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RESEARCH ARTICLE

STUDY OF SERUM SODIUM LEVELS AND ITS CLINICAL SIGNIFICANCE IN DECOMPENSATED CHRONIC LIVER DISEASE PATIENTS ADMITTED IN A TERTIARY CARE CENTRE OF NORTH EASTERN STATE, TRIPURA

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Abstract

Introduction: Chronic Liver Disease is a major source of death and morbidity globally. Hyponatremia is one of the most common electrolyte abnormalities in chronic liver disease patients. Various studies have established a correlation between serum sodium levels and survival in these patients. Hyponatremia is a marker of severity in CLD patients and studies have shown its relationship with MELD score and Child Pugh score. The complications of DCLD and mortality also increases with hyponatremia. The aim of this study was to study the serum sodium levels in patients with DCLD and to establish its significance.

Materials And Methods: Data was collected from 100 patients admitted in medical wards. Patients were divided into 3 groups based on serum sodium levels and the relevant parameters analyzed among the groups. OBSERVATIONS: Among 100 patients, 45 had serum sodium levels ≥136 mEq/L, while 32 had serum sodium levels between 131 and 135 mEq/L and 23 patients had serum sodium level ≤130. No patients had serum sodium levels greater than 145. Serum sodium levels were associated strongly with the severity of liver disease as assessed by Child Pugh and MELD scores. Serum sodium ≤130 indicated the existence of Hepatic Encephalopathy, Hepatorenal Syndrome and Spontaneous Bacterial Peritonitis. Patients with serum sodium less than 130 mEq/L had increased frequency of complications than those with ≥136 mEq/L. Patient with serum sodium levels ≤130 had increased mortality.

Conclusion: Hyponatremia is more common in DCLD and low serum sodium levels are associated with increased frequency of complications such as hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis and GI bleeding. Lower serum sodium levels were associated with increased MELD and Child Pugh score and mortality indicating the inverse relationship between serum sodium levels and severity of the disease.

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Introduction:-

Chronic liver disorders (CLD) are a major source of morbidity and death globally. Multiple etiological causes contribute to a similar clinicopathological pathophysiology in chronic liver disorders, albeit progression rates and clinical course may differ.[1]The majority of the rise in CLD mortality has been documented from Asia and Africa's poor and low-middle income (LMIC) nations. Disease burden is changing demographically and epidemiologically in LMIC. India is one of the epicentres of this transformation.[2]Reduced serum sodiumconcentration is a common finding in patients with cirrhosis, being the most common electrolyte disorder in this setting.[3]Hyponatremia in cirrhosis is currently defined as a serum sodium level of less than 130 meq/L.[4] It has been suggested that the prevalence of a serum sodium concentration less than 135, 130 and 120 meq/L in patients with cirrhosis and ascites is 49.4%, 21.6% and 1.2%, respectively.[5]Patients with cirrhosis may develop hyponatremia due to either hypovolemia (example: loss of extracellular fluid due to diuretics) or hypervolemia (expanded extracellular fluid volume due to the inability of the kidneys to excrete solute-free water proportionate to the amount of free water ingested).Patients with cirrhosis experience reduction in effective arterial blood volume because of splanchnic arterial vasodilation secondary to increased production of nitric oxide, endotoxins, and other vasodilators.[6,7,8] This leads to activation of the renin-angiotensin-aldosterone axis and impairment of free water excretion secondary to excessive antidiuretic hormone.[7]In 10% of cases, hyponatremia is hypovolemic,[3,8] typically from over diuresis.In cirrhosis, hyponatremia generally develops slowlyand gradually. Therefore, the brain can adjust to hypoosmolality and hypotonicity of the extracellular fluid sothat the incidence of neurological manifestations directlyattributable to hyponatremia is relatively low. However,since hyponatremia occurs in the setting of end-stage liverdisease, it is often difficult to define to what extent theclinical manifestations are due to reduced serum sodiumconcentration or to hepatic encephalopathy.Hyponatremia is a marker of the severity of cirrhosis and is more prevalent in patients with cirrhosis with Child-Pugh class C.[8,9,10] Patients with hyponatremia are less sensitive to diuretics and have higher rates of hospitalization with spontaneous bacterial peritonitis, hepatic encephalopathy, and hepatorenal syndrome.[10,11,12]According to recent research, hyponatremia isa significant predictive factor in individuals with chronic liver disease.There is a correlation between hyponatremia and the increased risk for mortality. Serum sodium has been found to be an independent predictor of mortality with a hazard ratio of 1.05 permmol reduction in serum sodium concentration between 125 and 140 mmol/L.[12,13] The current study was conducted to investigate blood sodium levels in chronic liver disease patients and determine their relationship with the disease severity in the such individuals.

