e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(9); 1579-1582

Original Research Article

# Dysnatremia in Patients with Chronic Liver Disease

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**Received: 25-06-2023 / Revised: 28-07-2023 / Accepted: 30-08-2023**

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**Conflict of interest: Nil**

**Abstract:**

**Background:** Chronic liver disease (CLD) is a prolonged impairment of liver function, leading to cirrhosis and fibrosis. The prevalence of CLD is increasing, especially in low-income countries such as India, where hyponatremia is a common electrolyte imbalance. Hyponatremia in cirrhosis is associated with disease severity and complications, impacting patient survival. However, the relationship between serum sodium levels and specific complications remains unclear.

**Materials and Methods:** We conducted a study at Narayan Medical College and Hospital, Sasaram, India, involving 50 CLD patients aged over 18 years. Patients with comorbidities affecting serum sodium levels were excluded. Demographic data, clinical findings, and laboratory results, including serum sodium levels, were collected. Complications were assessed using the Model for End-stage Liver Disease (MELD) and Child Pugh Score (CPS). Ascites severity was graded. Statistical analysis was performed to assess associations.

**Results:** Among the participants, 33% had serum sodium levels ≤130 mEq/L (Group A), 33% had levels between 131-135 mEq/L (Group B), and 34% had levels ≥136 mEq/L (Group C). No significant age or gender differences were observed between the groups. Patients in Group A exhibited higher rates of jaundice and altered sensorium. Hepatic encephalopathy, hepatorenal syndrome, and coagulopathy were significantly more common in Group A. Mean MELD and CPS scores were higher in Group A patients. Mortality was significantly higher in Group A (28.1%) compared to Group B (11.1%) and Group C (0%).

**Conclusion:** Decompensated CLD is linked to abnormal serum sodium concentrations, with hyponatremia being the most common electrolyte imbalance. Lower serum sodium levels are associated with higher MELD and CPS scores, as well as an increased risk of hepatic encephalopathy, hepatorenal syndrome, and coagulopathy. Mortality is significantly higher in patients with hyponatremia. Serum sodium levels serve as a valuable prognostic indicator in CLD management.

**Keywords:** Chronic liver disease, Hyponatremia, Complications, Severity, Mortality.



## Introduction

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months, which includes synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism, and excretion of bile.

Cirrhosis and fibrosis are the results of CLD, which is a chronic process of inflammation, liver parenchymal destruction, and regeneration. Chronic liver disease has a wide range of aetiologies, including toxins, long-term alcohol abuse, infection, autoimmune diseases, genetic abnormalities, and metabolic disorders. In the final stage of chronic liver disease called cirrhosis, the architecture of the liver is disrupted, there are numerous nodules that form, the blood vessels are reorganised, there is neo-angiogenesis, and an extracellular matrix is deposited. Cellularly, fibrosis and cirrhosis are caused by the recruitment of stellate cells and fibroblasts, whereas parenchymal regeneration is dependent on hepatic stem cells.

Most of the increase in CLD mortality has been linked to low-income (LMIC) countries in Asia and Africa. In LMIC, the epidemiology and demographics of disease burden are changing. One of the epicentres of this transformation is India. [1] Considering that the most prevalent electrolyte

disorder in this situation is cirrhosis, decreased serum sodium concentration is a frequent finding in patients with cirrhosis. [2] In fact, close to 20% of patients had blood sodium levels below 130 mmol/l, the standard for hyponatremia in cirrhosis. Although individuals with early or moderately severe cirrhosis from Child-Pugh classifications A and B can experience hyponatremia, those with advanced disease (Child-Pugh class C) are more likely to experience it. Further evidence for the relationship between hyponatremia and the severity of cirrhosis comes from its close relationship with the occurrence of complications: patients with serum sodium concentrations below 130 mmol/l have significantly higher rates of hepatic encephalopathy, hepatorenal syndrome, and spontaneous bacterial peritonitis than those with higher concentrations. According to recent research, hyponatremia is a significant predictive factor in individuals with chronic liver disease.

Additionally, patients with hyponatremia have lower survival rates than patients without the condition. [3] The clinical significance of serum sodium levels and whether they are associated with a higher likelihood of particular consequences in cirrhosis remain unknown, despite the medical literature supporting the role of blood sodium as a predictive factor in cirrhosis. There aren't many studies that have looked at the connection between blood sodium levels and the frequency and seriousness of liver cirrhosis complications. The aim of this present study was to study the serum sodium levels in chronic liver disease (CLD) patients and establish its association with the severity of disease in such patients with two objectives i.e. to estimate serum sodium levels in Chronic Liver Disease patients and to correlate serum sodium level with index event in IPD CLD Patients.

