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Original Article

Assessment of Various Factors Responsible for Hospital Admission in Patients of Chronic Liver Disease at Chandka Medical College Teaching Hospital, Larkana – An Analytical Cross-Sectional Study

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ABSTRACT

Chronic liver disease (CLD) is a major cause of hospital admission and in-hospital mortality in Pakistan, where chronic viral hepatitis is highly prevalent. **Objectives:** To assess factors responsible for hospital admission in CLD patients and their association with in-hospital outcome (Discharge vs Death). **Methods:** This analytical cross-sectional study was conducted in the Department of General Medicine Unit-III, Chandka Medical College Teaching Hospital, Larkana, from 5th January 2026 to 5th March 2026.. Seventy patients aged 18–60 years with CLD ≥6 months and decompensated cirrhosis (Child-Pugh A, B, or C) were enrolled by consecutive sampling after informed consent and IRB approval (IRB/96). The primary admission factor and in-hospital outcome (Discharge or Death) were recorded. Data were analysed in SPSS version 26.0 using the chi-square test; p≤0.05 was significant. **Results:** Mean age was 44.43 ± 11.23 years; 45 (64.3%) were male. HCV was the leading aetiology (57.1%), and 33 (47.1%) had Child-Pugh Grade C disease. Commonest admission factors were ascites (31.4%), hepatic encephalopathy (14.3%), and variceal bleeding (11.4%). In-hospital mortality was 10/70 (14.3%). Variceal bleeding was the only factor significantly associated with mortality (40.0% vs 6.7%; p=0.012). **Conclusions:** Decompensation complications, such as ascites, hepatic encephalopathy, and variceal bleeding, drove CLD admissions, and variceal bleeding was the only factor significantly associated with in-hospital death. Findings warrant larger multi-centre studies.

INTRODUCTION

Chronic liver disease (CLD) is a progressive and largely irreversible condition characterised by persistent hepatic inflammation, hepatocellular injury, and fibrotic remodelling of the liver parenchyma that ultimately leads to cirrhosis and hepatic failure [1]. Continuous hepatic insult drives architectural deformation and regenerative nodule formation, which impair normal hepatic function and predispose patients to multi-system complications. The principal aetiologies include chronic viral hepatitis, alcohol-related liver disease, non-alcoholic fatty liver disease, autoimmune hepatitis, and metabolic disorders, with chronic hepatitis C virus infection remaining the dominant cause of CLD in Pakistan and other low- and middle-income countries [2-5]. Globally, CLD is among the

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leading causes of liver-related morbidity and mortality [1, 3]. The decompensation phase typically results in hospital admission and represents a substantial proportion of liver-related healthcare expenditure because of prolonged stay, intensive monitoring, and frequent readmission [6, 7]. Recurrent admissions are associated with deterioration in quality of life, accelerated disease progression, and increased short-term mortality [8]. Complications of portal hypertension and impaired hepatocellular function are the most frequent triggers for hospitalisation in CLD. These include ascites, jaundice, variceal gastrointestinal bleeding, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, sepsis, coagulopathy, hepatorenal syndrome, and hepatopulmonary syndrome [6, 9]. Acute-on-chronic liver failure (ACLF) and hepatocellular carcinoma further raise the likelihood of admission and are associated with adverse outcomes [9, 10]. Among these, hepatic encephalopathy, infections, and variceal bleeding consistently emerge as major contributors to in-hospital mortality and early readmission [10, 11]. Despite advances in pharmacological and endoscopic management, clinical assessment of CLD patients remains challenging because disease severity may evolve rapidly and initial decompensation can be missed during routine outpatient visits [6, 12]. Prognostic instruments such as Child–Pugh, the Model for End-Stage Liver Disease (MELD/MELD-3.0), and CLIF-C ACLF scores are widely used but do not fully capture the multifactorial clinical and social determinants of hospital admission [13]. Delayed presentation, poor follow-up, sub-optimal treatment adherence, and limited access to specialised hepatology services further complicate disease management in resource-constrained environments. Although several international and regional reports suggest that a significant proportion of cirrhosis hospitalisations and readmissions can be averted through earlier identification of antecedent factors, optimised outpatient care, and timely intervention, the majority of available evidence is derived from high-income settings [14, 15].

