

## Correlation of Serum Sodium with Severity of Ascites in HCV-Related Liver Cirrhosis

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### Abstract

**Objective:** The objective of this study is to determine the frequency of hyponatremia among HCV-related chronic liver disease patients with ascites and to compare levels of serum sodium with different severity of ascites.

**Material and Methods:** This descriptive cross-sectional study was conducted in Holy Family Hospital. Indoor patients fulfilling the inclusion criteria were selected using consecutive sampling.

Patient information, clinical presentation and ascites grading, was recorded using a pre-designed questionnaire. Ascites was graded clinically and confirmed via ultrasound as mild, moderate, or severe. Serum sodium levels were measured using ISE (ion-specific electrode technology) at the hospital lab upon admission.

Statistical analysis was performed using SPSS, with a p-value of <0.05 considered statistically significant.

**Results:** A total of 291 patients were included. The mean age of patients was 48.82 (SD 14.94) years, whereas total male and female patients were 169 (58.1%) and 122 (41.9%) respectively. Frequency of hyponatremia (mild, moderate, severe) among HCV-related chronic liver disease patients with ascites was 135 (46.4%), 56 (19.2%), and 100 (34.4%) respectively whereas among patients with Grade 1 ascites, frequency of mild & severe hyponatremia was noted as 119 (62.8) and 54 (28.4) respectively and it was highly significant statistically (p-value 0.0001).

**Conclusion:** The study highlights a significant occurrence of hyponatremia among patients with HCV-related chronic liver disease, strongly associated with severity of ascites. In a resource-limited country like Pakistan, serum sodium emerges as a simple yet vital tool to promptly identify patients at risk of complications, enabling timely interventions.

**Keywords:** Ascites, Liver, Hyponatremia

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### Introduction

The pathological collection of fluid in the abdominal cavity is called ascites.<sup>1</sup> One of the most important complications of chronic liver disease is ascites along with variceal bleed and hepatic encephalopathy. Cirrhosis is the 12<sup>th</sup> leading cause<sup>1</sup> of death in the US, with 32,000 people dying each year.<sup>2</sup> Cirrhotic patients who develop

ascites have a probability of survival of 85% at one year & 56% at five years without a liver transplant. Underfill, overflow, and vasodilatation are three possible theories that are present in patients with ascites<sup>3</sup>. For successful mobilization of ascites, there should be a negative sodium balance that is achieved by dietary salt restriction and the use of diuretics. Renal function derangements and electrolyte imbalances intensify the clinical course of chronic liver disease. Dilutional hyponatremia is one of the main consequences of Chronic Liver Disease (CLD) which occurs only in advanced stage.<sup>4</sup> Hyponatremia is defined as serum sodium of less than 136meq/L while in cirrhosis, the relevant value is below 130meq/L. The hyponatremia occurring in cirrhosis is dilutional which occurs when serum is hypotonic

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and extracellular fluid volume is increased. There is Anti Diuretic Hormone (ADH) excess but free water excretion is abnormal.<sup>5</sup> Hyponatremia is a common finding in 57% of admitted and 40% of outpatients of chronic liver disease.<sup>6</sup>

Hyponatremia in cirrhosis is one of the risk factors predicting mortality in end-stage liver disease. The prevalence of serum sodium of less than 130mmol/L was 21.6%. while it was 25.3% in HCV-related liver cirrhosis. Ascites was resistant to diuretics and more often therapeutic paracentesis was required<sup>7</sup>. Therefore, serum sodium is incorporated into one of the most reliable prognostic scores, the MELD (Model for End Stage Liver Disease) score modified as MELD Sodium and patients with hyponatremia have poor survival as compared to non-hyponatremic patients.<sup>8</sup>

There was a study published in Egypt in Jan 2017 that correlated the serum sodium value with the severity of complications in liver cirrhosis. The results of the study showed that the severity of hyponatremia corresponded to a high risk of developing ascites.

Hepatitis C is a growing health crisis in Pakistan, with many patients developing complications like diuretic-resistant ascites. In busy outpatient clinics and emergency departments, there's an urgent need for simple, cost-effective tools to identify those at risk early. Hyponatremia is a common but overlooked marker of disease severity, yet no recent studies in Pakistan have explored its link to the severity of ascites. This study aims to fill that gap, highlighting how a basic test like serum sodium can guide timely interventions and improve outcomes for these vulnerable patients.

