Academic International Journal of Medical Science
ISSN: 2984-7583
Aca. Intl. J. Med. Sci. 2024; 2 (2) 09-21
Journal homepage: www.aipublishers.org/aijms

Acute-on-Chronic Liver Failure on Older Patients -an Overview

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Article Info.
Article history:
Received 10 May 2024
Revised 18 June 2024
Published 25 August 2024
Keywords:
Acute, Chronic, Liver, Failure, Older, Patients
How to cite:
Fadhl ALzamili. Acute-On-Chronic Liver Failure on Older Patients -An Overview. Aca. Intl. J. Med. Sci. 2024; 2 (2) 09-21.
DOI:
https://doi.org/10.59675/M222

Abstract

Acute-onset liver failure (ACLF), a severe manifestation of rapidly decompensating liver fibrosis, was not well reported until 2013. This disease is characterized by a rapid onset of death and failure of the hepatic system. Liver disease is a major cause of death in patients each year. More than 30 million Americans have liver disease, and more than 29 million Americans have chronic liver problems. Age-related changes in the liver include decreased cytochrome P450 activity that can affect drug metabolism and increase susceptibility to drug-induced liver injury, significant reductions in liver volume and blood flow, and decreased immune responses against infection or cancer cells. However, older adults may be more susceptible to autoimmunity due to decreased regulatory T cells and impaired maturation of dendritic cells. Because of changes in the liver, patients with liver disorders may experience a variety of clinical manifestations and outcomes. The pathophysiology of viral hepatitis, autoimmune liver disorders, and the onset of hepatocellular carcinoma may be influenced by these changes in immune function. Furthermore, treatment of liver disease is less appropriate for elderly patients due to the significantly reduced reserve functions of many organs. Age-related changes in the liver and other organs may have an impact on the treatment course and clinical features of liver disease in the elderly. An overwhelming systemic inflammatory response caused by clinically obvious etiological factors (such as confirmed microbiological infection associated with sepsis or severe alcohol-related hepatitis) or clinically unclear causes acute-chronic liver failure. Following the classification of acute-chronic liver failure (ACLF), several important studies have shown that patients with this condition should be stabilized as soon as possible in order to potentially benefit from liver transplantation. Receive comprehensive general care, which includes appropriate treatment in the intensive care unit and support of organ systems in the identified etiological factors.

Introduction

Acute-chronic liver failure (ACLF) was first described in 1995 and is a clinical disease of the liver. ACLF causes significant short-term mortality, estimated at 45% to 90%, as well as high rates of organ failure. It occurs in the context of persistent liver dysfunction. [1]. The disease is of clinical importance, but remains largely unclear, and its exact causes, clinical course, diagnostic parameters, and therapeutic approaches are still under debate. [2]. Patients admitted to hospital with severe manifestations of liver cirrhosis who also have extrahepatic or organ dysfunction are referred to as having acute-chronic liver failure (ACLF) [3]. These patients are very likely to die soon [4]. 1. The end stage of all chronic and advanced liver disorders is cirrhosis. Cirrhosis has a progressive natural history. Compensated cirrhosis is the term used to refer to the initial stage, while acute-onset liver failure and decompensated cirrhosis are the more advanced forms, each with its own clinical manifestations and prognosis [5]. Cirrhosis is the most common cause of hospitalization or liver transplantation among all liver disorders. Chronic hepatitis C, alcohol-related liver disease, and a combination of the two have been identified as the primary causes of cirrhosis [6]. Recent World Health Organization projections suggest that cirrhosis will rank ninth in the Western world by 2015, so it is reasonable to assume that this situation is unlikely to improve in the next 10 years [7]. Patients with cirrhosis who are brought to hospital involuntarily because of recent onset ascites, gastrointestinal bleeding, new-onset hepatic encephalopathy, bacterial infection, or any combination of these are referred to as having acute compensated cirrhosis [8–12]. The “golden signs” of aging are the significant cellular changes that occur in people as they age. The overlapping patterns of age-related disorders are associated with shared signaling pathways, dysregulated nutrition sensing, telomere shortening, genomic instability, protein homeostasis, and epigenetic changes. Stem cell depletion, impaired intercellular communication, persistent inflammation, impaired autophagy, and microbial dysregulation [13]. The overall prevention of these age-related disorders can be aided by interventions along these pathways.

