

Acute-on-Chronic Liver Failure in Zagazig University Hospital: A Single Center-Based Study

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ABSTRACT

Background : Chronic or acute liver failure is a common condition that has a number of contributing variables; a high death rate and a dismal prognosis. The mainstay of these individuals' survival chances is liver transplantation.

Objectives: To identify the prevalence of acute-on-chronic liver failure (ACLF) and to characterize patients admitted with ACLF according to the European association for the study of liver (EASL) definition of ACLF to determine the possible risk and precipitating factors and show the outcomes.

Patients and Method: Prospective study in a single tertiary University hospital was conducted for 1 year duration, comparing cirrhotic patients with or without ACLF according to EASL-ACLF criteria.

Results: The prevalence rate of ACLF was 57.9% of the studied populations. GIT bleeding, HE, and active infections were the most frequent precipitating factors. Patients who have ACLF had a high 28-day mortality rate (67.3%). The rate of mortality was significantly greater with the grade of ACLF. Chronic liver failure (CLIF) score of more than 5 was associated with 86.84% sensitivity, 45.95% specificity, 63% negative predictive value, 76.7% positive predictive value as well as 0.661 AUC.

Conclusion: A common illness with a high death rate is ACLF. The primary triggering causes include GIT hemorrhage, HE, and active infection. High sensitivity and positive predictive value, but low specificity and negative predictive value are associated with a CLIF score of more than five for mortality in ACLF patients.

Keywords: ACLF, Decompensated cirrhosis, Mortality.

INTRODUCTION

Distinct major international scientific associations offered numerous different criteria for acute on chronic liver failure (ACLF) in cirrhotic individuals in various geographic locations, although every definition identifies that ACLF is a separate clinical entity. The majority of these definitions consider ACLF as a serious type of acutely decompensated cirrhosis ⁽¹⁾. The clinical entity will change based on the etiological cause of underlying liver illnesses, the nature of various precipitating events, and the patient outcome and prognosis depending on the many types of precipitating events and organ failures covered in each description ⁽²⁾.

The frequency and mortality of patients with ACLF are significant on a global scale. The greatest 90-day death rate worldwide was in South America at 73 percent, therefore region-specific variances might be explained by the kind of distinct chronic liver disease (CLD) triggers or grade-related etiological factors ⁽³⁾.

Typically, it is impossible to pinpoint a precise triggering event. Uncontrolled inflammatory responses are believed to be a major contributing factor in inducing ACLF in cirrhotic individuals, despite the fact that the precise pathophysiological pathways of its development are still unclear ⁽²⁾.

In Egypt, the burden, the precipitating factors, the outcome, and mortality of ACLF have not been identified.

AIMS OF THE STUDY

We aim in this study to identify the prevalence of ACLF and to characterize patients admitted with ACLF according to the EASL definition of ACLF to determine the possible risk and precipitating factors and show the outcomes.

PATIENTS AND METHODS

At the Internal Medicine Department's gastroenterology and hepatic departments, as well as the Zagazig University hospitals, we conducted this prospective observational study during 1 year period from 2018-2019.

There were 254 patients hospitalized for decompensation of cirrhosis. The following conditions or combinations of conditions led to the exclusion of 59 patients (19 with hepatocellular carcinoma outside Milan criteria, 15 people were admitted for an appointment or treatment), 11 had insufficient data, (8 had ESRD, and six had chronic obstructive pulmonary disease (COPD)).

One-hundred ninety-five participants signed up and were counted in the sample population. 82 had no ACLF, whereas 113 had ACLF. Inclusion criteria: Patients who were hospitalized to the liver intensive care unit and who meet the criteria for ACLF as defined by the EASL. The study excluded patients with hepatocellular carcinoma or other malignancies, portal vein thrombosis, patients with COPD or renal failure.

All patients were subjected to the following: History, clinical examination, laboratory evaluation:

Complete blood count Biochemistry, of liver functions including S. bilirubin, albumin, total protein, AST, ALT, Alkaline phosphatase (ALP), PT, Prothrombin concentration (PC), and (INR). AFP (Alpha Feto Protein).

