

## ORIGINAL ARTICLE

**Severity of Hyponatremia and its Influence on Various Complications of Decompensated Chronic Liver Disease**MUHAMMAD AFFAN QAISER<sup>1</sup>, MUHAMMAD ASIF BAIG<sup>2</sup>, IMRAN ALI SYED<sup>3</sup>, SYED HAMMAD WAJID TALHA SHAH<sup>4</sup>, NAZISH BUTT<sup>5</sup>, FARAH NAJMI<sup>6</sup><sup>1</sup>Assistant professor, consultant gastroenterologist & transplant hepatologist, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat.<sup>2</sup>Assistant professor, consultant gastroenterologist & transplant hepatologist, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat.<sup>3</sup>Senior Registrar, Pakistan Kidney and Liver Institute, Lahore.<sup>4</sup>Assistant Consultant, Quaid-e-Azam International Hospital, Islamabad.<sup>5</sup>Post Graduate trainee, Radiology, Holy Family Hospital.<sup>6</sup>Medical officer, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat.

Correspondence to: Muhammad Affan Qaiser

**ABSTRACT****Objective** The study quantified the occurrence and intensity of hyponatremia in decompensated chronic liver disease patients**Study design:** Descriptive Cross sectional study**Place and Duration:** Department of Gastroenterology, Centre for Liver Diseases, Holy Family Hospital (CLD, HFH) for a total 6 months duration**Methodology:** Patients aged 13-75 years, both male and female presenting with Clinical, biochemical, and Ultrasonographic findings of cirrhosis were included in this study. Patients' ages, genders, levels of serum hyponatremia, rates of complications, Child-Pugh scores, and other contextual data were recorded in a standardized proforma. The tests were conducted in the hospital's lab, and a pathologist looked over the results.**Results:** Among 120 study cases, 72 (60 %) patients were male and 48 (40 %) were female patients. The mean age was 50.83 ± 10.50 years; ranging from 30 years to 70 years. Of these 120 study cases, 32 (26.7 %) were from rural areas while 88 (73.3 %) were from urban areas, 35 (29.2%) were poor, 69 (57.5%) were middle income and 16 (13.3%) were having rich socioeconomic status. Child-Pugh class B was noted in 77 (64.2 %) and Child-Pugh class C was noted in 43 (35.8%) of our study cases. The mean serum sodium level was 131.25 ± 4.34 mmol/L ranging from 118 mmol/L to 141 mmol/L and hyponatremia was noted in 64 (53.3%) of our study cases. Mild hyponatremia was noted in 12 (10%), moderate hyponatremia in 28 (23.3%) and severe hyponatremia in 24 (20%) of our study cases. Hepatic encephalopathy was noted in 16 (13.3%), spontaneous bacterial peritonitis in 36 (30%), variceal bleeding in 44 (36.7%) and Hepatorenal syndrome in 24 (20%).**Conclusion:** Our study found that people with liver cirrhosis were more likely to be hyponatremic than those without the condition. Hyponatremia was associated with being older age, having problems, and being labelled as a Child-Pugh class C. It was also revealed that the number of problems was strongly correlated with the degree to which the hyponatremia had progressed. Nurses, doctors, and anybody else providing care for cirrhotic patients should all keep a close check on their patients' sodium levels.**Keywords:** Hyponatremia, liver cirrhosis, Serum Sodium, Child-Pugh**INTRODUCTION**

About 57% of diabetic cirrhotic individuals develop hyponatremia (1). The first sign indicates low sodium levels and a decreased volume of plasma. This is a red flag that there's a problem with the body's ability to flush out water that doesn't have any solutes in it, which might lead to abnormal water retention. Patients with cirrhosis and ascites are disproportionately affected by this problem. (2) Poor renal perfusion and subsequent impaired sodium excretion combine with peripheral arterial vasodilation to reduce effective volume, leading to dilutional hyponatremia. These two factors both play a role in the kidneys' reduced salt processing.

