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Serum Sodium as a Prognostic Marker in Chronic Decompensated Cirrhosis of the Liver

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A B S T R A C T

Background: Serum sodium levels have been recognized as a prognostic marker in chronic liver disease, particularly in decompensated cirrhosis. This study aimed to investigate the association between serum sodium levels and clinical outcomes in patients with chronic decompensated cirrhosis.***Methods***: A prospective observational study was conducted on 90 patients with chronic decompensated cirrhosis. Serum sodium levels were measured, and patients were categorized into four groups: <125 mEq/L, 125-129 mEq/L, 130-134 mEq/L, and ≥135 mEq/L. The relationship between serum sodium levels and various clinical parameters, complications, mortality, hospital stay, and ICU requirement was analyzed. ***Results:*** The majority of patients (57.8%) were in the age group of 40-59 years, and males constituted 82.2% of the study population. Serum sodium levels showed a significant inverse correlation with Child-Pugh scores ($r=-0.723$, $p<0.001$) and MELD scores ($r=-0.739$, $p<0.001$). Patients with lower serum sodium levels had a significantly higher prevalence of complications, including hepatorenal syndrome (18.8% in patients with serum sodium <125 mEq/L), spontaneous bacterial peritonitis (12.5%), hepatic encephalopathy (68.8%), and coagulopathy (81.3%). Lower serum sodium levels were also associated with increased mortality, prolonged hospital stay, and higher ICU requirement ($p<0.001$). ***Conclusion***: Serum sodium is a valuable prognostic marker in patients with chronic decompensated cirrhosis. Lower serum sodium levels are associated with more advanced liver disease, higher prevalence of complications, increased mortality, prolonged hospital stay, and higher ICU requirement. Incorporating serum sodium levels into the assessment and management of these patients can aid in risk stratification and treatment decisions.

Keywords: Serum sodium, hyponatremia, decompensated cirrhosis, prognostic marker, liver disease.

INTRODUCTION

Chronic liver disease is a major global health concern, with cirrhosis representing the end-stage of various etiologies, including alcohol abuse, viral hepatitis, and non-alcoholic fatty liver disease [1]. Decompensated cirrhosis, characterized by the development of complications such as ascites, hepatic encephalopathy, and variceal bleeding, is associated with significant morbidity and mortality [2]. Accurate prognostic markers are crucial for assessing disease severity, predicting outcomes, and guiding treatment decisions in patients with decompensated cirrhosis.

Serum sodium levels have emerged as a promising prognostic marker in chronic liver disease, particularly in decompensated cirrhosis [3]. Hyponatremia, defined as a serum sodium concentration below 135 mmol/L, is a common electrolyte disturbance in patients with advanced liver disease [4]. The pathogenesis of hyponatremia in cirrhosis is multifactorial, involving a complex interplay between portal hypertension, neurohormonal activation, and renal dysfunction [5].

The prevalence of hyponatremia in patients with cirrhosis ranges from 22% to 50%, with increasing frequency as the disease progresses [6]. Hyponatremia has been associated with a wide range of adverse outcomes in cirrhosis, including increased risk of hepatic encephalopathy, refractory ascites, hepatorenal syndrome, and mortality [7].

The Model for End-Stage Liver Disease (MELD) score, which incorporates serum bilirubin, creatinine, and international normalized ratio (INR), has been widely adopted as a prognostic tool for assessing the severity of liver disease and prioritizing patients for liver transplantation [8]. However, the MELD score does not account for hyponatremia, which has been recognized as an independent predictor of mortality in patients with cirrhosis [9].

To address this limitation, the incorporation of serum sodium into the MELD score (MELD-Na) has been proposed to improve its prognostic accuracy [10]. Several studies have demonstrated the superiority of MELD-Na over the conventional MELD score in predicting mortality and other clinical outcomes in patients with decompensated cirrhosis [3, 7].

Serum sodium levels have emerged as a valuable prognostic marker in patients with chronic decompensated cirrhosis of the liver. Hyponatremia is associated with increased morbidity and mortality, and its severity correlates with the degree of liver dysfunction and cirrhosis-related complications. The incorporation of serum sodium into the MELD score has been shown to improve its prognostic accuracy, providing a more comprehensive assessment of disease severity. Monitoring serum sodium levels in patients with decompensated cirrhosis may aid in risk stratification, guiding treatment decisions, and improving patient outcomes.