Aim:

To study the serum sodium levels in patients with decompensated chronic liver disease and to study its relationship with the clinical outcome.

Materials and Methods:-

It was a cross-sectional descriptive type of study done in the department of General Medicine, Agartala Government Medical College and GBP Hospital.

The study duration was from January 2023 to June 2023.

Ethical Committee clearance was obtained from Institution.Patients were selected based on history, examination, laboratory investigations and imaging suggestive of the diagnosis of Decompensated Chronic Liver Disease. The presence of various complications and the outcome of the patients were monitored. The severity of the disease was calculated using MELD score and Child Pugh Score. The patients were included in the study after taking informed consent.

Inclusion Criteria:

All patients with Decompensated Chronic Liver Disease diagnosed by examination, laboratory investigations and radiological imaging belonging to the age group of 18-65.

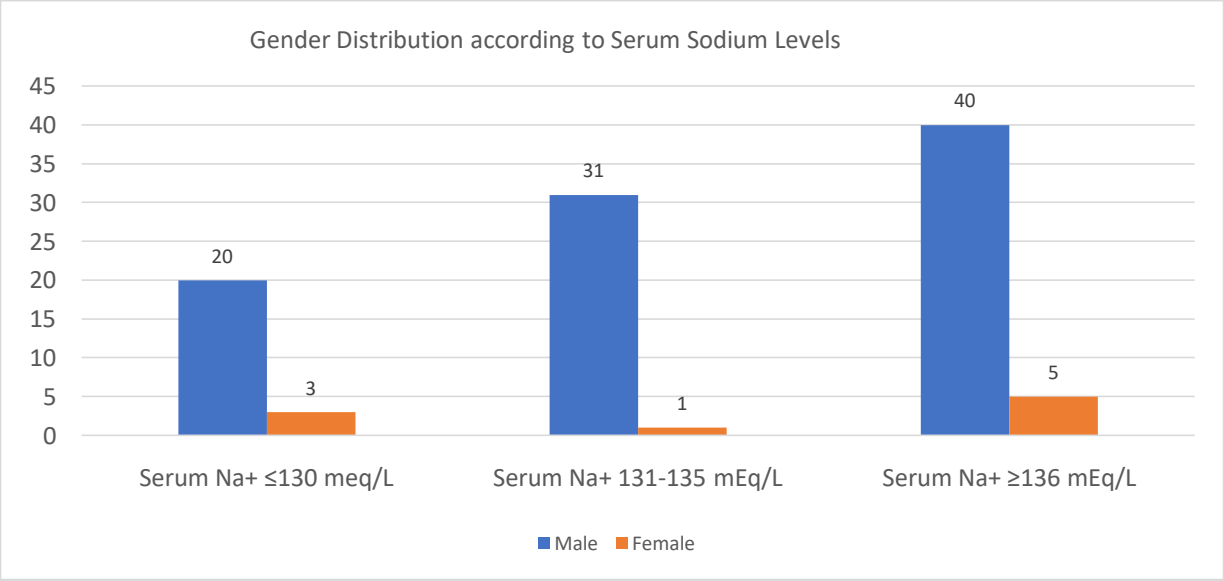
Exclusion Criteria:

1. Patients with cardiac failure
2. Patients with chronic kidney disease
3. Patients on drugs such as SSRIs, TCA, MAO inhibitors, cytotoxic drugs etc.