There is a relative scarcity of contemporary data from South Asian populations, including rural Sindh, Pakistan, where the spectrum of aetiologies, healthcare structure, and patient-related variables differ substantially. Chandka Medical College Teaching Hospital, Larkana, serves a predominantly rural catchment with a high background prevalence of HCV and other CLDs, and represents an ideal site to generate context-specific evidence. Therefore, the study aimed to assess the factors responsible for hospital admission in patients with chronic liver disease at this tertiary-care centre and to evaluate their association with in-hospital outcomes (Discharge vs Death), to inform preventive practice, resource allocation, and improve patient outcomes in similar settings.

METHODS

This was an analytical cross-sectional study conducted in the Department of General Medicine Unit-III, Chandka Medical College Teaching Hospital, Larkana, over six months from 5th January 2026 to 5th March 2026. The study commenced after obtaining ethical approval from the College of Physicians and Surgeons, Pakistan / Institutional Review Board (Ref No. SMBBMU/IRB/96, dated 29th December 2025), and written informed consent was obtained from every participant before enrolment. A total of 70 patients were enrolled using non-probability consecutive sampling. The sample size was calculated using the WHO sample-size formula for a single proportion, $n = Z^2.p.(1–p) / d^2$, where Z = 1.96 (95% CI), p=0.204 (expected prevalence of ascites as a reason for hospital admission, taken from Duah *et al.*), and d=0.10 (absolute precision). The calculated sample size of 62 was rounded up to 70 to allow for incomplete data [13]. Inclusion criteria: Patients of either gender aged 18–60 years with a confirmed diagnosis of chronic liver disease of ≥6 months' duration who were admitted electively or in emergency with decompensated cirrhosis (Child–Pugh A, B, or C). Exclusion criteria: Comatose patients, patients admitted for accidental causes, OPD/day-care patients, pregnant women, patients receiving treatment for hepatocellular carcinoma, liver transplant recipients, and self-reported drug abusers. CLD was defined as persistent hepatic dysfunction resulting from chronic parenchymal injury for ≥6 months, supported by (a) compatible clinical presentation (jaundice, hepatomegaly, splenomegaly, ascites, encephalopathy, or stigmata of chronic liver disease); (b) biochemical abnormalities — elevation of aspartate and alanine aminotransferases, raised total/direct bilirubin, prolonged prothrombin time / international normalised ratio (INR) ≥1.5, hypoalbuminaemia (serum albumin <3.5 g/dL), and/or thrombocytopenia; and (c) radiological findings on abdominal ultrasonography (coarse or nodular liver echotexture, surface irregularity, caudate-lobe hypertrophy, splenomegaly and/or features of portal hypertension such as portal-vein diameter >13 mm or collateral vessels), in accordance with the Lancet 2021 cirrhosis review and the British Society of Gastroenterology decompensated-cirrhosis guidance [6, 7]. The primary admission factor was defined as the single clinical complication of CLD deemed to be the most immediate, life-threatening reason for the index hospitalisation. Where two or more complications coexisted, the principal investigator and the supervising consultant jointly adjudicated the primary factor using a pre-specified hierarchy: (i) any actively bleeding lesion or haemodynamic instability; (ii) the complication associated with the highest acute mortality risk per Baveno VII8 and

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EASL ACLF guidance; (iii) the complication that necessitated admission according to the documented chief complaint. Disagreements were resolved by consensus after review of the medical record [9]. Specific definitions for admission factors: Ascites; clinically and/or sonographically detectable peritoneal fluid. Variceal bleeding; endoscopically confirmed bleeding from oesophageal or gastric varices [8]. Hepatic encephalopathy; overt encephalopathy graded by West Haven criteria (Grade ≥II) [11]. Spontaneous bacterial peritonitis (SBP); ascitic fluid polymorphonuclear count ≥250 cells/mm^3 with or without positive culture. Sepsis; Sepsis-3 criteria (suspected/confirmed infection plus SOFA ≥2). Acute-on-chronic liver failure (ACLF), EASL-CLIF definition (acute decompensation plus organ failure) [9, 10]. Hepatocellular carcinoma; radiological diagnosis on triphasic CT/MRI or histopathology. Hepatopulmonary syndrome; chronic liver disease with intrapulmonary vascular dilatation and arterial hypoxaemia. Coagulopathy; INR ≥1.5 with bleeding manifestations not attributable to variceal bleeding. Jaundice; admission predominantly for new or progressive jaundice without features fitting another category. COVID-19; RT-PCR-confirmed SARS-CoV-2 infection precipitating admission. Outcome variable: The in-hospital outcome was operationalised as the patient's final disposition at the end of the index hospital admission and was dichotomised into Discharge (survived to discharge) or Death (in-hospital mortality from any cause). The outcome was ascertained from the patient's medical record at the time of discharge or in-hospital death by the principal investigator, who reviewed the file daily until the patient left the ward. Data on demographic characteristics (age, gender, marital status, education, employment, monthly income), aetiology of CLD, Child–Pugh grade, comorbidities, duration of disease, duration of hospital stay, primary admission factor, and the in-hospital outcome were recorded on a structured, pre-designed proforma. Relevant laboratory and radiological investigations were performed as part of the routine inpatient care.

