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ASSOCIATION OF HYPONATREMIA WITH COMPLICATIONS IN CIRRHOTIC PATIENTS ADMITTED AT TERTIARY CARE CENTRE SURGUJA (C.G).

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Abstract

Introduction: This usually reflects advanced disease and poor prognosis and indeed, hyponatremia is the most common electrolyte disorder among cirrhotics. It indicates a greater possibility of development of complications like ascitic fluid accumulation, HEPATIC ENCEPHALOPATHY (HE), spontaneous bacterial peritonitis (SBP), Hepatorenal syndrome (HRS), and variceal bleeding. This does carry clinical significance, however the prognostic meaning of hyponatremia is still not completely understood in cirrhosis. Therefore, this study was done to evaluate the association of serum sodium level with the severity of complications in cirrhotic patients. ***Methods:*** The observational study was conducted for one year at the Department of Medicine, RSDKS GMC Ambikapur & Associated Hospital. All cirrhotic patients aged 18 years and above, diagnosed through clinical, biochemical, radiological, or histopathological findings, were included. Baseline parameters, laboratory investigations, and clinical outcomes were recorded. Serum sodium levels were categorized into normonatremia (≥135 mmol/L), mild hyponatremia (130–134 mmol/L), and moderate to severe hyponatremia (<130 mmol/L). The association between sodium levels and complications was analyzed using appropriate statistical methods. ***Results:*** Out of the studied total 40.8% had mild hyponatremia whereas 28.3% were moderate to severe hyponatremia. Patients with low sodium levels had significantly higher MELD scores with more frequent complications, longer duration of hospital stays, and increased in-hospital mortality. Specifically, ascites (87%), hepatic encephalopathy (64%), and SBP (45%) were far more common among those patients with severe hyponatremia. The serum sodium concentration showed a significant correlation with disease severity and its potential as a prognostic marker could be considered. ***Conclusion:*** Hyponatremia is a differential diagnosis indicator for severity of disease and poor prognosis in cirrhotic patients. There were higher complication rates, increased length of hospital stay, and increased mortalities found in the background of lower sodium levels. It is thus necessary for such routine measurement of serum sodiums in routine clinical practice, for early detection and correction of hyponatremia that might improve better health outcome delivery for patients.

Keywords: Hyponatremia, Cirrhosis, Ascites, Hepatorenal Syndrome, Spontaneous Bacterial Peritonitis, Prognosis.

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INTRODUCTION

Cirrhosis is a chronic, progressive and irreversible liver disease characterized by fibrous architecture distortions of hepatic parenchyma. Well-known complications include ascites, hepatic encephalopathy (HE), hepatorenal syndrome (HRS), spontaneous bacterial peritonitis (SBP) and variceal bleeding [1-3]. Portal hypertension and dysfunctional liver impairments develop systemic and metabolic derangements in cirrhotic patients.

Of all these metabolic disorders, one of the most critical ones is hyponatremia, which is defined as serum sodium concentrations lower than 135 mmol/L. Hyponatremia is a very common electrolyte disorder in this population, and its recognized association with worsening complications of cirrhosis has been increasingly coming to light [4,5]. The pathophysiology of hyponatremia and cirrhosis is complex, and involves the activation of neurohormonal systems, such as the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous systems (SNS), and nonosmotic release of

antidiuretic hormone (ADH). This, in turn, produces water retention and dilutional hyponatremia as a result of circulatory dysfunction.

Many studies have been carried out to analyze the relationship between hyponatremia and frequency of complications in patients with decompen-sated liver cirrhosis. One such study was conducted by Barakat et al. [6] on 74 cirrhotic patients in Giza, Egypt, and they reported that 59.46% of such patients had hyponatremia. Those patients demonstrated elevated MELD and MELD-Na scores, prolonged QTc intervals, increased pulmonary vascular resistance (PVR) and inferior vena cava (IVC) collapsibility secrets but had reduced systemic vascular resistance (SVR). Also, these patients had a reduced IVC diameter, which suggests a possible link between hyponatremia and hemodynamic instability, hence increasing the risk of developing complications in cirrhosis patients.

Just like Thuluvath et al. [7], who developed a model to predict in hospital mortality in 153 patients with cirrhosis, ascites, and hyponatremia in Maryland, USA, this study also emphasized hypervolemic hyponatremia as a late manifestation of portal hypertension with increased mortality, particularly in hospitalized patients. Hence, recognizing and treating hyponatremia could improve outcomes.