The collected datas were entered in a Microsoft Excel Sheet. Graphs and tables were generated using Microsoft Word and Microsoft Excel. Statistical analysis was done using medcalc 15.8, Minitab 17, IBM SPSS 22. Quantitative data was analysed using Mean, Median, Mode and Standard Deviation (SD). Qualitative data was analysed using Chi Square Test, One way ANOVA and Fisher's test. Difference between two variables is considered significant when 'p' value is less than 0.05.

Results:-

In this study 100 DCLD patients were included and they were divided into 3 groups according to their serum sodium concentrations. 23 % had serum sodium concentrations ≤130 meq/L (Group A), 32 % had serum sodium concentrations between 131 to 135 mEq/L (Group B) and 45 % had serum sodium concentrations ≥136 mEq/L (Group C)but none had serum sodium concentrations ≥145mEq/L.

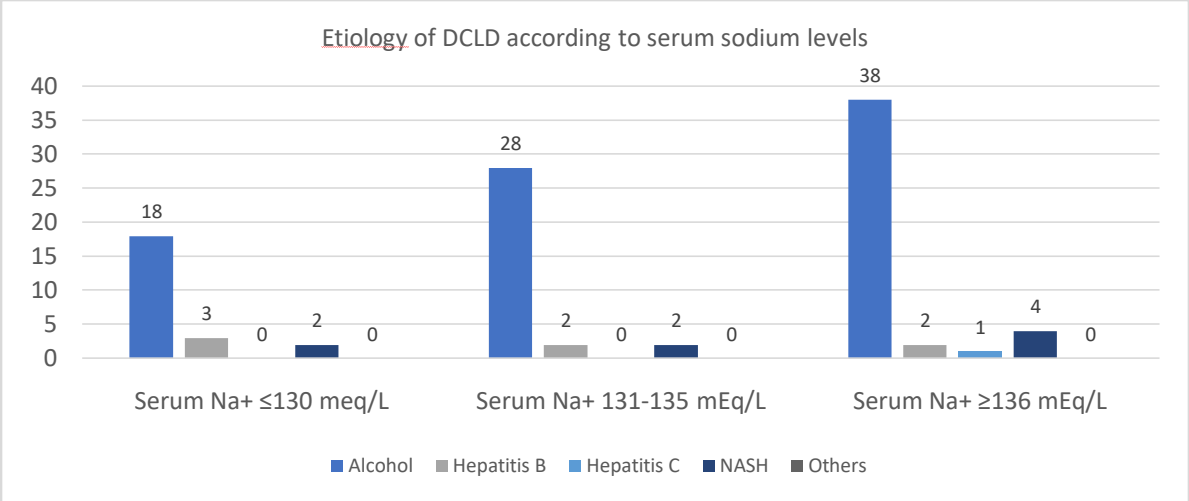


Among study subjects majority were males 91 % and only 9 % were females.

