

Characterization of Patients With Acute Liver Failure in a Quaternary-Care Hospital in Colombia

Santiago Escalante-Pérez,^{1*} Octavio Muñoz-Maya,² Óscar Santos-Sánchez,² Juan Ignacio Marín-Zuluaga,² Juan Carlos Restrepo-Gutiérrez,³ Jorge Hernando Donado-Gómez.⁴

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¹ Physician, Internal Medicine Resident, Universidad Pontificia Bolivariana. Hospital Pablo Tobón Uribe. Medellín, Colombia.

² Internist Hepatologist. Professor, Universidad de Antioquia, Hospital Pablo Tobón Uribe. Medellín, Colombia.

³ Surgeon and Specialist in Internal Medicine and Clinical Hepatology, Universidad de Antioquia. MSc in Organ and Tissue Transplantation, Universitat Autònoma de Barcelona; Hepatology and Liver Transplantation. PhD in Hepatic and Gastroenterological Diseases, Universitat de Barcelona. Hepatologist, Hospital Pablo Tobón Uribe. Full Professor, Universidad de Antioquia, Hospital Pablo Tobón Uribe. Medellín, Colombia.

⁴ Internist, MSc in Epidemiology. Professor, Universidad Pontificia Bolivariana, Hospital Pablo Tobón Uribe. Medellín, Colombia.

*Correspondence: Santiago Escalante-Pérez. santiago.escalante@upb.edu.co

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Abstract

Objective: To describe the etiology, management, and clinical course of patients diagnosed with acute liver failure (ALF) admitted to Hospital Pablo Tobón Uribe between January 2004 and December 2023. **Patients and Methods:** A retrospective observational study was conducted including all patients with ALF treated at a quaternary-care hospital in Medellín, Colombia. Demographic characteristics, etiologies, clinical evolution, therapeutic interventions—including liver transplantation—and survival outcomes were analyzed. **Results:** Eighty patients were included. The median age was 40 years, and 58% were women. The most frequent etiologies were viral hepatitis (20%), cryptogenic causes (18.8%), and autoimmune hepatitis (16.3%). Acetaminophen-induced toxicity was uncommon (5%). The clinical course was severe: 62.5% developed respiratory failure, and 57% required vasopressor support. Overall, 67.5% met criteria for urgent liver transplantation, of whom 57% ultimately underwent the procedure. Thirty-day overall survival was 55%, with significantly higher survival among transplanted patients (91%) compared with those not transplanted (49%). Leading causes of death included sepsis, intracranial hypertension, and multiorgan failure. **Conclusions:** This cohort, the largest reported in Colombia to date, underscores the critical importance of specialized management and timely access to liver transplantation to improve outcomes in patients with ALF.

Keywords

Acute liver failure, fulminant hepatic failure, liver transplantation, intensive care unit.

INTRODUCTION

Acute liver failure (ALF) is an infrequent but highly lethal clinical entity, characterized by rapid and severe liver dysfunction in patients without prior liver disease. Its classic definition includes the presence of coagulopathy (international normalized ratio [INR] >1.5), hepatic encephalopathy, and symptom onset within a period of less than 26

weeks. This condition may rapidly progress to multiorgan failure, intracranial hypertension, and death if timely access to liver transplantation is not achieved^(1,2). The term ALF encompasses different subtypes according to the timing of clinical presentation: hyperacute (<7 days), acute (8–28 days), and subacute (4–26 weeks), which has implications for both prognosis and transplant indication⁽³⁾. Global incidence is estimated at between 2,000 and 3,000 cases

annually and accounts for approximately 4%–6% of indications for adult liver transplantation^(4,5).

The causes of ALF vary significantly by geographic region. In developed countries, acetaminophen toxicity is the predominant etiology, accounting for up to 65% of cases in the United Kingdom and the United States⁽⁶⁾. In contrast, in middle- and low-income regions such as Latin America and Asia, acute viral hepatitis—particularly hepatitis A and B—is the leading cause^(7,8). This variability reflects not only differences in exposure to risk factors but also inequalities in access to early diagnosis, specialized management, and liver transplantation.

