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Original Research Article

To Study Predictors and Outcome of Renal Dysfunction in Patients of Chronic Liver Disease of Various Etiologies

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Abstract

Background: Chronic liver disease (CLD) represents a progressive spectrum of hepatic disorders that persist for months to years and frequently culminate in cirrhosis, portal hypertension, and multisystem complications. Among these, renal dysfunction is one of the most serious and prognostically significant complications, markedly increasing morbidity, mortality, length of hospital stay, and healthcare costs. Renal dysfunction in CLD encompasses a broad clinical spectrum ranging from potentially reversible acute renal failure to functional renal impairment such as hepatorenal syndrome and irreversible chronic kidney disease. Early identification of renal dysfunction in cirrhotic patients remains challenging because serum creatinine often underestimates renal impairment due to reduced muscle mass and altered hepatic creatine synthesis. Furthermore, renal dysfunction frequently develops in the setting of acute decompensation, making timely diagnosis and intervention difficult. Despite increasing recognition of its clinical importance, there is limited prospective data comprehensively evaluating predictors of renal dysfunction and associated outcomes across diverse etiologies of chronic liver disease, particularly in resource-limited tertiary-care settings.

Methodology: This cross-sectional prospective observational study was conducted over a one-year period in the Medicine Ward and Medical Intensive Care Unit of a tertiary-care teaching hospital after approval from the institutional ethics committee. Total of 110 Adult patients aged more than eighteen years admitted with liver parenchymal disease complicated by renal dysfunction were consecutively screened and enrolled after obtaining written informed consent. Ascitic fluid analysis was performed where indicated, including total leukocyte count, albumin, protein, and serum–ascites albumin gradient. Disease severity was assessed using the Model for End-Stage Liver Disease score. Patients were categorized into acute renal failure, hepatorenal syndrome, or chronic kidney disease based on clinical, biochemical, and radiological criteria. All patients received standard treatment protocols and were followed until discharge or death. Statistical analysis was performed using appropriate parametric and non-parametric tests, with significance defined as a p-value less than 0.05.

Results: total of 110 patients were included in the analysis, with a mean age of 48.6 years and a marked male predominance. Alcoholic liver disease emerged as the most common etiology. Ascites, jaundice, abdominal distension, pedal edema, and oliguria were the most frequently observed clinical manifestations, reflecting advanced hepatic decompensation. Acute renal failure was identified in 43.6% of patients, hepatorenal syndrome in 34.5%, and chronic kidney disease in 21.8%. Increasing age showed a significant association with more severe and chronic forms of renal dysfunction. Male gender predominated across all categories, particularly among patients with hepatorenal syndrome. Metabolic comorbidities such as diabetes mellitus, hypertension, obesity, and dyslipidemia were significantly associated with chronic kidney disease. Hepatorenal syndrome was strongly associated with severe ascites, oliguria, altered sensorium, prior episodes of ascites, previous acute kidney injury, and chronic alcohol consumption. Laboratory parameters differed significantly across renal dysfunction categories, with hepatorenal syndrome demonstrating higher serum bilirubin, INR, serum creatinine, blood urea, and MELD scores, along with lower serum sodium and albumin levels. Spontaneous bacterial peritonitis was significantly more frequent in patients with hepatorenal syndrome. Renal recovery was highest in acute renal failure, intermediate in chronic kidney disease, and lowest in hepatorenal syndrome. Requirement of dialysis and in-hospital mortality were significantly higher among patients with hepatorenal syndrome. Factors significantly associated with mortality included advanced age, presence of hepatorenal syndrome, acute kidney injury stage three, hepatic encephalopathy, hypotension, spontaneous bacterial peritonitis, severe hyponatremia, high MELD score, and requirement of renal replacement therapy.

Conclusions: Renal dysfunction is a frequent and serious complication of chronic liver disease and is closely linked to the severity of hepatic dysfunction and systemic derangements. Acute renal failure represents the most common and potentially reversible form, whereas hepatorenal syndrome is associated with the poorest outcomes, including high dialysis requirement and mortality. Advanced age, metabolic comorbidities, recurrent hepatic decompensation, severe liver dysfunction, hyponatremia, infection, and circulatory failure are key predictors of renal impairment and death. The strong association between hepatorenal syndrome and adverse outcomes underscores the importance of early recognition, prompt treatment of precipitating factors, and aggressive supportive care. Regular monitoring of renal function trends, early detection of infections, careful management of volume status, and avoidance of nephrotoxic agents are essential in patients with chronic liver disease.

Keywords: chronic liver disease, Model for End-Stage Liver Disease, non-alcoholic fatty liver disease, chronic kidney disease, Medical Intensive Care Unit.