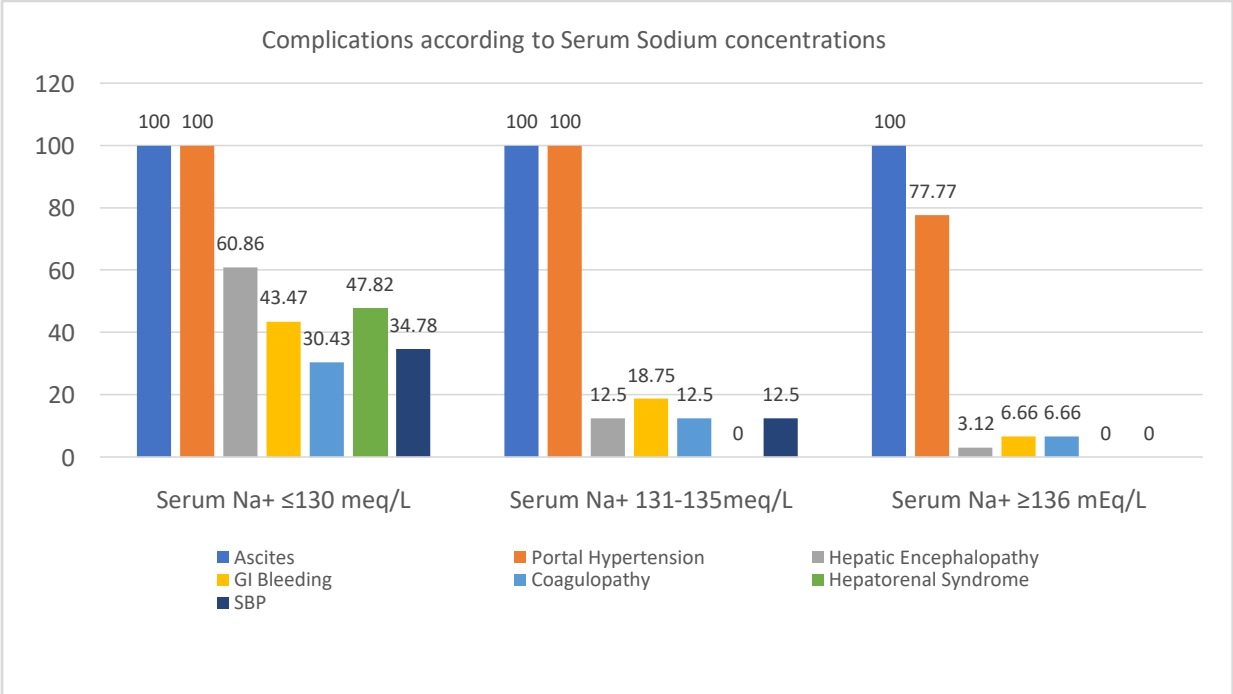
Table:- Characteristics of patients according to serum sodium concentration.

SL NO.	PARAMETERS	SERUM Na^+ ≤130 mEq/L (N=23)	SERUM Na^+ 131-135 mEq/L (N=32)	SERUM Na^+ ≥136 mEq/L (N=45)	P VALUE
1	Age(years)(Mean+SD)	53.20+11.46	50.11+11.10	52.82+10.78	
2	MELD Score(Mean+SD)	18.60+7.80	14.19+4.50	8.90+3.40	<0.0001
3	Child-Pugh Score	10.00 +1.92	8.42+1.20	7.22+1.23	<0.0001
4	Child-Pugh Class A	0	1	13	
	Child-Pugh Class B	9	21	27	
	Child-Pugh Class C	14	10	5	

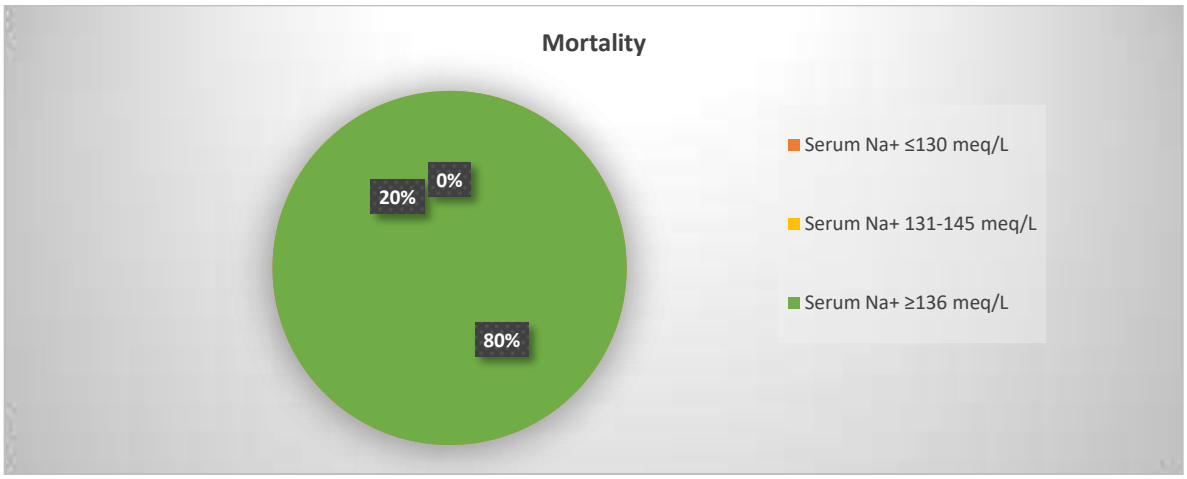
The mean age of patients with sodium levels ≤130 was 53.20+11.46 years, while in those with serum sodium levels 131- 135 and ≥136 were 50.11+11.10 years and 52.82+10.78 years respectively. The MELD Score was highest among patients having serum sodium levels ≤130 mEq/L (18.60+7.80) followed by patients having serum Na+ levels between 131-135 mEq/L (14.19+4.50) and by patients having serum Na+≥136 mEq/L (8.90+3.40). The association between MELD Score and P value was statistically significant (p value <0.0001). In Group A 60.87 % patients belonged to Child Pugh Class C and 39.13% belonged to Class B and none belonged to Class A. In group B 31.25% belonged to Class C, 65.63% belonged to class B and 3.12% belonged to Class A. In group C 11.11% belonged to class C, 60% belonged to class B and 28.89% belonged to class A.



