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Frequency of Hepatorenal Syndrome in Patients with Chronic Liver Disease

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ABSTRACT

Background: Hepatorenal syndrome (HRS) is a life-threatening functional renal failure occurring in advanced chronic liver disease (CLD) and is associated with high morbidity and mortality, particularly among hospitalized patients with hepatic decompensation. Early recognition and risk stratification using routine clinical and biochemical indicators are essential for timely intervention. Objective: To determine the frequency of hepatorenal syndrome among patients with chronic liver disease admitted to a tertiary-care hospital and evaluate associated demographic, clinical, and biochemical factors. Methods: A descriptive cross-sectional study was conducted from July 2024 to December 2024 in the General Medicine Department, Bolan Medical Complex Hospital, Quetta. A total of 142 adult CLD patients were enrolled using consecutive sampling. Patients were assessed clinically and biochemically, and HRS was diagnosed after applying predefined diagnostic criteria and exclusion of alternative causes of renal impairment. Group comparisons were performed using independent t-test and chi-square test with $p < 0.05$ as statistically significant. Results: HRS was present in 38 patients, yielding a frequency of 26.8%. Patients with HRS were significantly older (53.2 ± 10.9 vs 48.1 ± 11.6 years, $p = 0.01$) and had higher serum creatinine and bilirubin levels ($p < 0.001$). Ascites and hepatic encephalopathy were significantly more frequent among HRS patients ($p \leq 0.002$). HRS was associated with longer hospitalization, higher ICU admission, and increased mortality ($p \leq 0.01$). Conclusion: Hepatorenal syndrome is a frequent and severe complication in hospitalized CLD patients, strongly associated with decompensation and poor inpatient outcomes, highlighting the need for proactive renal surveillance and early escalation of care.

Keywords
Hepatorenal syndrome; Chronic liver disease; Cirrhosis; Renal failure; Ascites; Hepatic encephalopathy

INTRODUCTION

Liver cirrhosis and chronic liver disease (CLD) remain major contributors to morbidity and premature mortality, particularly in low- and middle-income settings where delayed presentation and limited access to specialized care accelerate progression to decompensation. Portal hypertension and its systemic consequences trigger profound circulatory dysregulation characterized by marked splanchnic vasodilation, reduced effective arterial blood volume, and compensatory neurohormonal activation that collectively impair renal perfusion and glomerular filtration despite structurally normal kidneys (1-6). Within this pathophysiological continuum, hepatorenal syndrome (HRS) represents a severe, potentially reversible form of functional renal failure that occurs in advanced liver disease and is associated with rapid clinical deterioration and high short-term mortality (7-9). Contemporary consensus frameworks recognize HRS primarily within the spectrum of acute kidney injury in cirrhosis and emphasize its dynamic nature, the need for early identification, and strict exclusion of alternative causes of kidney dysfunction, given the major prognostic implications and therapeutic time-sensitivity (2,6).

The clinical importance of HRS is underscored by evidence demonstrating that worsening renal indices in cirrhosis are not merely laboratory abnormalities but a pivotal inflection point in the natural history of decompensated CLD, strongly predicting intensive care utilization, prolonged hospitalization, and death (10-13). Even with advances in supportive therapies—such as vasoconstrictor strategies and albumin-based circulatory support—outcomes remain poor when diagnosis is delayed, when precipitating factors are not promptly recognized, or when escalation pathways such as transplant evaluation are not timely pursued (14-18). Prior literature has reported variable frequencies of HRS across hospitalized cirrhotic cohorts, reflecting heterogeneity in case mix, underlying etiology, diagnostic thresholds, and local care pathways (8,9). In regions where viral hepatitis remains prevalent and health-system constraints contribute to late-stage decompensation at first presentation, the expected burden of HRS may be amplified, yet locally relevant hospital-based estimates and correlates are not consistently reported in a way that can inform standardized renal monitoring and resource allocation policies (3,4,18-20).

From a PICO perspective, the population of interest comprises adults with clinically diagnosed CLD admitted to tertiary-care medical services, the exposure includes advanced decompensation features and biochemical evidence of liver dysfunction, and the outcome is the occurrence of HRS as a clinically meaningful marker of circulatory–renal failure with prognostic consequences. The knowledge gap is not the existence of HRS as a complication, but the lack of robust, context-specific estimates and the limited characterization of clinically actionable correlates—such as age, decompensation manifestations, and routinely available laboratory markers—that could support early suspicion and triage within high-burden tertiary hospitals. In this setting, defining the frequency of HRS and its association with pragmatic clinical indicators is essential to justify targeted renal surveillance, strengthen diagnostic stewardship, and support timely escalation of care. Accordingly, this study aimed to determine the frequency of hepatorenal syndrome among adults with chronic liver disease admitted to a tertiary-care hospital in Quetta and to evaluate its

association with demographic factors, decompensation features, and biochemical parameters available in routine inpatient practice. The research question was: among adults with chronic liver disease admitted to a tertiary-care medical unit, what is the frequency of hepatorenal syndrome and which demographic, clinical, and laboratory features are significantly associated with its occurrence?