In addition to the decreased ability to regenerate healthy tissue and survive whole organ transplants, older adults are at increased risk for chronic diseases. As people age, the structure and processes of every tissue, including the liver, change, leading to impaired metabolic and reproductive processes and an increased chance of developing chronic liver disorders [14]. Furthermore, the liver becomes more susceptible to harmful chemicals as its ability to withstand stress decreases. The accumulation of highly oxidized lipids is associated with the pathophysiology of alcohol-related liver disease (ALD) in the elderly, leading to the characteristic “brown atrophy” appearance of the liver [15]. Liver cirrhosis, along with liver disease, is responsible for 3.5% of cancer-related deaths worldwide. It is the fifth leading societal cause of death for patients aged 50–69 years and one of the top 10 causes of death worldwide [16]. Liver disorders are common worldwide due to a variety of factors, including drug abuse, immune system dysfunction, genetic vulnerability, sexually transmitted diseases, obesity, blood transfusion, liver transplantation, and excessive alcohol consumption. There are risk factors for nonalcoholic fatty liver disease (NAFLD) and hepatocellular carcinoma (HCC), as well as an estimated 400 million people with diabetes and 2 billion adults who are overweight or obese, according to [17]. It was proposed to rename nonalcoholic fatty liver disease (NAFLD) as metabolic-associated fatty liver disease (MASLD) in 2020. The overlapping biological mechanisms that lead to the development of both ALD and NAFLD served as inspiration for this idea. As a result, we refer to MASLD rather than NAFLD in the text for the sake of accuracy and clarity [18]. Figure 1 summarizes current views regarding the etiology of alcohol-related liver disease and acute-on-chronic liver failure.

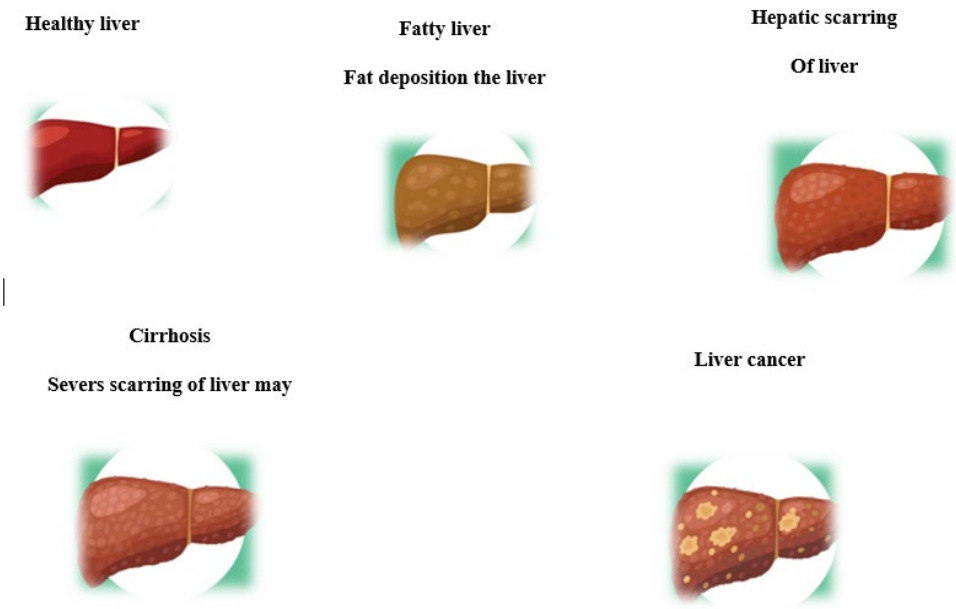


Figure 1: summarizes current theories about the etiology of both acute and chronic liver failure in relation to alcohol-related liver disease.