Aims and Objectives

The primary aim of this study was to investigate the correlation between serum sodium levels and the Model for End-Stage Liver Disease (MELD) scores in patients with chronic decompensated cirrhosis of the liver. The secondary objectives were to compare serum sodium levels between patients with MELD scores < 20 and ≥ 20, and to assess the potential of serum sodium as a prognostic marker in the management of patients with decompensated cirrhosis.

Materials and Methods

Study Design and Setting

A prospective observational study was conducted at a tertiary care center from September 2021 to August 2022. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants or their legal representatives.

Study Population

The study included 90 patients diagnosed with chronic decompensated cirrhosis of the liver. The diagnosis of cirrhosis was based on a combination of clinical, biochemical, and radiological findings. Patients were recruited from the outpatient and inpatient departments of the hospital.

Inclusion and Exclusion Criteria

The inclusion criteria for the study were as follows: (1) patients aged 18 years or above, (2) diagnosed with chronic decompensated cirrhosis of the liver, and (3) willingness to participate in the study. Patients were excluded if they had any of the following conditions: (1) acute liver failure, (2) hepatocellular carcinoma, (3) prior liver transplantation, (4) significant comorbidities such as severe cardiovascular disease or advanced renal failure, or (5) inability to provide informed consent.

Sample Size Calculation

The sample size was calculated using a correlation coefficient of 0.3, a significance level of 0.05, and a power of 80%. Considering a 10% dropout rate, a minimum of 90 patients were required for the study.

Data Collection

Demographic and clinical data were collected from each patient, including age, sex, etiology of liver disease, and presence of cirrhosis-related complications such as ascites, hepatic encephalopathy, and variceal bleeding. Serum sodium levels and other relevant laboratory parameters, including serum bilirubin, creatinine, and international normalized ratio (INR), were measured at the time of enrollment.

MELD Score Calculation

The MELD score was calculated using the following formula: $MELD = 3.78 \times \ln[\text{serum bilirubin (mg/dL)}] + 11.2 \times \ln[\text{INR}] + 9.57 \times \ln[\text{serum creatinine (mg/dL)}] + 6.43$. Patients were categorized into two groups based on their MELD scores: < 20 and ≥ 20.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Pearson's correlation coefficient was used to evaluate the relationship between serum sodium levels and MELD scores. Independent t-tests were used to compare serum sodium levels between the two MELD score groups. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The study included a total of 90 patients with chronic decompensated cirrhosis of the liver. Table 1 presents the distribution of patients by age, sex, and etiology of cirrhosis. The majority of patients (57.8%) were in the age group of 40-59 years, followed by 22.2% in the ≥60 years group and 20.0% in the 18-39 years group. Males constituted 82.2% of the study population, while females accounted for 17.8%. The most common etiology of cirrhosis was alcohol (44.4%), followed by non-alcoholic steatohepatitis (NASH) (40.0%), hepatitis B (8.9%), and hepatitis C (6.7%).

Table 2 shows the distribution of serum sodium levels by age, sex, and body mass index (BMI) categories. The highest proportion of patients with serum sodium levels <125 mEq/L was observed in the ≥60 years age group (20.0%), while the highest proportion of patients with serum sodium levels ≥135 mEq/L was found in the 18-39 years age group (27.8%). However, the differences in serum sodium levels across age groups were not statistically significant (p=0.703). Similarly, no significant differences were observed in the distribution of serum sodium levels between males and females (p=0.948) or across BMI categories (p=0.995).

The relationship between serum sodium levels, Child-Pugh scores, and Model for End-Stage Liver Disease (MELD) scores is presented in Table 3. A significant inverse correlation was found between serum sodium levels and both Child-Pugh scores (Pearson's r=-0.723, p<0.001) and MELD scores (Pearson's r=-0.739, p<0.001). The majority of patients with serum sodium levels <125 mEq/L had Child-Pugh C (81.3%) and MELD scores of 20-29 (75.0%). Conversely, 78.9% of patients with serum sodium levels ≥135 mEq/L had Child-Pugh A, and 57.9% had MELD scores of 10-19.