Tests for viral hepatitis: (HCVAb., HBsAg., HCV PCR for HCV ab+ve) -Kidney function test; creatinine, blood urea, and S. uric acid. -Arterial blood gases (SaO₂, PaO₂, PH, Na, K, etc.) -For ventilator patients, calculate O₂ consumption: (mask O₂-nasal O₂).

Radiological Examination of the Abdomen, Upper GIT Endoscopy if indicated. To diagnosis ACLF, the following criteria are used: a)-CLIF-OFs: (Chronic Liver Failure Consortium—Organ Failure [CLIF-C OF]) b) A Prognostic Score (Chronic Liver Failure Consortium—Acute-on-Chronic Liver Failure) [CLIF-C ACLF]. CLIF-c ACLFs = 10 times [0.33 x CLIF-OFs + 0.04 x Age + 0.63 x ln (WBCS count)-2].-CLIF-ACLF (Acute-on-chronic liver failure) score and expected mortality rates.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee (IRB#3864/30-07-2017). Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean \pm SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

One hundred and ninety five patients with decompensated cirrhosis who were admitted to the Internal Medicine Department and ICU were included in this research, Zagazige University for 1 year duration; eighty-two patients with chronic decomposition with chronic liver cell failure (non ACLF) and 113 patients with a history of CLD with acute decomposition (ACLF). Study populations show the rate of ACLF among the studied patients was present in 113 patients out of 195 patients, so the rate of ACLF was 57.9% (figure No. 1) distributed between 12.8% grade I, 33.8% grade II, and 11.3% grade III according to the EASL definition of ACLF.

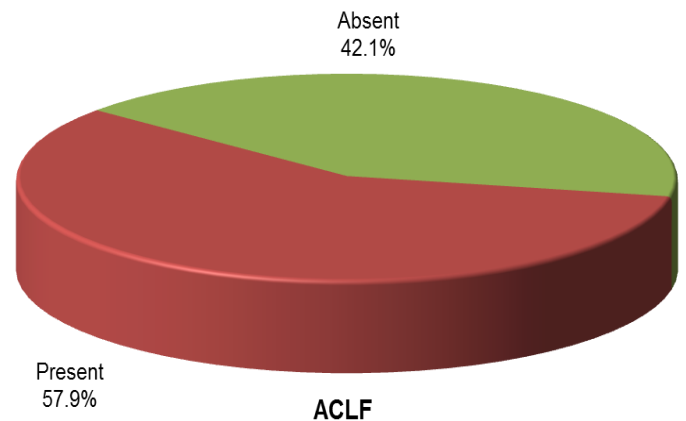


Figure (1): Frequency of ACLF among the studied patients.

The sociodemographic characteristics shows no statistically significant difference regarding age, sex, or residence (Table 1), also regarding HCV as an etiology [the most common cause of CLD in Egypt]; no statistically significant difference was found between groups ($p = 0.453$).

GIT bleeding and the occurrence of ACLF shows significant association where patients with hematemesis or melena had a more frequent rate of ACLF than patients without hematemesis or melena (80.8% versus 31.9% and 87.9% versus 31.7% respectively, p -value 0.001, 0.001 respectively). Hepatic encephalopathy and the occurrence of ACLF shows significant association where patients with hepatic encephalopathy had a more frequent rate of ACLF than patients without hepatic encephalopathy (94.9% versus 33.3%, respectively, p -value 0.001). Patients with ACLF had a mean CLIF score that was considerably higher than those without ACLF (mean: 8.20 versus 2.45, respectively, p -value 0.001) (Table 2).