## Material and Methods

This study was conducted in the Department of Medicine, Narayan medical college and hospital Jamuhar, Sasaram. After obtaining Institutional ethical committee approval and taking informed consent on the basis of inclusion criteria which includes patients having chronic liver disease and patients age more than 18 years attending medicine OPD included. Patients who are having comorbid cardiac failure, or with co morbid chronic kidney disease and patient taking drugs that alter serum sodium levels excluded from this study. A proper history was taken from the patients and other available sources. A thorough general physical and systemic examination was done and final diagnosis was made after doing all the necessary investigations.

The data of the patients were collected using a proforma. The first section of the proforma contains patient's demographic profile with detailed history. The second section contains detailed clinical examination that will be carried out at the time of admission. The third section contains investigations that were done to aid the diagnosis and the serum sodium level.

Patients were selected based on history, examination, laboratory investigations and imaging suggestive of the diagnosis of 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. Ascites was classified in to three grades:

Grade I- presence on examination not clear, but observed in imaging; Grade II- easily made out examination and palpation; Grade III- severe abdominal distension requiring large volume paracentesis.

## Result

In the present study, 50 patients were included. It was observed that 33% were in group A (≤ 130 mEq/l), 33% were in group B (131 to 135 mEq/l) and 34% were in group C (≥ 136 mEq/l). The age or gender of the patients was not associated with serum sodium levels.

**Table 1: Basic demographic details between groups based on serum sodium levels**

| Variables | | | Group A (≤ 130 mEq/l, n=33) | Group B (131-135 mEq/l, n=33) | Group C (≥ 136 mEq/l, n=34) | P- Value |
|---|---|---|---|---|---|---|
| Age | 25-40 | 28% | 9% | 11% | 8% | 0.6524 |
| | 41-60 | 59% | 17% | 19% | 23% | |
| | 61-80 | 13% | 6% | 4% | 3% | |
| Gender | Male | 81% | 27% | 27% | 27% | 0.8402 |
| | Female | 19% | 5% | 7% | 7% | |

All patients had abdominal distension. It was observed that patients from group A had jaundice ($p<0.05$) and altered sensorium ($p<0.05$) significantly more commonly as compared to those from group B and C. Alcohol consumption was reported by 88% of the patients. Serum sodium levels were not significantly associated with alcohol consumption. Among all examination findings, icterus ($p<0.05$) and clubbing ($p<0.05$) were found to be significantly more common among patients from group A, as compared to patients from group B or C. Pallor, pedal edema, signs of liver cell failure and organomegaly were not significantly associated with serum sodium levels in our study population.

**Table 2: Comparison of complication rate between groups based on serum sodium Levels**

| Complications | Group A(≤ 130 mEq/l, n=33) | Group B (131-135 mEq/l, n=33) | Group C(≥ 136 mEq/l, n=34) | Total | P Value |
|---|---|---|---|---|---|
| Portal Hypertension | 22 | 25 | 30 | 77 | 0.16 |
| Hepatic encephalopathy | 19 | 9 | 6 | 34 | <0.01 |
| Hepatorneal syndrome | 15 | 4 | 5 | 24 | <0.01 |
| Spontaneous bacterial peritonitis | 3 | 1 | 0 | 4 | 0.82 |
| Coagulopathy | 12 | 5 | 30 | 20 | <0.01 |

Portal hypertension was observed in 77%, hepatic encephalopathy in 34%, hepatorenal syndrome in 24%, spontaneous bacterial peritonitis in 4% and coagulopathy in 20%. Of these, hepatic encephalopathy ($p<0.01$), hepatorenal syndrome ($p<0.01$) and coagulopathy ($p<0.01$) were found to occur significantly more common among patients from group A, as compared to those in patients from group B or C.

We also observed that mean direct bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase were significantly higher among group A patients as compared to those from group B or C respectively. In addition, we observed that mean MELD (The Model for End-stage Liver Disease) score was significantly higher among group A patients (18.04±7.52) as compared to those with group B (13.24+5.02) and group C (12.04±4.72). We also observed that mean Child Pugh score (CPS) was significantly higher among group A patients (10.04±2.82) as compared to those with group B (8.72±1.45) and group C (7.34+2.02). Overall, 12% of the patients expired. It was observed that mortality as 28.1% among group a patients, which was significantly higher than that of group B patients (11.1%) or group C patients (0%).