Table 4 illustrates the association between serum sodium levels and various clinical complications. Statistically significant differences were observed in the prevalence of hepatorenal syndrome, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, and coagulopathy across different serum sodium levels (p<0.001). The highest prevalence of these complications was found in patients with serum sodium levels <125 mEq/L, with 18.8% having hepatorenal syndrome, 12.5% having SBP, 68.8% having hepatic encephalopathy, and 81.3% having coagulopathy.

The relationship between serum sodium levels and overall complications, mortality, hospital stay, and intensive care unit (ICU) requirement is shown in Table 5. Statistically significant differences were observed across serum sodium levels for all these parameters (p<0.001). All patients with serum sodium levels <125 mEq/L had complications, and 81.3% had mortality. The mean hospital stay was longest in patients with serum sodium levels <125 mEq/L (13.7 ± 1.3 days) and shortest in those with serum sodium levels ≥135 mEq/L (7.3 ± 1.9 days). The proportion of patients requiring ICU care decreased with increasing serum sodium levels, with 87.5% of patients with serum sodium levels <125 mEq/L requiring ICU care compared to none of the patients with serum sodium levels ≥135 mEq/L.

Table 6 presents the biochemical and hematological parameters across different serum sodium levels. Statistically significant differences were observed for all parameters (p<0.001). Patients with lower serum sodium levels had higher levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, creatinine, and international normalized ratio (INR), and lower levels of white blood cell count (WBC).

Table 7 shows the Pearson's correlation coefficients between serum sodium levels and various continuous variables. Serum sodium levels had a significant inverse correlation with Child-Pugh scores (r=-0.723, p<0.001), MELD scores (r=-0.739, p<0.001), AST (r=-0.744, p<0.001), ALT (r=-0.684, p<0.001), bilirubin (r=-0.759, p<0.001), creatinine (r=-0.732, p<0.001), INR (r=-0.719, p<0.001), and hospital stay (r=-0.602, p<0.001). A significant positive correlation was found between serum sodium levels and WBC (r=0.706, p<0.001). No significant correlations were observed between serum sodium levels and age (r=-0.139, p=0.192) or BMI (r=0.021, p=0.845).

Table 1: Distribution of Patients by Age, Sex, and Etiology of Cirrhosis

Age Group	Male (%)	Female (%)	Total (%)	Hepatitis B (%)	Hepatitis C (%)	Alcohol (%)	NASH (%)
18-39	13 (14.4%)	5 (5.6%)	18 (20.0%)	2 (2.2%)	1 (1.1%)	8 (8.9%)	7 (7.8%)
40-59	43 (47.8%)	9 (10.0%)	52 (57.8%)	3 (3.3%)	3 (3.3%)	22 (24.4%)	24 (26.7%)
≥60	18 (20.0%)	2 (2.2%)	20 (22.2%)	3 (3.3%)	2 (2.2%)	10 (11.1%)	5 (5.6%)
Total	74 (82.2%)	16 (17.8%)	90 (100%)	8 (8.9%)	6 (6.7%)	40 (44.4%)	36 (40.0%)

Table 2: Serum Sodium Levels and Distribution by Age, Sex, and BMI Categories

Category	<125 mEq/L (%)	125-129 mEq/L (%)	130-134 mEq/L (%)	≥135 mEq/L (%)	p-value
Age Group					
18-39	2 (11.1%)	4 (22.2%)	7 (38.9%)	5 (27.8%)	0.703
40-59	10 (19.2%)	16 (30.8%)	15 (28.8%)	11 (21.2%)	
≥60	4 (20.0%)	7 (35.0%)	6 (30.0%)	3 (15.0%)	
Sex					
Male	14 (18.9%)	22 (29.7%)	23 (31.1%)	15 (20.3%)	0.948
Female	2 (12.5%)	5 (31.3%)	5 (31.3%)	4 (25.0%)	
BMI (kg/m²)					
18.5-24.9	8 (17.0%)	14 (29.8%)	15 (31.9%)	10 (21.3%)	0.995
25.0-29.9	8 (18.6%)	13 (30.2%)	13 (30.2%)	9 (20.9%)	

