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## **EPIDEMIOLOGY OF ACLF IN THE EMERGENCY DEPARTMENT OF IBN SINA HOSPITAL IN RABAT**

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### **ABSTRACT**

**Background:** Acute-on-Chronic Liver Failure (ACLF) represents a critical syndrome characterized by acute decompensation of cirrhosis with organ failure and high short-term mortality. While extensively studied in Western and Asian populations, data from North African contexts remain scarce.

**Objective:** To describe the epidemiological, clinical, and biological characteristics of ACLF in a Moroccan tertiary care center.

**Methods:** We conducted a retrospective cross-sectional study of 27 cirrhotic patients admitted with ACLF to the Emergency Department of Ibn Sina University Hospital in Rabat between January 2022 and July 2023. ACLF was diagnosed using the EASL-CLIF criteria based on the CLIF-SOFA score. Data on demographics, clinical presentation, laboratory values, ACLF grades, and outcomes were analyzed.

**Results:** The mean age was  $52.4 \pm 14$  years; 63% were male. Viral hepatitis was the predominant etiology (36%). The precipitating factor remained unidentified in 55.5% of cases, with infections accounting for 37%. Neurological failure was the most frequent organ dysfunction (85.2%). ACLF grade distribution was: Grade 1 (33.3%), Grade 2 (25.9%), and Grade 3 (40.7%). The overall mortality rate was 48.1%, rising significantly with ACLF grade (Grade 1: 11.1%, Grade 2: 71.4%, Grade 3: 72.7%). CLIF-SOFA scores correlated strongly with mortality ( $p = 0.017$ ).

**Conclusion:** ACLF in Moroccan patients is associated with high mortality and often presents with neurological dysfunction. Early identification, particularly of infectious triggers, and timely intervention are essential. Despite the grave prognosis in advanced stages, favorable outcomes remain possible with appropriate management. Larger prospective studies are needed to better define ACLF epidemiology in North Africa.

## **KEYWORDS**

ACLF , Liver , cirrhosis

## **MAIN ARTICLE**

### **Introduction**

Cirrhosis represents the end stage of progressive hepatic fibrosis resulting from chronic liver diseases. It poses a major public health challenge due to its rising prevalence and severe complications (1). Decompensation, defined by the emergence of cirrhosis-related complications, can manifest singly or in combination (2). Among these, Acute-on-Chronic Liver Failure (ACLF) is associated with organ failure and high mortality rates. However, its definition remains inconsistent across North American, European, and Asian medical societies (1).

The CANONIC study in 2011, conducted under the European Association for the Study of the Liver (EASL)-Chronic Liver Failure (CLIF) Consortium, established ACLF diagnostic criteria using the CLIF-SOFA score (2). This landmark study emphasized the dynamic nature of ACLF, with mortality increasing proportionally to ACLF grade. Early diagnosis and intervention significantly reduce mortality, emphasizing the need for prompt and targeted management. This study aims to describe the clinical and biological characteristics of ACLF within a Moroccan context.

### **Materials and Methods :**

We conducted a retrospective cross-sectional study of patients admitted with cirrhosis decompensation and organ failure to the Emergency Department of Ibn Sina University Hospital, Rabat, between January 2022 and July 2023. Inclusion criteria encompassed patients aged 18 and older with decompensated cirrhosis and at least one organ failure. Patients with incomplete records, acute decompensation without organ failure, or non-cirrhotic pathologies were excluded.

The following data were extracted:

- Epidemiological data: Age, gender, medical history.
- Cirrhosis characteristics: Duration and etiology.

- Clinical and paraclinical data: Laboratory and radiological findings for CLIF-SOFA score calculation and ACLF grade determination.
- Outcomes: Overall and grade-specific mortality rates.

Statistical analyses were performed using Jamovi software. Qualitative variables were presented as counts and percentages and compared using the Chi-square or Fisher's exact test. Quantitative variables with normal distribution were expressed as mean  $\pm$  standard deviation (SD) and compared with Student's t-test. Non-normal variables were expressed as median [interquartile range] and compared using the Mann-Whitney test. Significant variables ( $p < 0.05$ ) in univariate analysis were further analyzed via multivariate logistic regression.

## **Results**

The study included 27 patients (17 men, 63%; 10 women, 37%) with a mean age of 52.4 years ( $\pm 14$  years). The duration of cirrhosis ranged from 1 to 72 months, with a mean of 35.2 months ( $\pm 22$  months). Viral hepatitis was the leading etiology (36%). Despite exhaustive testing, the decompensation trigger was undetermined in 55.5% of cases, while infections were identified as the primary trigger in 37% of cases.