MATERIAL AND METHODS

This descriptive cross-sectional observational study was conducted in the General Medicine Department of Bolan Medical Complex Hospital, Quetta, Pakistan, from July 2024 to December 2024. The study was designed to estimate the inpatient frequency of hepatorenal syndrome among adults with chronic liver disease and to examine its association with routinely documented demographic, clinical, and biochemical characteristics within a defined tertiary-care setting. Adult patients aged 18 years and above of either sex with a clinical diagnosis of chronic liver disease were enrolled using a consecutive sampling approach during the study period after obtaining written informed consent. Patients were excluded if they had established chronic kidney disease, acute kidney injury attributable to hypovolemia or septic shock, evidence of obstructive uropathy, recent exposure to nephrotoxic medications, or other clinical features suggesting intrinsic renal parenchymal disease, to ensure that the renal dysfunction assessed reflected the functional renal impairment spectrum consistent with hepatorenal syndrome (2,6,8).

Following enrollment, participants underwent standardized clinical assessment including documentation of age, sex, duration and etiology of chronic liver disease, and decompensation features such as ascites and hepatic encephalopathy recorded on admission and during inpatient evaluation. Blood sampling was performed as part of routine inpatient workup to determine serum creatinine and total bilirubin, and relevant clinical records were reviewed to support case ascertainment. Hepatorenal syndrome was diagnosed by applying predefined diagnostic criteria in cirrhotic chronic liver disease after exclusion of alternative causes of renal impairment and in the context of progressive renal dysfunction with no evidence of structural kidney disease, consistent with international consensus principles for HRS assessment in cirrhosis (2,8,9). The primary outcome was the frequency of hepatorenal syndrome among admitted chronic liver disease patients during the study period. Secondary outcomes included inpatient clinical course indicators including length of hospital stay, ICU admission requirement, in-hospital mortality, and renal function stabilization during admission, with stabilization determined by improvement in renal indices and clinical status under standard institutional management pathways.

The sample size was calculated using standard single-proportion estimation methods assuming a 25% anticipated frequency of hepatorenal syndrome, a 95% confidence level, and a 7% margin of error, yielding a required sample of 142 participants. Data were recorded on a structured proforma and entered into SPSS version 24.0 with verification procedures to reduce transcription errors and ensure data integrity. Quantitative variables were summarized as mean with standard deviation, and categorical variables as frequencies with percentages. Group comparisons between patients with and without hepatorenal syndrome were performed using the independent t-test for continuous variables and the chi-square test for categorical variables. To quantify the magnitude of associations, effect estimates were planned using mean differences for continuous variables and odds ratios with 95% confidence intervals for categorical exposures, with statistical significance set at $p < 0.05$. Missing values were handled through complete-case analysis for each comparison to preserve analytic transparency while maintaining reproducibility in a resource-limited clinical dataset. Ethical approval was obtained from the Institutional Research and Ethics Committee of Bolan Medical Complex Hospital, Quetta, and all study procedures complied with the Declaration of Helsinki, with confidentiality maintained through anonymized data handling and restricted access to study records (8,9).

RESULTS

A total of 142 adults with chronic liver disease were enrolled during the study period. Hepatorenal syndrome (HRS) was diagnosed in 38 patients, giving an overall inpatient frequency of 26.8%. The cohort had a mean age of 49.6 ± 11.8 years, and males comprised 66.2% of participants. Viral hepatitis was the most common reported etiology (60.6%), followed by alcohol-related liver disease (21.8%) and non-alcoholic fatty liver disease (17.6%). Clinical decompensation was frequent, with ascites present in 69.0% and hepatic encephalopathy in 29.6% (Table 1).