## Material & Methods

This descriptive cross-sectional study was conducted in Medical Unit 1 and department of Gastroenterology, Holy Family Hospital. The study was conducted after approval from the institute with ERB number RMU/2017-65. Informed consent was obtained from patients. A sample size of 291 was calculated with 80% power of the test and a 5% level of significance by taking 25.3% population proportion.

Patients with already diagnosed HCV-related chronic liver disease with ascites, of age more than 18-75 years were included. Exudative ascites, Heart failure (measured clinically by the presence of raised JVP, orthopnea, and abnormal ECG findings), Renal failure, Hepatitis B along with hepatitis C, or other causes of decompensated liver disease like NAFLD patients were excluded. At

the time of admission, serum sodium was measured. Patients were divided into 3 groups. Serum sodium of less than 125mmol/L, serum sodium between 125 and 129mmol/L, and serum sodium between 130mmol/L to 134mmol/L. Ascites were graded as per severity and detected by ultrasound. After history and relevant examination, investigations were carried out like full blood count, renal function tests, ultrasound abdomen for ascites grading and renal size, serum sodium level, urine routine examination, Hepatitis Serology by kit or by ELISA, Ascitic fluid albumin and serum albumin levels for calculating SAAG, Electrocardiography, and echocardiography if clinical suspicion of heart failure.

Information regarding the patient's presentation was noted on a pre-designed research questionnaire designed by the primary researcher. Serum sodium was sent to the hospital lab and was measured by ISE (ion-specific electrode technology).

Data was analyzed by SPSS 25.0. Mean + SD were calculated for age. Qualitative variables like gender, ascites severity, and serum sodium were measured by frequency and percentages. Post-stratification Pearson Chi-square was applied and a P value of less than 0.05 was considered significant. Effect modifiers were concurrent diuretic use, age, and gender were controlled by stratification. Post-stratification chi-square test was applied for P-value.

## Results

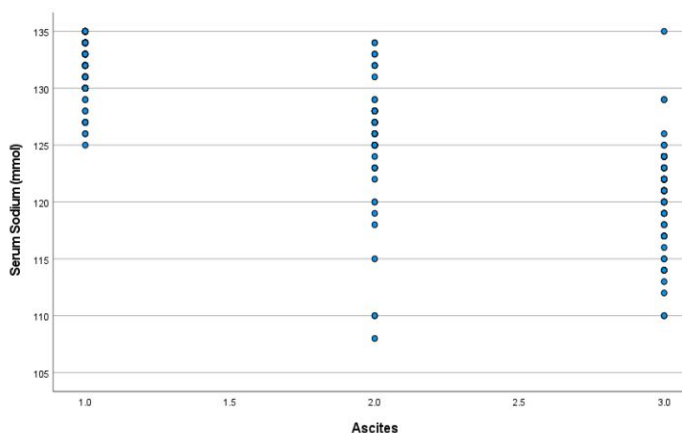
A total of 291 patients were included. The mean age was 48.82+14.24 years. There were 169 (58.1%) male and 122 (41.9%) female. Of the total 167 (57.4%) patients used diuretics while 124 (42.6%) did not. Frequency of hyponatremia (mild, moderate, severe) among HCV-related chronic liver disease patients with ascites was 135 (46.4%), 56 (19.2%), and 100 (34.4%) respectively (Table: 1). Ascites was also divided into mild, moderate and severe categories including mild 138 (47.4%), moderate 62 (21.3%), and severe 91 (31.3%) patients. Effect modifiers like age and gender stratification were done and compared with the frequency of hyponatremia among HCV-related chronic liver disease patients with ascites. Among patients with age below 18 years, frequency and percentage of hyponatremia (mild, moderate, severe) were 1 (50%), 1 (50%), and 0 (0%) respectively whereas among patients with age 18-50 years; frequency and percentage of hyponatremia (mild, moderate, severe) was 75 (44.1%), 32 (18.8%) and 63 (37.1%) respectively, in the age group above 50 years inferential analysis showed 59 (49.6%) of patients had mild hyponatremia,

23(19.3%) had moderate hyponatremia, 37(31.1%) had severe hyponatremia with p-value of 0.579 thus statistically insignificant respectively (Table 3). Similarly, there was no significant difference in the degree of hyponatremia in males and females (p-value 0.289). Likewise, ascites were not significantly associated with age and gender (p-value 0.814, 0.052). On the contrary, there was a significant difference in the degree of ascites between the diuretic users and nonusers (p-value <0.001). Table: 3