Table (1): Characteristics of studied populations

Basic characteristics	Acute on chronic liver failure				Test	p-value
	Absent (N=82)		Present (N=113)			
	No.	%	No.	%		
Sex						
Male	43	45.3%	52	54.7%	0.784	0.376
Female	39	39%	61	61%		
Age (days)						
Mean ± SD	61.36 ± 9.51		61.96 ± 10.01		-0.465	0.642
Median (Range)	62 (28 – 85)		62 (23 – 88)			
Residence						
Urban	44	46.3%	51	53.7%	1.383	0.240
Rural	38	38%	62	62%		
HCV						
Negative	40	44.9%	49	55.1%	0.562§	0.453
Positive	42	39.6%	64	60.4%		

Table (2): Comparison between patients with or without ACLF regarding clinical findings

Clinical findings	Absent (N=82)		Present (N=113)		Test	p-value
	No.	%	No.	%		
Ascites						
Present	76	43.4%	99	56.6%	1.328	0.249
Absent	6	30%	14	70%		
Jaundice						
Present	78	42.2%	107	57.8%	0.018	1.000
Absent	4	40%	6	60%		
Pleural effusion						
Present	1	100%	0	0%	1.385	0.421
Absent	81	41.8%	113	58.2%		
Hematemesis						
Present	20	19.2%	84	80.8%	47.62	<0.001
Absent	62	68.1%	29	31.9%		
Melena						
Present	11	12.1%	80	87.9%	62.864	<0.001
Absent	71	68.3%	33	31.7%		
HE						
Present	4	5.1%	74	94.9%	72.730	<0.001
Absent	78	66.7%	39	33.3%		
SBP (mmHg)						
Mean ± SD	111.40 ± 24.02		114.51 ± 27.81		-0.911	0.362
Median (Range)	105 (79 – 190)		110 (60 – 220)			
DBP (mmHg)						
Mean ± SD	68.78 ± 13.73		70.53 ± 14.01		-1.404	0.160
Median (Range)	70 (40 – 120)		70 (40 – 120)			
CLIF score						
Mean ± SD	2.45 ± 1.68		8.20 ± 3.02		-10.821	<0.001
Median (Range)	2.50 (0 – 10)		8 (0 – 16)			

Comparing laboratory tests between patients with and without ACLF reveals a statistically significant rise in AST and ALT levels ($p = 0.021$ and 0.007), respectively. Moreover, individuals with ACLF had higher levels of bilirubin and INR than those without ACLF, which was statistically significant ($p = 0.01, 0.030$), although there was no discernible difference between the two groups in the amount of serum albumin ($p = 0.291$). Patients with ACLF had mean serum creatinine levels that were noticeably greater than those without ACLF (mean: 2.88 versus 1.05 mg/dl, respectively; $p 0.001$). Patients with ACLF had mean PaO₂ values that were significantly greater than those without ACLF (mean: 54.24 versus 44.62 mmHg, respectively, p -value = 0.002) (Table 3).

Table (3): Comparison between patients with or without ACLF regarding liver function tests.

Liver function tests	Acute on chronic liver failure		Test•	p-value
	Absent (N=82)	Present (N=113)		
AST (U/L) Mean ± SD	77.16 ± 7.69	58.11 ± 12.24	-2.316	0.021
ALT (U/L) Mean ± SD	119.39 ± 23.85	72.30 ± 7.72	-2.718	0.007
TSB (mg/dl) Mean ± SD	1.80 ± 0.31	6.15 ± 1.31	-4.355	<0.001
Serum albumin (g/dl) Mean ± SD	2.67 ± 0.40	2.56 ± 0.61	-1.055	0.291
INR Mean ± SD	1.53 ± 0.31	2.01 ± 0.40	-2.175	0.030
PTT Mean ± SD	48.82 ± 8.52	48.97 ± 8.87	-0.630	0.529
S. creatinine (mg/dl) Mean ± SD	1.05 ± 0.21	2.88 ± 0.31	-6.549	<0.001
PaO ₂ (mmHg) Mean ± SD	44.62 ± 10.47	54.24 ± 12.07	-3.098	0.002
So ₂ (mmHg) Mean ± SD	60.18 ± 13.90	65.27 ± 15.93	-1.849	0.064
Na (mmol/L) Mean ± SD	133.90 ± 3.17	133.62 ± 7.53	-0.361	0.718

Among the studied population, the mean ICU stay duration was 5.16 days. One hundred patients (24 patients without ACLF, seventy-six patients with ACLF) (51.3%) died. The mean overall survival was 7.246 days. One-day overall survival was 96.4% while 10 days OS was 18.9% and 28-days OS was 16.5%.