Table 3: Serum Sodium Levels, Child-Pugh, and MELD Scores

Serum Sodium	Child-Pugh A (%)	Child-Pugh B (%)	Child-Pugh C (%)	MELD <10 (%)	MELD 10-19 (%)	MELD 20-29 (%)	MELD ≥30 (%)	p-value
<125 mEq/L	0 (0%)	3 (18.8%)	13 (81.3%)	0 (0%)	2 (12.5%)	12 (75.0%)	2 (12.5%)	<0.001
125-129 mEq/L	0 (0%)	11 (40.7%)	16 (59.3%)	0 (0%)	5 (18.5%)	21 (77.8%)	1 (3.7%)	
130-134 mEq/L	6 (21.4%)	16 (57.1%)	6 (21.4%)	2 (7.1%)	21 (75.0%)	5 (17.9%)	0 (0%)	
≥135 mEq/L	15 (78.9%)	4 (21.1%)	0 (0%)	8 (42.1%)	11 (57.9%)	0 (0%)	0 (0%)	
Pearson's r	-0.723	p<0.001	-0.739	p<0.001				

Table 4: Serum Sodium Levels and Clinical Complications

Serum Sodium	Hepatorenal Syndrome Present (%)	Hepatorenal Syndrome Absent (%)	SBP Present (%)	SBP Absent (%)	Hepatic Encephalopathy Present (%)	Hepatic Encephalopathy Absent (%)	Coagulopathy Present (%)	Coagulopathy Absent (%)	p-value
<125 mEq/L	3 (18.8%)	13 (81.3%)	2 (12.5%)	14 (87.5%)	11 (68.8%)	5 (31.3%)	13 (81.3%)	3 (18.8%)	<0.001
125-129 mEq/L	1 (3.7%)	26 (96.3%)	1 (3.7%)	26 (96.3%)	14 (51.9%)	13 (48.1%)	19 (70.4%)	8 (29.6%)	
130-134 mEq/L	0 (0.0%)	28 (100%)	1 (3.6%)	27 (96.4%)	6 (21.4%)	22 (78.6%)	12 (42.9%)	16 (57.1%)	
≥135 mEq/L	0 (0%)	19 (100%)	0 (0.0%)	19 (100%)	3 (15.8%)	16 (84.2%)	6 (31.6%)	13 (68.4%)	

Table 5: Serum Sodium Levels and Overall Complications, Mortality, Hospital Stay, ICU Requirement

Serum Sodium	Complications Present (%)	Complications Absent (%)	Mortality Present (%)	Mortality Absent (%)	Hospital Stay (Days) Mean ± SD	ICU Required (%)	ICU Not Required (%)	p-value
<125 mEq/L	16 (100%)	0 (0%)	5 (81.3%)	11 (18.8%)	13.7 ± 1.3	14 (87.5%)	2 (12.5%)	<0.001
125-129 mEq/L	24 (88.9%)	3 (11.1%)	3 (51.9%)	24 (48.1%)	12.3 ± 1.7	16 (59.3%)	11 (40.7%)	
130-134 mEq/L	18 (64.3%)	10 (35.7%)	1 (7.1%)	27 (92.9%)	9.4 ± 2.2	4 (14.3%)	24 (85.7%)	
≥135 mEq/L	8 (42.1%)	11 (57.9%)	0 (0%)	19 (100%)	7.3 ± 1.9	0 (0%)	19 (100%)	
Pearson's r	-0.669	p<0.001	-0.704	p<0.001	-0.602	p<0.001		

Table 6: Biochemical and Hematological Parameters by Serum Sodium Levels

Parameter	<125 mEq/L Mean ± SD	125-129 mEq/L Mean ± SD	130-134 mEq/L Mean ± SD	≥135 mEq/L Mean ± SD	p-value
AST (U/L)	171.9 ± 5.5	155.0 ± 11.8	122.4 ± 16.3	97.6 ± 12.7	<0.001
ALT (U/L)	112.1 ± 7.3	101.6 ± 8.8	89.5 ± 6.9	79.8 ± 6.5	<0.001
Bilirubin (mg/dL)	4.0 ± 0.3	3.2 ± 0.4	2.2 ± 0.5	1.7 ± 0.2	<0.001
Creatinine(mg/dL)	2.6 ± 0.2	2.1 ± 0.3	1.6 ± 0.2	1.3 ± 0.2	<0.001
INR	2.2 ± 0.2	1.9 ± 0.2	1.5 ± 0.2	1.3 ± 0.1	<0.001
CBC (WBC x10^3/uL)	3.2 ± 0.3	4.0 ± 0.4	5.0 ± 0.6	6.0 ± 0.4	<0.001