Neurological failure was the most prevalent organ dysfunction, observed in 23 patients (85.2%), followed by hepatic (37%), hemodynamic (25.9%), and coagulation failure (25.9%). The distribution of ACLF grades was as follows: Grade 1 (33.3%), Grade 2 (25.9%), and Grade 3 (40.7%).

The overall mortality rate was 48.1%, with higher rates in advanced grades: Grade 1 (11.1%), Grade 2 (71.4%), and Grade 3 (72.7%). CLIF-SOFA scores strongly correlated with mortality ( $p = 0.017$ ).

**Tables 1 and 2 summarize the clinical and biological characteristics found in our study.**

Factor	Total	Survivors	Deceased
Age	52.4 $\pm$ 13.9	57 $\pm$ 13.2	47 $\pm$ 13.3
Cirrhosis duration (months)	35.2 $\pm$ 22.3	32.6 $\pm$ 19.4	37.4 $\pm$ 25.6
Glasgow score	11 $\pm$ 2	12 $\pm$ 1	10 $\pm$ 2
Mean Arterial Pressure (MAP)	80 [60, 84]	80 [68, 85]	75 [50, 80]
SpO <sub>2</sub>	97 [94, 99]	98 [97, 99]	95 [90, 97]
Neurological failure	23 (85.2%)	10 (37%)	13 (48.2%)
Hemodynamic failure	7 (25.9%)	1 (3.7%)	6 (22.2%)
Respiratory failure	3 (11.1%)	1 (3.7%)	2 (7.4%)
Coagulation failure	7 (25.9%)	3 (11.1%)	4 (14.8%)
Hepatic failure	10 (37%)	4 (14.8%)	6 (22.2%)

Renal failure	6 (22.2%)	3 (11.1%)	3 (11.1%)
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**Table 1: Clinical characteristics**

Factor	Total	Survivors	Deceased
Hemoglobin (g/dL)	9.08 ± 2.26	8.68 ± 2.07	9.44 ± 2.46
Prothrombin Time (PT, %)	44.9 ± 16.9	42.4 ± 11.5	48.5 ± 21.5
INR	1.65 [1.35–2.56]	1.58 [1.31–2.25]	2 [1.5–3.24]
Urea (g/L)	0.7 [0.52–0.98]	0.7 [0.52–0.98]	0.74 [0.48–1.12]
Creatinine (μmol/L)	15 [8–18.3]	16 [8–17.8]	13.3 [11.1–19.7]
Total Bilirubin (μmol/L)	75 [21.8–197]	58 [20–127]	117 [40–333]
AST (U/L)	86 [51–119]	86 [62–103]	74 [40–180]
ALT (U/L)	33 [23–62]	31 [24–52]	42 [18–76]
ALP (U/L)	137 [100–217]	136 [110–230]	179 [85–213]
GGT (U/L)	40 [28–100]	37 [28–94]	50 [35–90]
Albumin (g/L)	20 [19–26]	20 [20–26]	20.5 [17.8–28.5]
Child-Pugh Score	11 [9–13]	10 [9–12]	12 [10–13]
MELD Score	23.6 ± 9.7	19 ± 7	27 ± 10
CLIF-SOFA Score	10 ± 3	8 ± 3	12 ± 3
ACLF Grade 1	9 (33.3%)	8 (29.6%)	1 (3.7%)
ACLF Grade 2	7 (25.9%)	2 (7.4%)	5 (18.5%)
ACLF Grade 3	11 (40.7%)	4 (14.8%)	7 (25.9%)

**Table 2 : Biological characteristics and scores**

## Discussion

The concept of ACLF was first introduced in 2002 by Jalan and Williams to describe the rapid clinical deterioration of patients with chronic liver disease due to a precipitating factor, leading to multi-organ failure and high short-term mortality (3). Definitions of ACLF vary across societies, but all emphasize its severe nature and association with multi-organ dysfunction.

The Asian Pacific Association for the Study of the Liver (APASL) defines ACLF as an acute hepatic insult (e.g., alcohol consumption or a hepatotropic viral infection) causing liver failure (manifested as jaundice or coagulopathy) that, within 4 weeks, progresses to ascites and/or encephalopathy in patients with or without pre-existing chronic liver disease or cirrhosis and is associated with a high 28 day mortality rate (4,5).

The American Association for the Study of Liver Diseases (AASLD), in conjunction with the European Association for the Study of the Liver (EASL), defines ACLF as the acute clinical deterioration of a patient with chronic liver disease, typically triggered by a precipitating

factor (including bacterial infections), and associated with multi-organ failure resulting in increased 3-month mortality (6).