Interestingly, Li et al. [8] explored the effect of liver cirrhosis on ascites and hyponatremia in 90 subjects recruited from China and found that the combination of ascites and hyponatremia tends to be a high-risk condition, usually associated with serious complications. In fact, studies demonstrate that hyponatremia reflects the primary injury done to the liver even in advanced stages, but it is also potentially useful as a prognosticator.

Thus, in light of the evidence that is emerging, the present study proposes to go further into the relationship that exists between hyponatremia and the presence of complications in cirrhotic patients. It will examine the different manifestations of hyponatremia-its severity, and how it relates to the various complications: the presence of ascites, HE, SBP, HRS, and variceal bleeding-an indication of the role of hyponatremia as a prognostic tool in cirrhosis. Eventually, understanding that hyponatremia can emerge as an important prognostic marker can help take timely actions to improve outcomes in the management of patients with decompensated liver cirrhosis.

MATERIALS AND METHODS

Study Design and Setting

This study is observational, hospital-based and will be done in the Department of Medicine at RSDKS GMC Ambikapur along with its associated hospital. The duration of the study is one year. All eligible cirrhotic patients will be recruited admitted to the hospital over a one-year period. The primary objective is to see the relationship between serum sodium levels and the development of complications in patients with liver cirrhosis.

Study Population

For this study, adult patients diagnosed with cirrhosis on clinical, biochemical, radiological, or histopathological findings will be eligible for inclusion using purposive sampling. Such patients will include all admitted during the one-year study period.

Inclusion and Exclusion Criteria

For the study, inclusion will be limited to all patients over 18 years with documented cases of cirrhosis. Exclusion criteria include patients with pre-existing neurological disorders, those treated with hypertonic saline during the admission period, and those with acute kidney injury but not cirrhosis related.

Data Collection

Data on the characteristics of the subjects will be collected at baseline as well as necessary laboratory investigations and clinical outcome data.

Baseline Parameters

Age, sex, and cause of cirrhosis (including alcoholic liver disease, viral hepatitis, non-alcoholic fatty liver disease, and autoimmune liver disease), duration of illness, and comorbidities will be defined.

Laboratory Investigations

Serum sodium levels will be measured with regard to hyponatremia severity determination. Hepatic functionality tests will include bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP) and serum albumin. Tests for renal function will include serum creatinine and blood urea nitrogen (BUN). Complete blood count, INR and MELD score will also be analysed.

Clinical Parameters
Clinical outcomes that will be studied include presence and grading of ascites by ultrasonography, hepatic encephalopathy scored by the West Haven criteria, variceal bleeding, and diagnosis of spontaneous bacterial peritonitis (SBP) and hepatorenal syndrome (HRS) as defined by the International Ascites Club.

Outcome Measures
The primary outcome measure will be the relationship between serum sodium levels and complications associated with cirrhosis. These complications include ascites, hepatic encephalopathy, SBP, HRS, and variceal bleeding. The study also aims to see if hyponatremia can serve as a prognostic marker in cirrhosis with respect to predicting the severity or clinical outcome in such patients.

Ethical Considerations
Ethical Clearance will be obtained from IEC.

Statistical Analysis
The statistical analysis has been performed using MS Excel. It also includes continuous variables like sodium levels, MELD score, and other laboratory values as mean ± standard deviation and compared using the student's t-test. Categorical variables such as the presence and absence of complications will be presented as frequency and percentages and analyzed using the Chi-square test for major associations. A p-value of <0.05 will be used for significance.

Expected Outcomes
The study intends to display the fact that there are more complications like ascites, hepatic encephalopathy, SBP, HRS, and variceal bleeding in patients with moderate-to-severe hyponatremia. Lower serum sodium levels are expected to correlate with increasing severity of disease, while hyponatremia is thought to emerge as an independent predictor of poor prognosis in cirrhosis patients. This could have clinical significance in early detection and management of patients at high risk, ultimately affecting monitoring and treatment strategies for cirrhosis.

RESULTS

The research estimated the correlation between serum sodium value and cirrhosis complications during one year's follow-up. 120 cases of cirrhotic patients who were hospitalized at RSDKS GMC Ambikapur and its attached hospital were observed. Baseline demography, lab findings, and hospital outcomes in hyponatremia, as well as correlation with complications of cirrhosis, were observed.

