HYPONATREMIA IN LIVER CIRRHOSIS: A RETROSPECTIVE STUDY AT A TERTIARY CARE HOSPITAL

Wiqas Ahmad[1], Naeem Jan[1], Jehan Mahmud Aurangzeb[2], Muhammad Iltaf[1]

ABSTRACT

Objective: This study's main objective was to ascertain the frequency of hyponatremia in patients with liver cirrhosis and to assess its relationship with the severity of liver cirrhosis and the duration of liver cirrhosis.

Materials and Methods: This retrospective study was carried out in Gastroenterology unit at Hayatabad Medical Complex Peshawar after approval from the hospital's ethical committee. A total of 175 patients with liver cirrhosis who fulfilled the inclusion criteria were included. Patients were categorized according to the Child-Pugh score into three classes. Serum sodium level was determined in the hospital laboratory. Patients were labeled to have hyponatremia if their blood sodium level was less than 135 mmol/L. The Statistical Package for the Social Sciences (SPSS) version 25 was used for data analysis.

Results: The participants in our study were from 18 to 60 years. The mean age was 46.68 ± 10.24 years. This study has more male participants than females. 48% of the participants in this study had hyponatremia. The mean serum sodium level was 131.36 ± 6.51 mmol/L. Disease duration and Child-Pugh class are significantly associated with hyponatremia ($p < 0.001$). Age, gender, and BMI had no significant association with hyponatremia.

Conclusion: Hyponatremia is a common electrolyte abnormality in liver cirrhosis. Prolonged duration of liver cirrhosis and patients with advanced liver disease (Child-Pugh class C) are more likely to have hyponatremia.

Keywords: Liver Cirrhosis, Hyponatremia, Chronic Liver Failure.

INTRODUCTION

Cirrhosis of the liver is a disorder involving the replacement of healthy liver tissue by fib-rous scar tissue. This leads to nodular regeneration and disruption of the organ's microvascular structure. Its causes include prolonged alcohol use, viral hepatitis, metabolic disorders, MASLD, DILI (drug-induced liver injury), inflammatory conditions, and in some cases, it is cryptogenic. Viral hepatitis is recognized as the leading cause of liver cirrhosis[1].

[1] Hayatabad Medical Complex, Peshawar, Pakistan
[2] Ipswich Hospital, East Suffolk North Essex Foundation Trust, NHS, United Kingdom

Address for Correspondence
Dr. Naeem Jan
Assistant Professor
Department of Gastroenterology, Hayatabad Medical Complex, Peshawar
naeemjan78.nj@gmail.com
+92 333 9376686

An estimated 1.6 million people die from liver cirrhosis worldwide each year. Cirrhosis-related consequences, such as hepatic encephalopathy, hepatorenal syndrome, variceal hemorrhage, and hepatocellular cancer, are responsible for most liver cirrhosis-related deaths. A common electrolyte imbalance that exacerbates the clinical course of liver cirrhosis is hyponatremia[2].

Hyponatremia is diagnosed when serum sodium level is less than 135 mmol/L. It is a common manifestation of liver cirrhosis. Hyponatremia is seen in approximately 20% of cases of liver cirrhosis[3]. Impaired renal sodium regulation because of renal hypo-perfusion and elevated arginine-vasopressin secretion due to reduced effective volume owing to peripheral arterial vasodilation represents the primary mechanism leading to dilutional hyponatremia[4].

Hyponatremia was observed in 48.4% of peopl e with liver cirrhosis in a study performed by Qureshi et al. (mean serum sodium level was 133.93 mmol/L)[5]. In another study by Mumtaz and his colleagues, hyponatremia was noted in 33.3% of patients[6].

The estimated prevalence of liver cirrhosis in Pakistan is approximately 27.5%[7]. The

association of hyponatremia with complications of liver cirrhosis has been demonstrated by Barakat et al. in their study[8]. So, we are conducting this study to find the burden of hyponatremia in patients with liver cirrhosis in our local population, as no study has been done on this subject in the last five years in our local population. The results of our study will give an estimate of the burden of hyponatremia in patients with liver cirrhosis in our local population and will provide a platform for future studies on this important topic.