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Introduction

Chronic liver disease (CLD) encompasses a spectrum of progressive liver disorders that persist for at least six months, eventually leading to cirrhosis, hepatic decompensation, and potentially hepatocellular carcinoma. Globally, CLD remains a significant cause of morbidity and mortality, exerting a tremendous burden on healthcare systems, particularly in regions where viral hepatitis, alcohol abuse, and metabolic syndromes are highly prevalent. [1] As CLD advances, it is often accompanied by a host of systemic complications involving multiple organ systems, with renal dysfunction standing out as one of the most ominous and life-threatening. The emergence of renal impairment in patients with chronic liver disease not only signals a severe decline in hepatic function but also drastically alters the clinical course, prognosis, and therapeutic strategy, making the study of its predictors and outcomes of paramount importance. [2] Renal dysfunction in the setting of chronic liver disease is multifactorial and complex. Traditionally, the classification includes functional disorders such as hepatorenal syndrome (HRS), and structural renal injuries such as acute tubular necrosis (ATN) and glomerulonephritis. Regardless of the type, renal dysfunction in CLD patients is strongly associated with poor outcomes, including increased risk of hospitalization, higher likelihood of developing hepatic encephalopathy, reduced response to treatment modalities, and decreased survival. The interplay between liver and kidney function is delicate and often disrupted in advanced liver disease, making early recognition, risk stratification, and prompt intervention critical for improving patient outcomes. [3] Chronic liver disease has a variety of etiologies, each contributing uniquely to its natural history and complications. These include chronic viral hepatitis (particularly hepatitis B and C), alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD), autoimmune liver disorders, cholestatic diseases like primary biliary cholangitis and primary sclerosing cholangitis, and inherited metabolic conditions such as Wilson's disease and hemochromatosis. [4] Among these, alcohol-related liver injury and NAFLD have gained increasing recognition in recent years due to shifting lifestyle patterns and the global obesity epidemic. These diverse etiologies not only influence the onset and progression of liver dysfunction but also have differing propensities to induce renal complications. The variability in pathogenesis highlights the importance of evaluating renal dysfunction within the context of specific etiological backgrounds. [5] The diagnosis of renal dysfunction in patients with chronic liver disease is complicated by several factors. Serum creatinine, the most widely used marker of renal function, is often unreliable in patients with cirrhosis due to reduced hepatic synthesis of creatine, muscle wasting, and altered renal handling. As a result, renal impairment may be underdiagnosed or misclassified in this population. [6] The outcome of renal dysfunction in patients with chronic liver disease is markedly influenced by its type, severity, reversibility, and timing of intervention. Hepatorenal syndrome, particularly type 1 (now categorized under HRS-AKI), carries an extremely poor prognosis if left untreated, with median survival often measured in weeks. [7] Furthermore, chronic kidney disease (CKD) is increasingly being recognized in cirrhotic patients, either as a consequence of longstanding functional impairment or due to coexisting systemic diseases such as diabetes and hypertension. The transition from AKI to CKD or the presence of CKD at baseline significantly affects transplant candidacy, increases the risk of cardiovascular complications, and shortens overall survival. Therefore, understanding the natural history and outcome trajectories of different forms of renal dysfunction is essential for optimizing care pathways in CLD patients. [8] Various clinical, biochemical, and imaging parameters have been proposed as predictors of

renal dysfunction in chronic liver disease. These include baseline severity of liver disease as assessed by scoring systems such as the Model for End-Stage Liver Disease (MELD) and Child-Pugh scores, presence of ascites and spontaneous bacterial peritonitis, systemic inflammatory response, serum sodium levels, and markers of circulatory dysfunction like low mean arterial pressure. [9] Emerging research is also exploring novel biomarkers and therapeutic strategies to address the limitations of current diagnostic and management paradigms. Biomarkers such as cystatin C, interleukin-18, and kidney injury molecule-1 (KIM-1) are being investigated for their ability to differentiate between functional and structural renal injury and to predict outcomes more accurately. [10] The present study seeks to address this gap by systematically analyzing the clinical profiles, biochemical parameters, and treatment outcomes of patients with chronic liver disease from various etiologies who develop renal dysfunction.

Materials and Methods

The present study was designed as a cross-sectional prospective observational study. The study was carried out at the medicine ward and medical intensive care unit (MICU) of GMERS medical college and general hospital, gotri, vadodara and was conducted over a period of one year. It was conducted among 110 adult patients admitted to the hospital with liver parenchymal disease complicated by renal dysfunction. Patients fulfilling the predefined inclusion criteria were enrolled after obtaining written informed consent or their legally acceptable representative. A detailed clinical history was obtained, and a thorough clinical examination was performed for each patient. Based on clinical evaluation, laboratory parameters, and predefined diagnostic criteria, patients were classified into three groups: Group A (Acute Renal Failure), Group B (Hepatorenal Syndrome), Group C (Chronic Kidney Disease). This classification was performed based on their respective diagnostic criteria and blood investigations.