In group A alcoholic liver disease was the commonest cause of DCLD in this study accounting for 78.26% while chronic hepatitis B and NASH was found to be the causative factor in 13.04% and 8.7% respectively.In group B alcoholic liver disease was the cause of DCLD in this study accounting for 87.50% while chronic hepatitis B and NASH was found to be the causative factor in 6.25% and 6.25% respectively.In group C alcoholic liver disease was the cause of DCLD in this study accounting for 84.44% while chronic hepatitis B, chronic hepatitis C and NASH was found to be the causative factor in 4.44%, 2.22% and 8.90% respectively.



Ascites was present in all the patients, portal hypertension was present in 100 % of patients in group A and group B but in 77.77% patients in group C. 60.86% of patients were suffering from hepatic encephalopathy in group A, 12.5% and 3.12% in group B and group Cwere having hepatic encephalopathy respectively.Complications like upper gastrointestinal bleeding and coagulopathy were maximum in group A patients followed by group B and C patients. Hepatorenal syndrome was present in 47.82% of group A patients and was not present in any of the group B or C patients. Spontaneous bacterial peritonitis was present in 34.78% patients of group A and 12.5% patients of group B and none of the patients of group C suffered from SBP.



10 patients died in our study and rest were discharged. Out of the 10 patients died 8 belonged to Group A and 2 belonged to Group B and no mortality was there in group C (p value 0.002).

Discussion:-

In the present study, 100 patients were included. It wasobserved that 23% were in Group A (≤130 mEq/L),32% were in Group B (131–135 mEq/L), and 45%were in Group C (≥136 mEq/L). Thus, hyponatremia wasobserved in 55% of the patients.

Bhandari A et al[14] in their study found that 41.22% patients had hyponatremia with mean age of 53.44±7.57years.Meganathan and Kumar established the prevalence ofhyponatremia in cirrhosis and to investigate if hyponatremiapredicts an increased rate and severity of complications incirrhosis.[15] They reported hyponatremia in 44%, normal serumsodium in 26%, and hypernatremia in 30% of the patients. The other studies showed:

STUDIES	DISTRIBUTIONOFPATIENTS		
	≤130mEq/L	131-135mEq/L	≥136mEq/L
PRESENTSTUDY	23%	32%	45%
ANGELIPET AL[4]	21.6%	27.8%	50.6%
JONGHOONKIM ET AL[16]	27.1%	20.8%	52.1%
SHAIKHET AL[17]	26.7%	24.9%	48.4%
BORRONIETAL[18]	29.8%		
UMEMURA ET AL[19]	4.7%	15.2%	80.1%
SINGH JP ET AL[20]	36.7%	30%	33.3%

The results of the present study extend the observations made by the above mentioned studies that decompensated liver disease is associated with abnormal serum sodium concentration. It also shows that hyponatremia is the common abnormality with more than half of the patients having serum sodium levels less than 135 mEq/L.