MATERIALS AND METHODS

It included all patients aged 18-60 with liver cirrhosis who were admitted in the last 6 months and fulfilled the inclusion criteria.

Patients were labeled as having liver cirrhosis if they had coarse shrunken liver on ultrasound, along with low serum albumin (<3.5g/dl) and an INR >1.2. During laboratory investigation, a serum sodium concentration of less than 135 mmol/L was called hyponatremia. The following inclusion and exclusion criteria were followed.

Inclusion Criteria: The study included patients aged 18 to 60, both males and females. It included all individuals diagnosed with liver cirrhosis (Child-Pugh Class A, B, and C), regardless of treatment status defined by the operational criteria.

Exclusion Criteria: Patients with incomplete records or specific medical conditions were excluded from the study. These conditions included a history of syndrome of inappropriate hypersecretion of ADH, hypothyroidism, chronic obstructive pulmonary disease, steroid intake, carcinoma of the lung, prostate, hepatocellular carcinoma, protein-losing enteropathy, or protein malnutrition.

Data Collection and Analysis: Patient information was retrieved from the Hospital management information system and from in-patient records. Standard demographic data, including gender, age, and body mass index (BMI), along with clinical parameters like Child-Pugh class and the etiology of liver cirrhosis, were also noted from the records. Similarly, laboratory parameters such as serum sodium and albumin levels were also noted from the records.

Data will be analyzed with SPSS version 25. For qualitative variables like gender, grade of severity of liver cirrhosis, and presence of hyponatremia, frequencies, and percentages will be calculated. Mean ± standard deviation will be computed for quantitative variables like age, height, weight, BMI, serum albumin, prothrombin time, and disease duration(months).

Effect modifiers (age, gender, BMI, and disease duration) will be controlled by stratification. The chi-square test will be applied after stratification. P-value ≤ 0.05 will be considered statistically significant.

RESULTS

Participants in our study were between the ag es of 18 and 60. Mean age was 46.68 ± 10.24 years, mean BMI was 24.87 ± 2.66 kg/m^2, mean duration of disease was 38.71 ± 15.35 months, mean serum albumin was 3.0680 ± 0.48281 gm/dL and mean serum sodium was 131.36 ± 6.51 mmol/L as shown in Table-1

Table 1: Mean and standard deviation of the study participants according to various Parameters (n=175)

Demographic/Baseline Parameters	Mean ± S.D
Age	46.68 ± 10.24
Mean Height (cm)	170.55 ± 7.88
Mean Weight (kg)	72.07 ± 6.47
Mean BMI (kg/m^2)	24.87 ± 2.66
Mean Disease duration (months)	38.71 ± 15.35
Mean Serum Sodium (mmol/L)	131.36 ± 6.51
Mean Serum Albumin	3.07 ± 0.48

S.D: standard deviation, BMI: body mass index

Among the study population, 118 patients were males, while 57 were females. Most of the patients had Child-Pugh class “C” (40%), followed by class “A” (32%). Hyponatremia was present in 48% of patients as shown in Table 2.

Table 2: Summarizes frequencies and percentages of the study population according to various parameters (n=175)

Variables/Parameters	(n, %)
Gender Male Female	 118 (67.4) 57 (32.4)
Child-Pugh Classification Class "A" Class "B" Class "C"	 56 (32) 49 (28) 70 (40)
Classification according to Age Age ≤ 40 years Age > 40 years	 53 (30.3) 122 (69.7)
Classification according to disease duration Disease duration ≤ 30 months Disease duration > 30 months	 64 (36.6) 111 (63.4)
Classification according to hyponatremia status Hyponatremia present Hyponatremia absent	 84 (48) 91 (52)

Patients with a longer disease duration (>30 months) had a higher percentage of patients with hyponatremia than those with a disease duration of 30 months or less and the difference between the two groups was statistically significant ($p < 0.001$). Similarly, the Child-Pugh Class of the patients had a significant association with hyponatremia with hyponatremia being more common in Child-Pugh class C patients than those with Class A and B ($p < 0.001$). Age, gender, and body mass index had no significant association with hyponatremia as shown in Table 3.