All enrolled patients were subjected to the following investigations: Complete Blood Count (CBC) with indices, Liver Function Tests (LFT), Renal Function Tests (RFT), Serum electrolytes, Ultrasonography (USG) of abdomen and kidneys, ureters, and bladder (KUB), Serum albumin and total protein, Serum glutamic-pyruvic transaminase (SGPT), Serum glutamic-oxaloacetic transaminase (SGOT), Prothrombin time (PT), International Normalized Ratio (INR), and Activated Partial Thromboplastin Time (aPTT), Serum calcium and serum phosphate, Serum parathyroid hormone (PTH), Urine routine microscopy, Urine albumin–creatinine ratio, Ascitic fluid analysis included: Ascitic fluid routine microscopy, Ascitic fluid albumin and protein, Viral markers including HBsAg, anti-HCV, and HIV were assessed. Additional parameters such as AST to Platelet Ratio Index (APRI) score and Serum–Ascites Albumin Gradient (SAAG) ratio were calculated. The APRI score was calculated using the following formula:

$$\text{APRI Score} = \left(\frac{\text{AST}}{\text{Upper limit of normal AST}}\right) \div \text{Platelet count} \times 100$$

All patients received appropriate treatment as per standard hospital protocols. Patients were monitored throughout their hospital stay, and outcomes were assessed at the time of discharge or death. The sample size was calculated using the formula:

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where: n = required sample size, Z = 1.96 for a confidence level of 95%, p = prevalence based on previous studies (8%), q = 100 – p, d = allowable error (15%). Based on this calculation, a minimum sample size of 110 patients was required to achieve a confidence level of 95% with an allowable error margin of 15%. Quantitative variables were expressed as mean ± standard deviation (SD). Comparison of quantitative data between groups was performed using the Student's t-test. Categorical variables were expressed as proportions and percentages and were analyzed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant. The study was conducted after obtaining approval from the institutional ethics committee of GMERS medical college and general hospital, gotri, Vadodara.

Results

A total of 110 patients were included in the study, with ages ranging from 18 years to over 60 years. The largest proportion of patients belonged to the 41–50 years age group, comprising 32 patients (29.1%). The mean age of the study population was 48.6 years with a standard deviation of ±11.2 years. males predominated with 82 cases (74.5%), while females accounted for 28 cases (25.5%). The calculated male-to-female ratio was 2.9:1, indicating a marked male preponderance in the study population. Ascites was the most frequently observed clinical feature, present in 96 patients (87.3%). Abdominal distension was noted in 90 patients (81.8%), followed by jaundice in 88 patients (80.0%). Oliguria was observed in 74 patients (67.3%). Altered sensorium was documented in 46 patients (41.8%), representing a substantial proportion of the cohort. Hematemesis was seen in 34 (30.9%) cases, fever in 50 (45.4%) cases, and fatigue in 40 (36.4%). Type 2 diabetes