In advanced liver disease, hyponatremia is common and is now understood to be a contributor to mortality in cirrhosis (3). Twenty-one percent of 997 cirrhotic patients in a 2006 study had blood sodium levels below 130 mmol/L. (5). Hepatic encephalopathy (odds ratio = 3.40; 95% CI: 2.35-4.92), Hepatorenal syndrome (odds ratio = 3.45; 95% CI: 2.04-5.82), and spontaneous bacterial peritonitis (SBP) (odds ratio = 2.36; 95% CI: 1.41-3.93) were all considerably more common in this patient population. Hyponatremia is an indication that a hospitalized patient with an infection may not recover. Researchers have shown that spontaneous bacterial peritonitis, is connected with serious outcomes such kidney failure and has a high death rate (6, 7). Hospitalized cirrhotic patients with skin and soft tissue infections had a higher risk of hyponatremia and renal failure compared to infection-free cirrhotic controls. In comparison to patients without either illness, those with hyponatremia and renal failure had a 45% higher risk of dying within three months (8).

Whether or not low serum sodium levels are linked to the onset and severity of cirrhotic effects, and how often they occur, has only been the subject of a small number of investigations to date. As such, we intend to investigate the connection between

serum hyponatremia and the aforementioned issues and submit our findings.

**METHODOLOGY**

This Descriptive Cross-sectional study was conducted at the Department of Gastroenterology, Centre for Liver Diseases, Holy Family Hospital (CLD, HFH). To determine the sample size, we used the parameters of 95% confidence and 6% precision. Our hyponatremia prevalence estimate for the cirrhotic population is 12.2% (9), therefore we will need a sample size of 120. We used Non-Probability Consecutive sampling technique. Patients aged 13-75 years, Both Male and female presenting with clinical, biochemical, and Ultrasonographic findings of cirrhosis were included in this study. Patients admitted after utilizing diuretics throughout the prior month **and** Patients with non-viral liver disease were excluded.

After the executive summary was accepted, a total of 120 consecutive cases of liver cirrhosis that met the inclusion and exclusion criteria were invited to take part in the experiment. All participants were given detailed information about the study's aims before giving their consent. Ultrasonography, liver function tests, and serum electrolytes were performed as baseline studies to ascertain whether or not the liver was deteriorating. Patients' ages, genders, levels of serum hyponatremia, rates of complications, Child Pugh scores, and other contextual data were recorded in a standardized proforma. The tests were conducted in the hospital's lab, and a pathologist looked over the results.

Data analysis was performed in SPSS 16 for Windows. Quantitative factors including age and serum salt levels were calculated using the mean and standard deviation. Both of these show instances of quantitative variables. Qualitative characteristics like gender, serum hyponatremia severity, and cirrhosis-related

sequelae were broken down by frequency and percentage to establish frequency and prevalence. Serum hyponatremia severity, gender, and the presence or absence of cirrhosis-related sequelae are all examples of qualitative factors to consider. We used both tables and graphs to show the information. Using characteristics including age, gender, and whether or not the patient was in child class B or C, a procedure called stratification was used to control the severity of hyponatremia in children. A Chi-square analysis was also done. P values at the 0.05 significance level were taken into account.

**RESULTS**

Our study included 120 people, all of whom were in good health and able to participate. Sixty percent of the study's patients were men, making up 72 of the total, while women made up 48 of the total (40%). The participants' average age was 50 years. The average age of men was determined to be 52.64± 10.40 years (p 0.020), while the average age of women was 48.10± 10.14 years. The bulk of the people we studied 71 (59.2%) were in their late 40s or early 50s. A total of 88 (73.3%) were from urban areas, while only 32 (6.6%) were from rural areas. From the total of 120 participants, 16 were extremely high class (13.3%), 69 were middle class (57.5%), and 35 (29.2%) were from a lower class.

In our investigation, we observed that Child-Pugh class B was present in 77 (64.2%) of the cases, while Child-Pugh class C was present in 43 (35.8%) of the cases. (As shown in Table 6) Our study found that hyponatremia occurred in 53.3% of patients, with a range of 118 mmol/L to 141 mmol/L. Sodium concentrations in the blood ranged from 118 to 141 millimole per litre (mmol/L), with a mean of 131.25 mmol/L. Our study found that mild hyponatremia affected 12 patients (10%), moderate hyponatremia affected 28 patients (23.3%), and severe hyponatremia affected 24 patients (20%).