Table 3: Summary of the association of hyponatremia with various variables

Parameter (n=175)	Hyponatremia (Present)	Hyponatremia (Absent)	p-value
Age Groups Age ≤ 40 years Age > 40 years	 26 58	 27 64	 0.854
Gender Male Female	 55 29	 63 28	 0.596
Disease duration Disease duration ≤30months Disease duration > 30 months	 15 69	 49 42	 <0.001
Child-Pugh Class Class (A) Class (B) Class (C)	 0 21 63	 56 28 07	 <0.001
Body Mass Index (kg/m^2) ≤ 25 >25	 44 40	 60 31	 0.068

DISCUSSION

Hyponatremia in liver cirrhosis is a frequent finding. The complex and multifactorial mechanism includes decreased renal excretion of salt-free water, antidiuretic effect of atrial natriuretic peptide, and increased sodium resorption in the proximal tubule. Hyponatremia in the setting of liver cirrhosis has implications in terms of precipitation of hepatic

encephalopathy, spontaneous bacterial peritonitis (SBP), and hepatorenal syndrome[9].

In our study, hyponatremia was observed in 48% of the patients diagnosed with liver cirrhosis. In this study, hyponatremia was found in a higher percentage of patients (48%) compared to the results of a study conducted by Mumtaz et al., where it was found in 33.3% of patients[6]. Similarly, in a study conducted by Azam et al., hyponatremia was found in 36.09% of patients[10]. A similar trend was reported in another study carried out by Shaikh et al[11]. The relatively higher frequency of hyponatremia may be because patients with a serum sodium less than 135 mmol/L were labeled hyponatremic in this study. In contrast, in the other studies, the hyponatremia cut-off was 130 mmol/L. If the cut-off value for these studies is raised to 135 mml/L, then the results are comparable to this study. Jenq et al. analyzed serum sodium levels in 126 cirrhotic patients who were admitted to the intensive care unit of a hospital. They observed a serum sodium concentration of less than 135 mEq/L in 53.2% of patients and < 130 mEq/L in 28.6%. This is in strong agreement with the results of this study [12].

Though this study could not demonstrate a significant association between hyponatremia and the gender of the patient ($p = 0.568$), the majority of the patients with hyponatremia in this study were male (65.5%). A study conducted by Azam and his colleagues reported a similar gender-based trend of hyponatremia[10].

In general, the rate of decompensated cirrhosis due to chronic viral hepatitis in women is less likely compared to men. Similar trends could be reflected in the sequelae of cirrhosis, including hyponatremia, in terms of decreased prevalence of complications. A significant association between hyponatremia was observed during the duration of the disease and Child-Pugh Class (p-value less than 0.001 in both cases). Patients with Child-Pugh class C disease and chronic illness are more at risk of hyponatremia. Similar findings have been reported in other studies [10,13,14]. Advanced cirrhosis is represented by Child-Pugh Class C. The kidneys' ability to remove solute-free water is compromised in these people.
Additionally, nonosmotic hypersecretion is associated with circulatory dysfunction in advanced cirrhosis causing them to produce more atrial natriuretic peptides from the neurohypophysis, which has natriuretic properties and causes hyponatremia.
Hyponatremia is not only a predictor of complications of cirrhosis like hepatic encephalopathy (HE), diuretic resistant ascites, SBP, and HRS but also a predictor of mortality in liver disease[14].In a developing country like ours, repeated hospital admission due to complications of cirrhosis precipitated by hyponatremia carries socio-financial implications both individually and in general for the community. Therefore, patients with liver cirrhosis should be vigorously monitored for electrolyte imbalance and promptly managed.