Research has been done on how aging affects both liver disorders and normal liver changes [19]. Aging is linked to a number of alterations in liver cells, such as hepatic sinusoidal endothelial cells, as well as a progressive shift in the structure and function of the liver [20]. Additionally, aging can raise the likelihood of developing a number of liver disorders and act as a negative prognostic factor, which raises the death rate [21–23]. We present updated data on the alterations in liver and liver disease caused by aging in this review.

Methods

The literature was found by searching English-language journals in PubMed and Google Scholar using keywords associated with the diagnosis of liver pathogenicity in elderly people.

Liver physiology with age

As we age, liver size and blood flow eventually decrease. Studies using ultrasound have shown that as people age, their liver capacity decreases by 20–40% [24]. These changes are associated with decreased hepatic blood flow, as evidenced by the fact that those aged 65 years or older have approximately 35% less hepatic blood volume than those aged under 40 years [25]. Under the microscope, older individuals have more hepatocytes with higher ploidy. Although there is no evidence of mitochondrial dysfunction, hepatocytes have fewer mitochondria overall but larger individual mitochondria. Hepatocytes from older individuals have thicker body compartments than those from younger participants, including lipofuscin and secondary lysosomes [26].

Elderly Populations with Liver Diseases

The development of liver issues may be influenced by age-related physiological changes. Furthermore, because most organs have a reduced reserve capacity as we age, managing liver problems may become more challenging for older adults. Lastly, older individuals are more likely than younger ones to have advanced liver disease.

Hepatic illness brought on by inflammation

PBC and autoimmune hepatitis (AIH) are two autoimmune liver disorders that are more common in older adults; on the other hand, primary sclerosing cholangitis is more common in those in their third or fourth decade of life [27–29]. However, the results of laboratory tests for these autoimmune liver diseases are unaffected by age, and treatment regimens for younger and older individuals are usually the same. The fecal-oral route—which involves consuming tainted food or water and contact with other people—is how HAV is spread.Because few incidences of transmission by blood transfusion have been recorded, blood donors are tested for polymerase chain reaction [30].

Hepatitis virus

Hepatitis A: Acute infections with the hepatitis A virus (HAV) typically resolve on their own. Elderly people with acute HIV infection, however, are more likely to develop comorbidities such as ascites, pancreatitis, and persistent cholestasis, as well as hepatic dysfunction with recurrent jaundice and coagulopathy [31]. There have been reports of higher hospitalization and fatality rates among elderly HAV patients. For instance, 42% of patients 70 years of age or older needed hospitalization during an HIV infection outbreak in the United States compared to 3%–20% of persons 40–49 years of age [32]. Hepatitis B virus (HBV) vaccinations are available, yet 290 million people worldwide still have a chronic HBV infection that can cause cirrhosis, hepatic failure, hepatitis, and hepatocellular carcinoma (HCC). In addition, HBV infection is thought to be the cause of 887,000 fatalities globally each year. The frequency of HBV infection is divided into three geographic categories: low (<2%: North America, Western Europe), medium (2-4%): Mediterranean, Eastern Europe, and high (>8%: East Asia, Africa) countries [33]. Over the past ten years, the epidemiology has changed due to the introduction of universal immunization, HBV screening programs, and population migration between high- and low-prevalence areas. Surprisingly, mother-to-child transmission (MTCT), which accounts for around half of all cases globally, is currently the most prevalent mechanism of HBV infection [34].