Table 1: Distribution of complications among study cases. (n = 120)

Complications	Frequency	Percentage
Hepatic Encephalopathy	16	13.3
SBP	36	30.0
Variceal bleeding	44	36.7
Hepatorenal syndrome	24	20.0
Total	120	100

Table 2: Stratification of hyponatremia with regards to gender. (n = 120)

Gender	Hyponatremia		P – value
	Yes (n=64)	No (n=56)	
Male (n=72)	40	32	0.580
Female (n=48)	24	24	
Total	120		

Table 3: Stratification of hyponatremia with regards to age. (n = 120)

Age	Hyponatremia		P – value
	Yes (n=64)	No (n=56)	
Up to 45 Years (n=49)	20	29	0.026
More than 45 Years (n=71)	44	27	
Total	120		

Table 4: Stratification of hyponatremia with regards to residential status. (n = 120)

Residential status	Hyponatremia		P – value
	Yes (n=64)	No (n=56)	
Rural (n=32)	17	15	1.000
Urban (n=88)	47	41	
Total	120		

A total of 16 (13.3%) of the cases in our study had hepatic encephalopathy, 30% had spontaneous bacterial peritonitis, 30% had a variceal hemorrhage, and 36% had Hepatorenal syndrome.

Hyponatremia was characterized according to a variety of factors, including gender, age, living circumstances, socioeconomic status, Child-Pugh classification, severity of hyponatremia, complications, and the severity of hyponatremia versus problems.

Table 5: Stratification of hyponatremia with regards to socioeconomic status. (n = 120)

Socioeconomic status	Hyponatremia		P – value
	Yes (n=64)	No (n=56)	
Poor (n=35)	19	16	0.958
Middle Income (n=69)	37	32	
Rich (n = 16)	08	08	
Total	120		

Table 6: Stratification of hyponatremia with regards to Child-Pugh classification. (n = 120)

Child Pugh classification	Hyponatremia		P – value
	Yes (n=64)	No (n=56)	
B (n=77)	25	52	0.001
C (n=43)	39	04	
Total	120		

Table No. 7: Stratification of hyponatremia with regards to complications. (n = 120)

Complications	Hyponatremia		P – value
	Yes (n=64)	No (n=56)	
Hepatic Encephalopathy (n=16)	08	08	0.002
SBP (n=36)	12	24	
Variceal bleed (n=44)	24	20	
Hepatorenal syndrome (n=24)	20	04	
Total	120		

Table 8: Stratification of the severity of hyponatremia with regard to complications. (n = 120)

Complications	Severity of hyponatremia				P value
	Mild (n=12)	Moderate (n=28)	Severe (n=24)	Normal (n=56)	
Hepatic Encephalopathy (n=16)	00	04	04	08	0.001
SBP (n=36)	08	00	04	24	
Variceal bleed (n=44)	04	16	04	20	
Hepatorenal syndrome (n=24)	00	08	12	04	
Total	120				

**DISCUSSION**

Hyponatremia occurs often in patients with advanced cirrhosis. When the kidneys don't filter waste products out of the blood effectively, this disease develops. This results in a lower blood sodium concentration and a lower osmotic pressure because the body retains more water than sodium. Because of the excess water retention brought on by hyponatremia, this is the case. Current therapeutic recommendations, including limiting fluid consumption, are insufficient. Researchers are looking at a new family of drugs called Vaptans in an effort to develop a cure for hyponatremia. The Vaptans function by blocking the actions of arginine vasopressin at the kidney's V2 receptors in the tubules. Improving hyponatremia is a side effect of Vaptans, which cause the kidneys to excrete more water without any solutes after a brief period of administration (10).

There are a variety of causes for ascites to appear in a cirrhotic patient. Sodium retention occurs as a coordinated effort of

the renin-angiotensin-aldosterone system, the sympathetic nervous system, and the antidiuretic hormone in response to portal hypertension and systemic vasodilation. In response, the body stores substantial amounts of sodium and water to make up for the diminished efficiency with which blood is being pumped. It may not be immediately apparent that the kidneys' ability to excrete water devoid of solutes is failing in the early stages of cirrhosis and ascites, but this is the case over time. To make up for the shortfall, the body adapts by creating new systems. One such process is the non-osmotic production of ADH, also called arginine vasopressin. In turn, this exacerbates the already severe symptoms of hyponatremia and water retention (11).