**Table 1:** Descriptive Analysis of Age & Gender

Total number of Patients		N	291
Age (Years)		Mean (SD)	48.8 (14.2)
Gender	Male	Frequency	169 (58.1%)
	Female	(Percentage)	122 (41.9%)
Diuretic Use	Yes	Frequency	167 (57.4%)
	No	(Percentage)	124 (42.6%)
Hyponatremia	Mild	Frequency	135 (46.4%)
	Moderate	(Percentage)	56 (19.2%)
	Severe		100 (34.4%)
Degree of Ascites	Mild		138 (47.4%)
	Moderate		62 (21.3%)
	Severe		91 (31.3%)

**Graph 1 Key:**  
 1.0= Mild Ascites  
 2.0= Moderate Ascites  
 3.0= Severe Ascites



**Graph 1:** Scatter Plot Between Degree of Ascites and Serum Sodium Level

### Discussion

Cirrhosis can develop from weeks to years after liver damage<sup>9</sup>. In developed countries, the most common causes of cirrhosis are Alcohol-associated Liver Disease (AALD), Hepatitis C Virus (HCV)&Non-Alcoholic

**Table 2:** Comparison of serum sodium among HCV-related chronic liver disease with Different severity of ascites

Degree of hyponatremia	Degree of Ascites		
	Grade 1	Grade 2	Grade 3
Mild	125 (90.6%)	9 (14.5%)	1 (1.1%)
Moderate	13 (9.4%)	38 (61.3%)	5 (5.5%)
Severe	0 (0%)	15 (24.2%)	85 (93.4%)
Total	138	62	91
P value	<0.001		

**Table 3:** Effect Modifier Age, Gender, and Diuretics use stratification with Ascites among HCV-related chronic liver disease

Diuretic Use	Age Groups	Ascites			P value
		Mild	Moderate	Severe	
Use	Below 18	1(50%)	1(50%)	0(0%)	0.814
	18-50 years	80 (47.1%)	35 (20.6%)	55 (32.4%)	
	Above 50	<b>57 (47.9%)</b>	<b>26 (21.8%)</b>	<b>36 (30.3%)</b>	
	No	Male	70(41.4%)	41(24.3%)	58(34.3%)
Female		68(55.7%)	21(17.2%)	33(27.0%)	
Yes		36 (21.6%)	53 (31.7%)	78 (46.7%)	<0.001
No		102(82.3%)	9 (7.3%)	13 (10.5%)	

Steatohepatitis (NASH).<sup>10</sup> In Pakistan, the most common cause of liver cirrhosis is HCV.<sup>9</sup> Cirrhosis over time leads to abdominal ascites, and consequently hyponatremia. Hyponatremia in the context of liver cirrhosis is primarily dilutional<sup>11</sup>, resulting from the body's inability to excrete free water effectively, leading to an excess of antidiuretic hormone (ADH). This condition not only reflects the severity of liver dysfunction but also poses a direct risk for increased mortality and morbidity.<sup>12</sup> Hyponatremia as a consequence of advanced liver disease results from reduced renal capacity to excrete solute-free water ultimately resulting in reduced serum sodium levels<sup>11</sup>. Serum sodium ranges from 135 to 145 mEq/L. A blood level of less than 135 mEq/L is called hyponatremia, and a level less than 125 mEq/L is considered severe hyponatremia.<sup>13</sup>

The findings of this study demonstrate the significant correlation between serum sodium levels and the severity of ascites in patients with HCV-related chronic liver disease. The data reveals a clear pattern where lower serum sodium levels are associated with more severe ascites. This relationship was statistically significant (p < 0.001), highlighting the potential of serum sodium

as a useful prognostic marker, similar results were obtained by Nareddy et al (2020).<sup>7</sup> Our study shows that hyponatremia is prevalent among patients with HCV-related liver cirrhosis and ascites. Specifically, severe hyponatremia was predominantly found in patients with grade 3 ascites (93.4%), while mild hyponatremia was more common in those with grade 1 ascites (90.6%). This monotonic pattern, confirmed through Spearman's rank-order correlation ( $r_s=0.899$ ,  $p<0.001$ ), suggests that as the severity of ascites increases, the serum sodium levels decrease significantly, as similarly noted in a study by Islam et al.<sup>14</sup>