This study has a few limitations, such as the retrospective nature of the study. Also, some of the patients with liver cirrhosis had used diuretics for cirrhosis-related complications like ascites before presentation to this hospital, which might have affected serum sodium concentration. Some patients were on dietary salt restrictions.

CONCLUSION

Hyponatremia is a commonly observed electrolyte abnormality in patients with liver cirrhosis. Hyponatremia in our study was noted in 48% of patients. It is more common in patients with advanced liver cirrhosis and also in patients with prolonged duration of illness. Gender, BMI, and age have no significant association with the prevalence of hyponatremia.

AUTHORS CONTRIBUTIONS

Wiqas Ahmad: Conception and design of study, manuscript drafting, data analysis/interpretation, critical revision, agree to be accountable for all aspects of work.

Naeem Jan: Conception and design of study, acquisition of data, data analysis/interpretation, critical revision, agree to be accountable for all aspects of work.

Jehan Mahmud Aurangzeb: Manuscript drafting, data analysis/interpretation, critical revision, agreeing to be accountable for all aspects of work.

Muhammad Iltaf: Conception and design of study, acquisition of data, critical revision, agree to be accountable for all aspects of work.

CONFLICT OF INTEREST

None

FUNDING

None

REFERENCES

1. Nishikawa H, Osaki Y. Liver cirrhosis: evaluation, nutritional status, and prognosis. Mediators of inflammation. 2015;2015(1):872152.
2. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. Journal of hepatology. 2019;70(1):151-71.
3. Bernardi M, Ricci CS, Santi L. Hyponatremia in patients with cirrhosis of the liver. Journal of clinical medicine. 2014;4(1):85-101.
4. Jiménez JV, Carrillo-Pérez DL, Rosado-Canto R, García-Juárez I, Torre A, Kershenobich D, et al. Electrolyte and acid–base disturbances in end-stage liver disease: a physiopathological approach. Digestive diseases and sciences. 2017;62:1855-71.
5. Qureshi MAM, Zubair N, Rafiq M. Frequency of Hyponatremia in Patients with Liver Cirrhosis. PJMHS. 2017;11(2):562-5.
6. Mumtaz M, Ahmad W, Khan AH. Frequency of Hyponatremia in patients of Chronic Liver Disease. Age (Years). 2017;46:15.82.
7. Butt AS. Epidemiology of viral hepatitis and liver diseases in Pakistan. Euroasian journal of hepato-gastroenterology. 2015;5(1):43.
8. Barakat AAE-K, Metwaly AA, Nasr FM, El-Ghannam M, El-Talkawy MD. Impact of hyponatremia on frequency of complications in patients with decompensated liver cirrhosis. Electronic physician. 2015;7(6):1349.
9. Ginés P, Berl T, Bernardi M, Bichet DG, Hamon G, Jiménez W, et al. Hyponatremia in cirrhosis: from pathogenesis to treatment. Hepatology. 1998;28(3):851-64.
10. Azam MU, Javed S, Memon MYY, Aftab MA, Shafqat MN, Sadiq HZ, et al. Hyponatremia Prevalence in Decompensated Chronic Liver Disease: Insights from a Tertiary Care Hospital. Cureus. 2024;16(9):e68907.
11. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatraemia and its influence on liver cirrhosis-related complications. JPMA The Journal of the Pakistan Medical Association. 2010;60(2):116-20.
12. Jenq CC, Tsai MH, Tian YC, Chang MY, Lin CY, Lien JM, et al. Serum sodium predicts prognosis in critically ill cirrhotic patients. Journal of clinical gastroenterology. 2010;44(3):220-6.
13. Guevara M, Baccaro ME, Torre A, Gómez-Ansón B, Ríos J, Torres F, et al. 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. 2009;104(6):1382-9.
14. Ginès P, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. Hepatology. 2008;48(3):1002-10.