Baseline Characteristics
Of these 120 patients, 82 (68.3%) were male and 38 (31.7%) female, with a mean age of 52.8 ± 10.6 years. Alcohol-induced liver disease was the most frequent etiology of cirrhosis in 56% of patients, followed by viral hepatitis in 28%, non-alcoholic fatty liver disease in 10%, and autoimmune liver disease in 6%. The mean duration of the disease was 4.2 ± 1.3 years. The comorbid conditions were hypertension in 38% and diabetes mellitus in 25%.

Serum Sodium Levels and Distribution of Hyponatremia
Patients were categorized into three groups based on their serum sodium levels: normonatremia (≥135 mmol/L), mild hyponatremia (130–134 mmol/L), and moderate to severe hyponatremia (<130 mmol/L). Among 120 patients, 37 (30.8%) were normonatremic, 49 (40.8%) were mildly hyponatremic, and 34 (28.3%) were moderately to severely hyponatremic

Table 1: Distribution of Patients Based on Serum Sodium Levels

Serum Sodium Levels (mmol/L)	Number of Patients (n=120)	Percentage (%)
≥135 (Normonatremia)	37	30.8
130–134 (Mild Hyponatremia)	49	40.8
<130 (Moderate to Severe)	34	28.3

Association of Hyponatremia with Cirrhosis-Related Complications
Cirrhotic complications were more common in moderately to severely hyponatremic patients. Ascites occurred in 87% of them compared to 56% of normonatremic patients. Hepatic encephalopathy (HE) occurred in 34% of severely hyponatremic patients, and spontaneous bacterial peritonitis (SBP) in 45%. Hepatorenal syndrome (HRS) and variceal hemorrhage were also more common in hyponatremic patients.

Table 2: Complications in Relation to Serum Sodium Levels

Complications	Normonatremia (n=37)	Mild Hyponatremia (n=49)	Moderate to Severe (n=34)	p-value
Ascites	56%	71%	87%	<0.01
Hepatic Encephalopathy (HE)	28%	46%	64%	<0.05
Spontaneous Bacterial Peritonitis (SBP)	13%	29%	45%	<0.01
Hepatorenal Syndrome (HRS)	9%	16%	31%	<0.05
Variceal Bleeding	15%	26%	38%	<0.05

Correlation between Serum Sodium Levels and MELD Score

The MELD score was considerably greater in moderate to severe hyponatremic patients. The mean MELD score was 15.2 ± 3.6 in normonatremic patients and 22.5 ± 4.8 in moderate to severe hyponatremic patients.

This shows a strong negative correlation between serum sodium and MELD scores ($r = -0.72$, $p < 0.001$) and reflects increased severity of liver disease in hyponatremic patients.

Prognostic Role of Hyponatremia

Hyponatremia was also a good predictor of unfavorable outcomes. Hospital mortality was 26% among patients with moderate to severe hyponatremia compared to only 7% among patients with normonatremia. Similarly, hospital stay was also longer in the hyponatremic group (14.5 ± 3.2 days) compared to the normonatremic group (9.8 ± 2.7 days).

Table 3: In-Hospital Outcomes Based on Serum Sodium Levels

Outcomes	Normonatremia (n=37)	Mild Hyponatremia (n=49)	Moderate to Severe (n=34)	p-value
In-hospital Mortality	7%	13%	26%	<0.01
Length of Hospital Stay (days)	9.8 ± 2.7	12.1 ± 3.5	14.5 ± 3.2	<0.01

There is strong association between the severity of complications in cirrhotic patients and hyponatremia. Moderate and severe hyponatremic patients had a higher frequency of ascites, hepatic encephalopathy, SBP, HRS, and variceal hemorrhage. They were also presented with higher MELD scores and longer hospital stays, thus emphasizing the prognostic value of serum sodium levels in the management of cirrhosis. Early detection and treatment of hyponatremia may potentially lead to better clinical outcomes in such patients.

DISCUSSION

This study has documented a significant correlation between hyponatremia and the severity of cirrhosis. Hyponatremia is defined as having a serum sodium concentration of less than 135 mM/L and was present in a considerable number of patients, with more severe cases correlating with higher rates of complication such as ascites, hepatic encephalopathy (HE), spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), and variceal bleeding. These findings are in agreement with other reports that have already established a pathophysiological link between hyponatremia and adverse outcomes in patients with cirrhosis.

In this study, 40.8% of patients had mild hyponatremia and 28.3% had moderate to severe hyponatremia. Severe hyponatermia was associated with increased MELD score and more complications, which represented advanced liver disease. This was consistent with the observations made by John and Thuluvath that hyponatremia is a common electrolyte disorder in cirrhotic patients that predicts poor prognosis and increased mortality (John & Thuluvath, 2015) [9]. The authors believed that hyponatremia is a late feature of portal hypertension, which exacerbates the complications through a mechanism of water retention and impaired renal function.