Table No. 4 There was an insignificant difference between patients without ACLF and patients with ACLF regarding ICU stay duration (mean: 5.32 versus 5.04 days respectively, p-value = 0.523), Nonetheless, there was a substantial link between ACLF and mortality, with individuals with ACLF dying more frequently than those without ACLF (67.3% versus 29.3% respectively, p-value 0.001). Patients with ACLF had considerably shorter overall survival on average than patients without ACLF (mean: 6.204 versus 9.071 respectively, p-value 0.001) (Table 4).

Table (4): Comparison between patients who have or free from ACLF regarding outcome.

Outcome	Acute on chronic liver failure				Test	p-value
	Absent (N=82)		Present (N=113)			
	No.	%	No.	%		
ICU Admission (days)						
Mean ± SD	5.32 ± 1.21		5.04 ± 1.01		-0.639	0.523
Median (Range)	5 (1 – 13)		5 (1 – 12)			
Mortality						
Alive	58	70.7%	37	32.7%	27.448	<0.001
Died	24	29.3%	76	67.3%		
Overall survival (OS)						
Mean OS	9.071 days		6.204 days		17.675	<0.001
(95%CI)	(7.968 – 10.173)		(5.575 – 6.832)			
Median OS	9 days		6 days			
(95%CI)	(7.332 – 10.668)		(5.181 – 6.819)			
1 day OS	98.8%		94.7%			
3 days OS	92.2%		74.4%			
7 days OS	61.6%		31.9%			
10 days OS	36.1%		10.5%			

Patients with hematemesis had ten times the chance of patients without hematemesis of developing ACLF (OR = 0.111). Melena patients had a one-in-fifteen chance of developing ACLF (OR = 0.064). Patients with chronic renal impairment had seven times as many chances of having ACLF as patients without CKD had (OR = 7.704). Those with hepatic encephalopathy had an ACLF risk that was 37 times higher than that of patients without hepatic encephalopathy. (OR = 37.000). Infections were more common among patients with ACLF as a main precipitating event of decompensation (p-value 0.025), and they were more common as more than one precipitating event (Table 5).

Table (5): Univariate logistic regression of predictors precipitating events for ACLF among the studied patients.

Predictors	N	ACLF		B	SE	OR	(Ninety-five percent CI)	Test	p-value
		No.	%						
Hematemesis									
Present	104	84	80.8%			Reference		42.818	<0.001
Absent	91	29	31.9%	-2.195	0.335	0.111	(0.058 – 0.215)		
Melena									
Present	91	80	87.9%					51.180	<0.001
Absent	104	33	31.7%	-2.750	0.384	0.064	(0.030 – 0.136)		
Renal impairment									
Present	159	81	50.9%					13.604	<0.001
Absent	36	32	88.9%	2.042	0.554	7.704	(2.603 – 22.797)		
HE									
Present	117	39	33.3%					43.178	<0.001
Absent	78	74	94.9%	3.611	0.550	37.000	(12.602 - `08.632)		
UTI									
Present	146	74	50.6%					13.602	<0.001
Absent	49	39	79.6%	2.042	0.554	7.702	(2.604- 22.797)		
SBP									
Present	182	102	56%					13.601	<0.001
Absent	13	11	84.6%	2.032	0.553	7.704	(2.606-22.792)		
Cellulites									
Present	14	13	92.9%					12.602	<0.001
Absent	181	100	55.2%	2.032	0.551	7.703	(2.604-22.791)		
Other precipitating factors									
NO PE	24	13	54.2%						
More>PE	52	34	65.4%						