Hepatitis B virus (HBV) infection is a major health issue worldwide. The sixth most common cause of death is viral hepatitis, specifically from hepatitis B virus (HBV) and hepatitis C virus (HCV). The mortality rate from viral hepatitis has been higher than that of tuberculosis and is higher than that of HIV infection, according to the World Health Organization (WHO) and the Global Burden of Disease Research [35, 36]. Since the advent of low-cost, short-course (3–6 months) direct-acting antiviral therapy for hepatitis C, dramatic results have been achieved. This therapy has improved treatment coverage in emerging and newly developed countries, reduced fibrosis and hepatocellular carcinoma, and maintained virological response rates of over 95%. There were 58 million people living with hepatitis C virus (HCV) as of 2019 [38]. Researchers have discovered metabolic abnormalities associated with hepatitis C. In Denmark, 50% of HCV patients, especially those taking intravenous medications, have not yet consulted a specialist [39]. Because HCV is transmitted through blood contact, such as blood transfusions (especially before 1992), intravenous drug use, tattooing, dialysis, and work in the medical sector, there are age-related differences in the incidence of infection. In the United States, patients aged 70 years or older had the lowest prevalence of HCV infection (0.9% and 1%, respectively), while patients aged 40–

49 years had the highest prevalence (4.3%) [40, 41]. Polyethylene-stabilized interferon and ribavirin are effective treatment regimens for the management of chronic HCV infection. On the other hand, adverse effects are more common in older patients [42]. Studies show that the rate of sustained virological response was lower in older adults (46% vs. 69.7%, respectively) compared to younger adults. The greater number of older patients who discontinued antiviral medications due to side effects may be responsible for this discrepancy [43]. Hepatitis E virus (HEV), a member of the Hepeviridae family, is the most common cause of acute viral hepatitis worldwide [44–46]. Although we are learning more about it and it is a major cause of hepatitis, its origin remains unknown [47]. After a common stool sample from a soldier with the virus was diagnosed, Russian virologists [48] examined one of their stools in 1983 and used an electron microscope to visualize the virus.

Hepatic illness brought on by inflammation

Adults in their third or fourth decade of life are more likely to develop primary sclerosing cholangitis, but older people are more likely to develop autoimmune liver diseases, including autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC) [49–51]. Nevertheless, age is not a factor in the outcomes of laboratory testing related to these autoimmune liver diseases, and treatment plans for younger and older patients are typically the same.

Primary biliary cholangitis (PBC)

According to [52], China has the second-highest PBC prevalence in the Asia-Pacific area, after Japan, at 20.5 per 100,000 people. Environmental elements, such as being exposed to potential risks, include smoking, exposure to chemicals [53], or poisons as a youngster [54], urinary tract infections [55], and poor environmental cleanliness, elements contributing to PBC growth [56].

The normal history of PBC was split into four stages prior to the UDCA.[57]. (1) The sole component in the preclinical stage was AMA positive. (2) There were increased liver enzymes during the asymptomatic stage, but no clinical signs were present. (3) Weariness and pruritus were among the symptoms of the symptomatic stage. (4) Hepatic encephalopathy, liver failure, and increasing jaundice were all part of the liver insufficiency stage. The natural history of PBC has been considerably changed by early detection and UDCA treatment. The survival rate of patients exhibiting biochemical reactions to UDCA is comparable to that of the matched control group [58]. Nonetheless, PBC patients' transplant-free survival with a subpar reaction to UDCA is substantially less than in healthy patients, even though it is still more than that of PBC that has not been treated patients [59].

Hepatocellular carcinoma (HCC)