Multiple studies have shown that prognosis in patients with ALF depends on etiology, the availability of specific treatments, intensive management in specialized units, and, most importantly, timely access to liver transplantation^(1,9,10). In the absence of transplantation, mortality may exceed 80% in patients with poor prognosis according to criteria such as those of King's College; by contrast, post-transplant survival may reach up to 90% in some series^(5,11).

In Latin America, information on ALF remains limited. Reported cohorts are scarce, with small sample sizes and high heterogeneity in etiology and outcomes. In Colombia in particular, there are no large studies that comprehensively describe the clinical characteristics, etiologies, and outcomes of patients with ALF. Therefore, the objective of this study is to characterize patients with ALF treated at a quaternary-care university hospital in Medellín, Colombia, over a 20-year period.

METHODOLOGY

We present an observational follow-up study of a cohort of patients with ALF hospitalized at a referral center. A search was conducted in the electronic medical records system to identify patients diagnosed with codes for acute or subacute liver failure (K720) or unspecified liver failure (K729), according to the International Classification of Diseases (ICD-10).

All patients older than 16 years hospitalized between January 1, 2004, and December 31, 2023, were included. Patients were required to meet diagnostic criteria for ALF, defined by the presence of jaundice, INR >1.5, hepatic encephalopathy, and a disease course of <26 weeks. Patients with a history of cirrhosis or other chronic liver diseases were excluded, except for cases of autoimmune hepatitis, Budd-Chiari syndrome, and Wilson disease.

Etiology was defined based on medical history and paraclinical test results obtained during hospitalization. ALF was classified by timing as hyperacute (less than 7 days), acute (8–28 days), and subacute (4–26 weeks). Prognostic

assessment was performed using the King's College criteria. Hepatic encephalopathy was graded according to the West Haven scale.

Data were collected through review of medical records in the hospital's electronic registry using a previously designed data collection instrument. Categorical variables were analyzed using absolute and relative frequencies. Continuous variables were described using means and standard deviations or medians and interquartile ranges, according to data distribution assessed with the Shapiro-Wilk test. For survival analysis and outcomes, time to event was estimated using the Kaplan-Meier curve.

Sample size was not estimated *a priori*, as all patients diagnosed with ALF and treated during the study period were included. The study followed the guidelines of the 2024 Declaration of Helsinki, as well as Resolution 008430 of 1993 on clinical research in Colombia, and was approved by the hospital's Ethics Committee.

RESULTS

A total of 80 patients older than 16 years were included in this study. Of these, 58% were women and 41% were men, with an age range of 16 to 71 years. Demographic, clinical, and paraclinical characteristics are shown in **Table 1**. Regarding the diagnostic criteria for ALF, the median prothrombin time (PT) at admission was 37 seconds; median total bilirubin was 37 mg/dL, and 63% of patients had grade I–II hepatic encephalopathy. Overall, 38.8% of patients were classified as having hyperacute ALF.

The main causes were viral hepatitis (20%), with hepatitis B being the most frequent; cryptogenic etiologies (18.8%); and autoimmune hepatitis (16.3%). Only 5% of patients had ALF due to acetaminophen. Ten percent of cases were attributed to other medications, including anti-convulsants (valproic acid, lamotrigine), antituberculous drugs, losartan in combination with captopril, antiretrovirals (efavirenz), antibiotics (levofloxacin combined with amoxicillin), amphetamine use, and the ABVD chemotherapy regimen. In 6.3% of cases, other causes were identified, including thyroid storm or combined etiologies (hepatitis A plus acetaminophen, herbal products plus hepatitis A). Of the four patients with acetaminophen-related ALF, all met King's College criteria; among the 76 patients with other etiologies, 50 patients (65.7%) met King's College criteria. All etiologies are shown in **Table 2**.