In astudy by Devadas AD et al.[21] among DCLD patientsshowed males constituted 80% and the rest were females. 67% of the patients were Alcoholics. HBsAg positive status was present in 11 patients, Hepatitis C Positive status in 7 patients and, 15 patients were cryptogenic. In this study, hyponatremia was seen in 70% of the patients which was higher as compared to our study. In our study 91% were males and only 9% were females. In our study also the predominant cause of DCLD was alcoholic liver disease which was 84% followed by chronic hepatitis B 7%.

In our study, the mean MELD score was significantly higheramong Group A patients (18.60+7.80) as compared to thosewith Group B (14.19+4.50) and Group C (8.90+3.40). Inanother study by Meganathan and Kumar, the mean MELDscore was 27.7±6.7 for patients with hyponatremia, which wassignificantly higher as compared to those with normal serumsodium levels and hypernatremia.Elkady et al.[22], also reportedthe mean MELD score to be 18.19±5.3 among patients withserum sodium ≤125 mEq/L as compared to 16.17±6.2 inpatients with serumsodium more than 125 mEq/L.

We observed that the Child-Pugh score was significantlyhigher among Group A patients (10.00 +1.92) as compared tothose with Group B (8.42+1.20) and Group C (7.22+1.23).In addition, Child-Pugh Class C was significantly morecommon in Group A patients (60.87%) as compared tothose with Group B (31.25%) and Group C (11.11%).In a similar study by Jenq et al., CPS was significantlyhigher in patients with serum sodium level ≤135 mEq/L(12.4±2.3) as compared to those with serum sodium level>135 mEq/L (11.1±2.1).[23] In the study by Kim et al., meanCPS was significantly higher in patients with hyponatremia(10.5±1.6) as compared to those with normal serum sodiumlevel (9.8±1.7) and hypernatremia (8.7±1.6), P<0.001.[16]

Kim et al found ascites in 88% of hyponatremia patients, spontaneous bacterial peritonitis in33%, and hepatic encephalopathy in 43%, allof which were considerablyhigher than inpatients with normal serum sodium and hypernatremia.[16]In the study by Jenq et al., a significantly higher proportionof patients with sodium level ≤135 mEq/L had hepaticencephalopathy as compared to those withsodium >135 mEq/L.[23] In another study, Elkady etal found that 91% of individuals with blood sodium levels less than125mEq/lhad hepatic encephalopathy, and50% had upper gastrointestinal bleed, which was considerably higher than those with serum sodium levels greater than 125 mEq/l.[24] In this study the complications like ascites, portal hypertension, hepatorenal syndrome, SBP, upper gastrointestinal bleeding and coagulopathy were more in group A than group B and C.

In our study 34.78%(n=8/23) patients of group A died while 6.25%(n=2/32) patients of group B died and all patients of group C were discharged without any mortality. In a similar study byKim et al., 3-year survival rate was 47.2% in patients witha serum sodium ≥136 mmol/L, 16.6% in patients with aserum sodium of 131–135 mmol/L, and 33.3% in patientswith a serum sodium ≤130 mmol/L and the associationwas statistically significant (P<0.001).[16] Inanother study by Eklady et al., the mortalities were26.4% among patients with serums sodium levels ≤125 mEq/Land 15.9% among patients with serum sodium levels morethan 125 mEq/L.[24]

Conclusion:-

Hyponatremia in DCLD is associated with increased frequency of complications such as hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis and GI bleeding. Lower serum sodium levels were associated with increased MELD and Child Pugh score and mortality indicating the inverse relationship between serum sodium levels and severity of the disease.