Table 7: Pearson's Correlation between Serum Sodium Levels and Continuous Variables

Variable	Pearson's Correlation Coefficient (r)	p-value
Age	-0.139	0.192
BMI	0.021	0.845
Child-Pugh Score	-0.723	<0.001
MELD Score	-0.739	<0.001
AST	-0.744	<0.001
ALT	-0.684	<0.001
Bilirubin	-0.759	<0.001
Creatinine	-0.732	<0.001
INR	-0.719	<0.001
CBC (WBC)	0.706	<0.001
Hospital Stay	-0.602	<0.001

DISCUSSION

The present study investigated the role of serum sodium as a prognostic marker in patients with chronic decompensated cirrhosis of the liver. The findings demonstrate a significant association between serum sodium levels and various clinical outcomes, including complications, mortality, hospital stay, and ICU requirement.

The majority of patients in this study were in the age group of 40-59 years (57.8%), and males constituted 82.2% of the study population. These demographic characteristics are consistent with previous studies on decompensated cirrhosis. A study by Qureshi *et al*., reported a mean age of 52.1 ± 12.3 years and a male predominance (63.3%) in their cohort of patients with decompensated cirrhosis [11].

The most common etiology of cirrhosis in the present study was alcohol (44.4%), followed by NASH (40.0%). These findings are in line with the increasing recognition of NASH as a significant contributor to the burden of chronic liver disease worldwide [12]. A study by Singal*et al*., reported alcohol (45.9%) and NASH (20.8%) as the leading etiologies of cirrhosis in their patient population [13].

The prevalence of hyponatremia (serum sodium <135 mEq/L) in the current study was 78.9%, which is higher than the reported prevalence in other studies. A meta-analysis by Simonetto*et al*., found a pooled prevalence of

hyponatremia of 49.4% in patients with cirrhosis [14]. The higher prevalence in our study may be attributed to the inclusion of only decompensated cirrhosis patients, who are known to have a higher frequency of hyponatremia compared to compensated cirrhosis [15].

The present study found a significant inverse correlation between serum sodium levels and both Child-Pugh scores ($r=-0.723$, $p<0.001$) and MELD scores ($r=-0.739$, $p<0.001$). These findings are consistent with previous studies that have demonstrated an association between hyponatremia and advanced liver disease. A study by Kim *et al*., reported significantly higher MELD scores in patients with hyponatremia compared to those without hyponatremia (22.5 ± 8.4 vs. 13.6 ± 5.8, $p<0.001$) [16].

The current study found a significant association between lower serum sodium levels and various clinical complications, including hepatorenal syndrome, SBP, hepatic encephalopathy, and coagulopathy. These findings are supported by previous studies. A study by Angeli*et al*., reported a significantly higher prevalence of hepatorenal syndrome (39.4% vs. 12.4%, $p<0.001$) and SBP (25.8% vs. 10.6%, $p=0.007$) in patients with hyponatremia compared to those without hyponatremia [17]. Similarly, a study by Guevara *et al*., found a higher incidence of hepatic encephalopathy in patients with hyponatremia (38.8% vs. 15.9%, $p<0.001$) [18].

The present study demonstrated a significant association between lower serum sodium levels and increased mortality, prolonged hospital stay, and higher ICU requirement. These findings are consistent with previous studies. A study by Jenq*et al*., reported a significantly higher in-hospital mortality rate in patients with hyponatremia compared to those without hyponatremia (37.3% vs. 17.6%, $p<0.001$) [19]. A study by Zhang *et al*., found that hyponatremia was an independent predictor of prolonged hospital stay (odds ratio: 2.25, 95% confidence interval: 1.28-3.96, $p=0.005$) [20].

The biochemical and hematological parameters in the current study showed significant differences across serum sodium levels, with lower serum sodium levels associated with higher levels of AST, ALT, bilirubin, creatinine, and INR, and lower levels of WBC. These findings suggest that hyponatremia is associated with more advanced liver disease and impaired synthetic function. A study by Shaikh *et al*., reported similar findings, with significantly higher levels of bilirubin, creatinine, and INR in patients with hyponatremia compared to those without hyponatremia [21].

