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DECOMPENSATED CHRONIC LIVER DISEASE: A COMPREHENSIVE REVIEW OF PATHOPHYSIOLOGY, SEVERITY ASSESSMENT, MANAGEMENT AND THE ROLE OF THE CLINICAL PHARMACIST

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Abstract: Background: Decompensated chronic liver disease (DCLD) is the advanced stage of cirrhosis in which loss of hepatic functional reserve and severe portal hypertension produce life threatening complications such as ascites, hepatic encephalopathy, variceal bleeding, spontaneous bacterial peritonitis and hepatorenal syndrome. It accounts for a large share of emergency admissions, intensive care utilisation and premature mortality, and may progress to acute-on-chronic liver failure (ACLF) with very high short-term mortality.
Objective: To review the definition, epidemiology, aetiology, pathophysiology, clinical presentation, diagnosis, severity assessment and management of DCLD, and to compare conventional prognostic scores (Child–Pugh, MELD) with objective biomarker-based scores (ALBI, PALBI) and ACLF-specific tools.
Methods: A narrative literature review was conducted to summarise relevant published evidence on DCLD. The review covered literature concerning disease mechanisms, epidemiology, risk factors, clinical complications, diagnostic investigations, prognostic assessment and therapeutic interventions. Conventional scoring systems, including Child– Pugh and Model for End-Stage Liver Disease (MELD), were evaluated alongside newer assessment tools such as Albumin–Bilirubin (ALBI), Platelet– Albumin–Bilirubin (PALBI) and Chronic Liver Failure Consortium (CLIF-C) scores.
Key findings: Alcohol-related and metabolic liver disease are the leading aetiologies in contemporary hospital cohorts, with viral hepatitis remaining important in endemic regions. About one third of hospitalised patients with decompensated cirrhosis meet ACLF criteria, and 28-day mortality rises from 10–15% in acute decompensation without organ failure to 76–86% in ACLF grade-3. Child–Pugh and MELD have recognised limitations; objective laboratory scores, CLIF-C scores, portal hypertension assessment and frailty evaluation improve risk stratification. Management rests on treating precipitants, nutritional support, alcohol cessation, vaccination, drug therapy for each complication, endoscopic and radiological interventions, and liver transplantation. Clinical pharmacists contribute through medication review, dose adjustment, monitoring and patient counselling.
Conclusion: DCLD is a multisystem condition that needs early recognition, objective multidimensional risk assessment and coordinated multidisciplinary care, including timely referral for transplant evaluation.

Keywords: *Decompensated chronic liver disease; cirrhosis; acute-on-chronic liver failure; portal hypertension; hepatic encephalopathy; ALBI score; PALBI score; clinical pharmacist.*

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1. INTRODUCTION

Definition of Chronic Liver Disease

Chronic liver disease (CLD) is a continuous process of inflammation, destruction and regeneration of liver parenchyma that lasts for more than six months, leading to progressive fibrosis and, ultimately, cirrhosis. Persistent injury caused by viral infections, alcohol consumption, metabolic dysfunction, autoimmune diseases or genetic disorders leads to chronic inflammation, hepatocyte death and fibrotic remodeling [1-3].

Definition of Decompensated Chronic Liver Disease

Decompensated chronic liver disease (DCLD), or decompensated cirrhosis, is an advanced stage of permanent liver scarring in which the liver can no longer maintain its normal metabolic, synthetic and clearance functions.

Decompensation marks the transition from an asymptomatic compensated phase to the development of major complications caused by severe portal hypertension [4,9].

The hallmark complications include:

- **Ascites:** Accumulation of fluid in the peritoneal cavity due to portal hypertension, reduced albumin levels and renal sodium retention [5].
- **Hepatic encephalopathy (HE):** Neuropsychiatric dysfunction ranging from mild cognitive impairment to coma, caused by the accumulation of ammonia and other toxins that the liver cannot adequately clear [3].
- **Variceal bleeding:** Life-threatening bleeding resulting from the rupture of oesophageal or gastric varices [4].
- **Spontaneous bacterial peritonitis (SBP):** Infection of ascitic fluid in the absence of an identifiable intra-abdominal source [5].
- **Hepatorenal syndrome (HRS):** Functional and rapidly progressive kidney failure resulting from splanchnic vasodilation [5].