mellitus was the most common comorbidity, identified in 42 patients (38.2%). Systemic hypertension was present in 36 patients (32.7%), while obesity (BMI ≥30 kg/m²) was observed in 28 patients (25.5%). Dyslipidemia was noted in 24 patients (21.8%). Chronic NSAID use was reported in 18 patients (16.4%), and ischemic heart disease was present in 12 patients (10.9%). Chronic alcohol intake was reported in 56 patients (50.9%). Previous episodes of ascites were documented in 62 patients (56.4%), while 40 patients (36.4%) had a history of prior acute kidney injury episodes. Nearly half of the patients, 48 cases (43.6%), had a history of prior hospitalization for chronic liver disease. Use of herbal or alternative medications was noted in 20 patients (18.2%). The mean total bilirubin level was 5.8 ± 3.2 mg/dL, with direct bilirubin averaging 3.4 ± 2.1 mg/dL. Mean AST and ALT levels were 96 ± 42 IU/L and 72 ± 38 IU/L, respectively. Alkaline phosphatase levels averaged 164 ± 56 IU/L. Serum albumin was reduced, with a mean value of 2.4 ± 0.4 g/dL. The mean INR was elevated at 2.0 ± 0.5. The mean MELD score for the study population was 24.1 ± 5.6. The mean serum creatinine level among patients was 2.8 ± 0.7 mg/dL, while mean blood urea was 82 ± 28 mg/dL. Serum sodium levels were reduced, with a mean value of 129 ± 5 mEq/L, whereas mean serum potassium was 4.6 ± 0.6 mEq/L. The urine albumin–creatinine ratio averaged 168 ± 72 mg/g. The mean estimated glomerular filtration rate was 42 ± 14 ml/min/1.73 m². Ascitic fluid albumin levels averaged 0.9 ± 0.3 g/dL, while ascitic fluid protein levels were 1.2 ± 0.4 g/dL. The mean serum–ascites albumin gradient was 1.5 ± 0.4 g/dL. Ascitic fluid total leukocyte count averaged 380 ± 160 cells/mm³. Neutrophil counts exceeding 250 cells/mm³ were observed in 28 patients (29.2%). Alcoholic liver disease was the most common etiology, identified in 46 patients (41.8%). Non-alcoholic fatty liver disease or non-alcoholic steatohepatitis was present in 24 patients (21.8%). Chronic hepatitis B infection accounted for 16 cases (14.5%), while chronic hepatitis C was noted in 10 patients (9.1%). Autoimmune liver disease was present in 8 patients (7.3%), and other causes, including Wilson's disease and cryptogenic cirrhosis, accounted for 6 cases (5.5%). Acute renal failure was the most common category of renal dysfunction, observed in 48 patients (43.6%). Hepatorenal syndrome was identified in 38 patients (34.5%), while chronic kidney disease was present in 24 patients (21.8%). Table 1 show that a statistically significant association was observed between age distribution and type of renal dysfunction ($p = 0.003$), and gender distribution also showed statistical significance ($p = 0.044$). Clinical features including ascites, oliguria, jaundice, pedal edema, abdominal distension, and altered sensorium were significantly associated with the type of renal dysfunction ($p < 0.05$). Among comorbidities, diabetes mellitus, hypertension, ischemic heart disease, obesity, and dyslipidemia showed statistically significant associations, whereas chronic NSAID use did not ($p = 0.639$). Past history variables such as chronic alcohol intake, previous ascites, prior AKI episodes, and prior hospitalization for CLD demonstrated statistically significant associations ($p < 0.05$), while herbal/alternative medicine use was not statistically significant ($p = 0.48$). Additionally, precipitating factors including gastrointestinal bleed with coagulopathy, severe anemia, and sepsis were significantly associated with the type of renal dysfunction ($p < 0.05$). Table 2 show that significant differences were observed across renal dysfunction categories for total bilirubin, serum albumin, INR, MELD score, serum creatinine, blood urea, serum sodium, eGFR, ascitic protein, and SAAG, with all parameters showing p-values <0.001. The presence of spontaneous bacterial peritonitis was also significantly associated with the type of renal dysfunction ($p = 0.003$). Table 3 show that recovery of renal function differed significantly among groups, with a p-value <0.001. Progression or non-recovery was also significantly different across categories ($p <0.001$). Requirement of dialysis showed a statistically significant association with renal dysfunction type ($p <0.001$). Survival and discharge rates as well as in-hospital mortality demonstrated statistically significant differences across groups ($p <0.001$). Partial recovery did not show a statistically significant difference ($p = 0.785$). Table 4 show that non-survivors were significantly older than survivors ($p = 0.02$). The presence of hepatorenal syndrome, AKI stage 3, hepatic encephalopathy, hypotension, spontaneous bacterial peritonitis, higher MELD scores, serum sodium levels below 130 mEq/L, and requirement of dialysis were all significantly associated with in-hospital mortality ($p <0.05$). Gender did not show a statistically significant association with mortality ($p = 0.18$).

Table 1: Association between sociodemographic and clinical parameters and type of renal dysfunction (N=110)