Patients with HRS were significantly older than those without HRS (53.2 ± 10.9 vs 48.1 ± 11.6 years, mean difference 5.1 years, 95% CI 0.98 to 9.22, $p = 0.01$) (Table 3). Biochemical parameters showed marked differences: serum creatinine was substantially higher in the HRS group (2.4 ± 0.6 vs 1.1 ± 0.3 mg/dL, mean difference 1.30, 95% CI 1.10 to 1.50, $p < 0.001$), and total bilirubin was also significantly higher (6.8 ± 2.1 vs 3.9 ± 1.8 mg/dL, mean difference 2.90, 95% CI 2.15 to 3.65, $p < 0.001$) (Table 3). Decompensation features were strongly associated with HRS: ascites was present in 89.5% of HRS patients versus 61.5% of non-HRS patients (OR 5.31, 95% CI 1.75 to 16.10, $p = 0.002$), and hepatic encephalopathy occurred in 55.3% versus 20.2%, respectively (OR 4.88, 95% CI 2.20 to 10.85, $p < 0.001$) (Table 3). Inpatient outcomes were significantly worse among patients with HRS (Table 4). Length of hospital stay was longer in the HRS group (9.6 ± 3.2 vs 5.4 ± 2.1 days, mean difference 4.20, 95% CI 3.11 to 5.29, $p < 0.001$). ICU admission was required in 42.1% of HRS patients compared with 17.3% of non-HRS patients (OR 3.47, 95% CI 1.53 to 7.89, $p = 0.001$). In-hospital mortality was higher in the HRS group (18.4% vs 4.8%, OR 4.47, 95% CI 1.32 to 15.09, $p = 0.01$). Renal function stabilization occurred less frequently among HRS patients (50.0% vs 88.5%, OR 0.13, 95% CI 0.05 to 0.31, $p < 0.001$) (Table 4).

Table 1. Baseline Demographic and Clinical Characteristics of Patients with Chronic Liver Disease (n = 142)

Variable	Overall (n = 142)
Age (years), mean ± SD	49.6 ± 11.8
Gender (Male/Female), n (%)	94 (66.2) / 48 (33.8)
Duration of CLD (years), mean ± SD	5.2 ± 2.1
Etiology of CLD, n (%)	
– Viral hepatitis	86 (60.6)
– Alcohol-related	31 (21.8)
– Non-alcoholic fatty liver disease	25 (17.6)
Presence of ascites, n (%)	98 (69.0)
Hepatic encephalopathy, n (%)	42 (29.6)

Table 2. Frequency of Hepatorenal Syndrome Among Study Participants (n = 142)

Variable	Frequency, n (%)
Hepatorenal syndrome present	38 (26.8)
Hepatorenal syndrome absent	104 (73.2)

Table 3. Comparison of Demographic, Clinical, and Biochemical Parameters Between HRS and Non-HRS Groups

Parameter	HRS (n = 38)	Non-HRS (n = 104)	Effect Estimate (95% CI)	p-value
Age (years), mean ± SD	53.2 ± 10.9	48.1 ± 11.6	Mean diff **5.10** (0.98 to 9.22)	0.01
Serum creatinine (mg/dL), mean ± SD	2.4 ± 0.6	1.1 ± 0.3	Mean diff **1.30** (1.10 to 1.50)	<0.001
Total bilirubin (mg/dL), mean ± SD	6.8 ± 2.1	3.9 ± 1.8	Mean diff **2.90** (2.15 to 3.65)	<0.001
Ascites present, n (%)	34 (89.5)	64 (61.5)	OR **5.31** (1.75 to 16.10)	0.002
Hepatic encephalopathy, n (%)	21 (55.3)	21 (20.2)	OR **4.88** (2.20 to 10.85)	<0.001

Table 4. Clinical Outcomes of Patients with and Without Hepatorenal Syndrome

Outcome	HRS (n = 38)	Non-HRS (n = 104)	Effect Estimate (95% CI)	p-value
Length of hospital stay (days), mean ± SD	9.6 ± 3.2	5.4 ± 2.1	Mean diff **4.20** (3.11 to 5.29)	<0.001
ICU admission required, n (%)	16 (42.1)	18 (17.3)	OR **3.47** (1.53 to 7.89)	0.001
In-hospital mortality, n (%)	7 (18.4)	5 (4.8)	OR **4.47** (1.32 to 15.09)	0.01
Renal function stabilization, n (%)	19 (50.0)	92 (88.5)	OR **0.13** (0.05 to 0.31)	<0.001

DISCUSSION

This study provides hospital-based evidence from a tertiary-care setting in Quetta demonstrating that hepatorenal syndrome occurred in 26.8% of admitted patients with chronic liver disease. This frequency is clinically substantial and aligns with the understanding that HRS is a relatively common complication in hospitalized decompensated cirrhosis, where systemic circulatory dysfunction and progressive portal hypertension predispose to functional renal failure (2,6,8). Importantly, the observed burden reinforces that HRS should be anticipated and actively screened in inpatient CLD populations, particularly in resource-constrained environments where late-stage presentation is frequent and opportunities for early stabilization may be limited.