DCLD is a multisystem condition. When acute decompensation occurs alongside extrahepatic organ failure, the condition progresses to acute-on-chronic liver failure (ACLF) [8,9].

Epidemiology

The most comprehensive global estimates published in 2025 are still based on the Global Burden of Disease (GBD) 2021 dataset. Global cirrhosis-related deaths increased from 1.02 million in 1990 to 1.43 million in 2021. Disability-adjusted life years (DALYs) increased from 36.3 million to 46.4 million, while incident cases increased from 36.9 million to 58.4 million. Over the same period, the age-standardised mortality rate decreased from 24.4 to 16.6 per 100,000 population.

A contemporary review published in 2025 reached a similar conclusion: although age-standardised death rates are declining in many regions, the absolute number of deaths continues to increase because of population growth and ageing. Metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease have also emerged as major contributors, replacing viral hepatitis as the leading drivers in several regions. These findings update the earlier estimate of more than 1.3 million deaths in 2017.

Table 01: Key epidemiological findings from 2025–2026 relevant to DCLD.

Topic	Finding	Source
Global deaths (2021)	1.43 million deaths; approximately 1.4 million in a separate 2025 review. Absolute deaths are increasing despite declining age-standardised mortality rates.	Duo 2025; Hepatology Communications 2025
Leading driver of new cirrhosis cases	NAFLD/MASLD, with 48.3 million incident cases in 2021.	Duo 2025
Alcohol-related deaths	Increased from 223,000 in 1990 to 354,000 in 2021.	Duo 2025
India: aetiology	Pooled estimates: alcohol-related liver disease, 43.2%; NAFLD/cryptogenic liver disease, 14.4%. Alcohol-related and metabolic causes are increasing, while viral causes are declining.	Journal of Clinical and Experimental Hepatology, 2024 meta-analysis
India: clinical presentation	Western India cohort (November 2025): mean age of 52.4 years, 71% male, with most patients presenting at the decompensated stage.	Cureus 2025
India: transplantation gap	Estimated annual requirement of approximately 100,000 liver transplants compared with approximately 2,500 procedures performed.	ILBS trial registry text
ACLF aetiology trend	A meta-analysis of 24 cohorts involving 4,398 patients reported persistently high mortality and a shift in aetiology from viral hepatitis towards alcohol-related causes.	Portal Hypertension & Cirrhosis 2025

DEFINITION AND CLASSIFICATION OF DCLD

Compensated Versus Decompensated Cirrhosis

The natural history of cirrhosis progresses from a compensated stage, which is generally asymptomatic and free from overt complications, to a decompensated stage characterised by ascites, variceal haemorrhage, jaundice and hepatic encephalopathy. The transition to decompensation is associated with a marked reduction in survival.[4,9]

Stages of Liver Disease

The progression of chronic liver disease is commonly described in the following stages:

1. **Chronic hepatitis/fibrosis:** Ongoing liver injury and inflammation accompanied by progressive collagen deposition.

2. **Compensated cirrhosis:** Established cirrhosis without overt complications. Compensated advanced chronic liver disease (cACLD) is the non-invasive term commonly used to describe this stage [4].
3. **Decompensated cirrhosis (DCLD):** Development of complications such as ascites, variceal bleeding, overt hepatic encephalopathy or jaundice.
4. **Further decompensation and ACLF:** Recurrent or multiple decompensating events, or the development of organ failure, resulting in a very high risk of short-term mortality [9].

Acute-on-Chronic Liver Failure (ACLF)

ACLF is a distinct clinical syndrome occurring in patients with cirrhosis. It is characterised by acute systemic inflammation, precipitating organ failure and extremely high short-term mortality.

Following acute deterioration, patients may progress along two main clinical trajectories: standard acute decompensation (AD) or ACLF. Mortality increases substantially with the number of failing organs [8,9].