Parameters	ARF n (%)	HRS n (%)	CKD n (%)	p-value
Age (years)				
18–30	8 (16.7)	3 (7.9)	1 (4.2)	0.003*
31–40	10 (20.8)	6 (15.8)	2 (8.3)	
41–50	16 (33.3)	10 (26.3)	6 (25.0)	
51–60	10 (20.8)	12 (31.6)	8 (33.3)	
>60	4 (8.3)	7 (18.4)	7 (29.2)	
Gender				
Male	34 (70.8)	32 (84.2)	16 (66.7)	0.044*
Female	14 (29.2)	6 (15.8)	8 (33.3)	
Clinical features at presentation				
Ascites	38 (79.2%)	38 (100%)	20 (83.3%)	<0.001*
Oliguria	28 (58.3%)	33 (86.8%)	15 (62.5%)	0.002*
Jaundice	35 (72.9%)	35 (92.1%)	18 (75.0%)	0.013*
Pedal edema	31 (64.6%)	33 (86.8%)	19 (79.2%)	0.012*
Abdominal distension	36 (75.0%)	38 (100%)	16 (66.7%)	<0.001*
Altered sensorium	14 (29.2%)	24 (63.2%)	8 (33.3%)	<0.001*
Comorbidities				
Type 2 diabetes mellitus	15 (31.3%)	13 (34.2%)	15 (62.5%)	0.014*
Systemic hypertension	12 (25.0%)	11 (28.9%)	13 (54.2%)	0.028*
Ischemic heart disease	3 (6.3%)	4 (10.5%)	6 (25.0%)	0.031*
Obesity (BMI ≥30 kg/m²)	10 (20.8%)	7 (18.4%)	11 (45.8%)	0.026*
Dyslipidemia	8 (16.7%)	7 (18.4%)	9 (37.5%)	0.043*
Chronic NSAID use	7 (14.6%)	6 (15.8%)	5 (20.8%)	0.639
Past history				
Chronic alcohol intake	20 (41.7%)	24 (63.2%)	11 (45.8%)	0.041*
Previous episodes of ascites	22 (45.8%)	30 (78.9%)	13 (54.2%)	0.003*
Previous AKI episodes	12 (25.0%)	16 (42.1%)	13 (54.2%)	0.012*

Table 2: Association between laboratory parameters and type of renal dysfunction (N=110)

Parameters (mean ± SD)	ARF (n=48)	HRS (n=38)	CKD (n=24)	p-value
Total bilirubin (mg/dL)	4.6 ± 2.4	7.8 ± 3.5	5.2 ± 2.6	<0.001*
Serum albumin (g/dL)	2.6 ± 0.4	2.1 ± 0.3	2.4 ± 0.4	<0.001*
INR	1.8 ± 0.4	2.4 ± 0.5	1.9 ± 0.4	<0.001*
MELD score	21.4 ± 4.2	28.6 ± 5.1	23.1 ± 4.6	<0.001*
Serum creatinine (mg/dL)	2.4 ± 0.6	3.1 ± 0.7	2.9 ± 0.5	<0.001*
Blood urea (mg/dL)	72 ± 24	94 ± 30	88 ± 26	<0.001*
Serum sodium (mEq/L)	132 ± 4	126 ± 5	130 ± 4	<0.001*
eGFR (ml/min)	48 ± 12	34 ± 10	38 ± 11	<0.001*
Ascitic protein (g/dL)	1.4 ± 0.4	0.9 ± 0.3	1.2 ± 0.4	<0.001*
SAAG (g/dL)	1.3 ± 0.3	1.7 ± 0.4	1.4 ± 0.3	<0.001*
Spontaneous Bacterial Peritonitis	8 (16.7)	17 (44.7)	6 (25)	0.003*

Table 3: Clinical outcomes in patients (N=110)

Parameters	ARF (n=48)	HRS (n=38)	CKD (n=24)	p-value
Recovery of renal function	29 (60.4%)	8 (21.1%)	8 (33.3%)	<0.001*
Partial recovery	9 (18.8%)	6 (15.8%)	5 (20.8%)	0.785
Progression / non-recovery	10 (20.8%)	24 (63.2%)	11 (45.9%)	<0.001*
Requirement of dialysis	9 (18.8%)	18 (47.4%)	10 (41.7%)	<0.001*
Survived and discharged	38 (79.2%)	17 (44.7%)	16 (66.7%)	<0.001*
In-hospital mortality	10 (20.8%)	21 (55.3%)	8 (33.3%)	<0.001*

Table 4: Factors associated with in-hospital mortality in patients with Chronic liver disease and renal dysfunction (N=110)

Parameters	Survivors (n=71)	Non-survivors (n=39)	p-value
Age (years, mean ± SD)	46.9 ± 10.8	51.7 ± 11.6	0.02
Male gender	50 (70.4%)	32 (82.1%)	0.18
Hepatorenal syndrome present	17 (23.9%)	21 (53.8%)	<0.001
AKI stage 3	13 (18.3%)	21 (53.8%)	<0.001
Hepatic encephalopathy	20 (28.2%)	26 (66.7%)	<0.001
Hypotension (MAP <65 mmHg)	16 (22.5%)	24 (61.5%)	<0.001
Spontaneous bacterial peritonitis	12 (16.9%)	16 (41.0%)	0.004
Mean MELD score (± SD)	22.1 ± 4.3	29.4 ± 5.2	<0.001
Serum sodium <130 mEq/L	20 (28.2%)	26 (66.7%)	<0.001
Requirement of dialysis	14 (19.7%)	23 (59.0%)	<0.001