The CANONIC study, conducted by the EASL-Chronic Liver Failure (CLIF) Consortium, established objective diagnostic criteria for ACLF using the CLIF-SOFA score (7,8):

Organ/System	0	1	2	3	4
Liver (bilirubin, mg/L)	<12	$\geq 12$ - $\leq 20$	$\geq 20$ -<60	$\geq 60$ -<120	$\geq 120$
Kidney (creatinine, mg/L)	<12	$\geq 12$ -<20	$\geq 20$ -<35	$\geq 35$ -<50	$\geq 50$ or renal replacement therapy
Brain (hepatic encephalopathy)	None	Grade I	Grade II	Grade III	Grade IV
Coagulation (INR)	<1.1	$\geq 1.1$ -<1.25	$\geq 1.25$ -<1.5	$\geq 1.5$ -<2.5	$\geq 2.5$ or platelets $\leq 20,000/\text{mm}^3$
Hemodynamics (MAP, mmHg)	$\geq 70$	<70	Dopamine $\leq 5$ $\mu\text{g/kg/min}$ , Dobutamine, or Terlipressin	Dopamine $> 5$ $\mu\text{g/kg/min}$ or Epinephrine $\leq 0.1$ $\mu\text{g/kg/min}$	Dopamine $> 15$ $\mu\text{g/kg/min}$ or Epinephrine $> 0.1$ $\mu\text{g/kg/min}$
Lungs ( $\text{PaO}_2/\text{FiO}_2$ or $\text{SpO}_2/\text{FiO}_2$ )	$> 400$ or $> 512$	$> 300$ -400 or 357- $\leq 512$	$> 200$ - $\leq 300$ or $> 214$ - $\leq 357$	$> 100$ - $\leq 200$ or $> 89$ - $\leq 214$	$\leq 100$ or $\leq 89$

A total score ranging from 0 to 24 can be calculated and reflect the severity of the disease.

ACLF severity is classified into three grades:

Grade 1: Includes three groups:

Patients with renal failure (serum creatinine  $\geq 20$  mg/L).

Patients with renal dysfunction (serum creatinine between 12–20 mg/L)

and failure

of another organ/system (liver, coagulation, lungs, or circulation).

Patients with renal dysfunction and cerebral failure.

Grade 2: Involves failure of two organs.

Grade 3: Involves failure of three or more organs.

It demonstrated a clear correlation between the severity of ACLF and short-term mortality:

22.1% for Grade 1, 32% for Grade 2, and 78.6% for Grade 3 (2).

While the CANONIC study identified renal failure as the most frequent organ dysfunction in ACLF, our findings highlight neurological failure (hepatic encephalopathy) as the predominant dysfunction, underscoring the need for heightened clinical vigilance in Moroccan settings.

Mortality rates in our study align with international data, including the findings of Masnou et al. in Spain, which reported an overall mortality rate of 46% and highlighted ACLF grade and CLIF-SOFA scores as significant mortality predictors (10).

Younger age and alcoholic cirrhosis are recognized risk factors for ACLF (11). In our cohort, the mean age was 52 years, with deceased patients being younger on average (47 years) than survivors (57 years), though this was not statistically significant. While infections were the most common precipitating factor (37%), a substantial proportion (55.5%) lacked an identifiable trigger compared to 42% in the CANONIC study, suggesting a need for improved diagnostic protocols. In Asia, hepatitis B virus reactivation predominates as a trigger for ACLF (12), other factors included excessive alcohol use in the previous 3 months and gastrointestinal bleeding.

The dynamic nature of ACLF, as evidenced in our cohort and in the literature (13), highlights its variable progression. The CANONIC study provides further insight, showing that 55% of patients with Grade 1 ACLF experience clinical improvement within a week, and even 32% of those with Grade 3 achieve marked recovery (2,13). These findings underscore the potential for favorable outcomes when early and intensive management is implemented in specialized centers, particularly for liver transplantation candidates. However, the prognosis becomes increasingly grim with advanced organ failure, as mortality rates rise to 90% for patients with 4 organ failures and approach 100% for those with 5 or more, emphasizing the limited benefits of intervention in such cases. While these data offer hope for recovery in milder grades of ACLF, they also emphasize the importance of prompt diagnosis and timely management.

Limitations of this study include its retrospective design and small sample size, which limit generalizability. A prospective multicenter study would provide more robust insights into ACLF epidemiology and outcomes in Morocco.

## **Conclusion**

ACLF is a severe and dynamic condition distinct from classic acute decompensation of cirrhosis. Early diagnosis, intensive management, and prompt identification of triggering factors, especially infections, are critical to improving outcomes. Despite its severity, ACLF is not invariably fatal, and liver transplantation remains a viable option with timely intervention. Future research should focus on optimizing management strategies and expanding access to specialized care in Morocco.

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