Aetiology (Causes)

The aetiology of chronic liver disease includes viral, metabolic, toxic, autoimmune and genetic factors. Persistent hepatic injury caused by any of these factors initiates chronic inflammation, hepatocyte death and progressive fibrotic remodelling, ultimately resulting in cirrhosis [3].

Aetiological Classification

- **Alcohol-related liver disease (ALD):** Sustained excessive alcohol consumption remains a major cause of hepatic parenchymal injury, steatohepatitis and rapid progression to cirrhosis [7].
- **MASLD/NAFLD/NASH:** Metabolic dysfunction-associated steatotic liver disease and steatohepatitis are leading causes of chronic liver injury, largely due to the increasing prevalence of obesity and diabetes [7].
- **Viral hepatitis (HBV, HCV and HDV):** Chronic HBV or HCV infection causes persistent hepatic necroinflammation, while HDV superinfection accelerates disease progression and decompensation in individuals infected with HBV [7].

Aetiology Distribution in Clinical Cohorts

A cross-sectional study of hospitalised patients with DCLD conducted by Balaji et al. (2026), involving 100 patients,[7] illustrates the clinical predominance of alcohol-related and metabolic aetiologies in contemporary patient populations (Table 02).

Table 02: Aetiology of DCLD in a hospital-based cohort (n = 100).

Aetiology	Frequency (n)	Percentage (%)
Alcohol-related liver disease	57	57.0
NASH/MAFLD/MASLD	31	31.0
Hepatitis B virus (HBV)	3	3.0
Cryptogenic	3	3.0
Autoimmune liver disease	2	2.0
Hepatitis C virus (HCV)	1	1.0
Alcohol + hepatitis B dual infection	1	1.0
Alcohol + hepatitis C dual infection	1	1.0
Wilson's disease	1	1.0
Total	**100**	**100.0**

Aetiology-Specific Prevalence of cACLD

The likelihood of progression to compensated advanced chronic liver disease (cACLD) varies according to the underlying aetiology.

In population-based screening studies, hepatitis C showed the highest prevalence (8.2% confirmed and 12.6% possible), followed by MASLD (5.09% confirmed and 7.14% possible), excessive alcohol consumption (2.79% confirmed and 3.69% possible) and active hepatitis B infection (1.6% confirmed and 1.59% possible).

Risk Factors

The development and progression of chronic liver disease and DCLD are associated with several risk factors. The major risk factors include chronic viral infections, particularly hepatitis B and hepatitis C, excessive alcohol consumption and metabolic disorders.

Obesity, type 2 diabetes mellitus, metabolic syndrome and non-alcoholic fatty liver disease (NAFLD/MASLD) increase the risk of hepatic damage. Other contributing factors include autoimmune liver diseases, genetic disorders such as Wilson's disease and haemochromatosis, and prolonged use of hepatotoxic drugs.

Exposure to toxins such as arsenic, advancing age, male sex, a sedentary lifestyle and a high-fat diet may also contribute to disease progression [2,6].

Pathophysiology of DCLD

Chronic liver injury caused by viral hepatitis, alcohol consumption, MASLD or autoimmune diseases leads to hepatocyte damage and hepatic stellate cell activation, resulting in fibrosis and cirrhosis.

The development of cirrhosis leads to portal hypertension, which causes splenic vasodilation, ascites and the formation of oesophageal varices. Reduced albumin synthesis decreases plasma oncotic pressure, further contributing to ascites formation.

Impaired hepatocyte function reduces ammonia clearance, resulting in hepatic encephalopathy. Reduced synthesis of clotting factors contributes to bleeding disorders, while impaired bilirubin metabolism leads to jaundice. Bacterial infections may result in spontaneous bacterial peritonitis.

Severe complications include hepatorenal syndrome, variceal haemorrhage and acute-on-chronic liver failure [3].

Integrated Picture of Decompensation

These complications are interconnected and may aggravate one another (Figure 6). Portal hypertension may cause gastrointestinal bleeding, SBP can precipitate hepatic encephalopathy, and HRS can worsen ascites. Even a single episode of decompensation is associated with a poorer prognosis. The interaction of these complications and additional systemic insults may ultimately lead to ACLF [3,9].