Table 3 presents the clinical outcomes during hospitalization. The median length of hospital stay was 13.5 days, with a maximum of 67 days. Sepsis occurred in 47.5% of patients, with the urinary tract being the most frequent source. Overall, 84% of patients received at least one anti-

Table 1. Demographic and Clinical Characteristics at the Time of Diagnosis

| Characteristic | (n = 80) |
|---|-------------------|
| Age in years, median (IQR) | 40 (27.25-51) |
| Sex, n (%) | |
| - Female | 47 (58.8) |
| - Male | 33 (41.3) |
| Comorbidities, n (%) | |
| - Neoplasms | 3 (3.8) |
| - Arterial hypertension | 9 (11.3) |
| - Dyslipidemia | 4 (5) |
| - Diabetes | 4 (5) |
| - Obesity | 1 (1.3) |
| - Chronic kidney disease | 1 (1.3) |
| Total bilirubin, mg/dL, median (IQR) | 18 (8.8-26.7) |
| PT, seconds, median (IQR) | 37 (25-56.5) |
| ALT, U/L, median (IQR) | 741 (228-2345) |
| AST, U/L, median (IQR) | 746 (211-2596) |
| Alkaline phosphatase, IU/L, median (IQR) | 152.5 (106.7-197) |
| Sodium, mEq/L, median (IQR) | 137 (133-140) |
| pH, median (IQR) | 7.45 (7.28-7.5) |
| Lactate, mmol/L, median (IQR) | 4.45 (2.7-9.6) |
| Ammonia, median (IQR) | 201 (131-355.5) |
| Serum creatinine, mg/dL, median (IQR) | 0.9 (0.7-2.1) |
| Encephalopathy grade, n (%) | |
| - Grade I | 35 |
| - Grade II | 28.7 |
| - Grade III | 23.8 |
| - Grade IV | 11.3 |
| Acute liver failure classification, n (%) | |
| - Hyperacute | 31 (38.8) |
| - Acute | 24 (30) |
| - Subacute | 25 (31.3) |

ALT: alanine aminotransferase; AST: aspartate aminotransferase; IQR: interquartile range (P_{25-75}); PT: prothrombin time. Author's own research.

Table 2. Etiology of Acute Liver Failure

| Etiology | (n = 80) n.º (%) |
|--------------------------------|------------------|
| Cryptogenic | 15 (18.8) |
| Hepatitis B | 13 (16.3) |
| Autoimmune hepatitis | 13 (16.3) |
| DILI | 8 (10) |
| Hypoxic-ischemic | 7 (8.8) |
| Acetaminophen | 4 (5.0) |
| Hepatitis A | 3 (3.8) |
| Herbal products | 3 (3.8) |
| Wilson's disease | 2 (2.5) |
| Acute fatty liver of pregnancy | 2 (2.5) |
| White phosphorus | 2 (2.5) |
| Cytomegalovirus | 1 (1.3) |
| Budd-Chiari syndrome | 1 (1.3) |
| Lymphoma | 1 (1.3) |
| Other causes | 5 (6.3) |

DILI: drug-induced liver injury. Author's own research.

Table 3. Clinical Outcomes

| Clinical Outcomes | (n = 80) n.º (%) |
|---|------------------|
| Sepsis | 38 (47.5) |
| Progression of encephalopathy | 53 (66.3) |
| Use of at least one antimicrobial agent | 70 (87.5) |
| Use of anticonvulsant prophylaxis | 1 (1.3) |
| Intracranial pressure (ICP) monitoring | 27 (33.8) |
| ICP value, median (IQR) | 18 (14- 27) |
| Use of at least one anti-cerebral edema measure | 45 (56.2) |
| Need for dialysis | 30 (37.5) |
| Respiratory failure | 50 (62.5) |
| Hemodynamic instability | 46 (57.5) |
| Transplantation | 31 (38.8) |
| Death during initial hospitalization | 42 (52.5) |
| Death after discharge | 4 (5) |

ICP: intracranial pressure. Author's own research.

microbial agent during hospitalization. Respiratory failure developed in 62% of patients, and 57% required vasopressor support. Although median creatinine at admission was within the normal range, 37.5% of patients required renal replacement therapy. At least one anti-cerebral edema measure—hypertonic saline, mannitol, or deep sedation—was administered to 56.2% of patients.

