Acute liver failure in adults

Ali Rıza Çalışkan, Murat Harputluoğlu
Department of Gastroenterology, İnönü University Turgut Özal Medical Center, Malatya, Turkey

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Acute liver failure (ALF) is defined as the acute development of jaundice, synthetic failure, and hepatic encephalopathy (HE) in patients without a previous history of liver disease. It is a severe and complex condition that results from acute and massive hepatocellular destruction (1). If untreated, its prognosis is poor; therefore, timely recognition and management of patients with ALF are crucial. Whenever possible, patients with ALF should be managed in an intensive care unit (ICU) at a facility capable of performing liver transplantation (2). Viral- and drug-induced hepatitis are the most common causes of ALF in adults. In Australia, Denmark, the United Kingdom, and the United States, acetaminophen is the most common cause of ALF, whereas in Asia and some other parts of Europe, viral hepatitis predominates (3).

A study published in Ann Intern Med, entitled "Outcomes in Adults With Acute Liver Failure Between 1998 and 2013; An Observational Cohort Study," investigated the changes in causes, disease severity, treatment, and 21-day outcomes that have occurred in recent years among adult patients with ALF referred to U.S. tertiary care centers (4). In this study, the authors aimed to update the experience in U.S. with regards to ALF at specialized liver disease and transplant centers since the last published overview by the Acute Liver Failure Study Group (ALFSG) in 2002. From January 1, 1998 to December 31, 2013, adult patients were consecutively enrolled in the ALFSG registry (2) from 31 U.S. academic liver centers. Clinical features, treatment, and 21-day outcomes were annually compared over time for trends and were also stratified into two 8-year periods (1998-2005 and 2006-2013).

All enrolled patients had both coagulopathy (international normalized ratio ≥1.5) and any grade of HE within 26 weeks of the first symptoms and had no evidence of significant chronic liver diseases, especially cirrhosis. Patients for whom prior liver transplantation failed (due to primary graft nonfunction or other causes) were excluded. During the patient enrollment in the study, the authors prospectively collected patient demographic characteristics (age, sex, race, and ethnicity); a complete medical history, including the timing of the first symptom of ill health, onset of jaundice and HE, and the number of days between the first symptom, hospital admission, transfer to the study site (where relevant), and enrollment in the study; and clinical features, including blood pressure and need for vasopressor support, mechanical ventilation, and renal replacement therapy, which allowed calculation of the systemic inflammatory response syndrome score.

During the 16-year study, a total of 2070 patients [median age, 39.0 years (IQR, 29.0-52.0 years)] were enrolled in the ALFSG registry. Among enrolled patients, 69.3% were women, and 76.4% were white. Patients did not differ in sex, race, or ethnicity between the two 8-year periods. The percentage of enrollment as a reflection of the most common causes of ALF did not change during the two 8-year periods. Hepatotoxicity due to n-acetyl-p-aminophenol (APAP) accounted for almost half the cases of ALF for the entire 16-year period. Hepatitis A virus infection was significantly less evident during the later period [9 cases (0.8%)] than the early period [28 cases (2.8%)] ($p<0.001$). Hepatic ischemia and autoimmune hepatitis increased modestly, whereas hepatitis B virus infection, drug-induced liver injury, Wilson disease, and Budd-Chiari syndrome were less frequently noted.

Over the entire 16-year period, the use of ventilator support, plasma and red blood cell transfusions, and vasopressors decreased ($p<0.001$ for all). The only use of renal replacement therapy (at any time) was unchanged. Approximately 90% of patients with APAP overdose were consistently treated with intravenous or oral N-acetylcysteine overall, and N-acetylcysteine use in patients without APAP toxicity showed a significant three-fold increase between the early and later periods largely due to a linear increase in administration from 18.2% in 2006 to 65.1% in 2010 that plateaued thereafter. Advanced life- and liver-support systems (such as extracorporeal

Corresponding Author: ***Ali Rıza Çalışkan; komamir308@gmail.com***

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membrane oxygenation, molecular adsorbent recycling, and extracorporeal liver-assist devices) were not used during the study.

Overall, 22.3% of patients received a transplant, and the 21-day postoperative survival was 92.0%. However, between the early and later periods, there was a reduction in the liver transplantation listing from 43.5% to 32.2% ($p<0.001$) accompanied by a slight but significant improvement in the post-transplantation survival. Overall survival and transplant-free survival (TFS) rates progressively improved over the 16-year study period. Overall survival significantly increased from 58.8% in 1998 to 75.0% in 2013 ($p<0.001$), and TFS increased from 32.9% in 1998 to 61.0% in 2013 ($p<0.001$). Causes of death from ALF were as follows: multiorgan failure (20.6%), neurologic cause (13.9%), multifactorial cause (11.2%), unspecified "liver-related" cause (10.8%), sepsis or infection (7.9%), and cardiac cause (5.3%). In 25% of cases, the cause of death was unknown or unspecified.

In a study conducted in Turkey, a total of 308 patients were analyzed. Hepatitis A (20.9%) for children and hepatitis B (34.7%) for adults were the most common causes of ALF. Cryptogenic (18%) and metabolic (14%) reasons were as follows: Wilson's disease was the most common cause of metabolic diseases. Mushroom intoxication was the most common factor for TLF in both adults and children (13%). Acetaminophen is not an emerging reason for ALF in Turkey (5).

In conclusion, ALF outcomes considerably improved over time in association with slightly improved survival after liver transplantation and especially with improved survival without transplantation, which, as it is speculated, relates mainly to a more effective ICU management.

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