-tailed). In our study we came to a conclusion that deficiency in the serum magnesium levels is associated with cirrhosis in alcoholic patients most of the studies like the study done by Iwasa M etal and Shechter M. etal are in accordance with us however multicentric studies with larger sample size are required to come to a conclusion Therefore, significant magnesium deficiency might be present even though the serum magnesium level is within normal limits

REFERENCES

1. Aldworth G. Hepatic encephalopathy. Ann Clin Biochem 2017; 54: 416.
2. Weiss N, Jalan R, Thabut D. Understanding hepatic encephalopathy. Intensive Care Med 2018; 44: 231-4.
3. Wijdicks EF. Hepatic Encephalopathy. N Engl J Med 2016;375: 1660-70.
4. Tapper EB, Jiang ZG, Patwardhan VR. Refining the ammoniahypothesis: a physiology-driven approach to the treatment ofhepatic encephalopathy. Mayo Clin Proc 2015; 90: 646-58.
5. Alsaad AA, Stancampiano FF, Palmer WC, Henry AM, Jackson JK, Heckman MG, Diehl NN, Keaveny AP. Serum Electrolyte Levels and Outcomes in Patients Hospitalized with Hepatic Encephalopathy. Annals of hepatology. 2018 Sep 13;17(5):836-42.
6. Shaker M, Carey WD. Hepatic encephalopathy.
7. Tamaoki S, Suzuki H, Okada M, Fukui N, Isobe M, Saito T. Development of an experimental rat model of hyperammonemic encephalopathy and evaluation of the effects of rifaximin. Eur J Pharmacol 2016; 779: 168-76.
8. Vilstrup H, Amodio P, Bajaj J, Cordoba J, Ferenci P, Mullen KD, Weissenborn K, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatology 2014; 60: 715-35.
9. Han KH. Mechanisms of the effects of acidosis and hypokalemia on renal ammonia metabolism. Electrolyte Blood Press 2011; 9: 45-9.
10. Iwasa M, Sugimoto R, Mifuji-Moroka R, Hara N, Yoshikawa K, Tanaka H, Eguchi A, et al. Factors contributing to the development of overt encephalopathy in liver cirrhosis patients. Metab Brain Dis 2016; 31: 1151-6.
11. Pantham G, Post A, Venkat D, Einstadter D, Mullen KD. A New Look at Precipitants of Overt Hepatic Encephalopathy in Cirrhosis. Dig Dis Sci 2017; 62: 2166-73.
12. Swaminathan R. Disorders of magnesium metabolism. CPD Bull Clin Biochem 2000; 2: 3-12.
13. Musso CG. Magnesium metabolism in health and disease. Int Urol Nephrol 2009; 41: 357-62.
14. Johnson S. The multifaceted and widespread pathology of magnesium deficiency. Med Hypotheses 2001; 56: 163-70.
15. Arnaud MJ. Update on the assessment of magnesium status. Br J Nutr 2008; 99 (Suppl 3): S24-36.
16. Cohen L. Physiological assessment of magnesium status in humans: a combination of magnesium load retention and renal excretion. IMAJ 2000; 938-9.
17. Shechter M. Body magnesium--the spark of life. Harefuah 2011; 150: 41-5, 67 [Hebrew].
18. Hashizume N, Mori M. An analysis of hypermagnesemia and hypomagnesemia. Jpn J Med 1990; 29: 368-72.

19. Pasqualetti P, Casale R, Colantonio D, et al. Serum levels of magnesium in hepatic cirrhosis. Quad Sclavo Diagn 1987; 23: 12-7.
20. Rocchi E, Borella P, Borghi A, et al. Zinc and magnesium in liver cirrhosis. Eur J Clin Invest 1994; 24: 149-55.
21. Aagaard NK, Andersen H, Vilstrup H, Clausen T, Jakobsen J, Dørup I. Muscle strength, Na,K-pumps, magnesium and potassium in patients with alcoholic liver cirrhosis -- relation to spironolactone. J Intern Med 2002; 252: 56-63.
22. Aagaard NK, Andersen H, Vilstrup H, Clausen T, Jakobsen J, Dørup I. Decreased muscle strength and contents of Mg and Na,K-pumps in chronic alcoholics occur independently of liver cirrhosis. J Intern Med 2003; 253: 359-66.
23. BOT TT, Ruth Hadary MD, Lotan S. Magnesium deficiency and minimal hepatic encephalopathy among patients with compensated liver cirrhosis.
24. Weisinger JR, Bellorin Front E. "Magnesium and phosphorus". Lancet; 352: 391-396. (1998)
25. Henry JB., Clinical Diagnosis and Management, 17th ed., W.B. Saunder Co. Philadelphia,157 (1984)
26. Galland L. "Magnesium and immune function: an overview. Magnesium" 7(5): 290- 299 (1988)
27. Elin R J. Magnesium: the fifth but forgotten electrolyte. Amer J Clin Pathol.; 102: 616- 629 (1994).
28. Saris NE, Mervaala E, Karppanen H, Khawaja JA, Lewenstam A. Magnesium. An update on physiological, clinical and analytical aspects. Clin Chim Acta.; 294 (1- 2): 1- 26 (2000)