The sex of patients and death among ACLF patients did not significantly correlate (p-value = 0.110). The age of deceased ACLF patients was significantly older than that of alive ACLF patients (p-value = 0.005). There was an insignificant association between residence and mortality among patients with ACLF (p-value = 0.083). Mean AST and ALT levels in deceased individuals were substantially higher than in living patients (p-value = 0.017, 0.001), respectively, and Patients who were still alive had mean serum creatinine levels that were significantly greater than those who had passed away (p-value = 0.011). No statistically significant difference between the two groups regarding the level of serum bilirubin, albumen

and INR, Na (p-value = 0.311, 0.472, 0.188, 0.425) respectively. The death rate in grades I, II, and III ACLF was 32 percent, 75.8 percent, and 81.8 percent, respectively, indicating a substantial relationship between the ACLF grade and mortality (p-value 0.001). Regarding the length of ICU stays, there was no difference between patients with ACLF who were still living and those who passed away (p-value = 0.968). The ROC curve analysis for CLIF as a predictor for mortality among ACLF patients. More than five CLIF scores were associated with 86.84% sensitivity, 45.95% specificity, 76.7% positive predictive value, 63% negative predictive value, and 0.661 AUC (Table 6).

Table (6): CLIF score as a predictor for mortality among ACLF patients: ROC curve analysis.

Cut-off Values	SN % (95% CI)	SP % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy (95% CI)	AUROC (95% CI)	p-value
CLIF score >5	86.84% (77.1-93.5)	45.95% (29.5-63.1)	76.7% (66.3-85.2)	63% (42-80.9)	73.5% (61.5-83.6)	0.661 (0.566-0.747)	0.002

There was a significant association between grades of ACLF and mortality where the death rate was 32%, 75.8%, and 81.8% among grade I, grade II, and grade III, respectively (p-value = 0.001). There was a significant difference between different grades of ACLF regarding overall survival, where the mean OS was 9.071, 8.621, 5.568, and 5.886 days, respectively (p-value 0.001) (Table 7).

Table (7): Comparison between different grades of ACLF as regard outcome

Outcome	Test						p-value
	Grade I (N=25)		Grade II (N=66)		Grade III (N=22)		
	No.	%	No.	%	No.	%	
ICU Admission (days)							
Mean ± SD	5.56 ± 1.12		4.77 ± 1.01		5.27 ± 1.11		1.785• 0.618
Median (Range)	5 (1 – 12)		4 (1 – 11)		5 (1 – 11)		
Mortality							
Alive	17	68%	16	24.2%	4	18.2%	43.662§ <0.001
Died	8	32%	50	75.8%	18	81.8%	
Overall survival (OS)							
Mean OS (95% CI)	8.621 days (7.047 – 10.195)		5.568 days (4.842 – 6.293)		5.886 days (4.566 – 7.206)		31.665‡ <0.001
Median OS (95% CI)	10 days (6.736 – 13.264)		5 days (3.415 – 6.585)		6 days (4.062 – 7.938)		
1 day OS	100%		92.4%		95.5%		
3 days OS	87.1%		72.2%		67.2%		
7 days OS	68.6%		20.7%		34.3%		
10 days OS	22.9%		6.5%		11.4%		

DISCUSSION

An initial loss in liver function is superimposed on CLD in the complicated illness known as acute-on-chronic liver failure. In both the short and long terms, it is linked to a death rate of 50–90% ⁽³⁾.

Out of 195 patients in this study, 113 had acute-on-chronic liver cell failure, making the rate of ACLF 57.9% distributed between 12.8% grade I, 33.8% grade II, and 11.3% grade III.

The study supported the findings of **Jalan et al.** ⁽⁴⁾, who revealed that patients who have or free from ACLF were similar in two groups in terms of male gender as well as age (P- 0.925, p-values 0.398 as well as residence, where ACLF occurred in 53.7% and 62.0% of urban and rural residents, respectively (p value = 0.240).

Our study was in line with **Sargenti et al.** ⁽⁵⁾, who found that there was a more frequent rate of ACLF in patients with than patients without hematemesis (80.8% versus 31.9%, respectively, p-value 0.001). Patients with hematemesis had a tenth chance of patients without hematemesis to have ACLF (OR =0.111). Also, patients with melena had a higher rate of ACLF than patients without melena (87.9 percent versus 31.7 percent, p-value 0.001), and they also had a 15% higher likelihood of developing ACLF (OR =0.064).

The study was concordant with **Cordoba et al.** ⁽⁶⁾, who found that there was a more frequent rate of ACLF in patients with than in patients without hepatic encephalopathy (94.9% versus 33.3%, respectively, p-value 0.001). Also, Patients with ACLF had a mean CLIF score that was considerably higher than those without ACLF (mean: 8.20 versus 2.45 respectively, p-value 0.001).