CLINICAL MANIFESTATIONS

Decompensated liver disease presents with clinical features associated with portal hypertension and hepatic failure.

Ascites causes abdominal distension, while peripheral oedema may result in swollen legs. Jaundice develops due to elevated bilirubin levels, causing yellow discolouration of the skin and eyes.

Hepatic encephalopathy ranges from mild confusion and sleep disturbances to coma due to the accumulation of toxins, particularly ammonia, which the damaged liver cannot adequately eliminate.

Variceal haemorrhage may present as haematemesis (vomiting of blood) or melaena (black, tarry stools). Patients are also highly susceptible to infections.

Other non-specific symptoms include fatigue, weight loss, pruritus and slurred speech [2,6].

COMPLICATIONS

- In addition to the defining events of decompensation, advanced DCLD is associated with several systemic complications.
- Dilutional hyponatraemia develops due to antidiuretic hormone (ADH)-mediated water retention. Hepatopulmonary syndrome, caused by intrapulmonary vascular dilatation, results in hypoxaemia. Portopulmonary hypertension is characterised by pulmonary arterial hypertension associated with portal hypertension.
- Hepatocellular carcinoma may develop in patients with underlying cirrhosis, while sepsis represents a major clinical threat.
- Together with ascites, SBP, hepatic encephalopathy, variceal bleeding and hepatorenal syndrome, these complications may ultimately lead to acute-on-chronic liver failure (ACLF) [6].

DIAGNOSIS

The diagnosis of DCLD begins with a comprehensive clinical evaluation. This includes a detailed medical history covering alcohol consumption, viral and metabolic risk factors, exposure to medications and herbal products, and relevant family history. Physical examination focuses on identifying jaundice, ascites, stigmata of chronic liver disease and altered mental status. Laboratory investigations include liver function tests (bilirubin, albumin, ALT and AST), renal function tests (creatinine and sodium), complete blood count (WBC count, neutrophils and platelet count), prothrombin time/international normalised ratio (PT/INR), electrolyte levels and screening tests for hepatitis B and C.

Liver biopsy is performed only in selected cases. Imaging investigations, including ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI), along with elastography (FibroScan) and upper gastrointestinal endoscopy for the detection of varices, complete the diagnostic evaluation [4,6].

SEVERITY ASSESSMENT AND PROGNOSTIC SCORING

Severity assessment in DCLD helps estimate prognosis, guide treatment intensity, determine the need for intensive care unit (ICU) admission and prioritise patients for liver transplantation.

The assessment begins with the identification of decompensating events, such as ascites, overt hepatic encephalopathy and gastrointestinal bleeding, along with routine laboratory investigations, including bilirubin, albumin, INR, creatinine and sodium levels.

- The Child–Pugh score uses five variables: bilirubin, albumin, INR, ascites and hepatic encephalopathy. It classifies patients into classes A, B or C, although some of its components are subjective.
- MELD, MELD-Na and MELD 3.0 are laboratory-based scoring systems that play important roles in assessing disease severity and prioritising patients for liver transplantation.
- ALBI and PALBI scores use objective parameters, including albumin and bilirubin, with PALBI additionally incorporating platelet count.

In patients with acute deterioration, CLIF-C scores are used to assess and grade ACLF. Portal hypertension assessment (HVPG and elastography), frailty and sarcopenia should also be evaluated, as no single scoring system is sufficient for comprehensive prognostic assessment [4,7,8].

CHILD–PUGH CLASSIFICATION

The Child–Pugh score remains one of the most widely used tools for assessing the severity of cirrhosis. It incorporates five variables: bilirubin, albumin, PT/INR, ascites and hepatic encephalopathy. Each variable is scored from 1 to 3, producing a total score ranging from 5 to 15 (Table 03).

- Class A: 5–6 points.
- Class B: 7–9 points.
- Class C: 10–15 points.

Class C indicates advanced hepatic dysfunction and is associated with a substantially poorer prognosis.

The limitations of this scoring system include the subjective assessment of ascites and hepatic encephalopathy and the use of broad categories rather than continuous variables [7].

Table 03: Child–Pugh scoring system.