Our study included 120 people, all of whom were in good health and able to participate. A total of 60% of the study's 120 patients were men, while 40% were women. Hussain and coworkers (12) found that there were disproportionately more male patients than female patients in their study of the same name conducted in Lahore. Consistent with our own findings, Khan et al. (13) from Jamshoro found that the majority of patients were male. The results of our investigation are consistent with those of a study conducted in Turkey by Topdagi et al. (14), who found a male-to-female ratio of 58%. We found that 60% of the population is comprised of males, which is in line with the findings of Zuberi and coworkers (15). Similar to our findings, Alam et al. (16) from Peshawar found that there were 64% more men than women.

The participants' average age was 50 years. The average age of men was determined to be 52.64 10.40 years ( $p < 0.020$ ), while the average age of women was 48.10 10.14 years. The bulk of the people we studied 71, (59.2%) were in their late 40s or early 50s, as determined by our research. Hussain and colleagues (12) found the same thing in their study of people with liver cirrhosis in Lahore: the average age was 51.12±6.03 years.

Our findings are slightly different from those of Khan et al. (14) from Jamshoro, who found that the average age of people with liver cirrhosis is 40.79±7.83 years. Similarly, Topdagi et al. (14) in Turkey found that patients with liver cirrhosis had an average age of 55.3±15.9 years, which is consistent with our own data. Similar results were found by Asgher et al. (17) in Lahore, Pakistan, who found that the average age of people with cirrhosis was 51 years, 5 months, and 1.22 days. Our findings are very similar to those of Naheed et al. (18) from Lahore, who found that the average age of cirrhotic patients was 45.0 ±10.95 years.

A total of 88 (73.3%) were from urban areas, while only 32 (6.6%) were from rural areas. From the total of 120 participants, 16 were extremely high class (13.3%), 69 were middle class (57.5%), and 35 (29.2%) were from a lower class. In our investigation, we observed that Child-Pugh class B was present in 77 (64.2%) of the cases, while Child-Pugh class C was present in 43 (35.8%) of the cases. Topdagi et al. (14) did a study in Turkey and found that 32 percent of patients were in Child-Pugh class B and 53 percent were in class C. This study also found that 53% of patients had class C. Our results suggested that Child-Pugh class B was the most common, but this turned out not to be the case. Seventy percent of patients were classed as Child-Pugh class B, while thirty percent were classified as Child-Pugh class C, as reported by Naheed et al. (18) from Lahore. Our findings corroborate this view. These findings are consistent with those reported by Ashger et al. (16), a group headquartered in Lahore.

Our study found that hyponatremia occurred in 53.3% of patients, with a range of 118 mmol/L to 141 mmol/L. Sodium concentrations in the blood ranged from 118 to 141 millimole per litre (mmol/L), with a mean of 131.25 mmol/L. Our study found that mild hyponatremia affected 12 patients (10%), moderate hyponatremia affected 28 patients (23.3%), and severe hyponatremia affected 24 patients (20%). A total of 16 (13.3%) of the cases in our study had hepatic encephalopathy, 30% had spontaneous bacterial peritonitis, 30% had a variceal hemorrhage,

and 36% had the Hepatorenal syndrome. Our results are consistent with those found by Angeli et al. (5), who found that about 57% of people with liver cirrhosis experienced hyponatremia.

Furthermore, Khan et al. (13) from Jamshoro found that patients with liver cirrhosis had an average serum sodium level of 129.73±83.51nmol/L. Our analysis found a similarly high value of hyponatremia in these people (72%), therefore these results are consistent. The serum sodium levels of 53.2% of patients were below 135 mEq/L, and the levels of 28.6% of patients were below 130 mEq/L, as reported by Jenq et al. (19). Our results are in agreement with those of Jenq et al. (19). Comparable results were found in a study by Kim et al. (9), where sodium concentrations of 135 mmol/L, 130 mmol/L, and 125 mmol/L were reported to be 20.8%, 14.9%, and 12.2%, respectively

## CONCLUSION

Our investigation revealed that patients with cirrhosis of the liver were more likely to experience hyponatremia. Hyponatremia was associated with being older age, experiencing difficulties, and being labelled as a Child-Pugh class C. Complication rates were shown to be significantly correlated with the severity of hyponatremia. Nurses, doctors, and anybody else providing care for cirrhotic patients should all keep a close check on their patients' sodium levels.