Among the 54 patients who met King’s College criteria, 31 patients (57%) underwent transplantation—one due to acetaminophen and the remainder due to other etiologies. Of the remaining patients, six died while on the waiting list, six died before they could be listed, seven had at least one contraindication, and four experienced spontaneous recovery (none in the acetaminophen group).

Outcomes among transplanted patients are shown in **Table 4**. The median waiting time on the transplant list was 2 days, with a maximum of 16 days. Three patients underwent retransplantation: one during the initial hospitalization due to severe ischemic cholangiopathy from hepatic artery thrombosis; another 10 years after the initial transplant due to graft cirrhosis secondary to ductopenia from chronic rejection; and in the third case, the cause was not specified.

Overall survival was 55% at 30 days (**Figure 1A**). Survival among transplanted versus non-transplanted patients at 30, 60, and 365 days was 91% versus 49%, 88% versus 48%, and 86% versus 28%, respectively (**Figure 1B**). The main causes of death across all patients were multiorgan failure, sepsis, and intracranial hypertension; among transplanted patients, mortality due to postreperfusion syndrome and primary graft dysfunction was also noted.

Table 4. Outcomes in Transplanted Patients

| Clinical Outcomes | (n = 31) n.° (%) |
|---|------------------|
| Transplant-related complications | 21 (68) |
| - Primary graft dysfunction | 2 (10) |
| - Acute cellular rejection | 14 (67) |
| - Chronic cellular rejection | 2 (10) |
| - Anastomotic stricture | 3 (14) |
| - Biliary leak | 1 (5) |
| - Non-anastomotic stricture | 1 (5) |
| - Thrombosis | 2 (10) |
| - Extrinsic obstruction of the hepatic artery | 1 (5) |
| - Arterial vasospasm | 1 (5) |
| - Ischemic necrosis of the hepatic parenchyma | 1 (5) |
| - Portal vein stenosis | 1 (5) |
| - Other | 11 (52) |
| Infections | 18 (51) |
| - CMV | 12 (67) |
| - Fungal | 2 (11) |
| - Bacterial | 11 (61) |
| - Tuberculosis | 1 (6) |
| Liver graft loss | 4 (13) |
| Liver retransplantation | 3 (10) |

CMV: cytomegalovirus. Author’s own research.