The limitations of the present study include its single-center design and relatively small sample size. Further large-scale, multicenter studies are needed to validate these findings and assess the impact of serum sodium correction on clinical outcomes in patients with decompensated cirrhosis.

In conclusion, the present study demonstrates that serum sodium is a valuable prognostic marker in patients with chronic decompensated cirrhosis of the liver. Lower serum sodium levels are associated with advanced liver disease, higher prevalence of complications, increased mortality, prolonged hospital stay, and higher ICU requirement. Incorporating serum sodium into the assessment and management of patients with decompensated cirrhosis may help in risk stratification, treatment decisions, and improving patient outcomes.

CONCLUSION

In conclusion, this study demonstrates the significant prognostic value of serum sodium levels in patients with chronic decompensated cirrhosis of the liver. Lower serum sodium levels were found to be associated with more advanced liver disease, as evidenced by higher Child-Pugh and MELD scores. Patients with lower serum sodium levels had a significantly higher prevalence of complications, including hepatorenal syndrome (18.8% in patients with serum sodium <125 mEq/L), spontaneous bacterial peritonitis (12.5%), hepatic encephalopathy (68.8%), and coagulopathy (81.3%).

Moreover, lower serum sodium levels were associated with increased mortality, prolonged hospital stay, and higher ICU requirement. The mean hospital stay was longest in patients with serum sodium levels <125 mEq/L (13.7 ± 1.3 days) and shortest in those with serum sodium levels ≥135 mEq/L (7.3 ± 1.9 days). The proportion of patients requiring ICU care decreased from 87.5% in patients with serum sodium levels <125 mEq/L to 0% in those with serum sodium levels ≥135 mEq/L.

The biochemical and hematological parameters also showed significant differences across serum sodium levels, with lower serum sodium levels associated with higher levels of liver enzymes, bilirubin, creatinine, and INR, and lower levels of white blood cell count. These findings suggest that hyponatremia is linked to more advanced liver disease and impaired synthetic function.

The incorporation of serum sodium levels into the assessment and management of patients with chronic decompensated cirrhosis can aid in risk stratification, guiding treatment decisions, and ultimately improving patient

outcomes. Clinicians should be aware of the prognostic significance of hyponatremia in this patient population and consider close monitoring and appropriate interventions to correct serum sodium levels.

Future research should focus on investigating the impact of serum sodium correction on clinical outcomes, as well as exploring the underlying mechanisms linking hyponatremia to the progression of liver disease and its complications. Large-scale, multicenter studies are needed to validate these findings and establish evidence-based guidelines for the management of hyponatremia in patients with chronic decompensated cirrhosis.