Referrences:-

1.Propst A, Propst T, Zangerl G, Ofner D, Judmaier G, Vogel W. Prognosis and life expectancy in chronic liver disease. Dig Dis Sci. 1995;40(8):1805-15.
2.James K S. India's demographic change: opportunities and challenges. Science. 2011;333(6042):576-80.
3.Ginés P, Berl T, Bernardi M, Bichet DG, Hamon G, Jiménez W et al. Hyponatremia incirrhosis: from pathogenesis to treatment. Hepatology. 1998;28(3):851-64.
4. Angeli P, Wong F, Watson H, Ginès P. Hyponatremia in cirrhosis: Results of a patient population survey. Hepatology. 2006;44:1535–1542.
5. Abelmann WH. Hyperdynamic circulation in cirrhosis: a historical perspective.Hepatology. 1994;20:1356–1358.
6. Schrier RW, Gross P, Gheorghiade M, et al. Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. N Engl J Med 2006;355:2099-2112.
7. Iwakiri Y. The molecules: Mechanisms of arterial vasodilatation observed in the splanchnic and systemic circulation in portal hypertension. J Clin Gastroenterol 2007;41(Suppl. 3):S288-S294.
8. Ginès P, Cárdenas A. The management of ascites and hyponatremia in cirrhosis. Semin Liver Dis 2008;28:43-58.
9. Ginès P, Guevara M. Hyponatremia in cirrhosis: Pathogenesis, clinical significance, and management. Hepatology 2008;48:1002-1010.
10. Guevara M, Baccaro ME, Torre A, et al. Hyponatremia is a risk factor of hepaticencephalopathy in patients with cirrhosis: A prospective study with time-dependent lysis. Am J Gastroenterol 2009;104:1382-1389.
11. Ginès A, Escorsell A, Ginès P, et al. Incidence, predictive factors, and prognosis of the hepatorenal syndrome in cirrhosis with ascites. Gastroenterology 1993;105:229-236.
12. Sinha VK, Ko B. Hyponatremia in cirrhosis—pathogenesis, treatment, and prognostic significance. Adv Chronic Kidney Dis 2015;22:361-367.
13. Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med 2008;359:1018-1026.

14. Bhandari A, Chaudhary A. Hyponatremia in Chronic Liver Disease among Patients Presenting to a Tertiary Care Hospital: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2021 Dec 11;59(244):1225-1228.
15. Meganathan A and Kumar VS. Hyponatremia incirrhosis- prevalence and correlation with the complications ofcirrhosis. J Evol Med Dent Sci. 2018;7(18):2197-2202.
16. Jong Hoon Kim, June Sung Lee, Seuk Hyun Lee, Won Ki Bae, Nam- Hoon Kim, Kyung-Ah Kim, and Young-Soo Moon. The Association Between the Serum Sodium Level and the Severity of Complications in Liver Cirrhosis Korean J Intern Med. Jun 2009; 24(2): 106–112.
17. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatraemia and its influence on liver cirrhosis-related complications. J Pak Med Assoc. 2010 Feb;60(2):116-20.
18. Borroni, G., Maggi, A., Sangiovanni, A., Cazzaniga, M, Salerno F. Clinical relevance of hyponatraemia for the hospital outcome of cirrhotic patients. Digestive and Liver Disease. 2000; 32: 605–610.
19. Umemura T, Shibata S, Sekiguchi T, Kitabatake H, Nozawa Y,Okuhara S, et al. Serum sodium concentration is associated withincreased risk of mortality in patients with compensated livercirrhosis. Hepatol Res. 2015;45(7):739-744.
20. Singh JP, Khurana A, Singh D. Frequency of hyponatremia and its influence on liver cirrhosis-related complications. Int J Adv Res. 2016;4(2):1113–8.
21. Devadas AD, Srividya, Raja G, Kumar S, Sindhu, Shanmugasundaram, et al. A Study on Hyponatremia in Decompensated Liver Disease. J Med Sci Clin Res. 2017 Apr;5(4):19832–6.
22. Elkady MS, El-Toukhy NE and Rashed SE. Serum sodiumconcentration profile incirrhotic patients and its effecton the prognostic value of the MELD score. SAS J Surg.2016;2(6):266-277.
23. Jenq CC, Tsai MH, Tian YC, Chang MY, Lin CY, Lien JM, et al.Serum sodium predicts prognosis in critically ill cirrhotic patients.J Clin Gastroenterol. 2010;44(3):220-226.
24. Elkady MS, El-Toukhy NE and Rashed SE. Serum sodiumconcentration profile in cirrhotic patients and its effecton the prognostic value of the MELD score. SAS J Surg.2016;2(6):266-277.