Parameter	1 point	2 points	3 points
Bilirubin	<2 mg/dL	2–3 mg/dL	>3 mg/dL
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
INR	<1.7	1.7–2.3	>2.3
Ascites	None	Mild/moderate	Severe/refractory
Hepatic encephalopathy	None	Grade I–II	Grade III–IV

Ascites Severity

Ascites should be assessed clinically and, where appropriate, through ultrasonography. It is classified into the following grades:

- **Grade 1:** Mild ascites, detectable mainly through ultrasonography.
- **Grade 2:** Moderate ascites, causing symmetrical abdominal distension.
- **Grade 3:** Large or tense ascites, characterised by marked abdominal distension.

Refractory ascites indicates advanced circulatory and renal dysfunction and is associated with a poor prognosis.

Diagnostic paracentesis is particularly important in patients with new-onset ascites, those requiring hospitalisation and those experiencing clinical deterioration. This is because SBP may occur without prominent symptoms. An ascitic fluid polymorphonuclear (PMN) cell count of ≥250 cells/mm³ is diagnostic of SBP in the appropriate clinical context [5].

Hepatic Encephalopathy Assessment

Hepatic encephalopathy (HE) is an important indicator of advanced liver dysfunction and portosystemic shunting. It is graded using the West Haven criteria (Table 04). Higher grades are associated with increased morbidity and mortality. Serum ammonia levels may support the assessment in selected clinical circumstances; however, they should not be used alone to determine the clinical grade of hepatic encephalopathy [6].

Table 04: West Haven criteria for grading hepatic encephalopathy.

Grade	Typical manifestations
Grade 0	No clinically apparent HE; subtle cognitive abnormalities may be detected through specialised testing.
Grade I	Mild confusion, impaired attention and altered sleep patterns.
Grade II	Lethargy, disorientation, personality changes and asterixis.
Grade III	Marked confusion, somnolence and gross disorientation.
Grade IV	Coma.

ACLF, CLIF-C OF, CLIF-C ACLF and CLIF-C AD Scores

The EASL-CLIF approach evaluates six organ systems: liver, kidney, brain, coagulation, circulation and respiration.

The CLIF-C Organ Failure (CLIF-C OF) score identifies and grades organ failures, while the CLIF-C ACLF score combines organ dysfunction with inflammatory response variables to provide prognostic information. The CLIF-C ACLF score may outperform conventional scoring systems in predicting short-term mortality. A systematic review and meta-analysis published in 2025 reported good discriminatory performance for predicting both 28-day and 90-day mortality [8]. Not all patients with acute decompensation meet the diagnostic criteria for ACLF. In patients without ACLF, the CLIF-C AD score provides additional prognostic information. Therefore, the choice of scoring system should be based on the patient's clinical phenotype rather than applying a single scoring system to all patients with DCLD [8].

MANAGEMENT

General Management

- Identify and treat the precipitating causes of decompensation, including infections, gastrointestinal bleeding, alcohol relapse, drug-induced liver injury and portal vein thrombosis [1,9].
- Regularly monitor renal function, electrolyte levels, coagulation parameters and mental status [5].
- Avoid hepatotoxic and nephrotoxic medications, NSAIDs and sedatives, as benzodiazepines may precipitate hepatic encephalopathy [5].

RECENT TREATMENT ADVANCES (2025–2026)

Recompensation as a Treatment Goal

- The Baveno VII consensus defined recompensation as the sustained removal or cure of the underlying aetiology, resolution of ascites and hepatic encephalopathy, absence of variceal bleeding and stable improvement in liver function [4].
- Recent studies indicate that recompensation is achievable, although it remains uncommon when strict diagnostic criteria are applied.
- In an Italian cohort of 525 decompensated outpatients, 298 patients received effective aetiological treatment. However, only 21 patients (7%) met the strict Baveno VII criteria, compared with 112 patients (37.6%) who met the expanded criteria.
- In patients with hepatitis C, approximately two-thirds of those with decompensated disease achieved recompensation 12 months after attaining a sustained virological response (SVR). Their survival was better than that of patients who remained decompensated but was still poorer than that of patients with compensated cirrhosis. Furthermore, the risk of hepatocellular carcinoma (HCC) did not decrease, indicating that regular surveillance must continue.
- A 2025 review confirmed that evidence supporting recompensation is primarily available for alcohol-related, HBV-related and HCV-related liver disease. A 2026 meta-analysis also examined differences in recompensation rates according to aetiology.
- The 2025 Chinese guidelines now recommend recompensation as the treatment goal for patients with decompensated cirrhosis through aetiological and antifibrotic therapy, along with appropriate management of complications.