Data were analysed using IBM SPSS Statistics version 26.0. Continuous variables (age, BMI, income, duration of disease, hospital stay) are presented as mean ± standard deviation with 95% confidence intervals; categorical variables as frequencies and percentages. The chi-square test (or Fisher's exact test where cell counts were <5) was used to assess the association between each admission factor and the binary in-hospital outcome (Discharge vs Death). Stratification for age, gender, Child–Pugh grade, and aetiology was performed, and post-stratification chi-square testing was applied. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 70 patients with chronic liver disease who were admitted during the study period and met the eligibility criteria were enrolled and analysed. The mean age was 44.43 ± 11.23 years (95% CI 41.75–47.11), and the mean BMI was 26.06 ± 3.62 kg/m^2 (25.19–26.92). The mean monthly income was PKR 38,586 ± 10,103 (36,177–40,995). Mean disease duration was 19.33 ± 8.43 months (17.32–21.34), and mean hospital stay was 6.56 ± 1.93 days (6.10–7.02). Forty-five (64.3%) patients were male, and 25 (35.7%) females; 48 (68.6%) were married. Educational attainment was higher among 24 (34.3%), secondary among 21 (30.0%), primary among 17 (24.3%), and graduation or above among 8 (11.4%); 48 (68.6%) were employed. Hepatitis C virus was the leading aetiology (57.1%), followed by hepatitis B virus (28.6%), NAFLD/NASH (8.6%), and alcohol-related disease (5.7%). Thirty-three patients (47.1%) had Child–Pugh Grade C disease, 26 (37.1%) Grade B, and 11 (15.7%) Grade A. Diabetes mellitus (40.0%) and hypertension (34.3%) were the leading comorbidities. The overall in-hospital outcome was Discharge in 60 patients (85.7%) and Death in 10 patients (14.3%).

Table 1: Demographic, Socioeconomic, Clinical Profile, and In-Hospital Outcomes of the Study Participants with Chronic Liver Disease (n=70)

Characteristics	Mean ± SD	95% Confidence Interval / n (%)
Continuous Variables		
Age (Years)	44.43 ± 11.23	41.75–47.11
BMI (kg/m^2)	26.06 ± 3.62	25.19–26.92
Monthly Income (PKR)	38,586 ± 10,103	36,177–40,995
Duration of Disease (Months)	19.33 ± 8.43	17.32–21.34
Duration of Hospital Stay (Days)	6.56 ± 1.93	6.10–7.02
Categorical Variables		
Gender	Male	45 (64.3%)
	Female	25 (35.7%)
Marital Status	Married	48 (68.6%)
	Unmarried	14 (20.0%)
	Widowed	5 (7.1%)
	Divorced	3 (4.3%)
Educational Status	Higher	24 (34.3%)
	Secondary	21 (30.0%)
	Primary	17 (24.3%)
	Graduation or above	8 (11.45%)
Employment	Employed	48 (68.6%)
	Unemployed	22 (31.4%)
Aetiology of CLD	Hepatitis C Virus (HCV)	40 (57.1%)
	Hepatitis B Virus (HBV)	20 (28.6%)
	NAFLD/NASH	6 (8.6%)
	Alcohol-related disease	4 (5.7%)
Child–Pugh Grade	Grade A	11 (15.7%)