The study supported the findings of **Vasu et al.** ⁽⁷⁾, who discovered that individuals with chronic renal impairment experienced an increased risk of ACLF compared to those without CKD (88.9 percent versus 50.9 percent, respectively, p-value 0.001). Also, patients with ACLF had mean serum creatinine levels that were considerably greater than those without ACLF (mean: 2.88 versus 1.05 mg/dl, respectively, p-value 0.001). Our findings were contrary to those of **Yan et al.** ⁽⁸⁾, who found that one of the main causes (precipitating events) of acute-on-chronic liver failure has been HBV reactivation. Patients with ACLF had a greater incidence of infection as a precipitating event in our research (p-value 0.025), as well as a higher prevalence of multiple precipitating events.

Also, our study matched with another Egyptian study which showed that infection and GIT bleeding were the most precipitating factors for ACLF ⁽⁹⁾.

Solé and Solà ⁽¹⁰⁾, also showed The most frequent precipitating factors in ACLF are bacterial infections, alcoholism, and reactivation of viral hepatitis, although in up to 40% of patients in his study, no precipitating factor could be identified. This correlated with our study, where some patients had no clear precipitating factor while others had multiple precipitating factors.

Kumar et al. ⁽¹¹⁾ showed that Bacterial infection and active alcohol use are the most prevalent events that cause ACLF in western nations, whereas hepatitis B flare, sepsis, and active alcohol consumption are the most often recognised precipitating events in the east and south. However, there were roughly 40% of individuals with ACLF who had no known triggering factors.

In his study, **Masnou et al.** ⁽¹²⁾ showed that approximately 83 percent of cases had nearly identifiable triggering circumstances gastrointestinal bleeding (53 percent) and infection were the most common triggering causes (19 percent). Sepsis (50 percent) was the most frequent factor that caused ACLF, according to **Chirapongsathorn et al.** ⁽¹³⁾ across all grades of ACLF, the frequency of multiple organ failures other than liver failure was significantly higher in ACLF patients. The variables that demonstrated a significant correlation with ACLF across grades were total leukocyte count, INR, and serum creatinine. This finding is consistent with the research of **Moreau et al.** ⁽¹⁴⁾, and elevated serum creatinine points to a critical role for renal failure in the increased mortality linked to the ACLF syndrome.

Researchers **Kamath et al.** ⁽¹⁵⁾ did the investigation, and they discovered that the mean AST was substantially greater in deceased patients than in living individuals (mean: 62.07 versus 49.98 U/L, respectively, p-value = 0.017). Additionally, mean ALT was much greater in deceased individuals compared to living patients (mean: 83.20 versus 49.90 U/L, respectively, p-value = 0.001).

The study agreed with **Jalan et al.** ⁽¹⁶⁾ who found that Patients with and without ACLF did not vary substantially in terms of the presence of liver failure as a single failure, with a p-value of 0.237. However, the ACLF group had much more occurrences of all other individual organ failures.

Our findings coincides with **Moreau et al.** ⁽¹⁴⁾ who found that there was a significant higher statistical difference between grades of ACLF regarding ALT, total serum bilirubin, and INR. Whereas the mean ALT was 119.39, 63.36, 66.07, and 101.15 U/L (p-value = 0.011), the mean TSB was 1.80, 2.90, 7.23, and 6.59 mg/dl (p-value 0.001), and the mean INR was 1.53, 2.28, 1.67, and 2.75 (p-value = 0.033).

The study coincided with **Vasu et al.** ⁽⁷⁾ who found that there was a variation between different grades of ACLF regarding serum creatinine where mean serum creatinine was 1.05, 4.23, 2.01, and 3.63 mg/dl respectively (p-value > 0.0011). Additionally, mean blood creatinine levels in deceased patients were much greater than those in surviving individuals. (mean: 3.68 versus 2.50 mg/dl, respectively, p-value = 0.011). Renal dysfunction was the most prevalent organ failure (49 percent) among patients with ACLF, according to a meta-analysis by **Mezzano et al.** ⁽³⁾ according to **Hernaes et al.** ⁽¹⁷⁾, patients with ACLF had high 28- and

90-day death rates of 25.52 percent and 40.02 percent, respectively. Mortality risk is also much higher the more organ failures (OFs) there are, ranging from 17 to 53 percent at 28 days and 31 to 69 percent at 90 days, respectively.