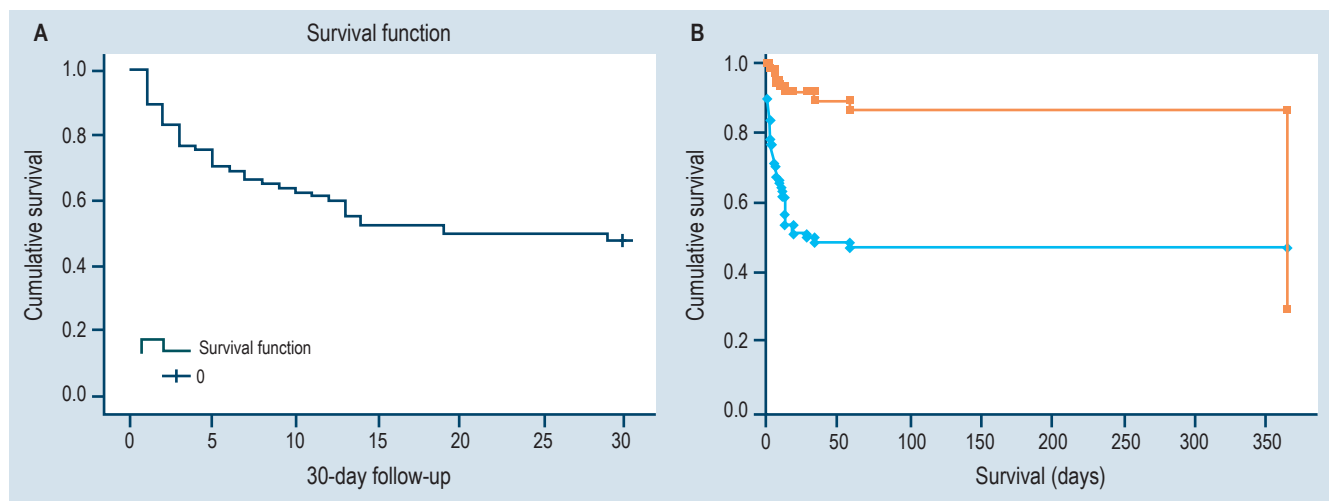


Figure 1. Kaplan-Meier Survival Curves. **A.** Overall 30-day survival. **B.** Cumulative survival according to whether transplantation was performed (orange) or not (blue). Author’s own research.

DISCUSSION

Acute liver failure (ALF) remains a severe disease, characterized by abrupt onset, rapid progression, and high mortality⁽⁵⁾. Despite its low incidence, its clinical relevance lies in the need for immediate specialized care and the potential requirement for urgent liver transplantation. Regarding demographic characteristics, it is noteworthy that, consistently in this and other series, ALF predominantly affects young adults and women^(9–11). In this cohort, a median age of 40 years was observed, with 58% of patients being female.

Bilirubin, transaminase, and creatinine levels were similar to those reported in other cohorts, with mean creatinine levels close to 2 mg/dL in a study of the Nordic population^(10,12). These biochemical similarities reinforce clinical comparability across populations, despite etiological differences and structural variations among health care systems.

With respect to etiology, marked differences are evident between developed countries and those in the developing world. In the former, acetaminophen is the most common cause of ALF, with frequencies of 65% in the United Kingdom and 46% in the United States, as consistently described in multiple series^(9,11,12). In contrast, in the present Colombian cohort, acetaminophen accounted for only 5% of cases, being surpassed by viral hepatitis (20%), cryptogenic etiology (18.8%), and autoimmune hepatitis (16.3%). These findings are similar to those reported by Mendizábal and colleagues in Argentina, where the main causes were viral hepatitis (32%), autoimmune hepatitis (26%), and indeterminate etiologies (26%)⁽¹⁰⁾. Differences in etiology may have important prognostic implications. Acetaminophen toxicity is associated with a better prognosis and higher rates of spontaneous recovery, with transplant-free survival reaching up to 89% at two years in some series^(6,12,13). In contrast, other etiologies, such as autoimmune hepatitis, tend to follow a more protracted and severe course. In this cohort and in the Argentine series, a significant prevalence of autoimmune hepatitis was observed. It is now recognized that this condition may initially present as acute hepatitis and progress to severe forms (INR >1.5), and even to ALF⁽¹⁴⁾. Although this disease is potentially treatable with corticosteroids, most patients progress and require liver transplantation or die. This suggests that autoimmune hepatitis is a frequent etiology of ALF in Latin America, with severe and late presentations that require transplantation and with a low likelihood of recovery with specific therapy.

Clinical course was severe in this cohort. Sepsis occurred in 47.5% of patients, 62.5% developed respiratory failure, 57% required vasopressor support, and 37.5% required renal replacement therapy (RRT). These figures reflect greater severity compared with other series, such as the

Argentine cohort (25% RRT, 24% ventilatory support, and 14% vasopressor use at admission) or the Nordic cohort (21% RRT and 41% mechanical ventilation)^(10,12).