LONG-TERM ALBUMIN AND HYPONATRAEMIA

- The PRECIOSA phase III trial, involving 410 patients across 14 countries, evaluated the administration of 20% albumin at a dose of 1.5 g/kg every 10 days for up to 12 months, in addition to standard care.
- The primary endpoint, one-year transplant-free survival, was not statistically significant (HR 0.80, 95% CI 0.58–1.10). However, the incidence of complications decreased, including spontaneous bacterial peritonitis (OR 0.28, 95% CI 0.09–0.86) and hepatorenal syndrome (OR 0.24, 95% CI 0.09–0.64). No new safety signals were identified.
- In the ALBUCAT randomised controlled trial, involving 52 patients with dilutional hyponatraemia (Na ≤133 mEq/L), daily intravenous albumin administration resulted in the resolution of hyponatraemia in 48% of patients, compared with 15% in the standard-care group.
- Both findings were reported at scientific conferences in 2025 and should be verified against the full publications.

NEGATIVE TRIALS: SIMVASTATIN PLUS RIFAXIMIN

- The LIVERHOPE randomised controlled trial, involving 237 patients with Child–Pugh B/C decompensated cirrhosis across 14 European centres, found no significant benefit from the combination of simvastatin 20 mg and rifaximin 1,200 mg daily for 12 months.
- ACLF occurred in 17.9% of patients receiving the combination compared with 14.2% in the placebo group (HR 1.23, p = 0.52). The rates of transplantation or death were 18.8% versus 24.2% (p = 0.32), while the occurrence of any cirrhosis-related complication was 42.7% versus 45.8%.
- Adverse events were similar between the groups. Therefore, this combination is not recommended for the routine prevention of complications in patients with decompensated cirrhosis.
- The 2026 KASL guidelines continue to permit the use of statins when there is an appropriate cardiovascular indication.

HEPATIC ENCEPHALOPATHY: ACG 2026 UPDATE

- The 2026 American College of Gastroenterology (ACG) guideline update suggests avoiding routine brain imaging in patients with cirrhosis who present with confusion but have no new focal neurological deficits.
- It also suggests the use of outpatient rifaximin to prevent the recurrence of overt hepatic encephalopathy.

- The guideline recommends initiating rifaximin 14 days before elective TIPS and continuing it for at least six months in patients with decompensated cirrhosis. It also suggests embolisation of extrahepatic collaterals during TIPS to reduce the risk of post-TIPS hepatic encephalopathy.
- Furthermore, the guideline suggests exercise interventions, highlighting their potential benefits in reducing falls, lowering portal pressure and improving skeletal muscle ammonia handling.

HRS-AKI AND TERLIPRESSIN

- Terlipressin remains the first-line vasoconstrictor used in combination with albumin for the management of hepatorenal syndrome (HRS). However, safety recommendations have become more stringent.
- In 2022, European regulators warned that terlipressin could cause serious or fatal respiratory failure in patients with type 1 HRS. They advised avoiding its use in patients with ACLF grade 3 and/or a high MELD score (≥39), unless the expected benefits outweighed the risks.
- Continuous infusion has been associated with fewer severe adverse events than bolus administration. The recommended starting dose is 2 mg/24 hours, which may be increased to a maximum of 12 mg/24 hours.[5]
- A pilot randomised study published in 2025, involving 56 patients, found that continuous infusion and bolus administration had similar efficacy, without significant differences in adverse effects.
- The study also reported that early initiation of terlipressin, when AKI persisted after 12 hours of albumin-based volume expansion, was associated with reduced short-term mortality and improved AKI reversal in patients with ACLF.
- The DROP-AKI trial, which evaluates droxidopa for increasing mean arterial pressure, is currently underway following its registration in 2025.