Our study matched with another study conducted in Egypt, which showed a significant high mortality rate of ACLF. The death rates among ACLF patients at 28 and 90 days were 86.5 and 96.2 percent, respectively⁽⁹⁾.

This study was agreed with by **Garg *et al.***⁽¹⁸⁾, who found that there was a high mortality rate between ACLF grade among ACLF patients, where the death rate in grade I, grade II, and grade III ACLF was 32%, 75.8%, and 81.8%, respectively.

The findings agrees with **Kumar *et al.***⁽¹⁹⁾ who discovered that having one organ fail carried a death risk of 8.3 percent, while having two organ failures carried a mortality rate of more than 50 percent, and having three or more organ failures carried an 80 percent mortality rate.

The findings concurred with **Sargenti *et al.***⁽⁵⁾, who discovered that people with ACLF grades 2 and 3 had an infection as a precipitating event in a much greater percentage. More frequently, those with ACLF 3 had >1 precipitating incident (p-value 0.025). When compared to other ACLF grades or patients without ACLF, individuals with ACLF grade 3 had a considerably greater prevalence of all individual organ failures, except for liver failure.

The study was also matched with **Cholongitas *et al.***⁽²⁰⁾, who discovered that the CLIF-SOFA score had a higher sensitivity in predicting mortality as compared to both MELD and CPs scores, where a CLIF score greater than 5 was associated with 86.84 percent sensitivity, 45.95 percent specificity, 76.7 percent positive predictive value, 63 percent negative predictive value, and 0.661 AUC.

The results of our study were in agreement with those of **Bajaj *et al.***⁽²¹⁾, who discovered a substantial difference between the grades of ACLF in terms of overall survival. For these grades, the mean (OS) was 9.071, 8.621, 5.568, and 9.071 days, respectively (p-value 0.001). The study is in line with **Sliva *et al.***⁽²²⁾ work's which developed the CLIF-C OFs, a novel, straightforward score for diagnosing organ failure and ACLF in patients with cirrhosis. Additionally, the CLIF-C ACLF was created as a particular prognostic score for ACLF patients by combining the CLIF-C OFs with age and white blood cell count. This permitted a considerable increase in the discriminating capacity in comparison to the MELDs, MELD- Na, and CPs.

Study limitations: This study has a number of limitations. First, there weren't many patients enrolled (195). This could have distorted some of the results. We only performed a 28-day follow-up since the trial was conducted in a single site, and we used 28-day mortality as our endpoint. We did not experience numerous viral hepatitis B virus (HBV), which makes up a large

fraction in this region of the world. We didn't look out for (HEV and HAV).

CONCLUSION

GIT bleeding, HE, and active infections were more common in ACLF patients. Overall survival (OS) was significantly higher in patients without ACLF. CLIF score of more than 5 was associated with 86.84% sensitivity, 45.95% specificity, 63% negative predictive value, 76.7% positive predictive value as well as 0.661 AUC.

RECOMMENDATIONS

The outcome of patients with ACLF can be predicted better by ACLF-specific ICU scores (such CLIF-C ACLF) than by general ICU ratings. However, as there is still significant variation in the survival rate of patients with comparable scores, the discrimination of the existing CLIF-C ACLF may be improved. The ability to identify a precipitating cause (that may be treated) should be taken into account when interpreting prognostic ratings. It is also important to consider whether liver transplantation is an option when interpreting scores. The choice of whether to continue or stop providing intensive life support is based on dynamic evaluation. Long-term outcomes from transplanting cirrhotic individuals who meet certain criteria for critical illness are excellent. Nevertheless, prognostic techniques are required to better determine who is likely to benefit from transplantation and who is too sick to be transferred, namely, at too great of a risk to justify organ allocation in a setting of organ shortage.

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