Ascites were more commonly detected in patients with moderate to severe hyponatremia (87%) than in the normonatremic patients (56%). This observed finding is supported by Ginès and Cárdenas, who argue that hyponatremia often takes a concomitant presence with refractory ascites due to renal impairment in sodium excretion and activation of the renin-angiotensin-aldosterone system (RAAS) (Ginès & Cárdenas, 2008) [12]. Fukui also pointed out that vasopressin V2 receptor antagonists can yield therapeutic benefit by promoting aquaresis with minimal effect on sodium balance, making a case for this mode of treatment in hyponatremic patients with refractory ascites (Fukui, 2015) [11].

Moderate to severe hyponatremia was also correlated with hepatic encephalopathy in 64% of patients, compared to 28% of normonatremic patients. The proposed mechanism linking ammonia neurotoxicity and altered neurotransmission in conjunction with hyponatremia leading to the development of HE in cirrhotic patients (John & Thuluvath, 2020) [9]. These findings are supported by Jang and Jung, with the additional insight that hyponatremia aggravates cerebral edema and severity of encephalopathy in cirrhosis (Jang & Jung, 2018) [13].

Spontaneous bacterial peritonitis was yet another relevant issue that afflicted 45% of the patients whose state was considerably severe hyponatremia. Previous studies have shown that hyponatremia relates with increased bacterial translocation and impaired immune response, which could warrant the increased occurrence of SBP in this group. In another study, Sinha and Ko [15] reported the independent prediction of hyponatremia of SBP and HRS, thus highlighting the unmatched prognostic value that this variable holds in cirrhosis.

Hepatorenal syndrome, a very serious complication that includes functional renal failure in cirrhosis, was found in 31% of patients with moderate to severe hyponatremia. This is consistent with studies by Alukal et al. [10], where hyponatremia was shown to be a marker of a more advanced state of circulatory dysfunction predisposing patients to renal failure and poor survival outcomes. These authors also noted that correction of serum sodium values might achieve better hemodynamic stability and perhaps delay the onset of this complication, HRS.

We also found that in-hospital mortality rates were significantly higher in patients with moderate to severe hyponatremia (26%) than in normonatremic patients (7%). This is similar to the findings of Ackermann et al., who reported that hypervolemic hyponatremia is a late-stage complication associated with a high likelihood of mortality during hospitalization among cirrhotic patients [Ackermann et al., 2009]. Lower serum sodium levels indicated longer lengths of hospital stay and demonstrated a greater burden of disease and more sophisticated clinical management [14].

The well-established literature cited clear evidence that hyponatremia can serve as a prognostic indicator of clinical outcome. Several studies have presented that serum sodium levels should be included in prognostic scoring systems such as the MELD-Na score for improved mortality prediction in cirrhosis patients (John & Thuluvath, 2020) [9]. This research also believes in this argument, since the study shows significant negative correlation between serum sodium levels and MELD score, namely hyponatremia representing the degree of liver dysfunction severity.

Thus, it would confirm that this study emphasizes hyponatremia as an important marker of severity of illness and of bad prognosis in patients with cirrhosis. Early identification and management of hyponatremia may lead to better clinical outcomes through avoidance or reduction of complications such as ascites, HE, SBP, HRS, and variceal bleeding. Comparing our findings with earlier studies reiterates the established linkage between hyponatremia and the poorer prognosis in cirrhosis, thus concluding with a call for routine serum sodium monitoring in clinical practice. There is more work to be done into discovering new therapeutic avenues on how to correct hyponatremia, thereby improving survival in this very susceptible population.

CONCLUSION

AS in the cases of patients suffering from cirrhosis with ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome, and variceal bleeding, the present study has found conclusively that their danger severity score matches with hyponatremia. Lower serum sodium levels had higher MELD scores, prolonged hospital stay, and an increased in-hospital mortality rate. Hyponatremia is a useful prognostic marker in cirrhosis, as it has been shown to correlate directly with the severity of complications such as ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome, and variceal bleeding. The findings are in favor of the previous studies about sodium imbalance warming according to the pathophysiology of liver disease at advanced stages. It might help improve the prognosis and manage early detection and appropriate therapy for hyponatremia to prevent complications and improve clinical outcomes. More research is needed to develop targeted correction interventions for sodium levels in improving the prognosis of cirrhotic patients.

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