ASCITES AND PORTAL HYPERTENSION

- The 2026 KASL guidelines on ascites management recommend treating the underlying liver disease, including antiviral therapy for HBV infection.
- In one study involving 267 patients with decompensated HCV-related cirrhosis, 12 weeks of sofosbuvir/velpatasvir treatment improved the MELD score in 51% of patients and the Child–Pugh score in 47%.
- The guidelines also recommend limiting acetaminophen intake to 2–3 g/day and exercising caution when prescribing NSAIDs, opioids and oral hypoglycaemic agents.
- The 2025 Chinese guidelines further highlight the anti-inflammatory and endothelial-stabilising effects of albumin. They also report that antiviral therapy combined with carvedilol delays variceal progression in patients with compensated HBV-related cirrhosis.
- Two trials investigating carvedilol for the prevention of decompensation in compensated patients with liver stiffness ≥25 kPa (CARVECIR, involving 290 patients) were initiated in 2025 and are currently ongoing.

REGENERATIVE AND EXPERIMENTAL APPROACHES

- The Institute of Liver and Biliary Sciences (ILBS), New Delhi, registered randomised controlled trials in 2025 to evaluate granulocyte colony-stimulating factor (G-CSF) combined with darbepoetin in patients with early decompensated cirrhosis (MELD <16).
- These trials compare single and repeated treatment cycles, with primary outcomes including changes in immune profiles and improvements in Child–Pugh and MELD scores.
- As results are not yet available, these approaches should be considered investigational.

Table 05: Summary of treatment evidence from 2025–2026.

Intervention	Key result	Study design	Status
Aetiological therapy (recompensation)	7% strict and 37.6% expanded recompensation; approximately two-thirds after HCV SVR.	Cohort studies	Practice-supporting
Long-term albumin	Reduced SBP and HRS events; survival endpoint was neutral.	Phase III RCT, n = 410	Conference data
IV albumin for hyponatraemia	Resolution in 48% versus 15%.	RCT, n = 52	Conference data
Simvastatin + rifaximin	No reduction in ACLF, transplantation/death or complications.	RCT, n = 237	Negative
Rifaximin before TIPS	Initiation 14 days before TIPS and continuation for at least 6 months.	ACG 2026 guideline	Guideline recommendation
Early terlipressin infusion	Fewer severe adverse events; early initiation may improve outcomes in ACLF-associated AKI.	RCTs and regulatory guidance	Clinical use with caution in ACLF

Carvedilol to prevent decompensation	Results are awaited.	Ongoing RCT, n = 290	Investigational
G-CSF + darbepoetin	Results are awaited.	Ongoing RCTs	Investigational

ROLE OF THE CLINICAL PHARMACIST

The clinical pharmacist plays an important role in the multidisciplinary management of patients with DCLD.
The responsibilities of the clinical pharmacist include:

- Performing medication reconciliation and screening for hepatotoxic, nephrotoxic and contraindicated medications.
- Adjusting drug doses according to renal and hepatic function, including the patient's Child–Pugh and MELD status.
- Monitoring potential drug interactions, such as those involving diuretics and NSAIDs, and rifaximin with other antibiotics.
- Performing therapeutic drug monitoring wherever applicable.
- Identifying and managing adverse drug reactions, such as diuretic-induced electrolyte imbalances and lactulose-induced diarrhoea.
- Promoting rational antibiotic use and antimicrobial stewardship in the management of SBP and other infections.
- Participating in multidisciplinary ward rounds and liver transplantation evaluation teams.
- Contributing to the development of institutional protocols and guidelines for cirrhosis-related pharmacotherapy.
- Reporting adverse drug reactions through pharmacovigilance programmes.

PATIENT COUNSELLING

Patient counselling is an essential component of DCLD management.