A key demographic finding was the significantly higher mean age in the HRS group, with an absolute difference of 5.1 years. This pattern is consistent with the biologically plausible concept that older cirrhotic patients may have reduced physiological reserve, greater vulnerability to circulatory dysfunction, and higher susceptibility to renal hypoperfusion when exposed to systemic vasodilation and neurohormonal activation that characterize advanced liver disease (2,8). Older age may also reflect accumulated comorbidity burden, which can amplify renal vulnerability even in the absence of established chronic kidney disease, thereby increasing the likelihood that cirrhotic decompensation manifests with renal dysfunction.

The study also demonstrated that HRS was strongly associated with both biochemical derangement and decompensatory clinical features. Patients with HRS had significantly higher serum creatinine and total bilirubin levels, indicating concurrent renal impairment and reduced hepatic excretory function—markers repeatedly linked to poor short-term prognosis in advanced cirrhosis (6,8). Total bilirubin elevation reflects severe hepatocellular dysfunction and impaired bile excretion, which often parallels systemic inflammation and circulatory dysregulation, while creatinine elevation is central to recognizing HRS as a clinical state of renal vasoconstriction and reduced glomerular filtration without primary structural kidney disease (2,6). These findings suggest that routine inpatient monitoring of creatinine trends and liver biochemistry—when interpreted within appropriate clinical context—can support earlier suspicion of HRS and prompt escalation to supportive strategies.

Notably, ascites and hepatic encephalopathy were significantly more common among patients with HRS, with odds of HRS approximately five-fold higher in those with ascites and nearly five-fold higher in those with encephalopathy. These complications represent advanced portal hypertension and hepatic insufficiency, respectively, and they integrate mechanistically with the hemodynamic and neurohumoral changes driving HRS pathogenesis (8,17). The strong association observed in this cohort supports the interpretation of HRS not as an isolated renal condition but as a marker of advanced multi-organ dysfunction in cirrhosis, thereby emphasizing the importance of integrated inpatient management rather than kidney-directed care alone.

Clinical outcomes were significantly poorer in patients with HRS, including longer hospitalization, higher ICU admission rates, and increased in-hospital mortality. The mean length of stay was 4.2 days longer among HRS patients, reflecting greater complexity of management and higher acuity. ICU admission and mortality were also markedly increased, with HRS associated with 3.47-fold higher odds of ICU admission and 4.47-fold higher odds of death. These findings align with the established prognostic severity of HRS as one of the strongest predictors of short-term mortality in decompensated cirrhosis (8,9). Furthermore, renal function stabilization occurred substantially less often among HRS patients, highlighting that once HRS develops, reversal may be incomplete without timely initiation of targeted therapy and definitive pathways such as transplant evaluation, which may not be readily accessible in many settings (3,4,20).

From a clinical and health-system perspective, these results support strengthening hospital-based diagnostic vigilance for HRS in CLD admissions, particularly in older patients and those with clear evidence of decompensation. Standardizing renal monitoring protocols, ensuring early exclusion of reversible causes of renal impairment, and establishing escalation pathways for patients with rising creatinine and advanced decompensation may reduce preventable mortality. Moreover, integrating HRS recognition into broader CLD management strategies—including early decompensation prevention and timely referral—remains essential to reduce downstream burden and improve survival (8,21,22).

Although the study provides pragmatic and locally relevant estimates, interpretation should remain aligned with its cross-sectional observational nature and single-center setting. The associations observed represent unadjusted relationships and should not be interpreted as independent predictors without multivariable modeling. Additionally, variability in diagnostic thresholds and the complexity of excluding competing causes of renal injury in cirrhosis may influence frequency estimates. Nonetheless, the demonstrated burden and its strong relationship with decompensation

markers and adverse outcomes provide compelling evidence for improving standardized inpatient surveillance and early management of renal dysfunction in chronic liver disease.

CONCLUSION

Hepatorenal syndrome was identified in approximately one-quarter of hospitalized patients with chronic liver disease at a tertiary-care center in Quetta, confirming that HRS is a frequent and clinically severe complication in this setting. Its occurrence was significantly associated with older age, higher serum creatinine and bilirubin levels, and markers of hepatic decompensation including ascites and hepatic encephalopathy, and it was linked to substantially worse inpatient outcomes such as prolonged hospitalization, higher ICU admission, lower renal stabilization rates, and increased in-hospital mortality. These findings emphasize the need for standardized inpatient renal monitoring, early recognition of functional renal decline in cirrhosis, and timely escalation of supportive and definitive care pathways to reduce preventable mortality among patients with advanced chronic liver disease.

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