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	Grade B	26 (37.1%)
	Grade C	33 (47.1%)
Comorbidities	Diabetes Mellitus	28 (40.0%)
	Hypertension	24 (34.3%)
	Chronic Kidney Disease	4 (5.7%)
	Cardiovascular Disease	3 (4.3%)
	Chronic Respiratory Disease	2 (2.9%)
	Thyroid Disease	2 (2.9%)
	Non-HCC Malignancy	1 (1.4%)
Other CLD-Related Conditions (Specified)	Portal Hypertension without Variceal Bleeding	2 (2.9%)
	Oesophageal Varices without Bleeding	1 (1.4%)
	— Thrombocytopenia	1 (1.4%)
	— Splenomegaly	1 (1.4%)
	Other Specified Non-CLD Comorbidity	1 (1.4%)
	Total Other Comorbidities	18 (25.7%)
Primary Admission Factor	Ascites	22 (31.4%)
	Hepatic Encephalopathy	10 (14.3%)
	Variceal Bleeding	8 (11.4%)
	Spontaneous Bacterial Peritonitis (SBP)	6 (8.6%)
	Sepsis	5 (7.1%)
	Acute-on-Chronic Liver Failure (ACLF)	4 (5.7%)
	Hepatocellular Carcinoma (HCC)	3 (4.3%)
	Other Specified Admission Factors*	12 (17.1%)
In-Hospital Outcome	Discharge	60 (85.7%)
	Death	10 (14.3%)

Ascites was the most frequent primary factor leading to Hospitalisation, accounting for 22 (31.4%) of admissions, followed by hepatic encephalopathy in 10 (14.3%) and variceal bleeding in 8 (11.4%). Spontaneous bacterial peritonitis was responsible for 6 (8.6%) admissions; sepsis and jaundice each accounted for 5 (7.1%). Acute-on-chronic liver failure was noted in 4 (5.7%) patients (correcting the earlier typographical error). Coagulopathy and hepatocellular carcinoma each accounted for 3 (4.3%); COVID-19 infection was the primary admission factor in 2 (2.9%) patients; and hepatopulmonary syndrome was the least frequent, occurring in 1 (1.4%) patient.

Table 2: Factors Responsible for Hospitalization Among Patients with Chronic Liver Disease (n=70)

The Factor Responsible for Hospitalisation	Frequency, n (%)
Ascites	22 (31.4%)
Hepatic Encephalopathy	10 (14.3%)
Variceal Bleeding	8 (11.4%)
Spontaneous Bacterial Peritonitis (SBP)	6 (8.6%)
Sepsis	5 (7.1%)
Jaundice	5 (7.1%)
Acute-on-Chronic Liver Failure (ACLF)	4 (5.7%)
Coagulopathy	3 (4.3%)
Hepatocellular Carcinoma (HCC)	3 (4.3%)
COVID-19 Infection	2 (2.9%)
Hepatopulmonary Syndrome	1 (1.4%)

Most clinical features did not show a statistically significant association with in-hospital outcome ($p>0.05$). Acute-on-chronic liver failure was present in 3/60 (5.0%) discharged patients and 1/10 (10.0%) deaths (95% CI 0.044–5.066; $p=0.468$). Ascites was present in 18/60 (30.0%) discharged patients and 4/10 (40.0%) deaths (0.162–2.556; $p=0.528$). The wide 95% confidence intervals for low-frequency factors reflect imprecision due to the small number of events rather than a true absence of effect. No significant association was observed for coagulopathy, COVID-19, hepatic encephalopathy, hepatocellular carcinoma, hepatopulmonary syndrome, jaundice, SBP, or sepsis. In contrast, variceal bleeding was significantly associated with in-hospital mortality — present in 4/10 (40.0%) deaths versus 4/60 (6.7%) discharges (95% CI 0.021–0.542; $p=0.012$).

Table 3: The Association Between Each Admission Factor and the Dichotomous In-Hospital Outcome (Discharge vs Death)