## Discussion

Chronic liver disease is a condition that gradually destroys and regenerates the liver's parenchyma, resulting in fibrosis and cirrhosis. When the disease process lasts for six months, chronic liver disease is said to be present. Clinicians should distinguish between chronic liver disease patients with compensated liver function and those with decompensated liver function.

Hepatocellular injury due to various etiologies is followed by degeneration or necrosis of the hepatocyte. Necrosis leads to kupffer cell activation and macrophage immigration. T lymphocytes are also attracted. They are stimulated by IL-1. Fibroblasts are drawn to the area and change into myofibroblasts, which boost collagen and extracellular matrix synthesis. When symptoms of decompensation start to appear, the course of chronic liver disease becomes more complicated. No matter the primary cause, these complications always develop. [4] A common side effect in patients with decompensated liver disease is hyponatremia. It happens as a result of the renal tubules' impaired ability to remove free water, which causes disproportionately more water to be retained than sodium. Hypoosmolality and the level of serum sodium decrease as a result. Despite the fact that decompensated liver disease and hyponatremia were first described 50 years ago, interest in this topic grew after studies from the 1980s showed that hyponatremia is a significant prognostic indicator. Recent studies have also demonstrated that hyponatremia is linked to poor outcomes in both post-transplant patients and patients who have not yet received a transplant. [5]

Hepatic encephalopathy, hepatorenal syndrome, and coagulopathy were shown to be considerably more prevalent in group a patients than in group B or C patients in the current study. In a different study, Elkady et al [6] discovered that the prevalence of hepatic encephalopathy in people with blood sodium levels below 125 mEq/l was significantly higher than that in people with serum sodium levels above 125 mEq/l, at 91% and 50%, respectively. Ascites were shown to be considerably less prevalent in individuals with blood sodium levels of 139 mEq/l, according to Umemura et al [7] (45 vs 65%). Jenq et al [8] found that a substantially larger proportion of individuals with sodium levels less than 135 mEq/l (52/67) developed hepatic encephalopathy than those with sodium levels more than 135 mEq/l (35/59)5.

Meganathan and Kumar [9] established the prevalence of hyponatremia in cirrhosis and to investigate if hyponatremia predicts an increased rate and severity of complications in cirrhosis. They reported hyponatremia in 44%, normal serum sodium in 26%, and hypernatremia in 30% of the patients. In another study, Umemura et al [7]. Assessed mortality in cirrhosis patients taking conventional diuretics and found correlations between clinical traits and serum sodium levels. In their study, 26 of the 171 patients (15.2%) had sodium levels below the lower limit of the normal range (135 mEq/L), and 8 of the 171 patients (4.7%), had sodium levels of 130 mEq/L or less, the cut-off value typically used to define hyponatremia.

In our study, we observed that mean MELD score was significantly higher among group a patients (18.04±7.52) as compared to those with group B

(13.24±5.02) and group C (12.04±4.72). In another study by Meganathan and Kumar [9], the mean MELD score was 27.7±6.7 for patients with hyponatremia, which was significantly higher as compared to those with normal serum sodium levels and hypernatremia Elkady et al. [6], also reported the mean MELD score to be 18.19±5.3 among patients with serum sodium ≤125 mEq/L as compared to 16.17±6.2 in patients with serums sodium more than 125 mEq/L.

A large study done on patients admitted for cirrhosis, has shown that the prevalence of hyponatremia to be 29.8%. [10] Low serum sodium levels were found to be an indicator of poor prognosis and short term in-hospital mortality. Low serum sodium levels were not found to be an independent predictor of mortality when compared with CPS. [11] Biggins et al showed that the ability of MELD score to predict three month waiting list mortality improved when serum sodium was added to it. [12]

The mortality risk for patients with decompensated liver disease was found to be higher in patients with hyponatremia irrespective of the disease severity. [13] In this study also, 12% of the patients expired. It was observed that mortality was 28.1% among group A patients, which was significantly higher than that of group B patients (11.1%) or group C patients (0%). [14]

## Conclusion

Decompensated Chronic Liver Disease is associated with abnormal serum sodium concentration. Hyponatremia is the most common abnormality in this study. Age and gender did not have any association with serum sodium levels. Individuals with lower serum salt levels had a substantially higher MELD score and CPS. Furthermore, hepatic encephalopathy, hepatorenal syndrome, and coagulopathy were shown to be considerably more prevalent in individuals with blood sodium levels more than 136 mEq/l than in other patients.

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