Discussion

The age distribution in the present study showed a predominance of middle-aged individuals, with the highest proportion between 41 and 50 years. This finding was consistent with observations reported by Amarapurkar et al., who noted that acute decompensation and renal complications frequently occurred in patients in the fifth decade of life, reflecting cumulative liver injury and progressive circulatory dysfunction. [13] Jalan et al. similarly observed that patients developing organ failure during acute deterioration of cirrhosis were typically in the middle-age group, emphasizing that advancing age increased vulnerability to systemic inflammation and hemodynamic instability. [12] The relatively lower representation of younger patients suggested that renal dysfunction was uncommon without prolonged liver disease, while older patients above 60 years possibly reflected survivorship bias or earlier mortality in severe cases. A marked male predominance was observed in the study population. This pattern aligned with findings from multiple studies, including Shetty et al., where male patients constituted the majority of cirrhotic individuals with acute kidney injury. [17] Amarapurkar et al. also reported higher male representation, attributed to increased alcohol consumption and metabolic risk factors among men. [13] The gender skew likely reflected etiological patterns, particularly alcoholic liver disease, rather than gender-specific susceptibility to renal dysfunction. Yoo et al. further highlighted that male cirrhotic patients exhibited greater muscle mass variability, influencing creatinine-based renal assessment and potentially contributing to higher detection rates of renal dysfunction. [18]

Ascites and abdominal distension were the most prevalent clinical features, indicating advanced portal hypertension. Piano et al. reported ascites as an independent predictor of acute-on-chronic liver failure, reinforcing its role as a marker of circulatory dysfunction. [16] Oliguria was observed in over two-thirds of patients, paralleling findings by Shetty et al., who identified oliguria as a strong predictor of mortality in cirrhotic patients with AKI. [17] Altered sensorium was noted in a substantial proportion, consistent with Amarapurkar et al., where hepatic encephalopathy was significantly associated with poor outcomes. [13] These findings underscored that renal dysfunction frequently occurred in the context of multisystem decompensation rather than isolated kidney injury. Metabolic comorbidities were common in the study population. Targher et al. demonstrated that diabetes mellitus independently increased the risk of chronic kidney disease in patients with NAFLD, supporting the high prevalence of diabetes observed. [11] Huh et al. similarly linked metabolic risk factors to progressive renal impairment. [15] Hypertension and dyslipidemia reflected shared vascular and inflammatory pathways contributing to renal vulnerability. The presence of ischemic heart disease further suggested compromised systemic perfusion. Chronic NSAID use, though less frequent, represented an avoidable nephrotoxic risk, as highlighted in prior cirrhotic AKI cohorts reported by Shetty et al. [17] A significant proportion of patients had chronic alcohol intake and previous episodes of ascites and AKI. Jalan et al. emphasized that prior decompensations predisposed patients to subsequent organ failure due to reduced physiological reserve. [12] Maiwall et al. demonstrated that previous AKI episodes strongly predicted progression to chronic kidney disease, aligning with the current findings. Prior hospitalizations reflected disease severity and recurrent insults.20 Herbal medicine use, although present, did not show a significant association, similar to observations in other tertiary-care cohorts where standardized nephrotoxicity assessment was limited. The study population demonstrated markedly deranged liver function tests, including hyperbilirubinemia, hypoalbuminemia, elevated INR, and high MELD scores. Amarapurkar et al. identified elevated INR and creatinine as key predictors of mortality in ACLF. [13] Piano et al. reported that higher MELD scores were independently associated with ACLF development and reduced survival. [16] Hypoalbuminemia reflected impaired synthetic function and circulatory dysfunction, both critical in renal