Admission Factor	Discharge (n=60), n (%)	Death (n= 10), n (%)	95% CI	p-value
Acute-on-Chronic Liver Failure	3 (5.0%)	1 (10.0%)	0.044–5.066	0.468
Ascites	18 (30.0%)	4 (40.0%)	0.162–2.556	0.528
Coagulopathy	3 (5.0%)	0 (0.0%)	1.063–1.299	0.625
COVID-19 infection	2 (3.3%)	0 (0.0%)	1.062–1.294	0.733
Hepatic encephalopathy	10 (16.7%)	0 (0.0%)	1.072–1.344	0.190
Hepatocellular carcinoma	3 (5.0%)	0 (0.0%)	1.063–1.299	0.625
Hepatopulmonary syndrome	1 (1.7%)	0 (0.0%)	1.061–1.289	0.857
Jaundice	5 (8.3%)	0 (0.0%)	1.065–1.311	0.343
Spontaneous Bacterial Peritonitis	6 (10.0%)	0 (0.0%)	1.067–1.317	0.382
Sepsis	5 (8.3%)	0 (0.0%)	1.065–1.311	0.451
Variceal bleeding	4 (6.7%)	4 (40.0%)	0.021–0.542	0.012*

*$p \leq 0.05$ is considered statistically significant. 95% CI = 95% confidence interval for the odds ratio of mortality vs discharge. Wide confidence intervals reflect low event counts in some categories and should be interpreted with caution

DISCUSSION

Chronic liver disease is a major cause of morbidity and mortality worldwide, with disproportionate impact in low- and middle-income countries where late presentation and limited access to specialised hepatology services persist [1-3]. Cirrhosis represents the end-stage of progressive hepatic fibrosis and is associated with frequent decompensation, hospital admission, and high resource utilisation [6, 14]. Identifying the principal factors that precipitate hospital admission is therefore central to risk stratification and preventive planning. The mean age in our

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cohort was 44.43 ± 11.23 years, appreciably younger than typical Western cirrhosis-admission cohorts, in which the fifth and sixth decades predominate [1, 14]. This younger age pattern most likely reflects the high background prevalence of chronic viral hepatitis (particularly HCV) in Pakistan and other South Asian populations [4, 5]. The male predominance (64.3%) is consistent with regional reports [4, 5]. Hepatitis C was confirmed as the aetiology in 57.1% of patients, reinforcing the well-documented role of HCV as the principal driver of CLD in Pakistan [5]. A particularly striking finding was the predominance of Child–Pugh Grade C disease (47.1%) at the time of admission, with another 37.1% in Grade B. This pattern indicates that almost half of the admitted patients had advanced hepatic decompensation at first contact with hospital services. Several factors likely contribute to this: limited primary-care infrastructure in rural Sindh, low patient awareness of CLD, financial barriers to outpatient hepatology follow-up, and a tendency to present only when overt complications develop. The skew toward Grade C disease has important implications — it explains the relatively high in-hospital mortality (14.3%), the dominance of decompensation complications such as ascites, hepatic encephalopathy, and variceal bleeding in our admission spectrum, and supports the case for community-level HCV screening, structured cirrhosis registries, and earlier outpatient referral pathways in this catchment population [6, 7]. Ascites was the leading admission factor in our study (31.4%), a figure somewhat higher than the 20–30% range reported from Western tertiary-care cohorts [13, 14]. Pathophysiologically, portal hypertension drives splanchnic vasodilatation and neurohormonal activation, leading to renal sodium retention and progressive fluid accumulation; in resource-limited settings, late presentation and limited use of long-term diuretic therapy may further increase the admission burden [6, 8]. Hepatic encephalopathy accounted for 14.3% of admissions, which lies within the internationally reported range of 10–20% [11, 14]. Although encephalopathy did not reach statistical significance for in-hospital mortality in our analysis ($p>0.05$), its presence signals advanced hepatocellular insufficiency and impaired ammonia detoxification, and larger cohorts have consistently demonstrated that recurrent encephalopathy is a major predictor of readmission and adverse long-term outcomes [11, 16]. Variceal bleeding occurred in 11.4% of patients and was the only admission factor significantly associated with in-hospital mortality (40.0% of in-hospital deaths vs 6.7% of discharges; $p=0.012$). Acute variceal haemorrhage is one of the most life-threatening complications of portal hypertension, resulting from elevated portal pressure and rupture of fragile collateral vessels [8]. The 40% in-hospital mortality rate observed here is substantially higher than the 10–20% six-week mortality reported from high-income centres. Duah *et al.* in Ghana similarly identified gastrointestinal bleeding as a leading cause of admission and in-hospital death in cirrhotic patients, while Balane *et al.* from the Philippines reported analogously high in-hospital mortality from variceal bleeding in their tertiary-care cohort [13, 15]. The disparity between our figure and the international benchmark most likely reflects delayed presentation, limited round-the-clock endoscopic services, unavailability of pre-emptive TIPS, and the high background severity of disease (Child–Pugh C in nearly half the cohort). These findings underscore the need to adhere to Baveno VII recommendations early endoscopy within 12 hours, vasoactive drugs, antibiotic prophylaxis, endoscopic band ligation, and consideration of pre-emptive TIPS in high-risk patients, and to strengthen referral networks for definitive management [8]. Other decompensation complications, such as SBP (8.6%), sepsis (7.1%), ACLF (5.7%), and HCC (4.3%), did not reach statistical significance for in-hospital mortality. ACLF is well established as a syndrome of high short-term mortality in larger series (28-day mortality 38–52% across EASL-CLIF, APASL, and NACSELD definitions), and infections are consistently associated with adverse prognosis in cirrhosis [11, 12, 17]. The absence of a detectable statistical association in our cohort almost certainly represents a Type-II (false-negative) finding driven by the modest sample size (n=70), the small absolute number of in-hospital deaths (n=10), and the low frequency of these complications (3–9 patients each). The very wide 95% confidence intervals around the point estimates for these factors, for example, ACLF (0.044–5.066) and ascites (0.162–2.556), illustrate the imprecision rather than the absence of effect, and our findings should be interpreted in that light. Adequately powered multi-centre studies will be needed to characterise the mortality contribution of these less frequent admission factors in similar populations [9, 10, 17]. The overall in-hospital mortality of 14.3% is broadly comparable to figures reported from comparable settings (Ghana 12–15%, Philippines 11–17%) and from large US administrative databases (10–15%), suggesting that while individual admission factors may not have reached significance, the aggregate clinical burden of admitted CLD patients is high and clinically meaningful [13, 14, 18]. The strengths of this study include the provision of context-specific data from a tertiary hospital that serves a predominantly rural catchment, systematic assessment of admission factors using pre-specified operational definitions, and direct evaluation of their association with in-hospital outcomes [19, 20].