Moreover, our findings align with previous studies, such as those conducted by Ibrahim et al. (2017) and Nareddy et al. (2020), which also reported a high prevalence of hyponatremia in cirrhotic patients with severe ascites. These studies emphasize the role of serum sodium as an independent prognostic factor in chronic liver disease, further validating our results. Incorporating serum sodium levels into routine assessment provides a simple, cost-effective tool for early identification of patients at higher risk of complications, thereby enabling timely and targeted interventions, as previously demonstrated by Nareddy et al. (2020).<sup>7</sup>

Given the resource constraints in Pakistan and the high prevalence of HCV, the use of serum sodium measurement is particularly advantageous. It offers a readily available and non-invasive prognostic measure that can guide clinical decision-making. In settings where advanced treatments like liver transplantation or transjugular intrahepatic portosystemic shunt (TIPS) are not readily accessible, serum sodium levels can help prioritize patients for more intensive monitoring and management. The significant difference in the degree of ascites between diuretic users and non-users ( $p < 0.001$ ) also highlights the importance of managing diuretic therapy effectively to mitigate the progression of ascites and prevent severe hyponatremia. Future research should focus on optimizing diuretic use and other interventions to manage serum sodium levels, potentially improving outcomes for patients with chronic liver disease. The results of this study highlight the prevalence of hyponatremia in patients with varying grades of ascites. The mean serum sodium level was  $132.23 \pm 5.89$  mmol/L, with 29% of patients having serum sodium below 130 mmol/L, 46.5% between 130 and 135 mmol/L, and 24.5% above 135 mmol/L. Patients with grade 3 ascites demonstrated a notable prevalence of severe hyponatremia, as 14 of them had serum sodium

levels below 130 mmol/L. Comparatively, only 2 patients with grade 1 ascites and 12 with grade 2 ascites had serum sodium levels in this range.

The literature further supports the frequent occurrence of hyponatremia in cirrhotic patients<sup>15</sup>, attributing it primarily to dilutional mechanisms and the dysregulation of water balance. It is seldom a spontaneous finding but rather an indicator of worsening pathophysiology in chronic liver disease<sup>16</sup>. This highlights its prognostic relevance, as hyponatremia correlates with an increased burden of cirrhosis-related complications, including hepatic encephalopathy and spontaneous bacterial peritonitis. This negative influence on clinical outcomes highlights the critical role of sodium management in mitigating morbidity among cirrhotic patients. The results of previous large observational studies<sup>16</sup> are consistent with our findings, emphasizing that low serum sodium levels are a common feature in both inpatient and outpatient cirrhotic populations. Patients with serum sodium concentrations below 135 mmol/L were shown to have poorer control of ascites, a higher incidence of hepatic encephalopathy, and increased risk of hepatorenal syndrome compared to those with sodium levels within the normal range. Our study aligns with these findings, further demonstrating that patients with mild reductions in serum sodium levels, even within the 130–135 mmol/L range, should be regarded as high-risk. This group exhibited more severe ascites and higher rates of major complications compared to those with normal sodium levels, necessitating closer monitoring and early intervention.

Hyponatremia's strong association with poor prognosis in cirrhotic patients suggests its potential as a valuable clinical marker to guide decision-making in resource-constrained settings. Identifying patients at risk through simple serum sodium measurements can facilitate timely interventions and potentially reduce the progression of complications. This approach is particularly relevant in regions like Pakistan, where advanced treatment options, such as liver transplantation, remain limited. By integrating serum sodium evaluation into routine clinical practice, healthcare providers can prioritize high-risk patients for closer monitoring, optimize treatment plans, and potentially improve overall outcomes.

In conclusion, this study reinforces the utility of serum sodium as a prognostic tool in HCV-related liver cirrhosis with ascites. Its simplicity and cost-effectiveness make it an invaluable asset in resource-limited settings, which can potentially aid in the timely identification of patients

at risk of severe complications and improving the overall management of chronic liver disease.

## Conclusion

The conclusion of the study is that a substantial frequency of hyponatremia was noted among HCV-related chronic liver disease patients corresponding with the severity of ascites. As Pakistan is a resource-constrained country with an increasing prevalence of HCV and treatment options like liver transplant and Trans jugular intra-hepatic portosystemic shunting (TIPS) are not readily available. So a simple tool like serum sodium is required to identify those patients who are at risk of developing complications of chronic liver disease timely.

**Conflict of Interest:** None

**Funding Source:** None

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## Authors Contribution

**IA:** Conceptualization of Project

**SA:** Data Collection

**AM:** Literature Search

**KURK:** Statistical Analysis

**FI, AJ:** Drafting, Revision

**HBR:** Writing of Manuscript