hypoperfusion. These findings reinforced that renal dysfunction occurred predominantly in patients with advanced hepatic failure. Elevated serum creatinine and reduced eGFR characterized renal dysfunction in the cohort. Yoo et al. demonstrated that creatinine-based eGFR often overestimated renal function in cirrhosis, suggesting that true renal impairment might have been even more severe. [18] Markwardt et al. highlighted cystatin C as a superior predictor of renal dysfunction and mortality, emphasizing limitations of conventional markers. [14] Hyponatremia, observed in most patients, reflected severe circulatory dysfunction and neurohormonal activation, consistent with findings by Piano et al., who identified low sodium as a predictor of ACLF. [16] Low ascitic fluid protein and elevated SAAG indicated portal hypertensive ascites. The high prevalence of neutrocytic ascites aligned with Napoleone et al., who reported frequent AKI in the presence of infection during acute decompensation. [21] Amarapurkar et al. also noted bacterial infections as major precipitants of organ failure. [13] Low ascitic protein levels suggested impaired opsonic activity, predisposing patients to spontaneous bacterial peritonitis and subsequent renal dysfunction through systemic inflammation. Alcoholic liver disease emerged as the predominant etiology. This finding was consistent with Amarapurkar et al. and Shetty et al., who reported alcohol as the leading cause of cirrhosis complicated by renal dysfunction in Indian cohorts. [13,17] NAFLD constituted a significant proportion, supporting observations by Targher et al. that metabolic liver disease increasingly contributed to renal impairment. [11] Viral hepatitis accounted for a smaller fraction, possibly reflecting improved antiviral therapy availability. Autoimmune and genetic causes were less common but associated with advanced disease at presentation. Acute renal failure was the most frequent category, followed by hepatorenal syndrome and chronic kidney disease. Shetty et al. similarly reported a predominance of ATN and HRS among cirrhotic AKI cases. [17] Napoleone et al. demonstrated that AKI was nearly universal in ACLF, highlighting its central role in decompensation.21 The proportion of CKD reflected cumulative renal injury, consistent with Maiwall et al., who documented high CKD incidence following repeated AKI episodes in cirrhosis. [20] The present study demonstrated a significant association between sociodemographic and clinical variables and the type of renal dysfunction in patients with chronic liver disease. Increasing age was significantly associated with chronic kidney disease and hepatorenal syndrome, indicating that advancing age predisposed patients to more persistent and severe renal impairment. This observation was consistent with the findings of Maiwall et al., who reported that older cirrhotic patients were more likely to develop chronic kidney disease following acute kidney injury due to reduced renal reserve and repeated ischemic insults. [20] Jalan et al. similarly observed that advanced age contributed to higher susceptibility to organ failure during acute decompensation of cirrhosis 12 Male predominance was noted across all categories of renal dysfunction, particularly in hepatorenal syndrome. This pattern mirrored observations by Shetty et al. and Amarapurkar et al., where male patients constituted the majority of cirrhotic individuals with renal failure, largely attributable to higher prevalence of alcoholic liver disease among men. [13,17] Yoo et al. further highlighted that male cirrhotic patients often exhibited sarcopenia-related inaccuracies in creatinine-based renal assessment, which could influence detection and staging of renal dysfunction. [18] Among clinical features, ascites and abdominal distension were universally present in patients with hepatorenal syndrome, underscoring the role of severe portal hypertension and circulatory dysfunction. Piano et al. identified ascites as an independent predictor of acute-on-chronic liver failure, reflecting systemic vasodilation and effective hypovolemia. [16] Oliguria and altered sensorium were significantly more common in hepatorenal syndrome, findings consistent with Shetty et al., who identified oliguria as an independent predictor of mortality in cirrhotic patients with acute kidney injury. [17] Amarapurkar et al. similarly reported hepatic encephalopathy as a marker of multiorgan failure and poor prognosis. [13] Metabolic comorbidities such as diabetes mellitus, hypertension, obesity, and dyslipidemia were significantly associated with chronic kidney disease. Targher et al. demonstrated that diabetes and metabolic syndrome independently increased the risk of chronic kidney disease in patients with NAFLD, even after adjusting for traditional risk factors. [11] Huh et al. further supported this association by showing that higher fatty liver index scores predicted incident chronic kidney disease over long-term follow-up. [15] These findings suggested that intrinsic renal pathology played a greater role in chronic kidney disease than in functional renal failure. Past history variables such as previous ascites, prior acute kidney injury, and prior hospitalizations were significantly associated with hepatorenal syndrome and chronic kidney disease. Maiwall et al. emphasized that recurrent AKI episodes strongly predicted progression to chronic kidney disease and increased mortality. [20] Jalan et al. also reported that repeated hospitalizations and prior decompensations reflected diminished physiological reserve, predisposing patients to severe renal dysfunction. [12] The laboratory profile differed significantly across renal dysfunction categories, reflecting varying degrees of hepatic and circulatory failure. Patients with hepatorenal syndrome exhibited significantly higher total bilirubin, INR, and MELD scores compared to those with acute renal failure or