Nevertheless, several limitations must be acknowledged: (i) the cross-sectional design precludes causal inference and only allows reporting of associations; (ii) the modest

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sample size (n=70) and small number of in-hospital deaths (n=10) limit statistical power, particularly for lower-frequency complications such as SBP, sepsis, ACLF and HCC; (iii) the single-centre design limits generalisability beyond similar rural-catchment tertiary centres; (iv) prognostic indices such as the MELD, MELD-3.0, CLIF-C ACLF and Albumin–Bilirubin (ALBI) scores were not calculated, which would have permitted finer mortality prediction; and (v) longer-term outcomes such as 30- or 90-day mortality and readmission rates were not captured. Future work in this region should focus on multi-centre prospective cohort studies in rural Sindh and other comparable LMIC catchment areas, with substantially larger sample sizes, prospective collection of MELD-3.0 and CLIF-C ACLF scores at admission, standardised endoscopic-management bundles for variceal bleeding (Baveno VII), and structured 30- and 90-day post-discharge follow-up to capture early readmission and short-term mortality. Embedded community-screening sub-studies targeting HCV and earlier identification of compensated cirrhosis could further inform preventive strategy and reduce the burden of late, decompensated admissions.

CONCLUSIONS

In this analytical cross-sectional study of 70 patients admitted with chronic liver disease at Chandka Medical College Teaching Hospital, Larkana, hospitalisation was driven principally by decompensation complications, most commonly ascites (31.4%), hepatic encephalopathy (14.3%), and variceal bleeding (11.4%). The overall in-hospital mortality was 14.3%. Variceal bleeding was the only admission factor significantly associated with in-hospital death (40.0% vs 6.7%; p=0.012), whereas other complications did not reach statistical significance, most likely because of the modest sample size and low event counts. Given the cross-sectional design and limited sample, these findings should be interpreted as associations rather than causal relationships, and they highlight the need for larger multi-centre prospective studies incorporating MELD-based prognostic scoring and longer-term follow-up to inform targeted preventive and management strategies in similar resource-constrained settings.

Authors' Contribution

Conceptualization: SAS, KG
Methodology: SAS, PG, AL, KG, BG
Formal analysis: SAS, KG, PG, KG, SAL, BG
Writing and Drafting: SAS, AL
Review and Editing: SAS, KG, PG, AL, KG, SAL, BG

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflict of Interest

All the authors declare no conflict of interest.

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