**Funding source:** None

**Permission:** Taken from the ethical committee

**Conflict:** Nothing to declare

## REFERENCES

- 1) Barakat AAE-K, Metwaly AA, Nasr FM, El-Ghannam M, El-Talkawy MD, taleb HA. Impact of hyponatremia on frequency of complications in patients with decompensated liver cirrhosis. *Electronic Physician*. 2015; 7(6):1349-1358.
- 2) Piano S, Morando F, Angeli P. Cirrhosis: A practical guide to management. First Edition. chapter 18. John Wiley & Sons, Ltd Published; 2015. Hyponatremia and other electrolyte/ion disorders.
- 3) Bernardi, Mauro, Carmen Serena Ricci, and Luca Santi. "Hyponatremia in Patients with Cirrhosis of the Liver." Ed. Lewis S. Blevins. *J Clin Med*. 2015; 4(1):85-101.
- 4) John S, Thuluvath PJ. Hyponatremia in cirrhosis: Pathophysiology and management. *World J Gastroenterol*. 2015; 21(11):3197-3205.
- 5) Angeli P, Wong F, Watson H, Ginès P. Hyponatremia in cirrhosis: Results of a patient population survey. *Hepatology (Baltimore, Md.)* 2006; 44(6):1535-42.
- 6) Merola J, Chaudhary N, Qian M, Jow A, Barboza K, Charles H, et al. Hyponatremia: A Risk Factor for Early Overt Encephalopathy after Transjugular Intrahepatic Portosystemic Shunt Creation. *J Clin Med*. 2014; 3(2):359-72.
- 7) Sola E, Watson H, Graupera I, Turon F, Barreto R, Rodríguez E, et al. Factors related to quality of life in patients with cirrhosis and ascites: relevance of serum sodium concentration and leg edema. *J Hepatol*. 2012; 57(6):1199-1206.
- 8) Pereira G, Guevara M, Fagundes C, Solá E, Rodríguez E, Fernández J, et al. Renal failure and hyponatremia in patients with cirrhosis and skin and soft tissue infection. A retrospective study. *J Hepatol*. 2012; 56(5):1040-46.
- 9) Kim JH, Lee JS, Lee SK, Bae WK, Kim NH, Kim KA, et al. The association between the serum sodium level and the severity of complications in liver cirrhosis. *Kor J Intern Med*. 2009; 24:106-12.
- 10) Ginès P1, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. *Hepatology*. 2008 Sep; 48(3):1002-10.
- 11) John S1, Thuluvath PJ1. Hyponatremia in cirrhosis: pathophysiology and management. *World J Gastroenterol*. 2015 Mar 21; 21(11):3197-205.
- 12) Hussain A, Nadeem MA, Nisar S, Tauseef HA. Frequency of gallstones in patients with liver cirrhosis. *J Ayub Med Coll Abbottabad*. 2014 Jul-Sep; 26(3):341-3.
- 13) Khan AH, Hayat AS, Humaira M, Pathan GN, Akbar A. Hyponatremia; frequency and outcome in patients with liver cirrhosis. *Professional Med J*. 2016; 23(6):669-672.
- 14) Topdagi O1, Okcu N1, Bilen N1. The frequency of complications and the etiology of disease in patients with livercirrhosis in erzurum. *Eurasian J Med*. 2014 Jun; 46(2):110-4.
- 15) Zuberi FF1, Zuberi BF, Khan MA, Khan MH. Frequency of rectal varices in patients with cirrhosis. *J Coll Physicians Surg Pak*. 2004 Feb; 14(2):94-7.
- 16) Alam I, Razaullah, Haider I, Humayun M, Taqweem A, Nisar M. Spectrum of precipitating factors of Hepatic Encephalopathy in liver cirrhosis. *Pak J Med Res*. 2005; 44(2):96-100.
- 17) Asgher SA, Saleem MK, Hussain A. Accuracy of rockall score for in hospital re-bleeding among cirrhotic patients with variceal bleed. *Ann King Edward Med Uni*. 2015; 21(1):14-9.
- 18) Naheed T, Akbar N, Akbar N. Frequency of Gallstones in patients of liver cirrhosis - a study in Lahore. *Pak J Med Sci*. 2004; 20(3):215-8.
- 19) Jenq CC, Tsai MH, Tian YC, Chang MY, Lin CY, Lien JM. Serum sodium predicts prognosis in critically ill cirrhotic patients. *J Clin Gastroenterol*. 2010; 44:220-6.