chronic kidney disease. Amarapurkar et al. identified elevated INR and MELD score as strong predictors of short-term mortality in acute-on-chronic liver failure, emphasizing their role as markers of severe hepatic dysfunction. [13] Piano et al. similarly demonstrated that higher MELD scores were independently associated with development of acute-on-chronic liver failure and reduced transplant-free survival. [16] Hypoalbuminemia was most pronounced in hepatorenal syndrome, reflecting impaired hepatic synthetic function and reduced oncotic pressure. Markwardt et al. emphasized that hypoalbuminemia contributed to circulatory dysfunction and renal hypoperfusion, increasing the risk of renal failure and mortality. [14] Elevated serum creatinine and blood urea levels in hepatorenal syndrome indicated advanced renal impairment, although Yoo et al. cautioned that creatinine-based measures often underestimated renal dysfunction in cirrhotic patients, particularly those with sarcopenia. [18] Their study demonstrated superior prognostic accuracy of cystatin C–based renal assessment in predicting acute kidney injury and mortality. Hyponatremia was significantly more severe in hepatorenal syndrome. Piano et al. identified low serum sodium as a marker of advanced circulatory dysfunction and a predictor of acute-on-chronic liver failure. [16] Jalan et al. similarly reported that hyponatremia reflected intense neurohormonal activation and was associated with increased mortality. [12] Reduced eGFR values in hepatorenal syndrome further supported the presence of profound functional renal impairment. Ascitic fluid analysis revealed significantly lower ascitic protein levels and higher SAAG in hepatorenal syndrome. Amarapurkar et al. reported similar findings, noting that low ascitic protein predisposed patients to spontaneous bacterial peritonitis due to impaired opsonic activity. [13] Napoleone et al. demonstrated that acute kidney injury associated with infection during acute decompensation carried a significantly worse prognosis. [21]

The higher prevalence of spontaneous bacterial peritonitis in hepatorenal syndrome reinforced the role of infection-triggered systemic inflammation in precipitating renal failure. Renal recovery was highest in acute renal failure and lowest in hepatorenal syndrome. Shetty et al. reported similarly poor recovery and high mortality in HRS patients. [17] Napoleone et al. demonstrated reduced AKI resolution in ACLF-associated AKI. Dialysis requirement was significantly higher in HRS and CKD, reflecting irreversible injury. [21] Survival rates were lowest in HRS, consistent with Amarapurkar et al., who reported mortality exceeding 70% in patients with multiple organ failure. [13] In-hospital mortality was significantly associated with multiple clinical and biochemical factors reflecting advanced disease severity and multiorgan dysfunction. Non-survivors were significantly older, consistent with findings by Maiwall et al., who reported age as an independent predictor of mortality in cirrhotic patients with renal dysfunction. [20] Although male gender was more frequent among non-survivors, it did not reach statistical significance, a finding similar to that reported by Shetty et al. [17]

The presence of hepatorenal syndrome was strongly associated with mortality. Amarapurkar et al. demonstrated that patients with multiple organ failures, including renal dysfunction, had mortality rates exceeding 70%. [13] Napoleone et al. similarly reported markedly reduced three-month survival in patients with acute kidney injury occurring in the setting of acute-on-chronic liver failure. [21] Advanced AKI stage 3 was another strong predictor of death, consistent with findings by Shetty et al. and Hadem et al., both of whom identified severe AKI as the most powerful determinant of short-term mortality. [17,19] Hepatic encephalopathy and hypotension were significantly more common among non-survivors. Jalan et al. emphasized that systemic inflammation and circulatory failure played central roles in progression to organ failure and death. [12] Spontaneous bacterial peritonitis was also significantly associated with mortality, reinforcing observations by Amarapurkar et al. and Napoleone et al., who highlighted infection as a key precipitating factor for renal failure and poor outcomes. [13,21] Non-survivors had significantly higher MELD scores and more severe hyponatremia. Piano et al. demonstrated that elevated MELD and low sodium levels independently predicted reduced transplant-free survival. [16] Requirement of dialysis was another strong mortality predictor, consistent with Shetty et al., who reported high mortality among cirrhotic patients requiring renal replacement therapy. [17] the present study demonstrated that renal dysfunction in chronic liver disease occurred predominantly in advanced hepatic failure, was influenced by metabolic and hemodynamic factors, and was strongly associated with poor outcomes. Findings were consistent with existing literature and emphasized the importance of early detection, infection control, and risk stratification to improve survival in this high-risk population.

Conclusion

Renal dysfunction is a frequent and serious complication of chronic liver disease and is closely linked to the severity of hepatic dysfunction and systemic derangements. Acute renal failure represents the most common and potentially reversible form, whereas hepatorenal syndrome is associated with the poorest outcomes, including high dialysis requirement and mortality. Advanced

age, metabolic comorbidities, recurrent hepatic decompensation, severe liver dysfunction, hyponatremia, infection, and circulatory failure are key predictors of renal impairment and death. The strong association between hepatorenal syndrome and adverse outcomes underscores the importance of early recognition, prompt treatment of precipitating factors, and aggressive supportive care. Regular monitoring of renal function trends, early detection of infections, careful management of volume status, and avoidance of nephrotoxic agents are essential in patients with chronic liver disease.

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