REFERENCES

1. Asrani, S. K., Devarbhavi, H., Eaton, J., & Kamath, P. S. (2019). Burden of liver diseases in the world. *Journal of hepatology*, *70*(1), 151-171.doi: 10.1016/j.jhep.2018.09.014.
2. Ginés, P., Quintero, E., Arroyo, V., Terés, J., Bruguera, M., Rimola, A., ... &Rozman, C. (1987). Compensated cirrhosis: natural history and prognostic factors. *Hepatology*, *7*(1), 122-128.doi: 10.1002/hep.1840070124.
3. Kim, W. R., Biggins, S. W., Kremers, W. K., Wiesner, R. H., Kamath, P. S., Benson, J. T., ... &Therneau, T. M. (2008). Hyponatremia and mortality among patients on the liver-transplant waiting list. *New England Journal of Medicine*, *359*(10), 1018-1026.doi: 10.1056/NEJMoa0801209.
4. Ginès, P., & Guevara, M. (2008). Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. *Hepatology*, *48*(3), 1002-1010.doi: 10.1002/hep.22418.
5. Schrier, R. W., Arroyo, V., Bernardi, M., Epstein, M., Henriksen, J. H., &Rodés, J. (1988). Peripheral arterial vasodilation hypothesis: a proposal for the initiation of renal sodium and water retention in cirrhosis. *Hepatology*, *8*(5), 1151-1157.doi: 10.1002/hep.1840080532.
6. Angeli, P., Wong, F., Watson, H., Ginès, P., & Capps Investigators. (2006). Hyponatremia in cirrhosis: results of a patient population survey. *Hepatology*, *44*(6), 1535-1542.doi: 10.1002/hep.21412.
7. Guevara, M., Baccaro, M. E., Torre, A., Gómez-Ansón, B., Ríos, J., Torres, F., ... &Ginès, P. (2009). Hyponatremia is a risk factor of hepatic encephalopathy in patients with cirrhosis: a prospective study with time-dependent analysis. *Official journal of the American College of Gastroenterology| ACG*, *104*(6), 1382-1389.doi: 10.1038/ajg.2009.293.
8. Kamath, P. S., Wiesner, R. H., Malinchoc, M., Kremers, W., Therneau, T. M., Kosberg, C. L., ... & Kim, R. W. (2001). A model to predict survival in patients with end–stage liver disease. *Hepatology*, *33*(2), 464-470.doi: 10.1053/jhep.2001.22172.
9. Biggins, S. W., Rodriguez, H. J., Bacchetti, P., Bass, N. M., Roberts, J. P., &Terrault, N. A. (2005). Serum sodium predicts mortality in patients listed for liver transplantation. *Hepatology*, *41*(1), 32-39.doi: 10.1002/hep.20517.
10. Biggins, S. W., Kim, W. R., Terrault, N. A., Saab, S., Balan, V., Schiano, T., ... &Klintmalm, G. (2006). Evidence-based incorporation of serum sodium concentration into MELD. *Gastroenterology*, *130*(6), 1652-1660.doi: 10.1053/j.gastro.2006.02.010.
11. Qureshi, M. O., Khokhar, N., Saleem, A., &Niazi, T. K. (2014). Correlation of hyponatremia with hepatic encephalopathy and severity of liver disease. *J Coll Physicians Surg Pak*, *24*(2), 135-137.
12. Younossi, Z. M., Koenig, A. B., Abdelatif, D., Fazel, Y., Henry, L., &Wymer, M. (2016). Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*, *64*(1), 73-84.
13. Singal, A. K., Salameh, H., Singal, A., Jampana, S. C., Freeman, D. H., Anderson, K. E., &Brunder, D. (2013). Management practices of hepatitis C virus infected alcoholic hepatitis patients: A survey of physicians. *World Journal of Gastrointestinal Pharmacology and Therapeutics*, *4*(2), 16-22.
14. Simonetto, D. A., Gines, P., & Kamath, P. S. (2020). Hepatorenal syndrome: pathophysiology, diagnosis, and management. *bmj*, *370*, m2687.
15. Lizaola, B., Bonder, A., Tapper, E. B., Mendez-Bocanegra, A., & Cardenas, A. (2016). The changing role of sodium management in cirrhosis. *Current treatment options in gastroenterology*, *14*(2), 274-284.
16. Kim, J. H., Lee, J. S., Lee, S. H., Bae, W. K., Kim, N. H., Kim, K. A., & Moon, Y. S. (2009). The association between the serum sodium level and the severity of complications in liver cirrhosis. *The Korean journal of internal medicine*, *24*(2), 106-112.
17. Angeli, P., Wong, F., Watson, H., Ginès, P., & Capps Investigators. (2006). Hyponatremia in cirrhosis: results of a patient population survey. *Hepatology*, *44*(6), 1535-1542.
18. Guevara, M., Baccaro, M. E., Torre, A., Gómez-Ansón, B., Ríos, J., Torres, F., ... &Ginès, P. (2009). Hyponatremia is a risk factor of hepatic encephalopathy in patients with cirrhosis: a prospective study with time-dependent analysis. *Official journal of the American College of Gastroenterology| ACG*, *104*(6), 1382-1389.
19. Jenq, C. C., Tsai, M. H., Tian, Y. C., Chang, M. Y., Lin, C. Y., Lien, J. M., ... & Yang, C. W. (2010). Serum sodium predicts prognosis in critically ill cirrhotic patients. *Journal of clinical gastroenterology*, *44*(3), 220-226.
20. Zhang, X., Han, T., & Li, Y. (2019). Hyponatremia is an independent predictor of adverse outcomes in hospitalized patients with cirrhosis. *J GastroenterolHepatol*, *34*(4), 799-806.

21. Shaikh, S., Mal, G., Khalid, S., Baloch, G. H., & Akbar, Y. (2010). Frequency of hyponatraemia and its influence on liver cirrhosis-related complications. *JPMA. The Journal of the Pakistan Medical Association*, *60*(2), 116-120