- **Alcohol abstinence:** Patients should be advised to strictly avoid alcohol and other hepatotoxic substances, including potentially harmful herbal remedies.
- **Medication adherence:** Patients should be educated about the correct dosage and timing of medications, including diuretics, lactulose and beta-blockers. Lactulose should be titrated to achieve 2–3 soft stools per day.
- **Dietary counselling:** Patients should maintain adequate protein intake, restrict dietary sodium and avoid prolonged fasting.
- **Recognition of warning signs:** Patients and caregivers should be educated about symptoms requiring urgent medical attention, including confusion or altered behaviour, black tarry stools, vomiting blood, increasing abdominal distension, fever and reduced urine output.
- **Avoidance of self-medication:** Patients should avoid self-medication, particularly with NSAIDs and unregulated dietary supplements.
- **Regular follow-up:** The importance of regular clinical follow-up, laboratory monitoring and HCC surveillance using ultrasonography and AFP testing should be emphasised.
- **Family and caregiver education:** Family members and caregivers should be educated about recognising hepatic encephalopathy and ensuring patient safety [5].

RECENT ADVANCES

Recent advances in the management and assessment of DCLD include:

- **Non-invasive assessment tools:** Transient elastography, magnetic resonance elastography and serum biomarker panels have reduced reliance on liver biopsy.
- **Recognition of ACLF:** ACLF is now recognised as a distinct clinical entity, with dedicated EASL-CLIF and APASL diagnostic and prognostic frameworks.
- **Albumin-based strategies:** Newer albumin-based approaches, including long-term albumin therapy trials, are being investigated for the management of ascites.
- **Terlipressin therapy:** The use of terlipressin for hepatorenal syndrome has been refined, including the evaluation of newer formulations and administration strategies.
- **TIPS:** The wider use of TIPS with covered stents has improved stent patency and clinical outcomes.
- **Microbiome-targeted therapies:** Rifaximin and probiotics are used or investigated for hepatic encephalopathy, while faecal microbiota transplantation remains under investigation.
- **Artificial intelligence and machine learning:** AI-based prognostic models are being explored to improve mortality prediction beyond conventional MELD scoring.
- **Extracorporeal liver support systems:** Techniques such as the Molecular Adsorbent Recirculating System (MARS) and plasma exchange are being investigated as bridging therapies.

- **Liver transplantation:** Living-donor liver transplantation and normothermic machine perfusion are expanding the possibilities for organ preservation and transplantation.[1,8]

FUTURE PERSPECTIVES

Future developments in DCLD management may include:

- Precision medicine approaches that tailor treatment according to individual genetic and biomarker profiles.
- Regenerative medicine and bioartificial liver support systems as bridging options to transplantation or recovery.
- Further refinement of ACLF definitions and the development of targeted therapies for organ-specific failure.
- Wider validation and adoption of artificial intelligence and machine-learning-based prognostic tools in routine clinical practice.
- Expansion of the donor pool through machine perfusion techniques and the utilisation of marginal donor organs.
- Greater integration of clinical pharmacists into multidisciplinary hepatology teams.
- Increased focus on the early detection and reversal of decompensation to prevent progression to ACLF.
- Development of antifibrotic and disease-modifying therapies to alter the natural history of chronic liver disease [1].

CONCLUSION

Decompensated chronic liver disease is a multisystem condition associated with high morbidity, frequent hospitalisation and substantial short-term mortality, particularly when it progresses to acute-on-chronic liver failure (ACLF).

The aetiological pattern is shifting towards alcohol-related and metabolic liver diseases, although viral hepatitis remains an important contributor in endemic regions.

Conventional scoring systems, such as Child–Pugh and MELD, have recognised limitations. Objective measures, including ALBI, PALBI, MELD 3.0 and CLIF-C scores, along with portal hypertension assessment and frailty evaluation, provide more accurate and multidimensional risk stratification.

Effective management requires a comprehensive approach involving the identification and treatment of precipitating factors, nutritional support, alcohol cessation, vaccination, targeted pharmacotherapy, endoscopic and radiological interventions, and timely referral for liver transplantation.

These interventions should be delivered through a multidisciplinary healthcare team in which clinical pharmacists and patient counselling play important roles in improving treatment outcomes and quality of life.

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CONFLICT OF INTEREST

Nil

INFORMED CONSENT

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ETHICAL STATEMENT

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