Infections were among the leading causes of death in this and other cohorts. Despite antimicrobial use in 84% of patients, sepsis persisted as a major cause of fatal outcomes, consistent with findings reported by Mendizábal and colleagues⁽¹⁰⁾. Multiple studies have shown that infections negatively impact the natural history of ALF by promoting worsening hepatic encephalopathy, renal failure, and mortality⁽¹⁵⁾. Across reviewed cohorts, the main causes of death were sepsis, intracranial hypertension, and multiorgan failure⁽¹⁰⁾. Although universal antimicrobial prophylaxis remains controversial, some centers use it in patients on the transplant waiting list or with multiorgan dysfunction^(5,7). Our findings support the need for studies evaluating the systematic use of broad-spectrum antibacterial and antifungal prophylaxis to reduce the incidence of sepsis and preserve transplant eligibility in suitable candidates.

The use of intracranial pressure (ICP) monitoring was another relevant aspect. In this series, 35.1% of patients had grade III–IV encephalopathy, a figure comparable to other cohorts reporting rates between 38% and 47%^(10,11). ICP monitoring was implemented in 33.8% of cases, and 56.2% received at least one measure for cerebral edema. ICP monitoring remains controversial due to bleeding and infection risks and the lack of conclusive evidence regarding its impact on survival^(5,16). Its use varies widely among studies, ranging from 14% to 65%^(11,17). Current guidelines recommend noninvasive prophylactic measures such as head-of-bed elevation to 30°, deep sedation, normovolemia, adequate mean arterial pressure, and correction of hyponatremia⁽⁵⁾. However, patients with advanced encephalopathy, ammonia levels >150 µmol/L, hyperacute ALF, hemodynamic instability, or need for RRT may benefit from ICP monitoring to optimize management.

Regarding liver transplantation, 57% of patients meeting King's College criteria underwent transplantation, a proportion comparable to the Argentine (54%) and U.S. (59%) series, but lower than that reported in Nordic countries (73%)^(10–12). Twelve patients died while on the waiting list or before listing, reflecting limitations in timely access to transplantation, a phenomenon also described in other series^(10,11). Median waiting time was two days, shorter than that reported in Argentina (3.8 days)⁽¹⁰⁾.

Overall, 30-day survival was 55%, lower than that reported in the United Kingdom (62%), the United States (75%), and Argentina (73%)^(9–11). This difference may be related to prevailing etiology, access to transplantation, and sample size; notably, the British and U.S. cohorts included more than 2,000 patients. Post-transplant survival was 91%, compared with 49% in non-transplanted patients, similar

to other series such as that from the United States (96% vs. 56%), with two-year survival rates of up to 92% among transplanted patients^(11,13). Better transplant-free survival has been documented in acetaminophen-related cases, an etiology that was infrequent in this cohort^(12,18).

LIMITATIONS

Among the main limitations of this study are its retrospective, single-center design and relatively small sample size, which limit subgroup analyses and the generalizability of the results. However, this represents one of the largest single-center series reported in Latin America and the most extensive in Colombia. The findings provide valuable data on the clinical, etiological, and outcome characteristics of ALF in a context where causes differ from those observed in developed countries and where barriers to timely access to liver transplantation persist.

CONCLUSION

ALF is an infrequent but highly lethal disease. In recent years, improvements in overall survival have been observed, attributable to specialized intensive care, specific therapies,

and the availability of liver transplantation. However, these benefits are not evenly distributed across all settings. In this Colombian cohort, outcomes were consistent with the international literature regarding clinical course and transplant results, while also highlighting specific challenges related to etiology and timely access to treatment.

Early diagnosis, rapid referral to high-complexity centers, and specialized interdisciplinary management are required. In addition, prospective regional studies are needed to evaluate the validity of prognostic models, the role of intracranial pressure monitoring, and the utility of antimicrobial prophylaxis strategies to improve outcomes in this highly complex condition.

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Conflict of Interest

The authors report no conflicts of interest in relation to this article.

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