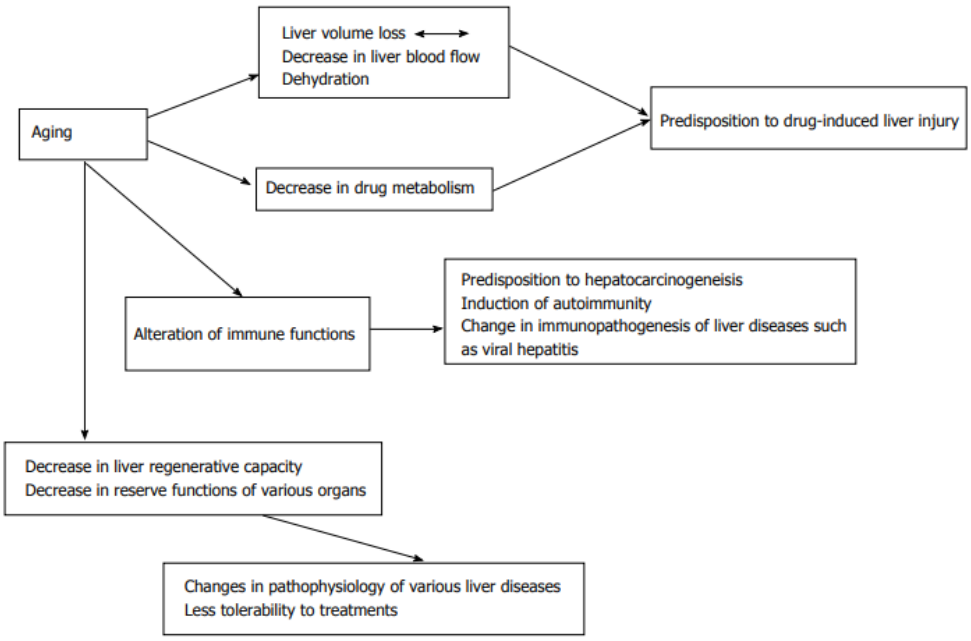
75%–85% of initial liver malignancies are caused by hepatocellular carcinoma (HCC). In the past 30 years, the occurrence of HCC has increased globally by over 75%, particularly in Western countries (60-62). This growth is anticipated to continue in the near future. Regretfully, only 30%–34% of individuals with HCC survive five years following analysis, and survival rates for these patients have remained basically stable for the past thirty years in the United States [63,64]. Around a number of explanations for the high death rates from HCC, but one major one is the delayed detection of the disease at more advanced stages[65,66]. Usually, HCC develops in the context of cirrhosis of the liver, where fibrosis and persistent inflammation cause genetic changes that make hepatocytes susceptible to cancerous transformation[67,68].The greatest risk factor for HCC is cirrhosis; 90% of HCCs develop in livers with cirrhosis[69].

Portal hypertension

Elderly individuals do not have a advanced hazard of developing portal hypertension and have a abridged portal velocity[70,71]. Worldwide, the approach to treatment is the same [72]. Despite a number of warnings, side effects, and increased risk of hospitalization (including cardiovascular and pulmonary events), beta blockers are nonetheless allowed [73]. Similar to younger adults, older patients should not get beta-blockers if they have hyponatremia, hypotension, or renal insufficiency [74]. According to the [75], the main cause of variceal and non-variceal upper gastrointestinal bleeding in the elderly is liver cirrhosis.Infection risk is raised when using proton pump inhibitors, anden cephalopathy in individuals with cirrhosis, regardless of age. In elderly individuals, the respecting therapeutic advice is necessary to avoid incorrect prescription drugs [76].

Alcohol-Related Liver Conditions

A wide range of clinical conditions are included in alcohol-associated liver disease, such as steatosis, ASH, AH with varied degrees of severity, and AC made worse by HCC. ALD is the primary cause of a significant proportion of cirrhosis cases globally, including in the US. It is also the cause of the rising rates of liver-related death, particularly in younger patients [77-79]. In AH, corticosteroids have been the subject of the most research, having been the subject of over 20 clinical trials spanning over 40 years, twelve of which were placebo-controlled. These trials have produced a range of results, and because of heterogeneity and limited power to detect changes in survival, most of them carry a substantial risk of bias [80]. The declining death rate of severe acute hemorrhage (several AH) over time (from 30%–50% at 28 days in early studies to 14%–18% more recently) complicates data interpretation and has implications for future trial design. Several meta-analyses have produced contradictory results [81, 82]. (Figure 2).



Aca. Intl. J. Med. Sci. 2024; 2 (2) 09-21: https://doi.org/10.59675/M222

Figure 2: illustrates the physiological alterations in aged participants linked to the emergence or pathophysiological alteration of liver disorders. Reductions in liver capacity, blood flow, drug metabolism, re-forming capacity, and immunological function are all linked to elderly. Modifications brought about by reduced reserve functions of different organs may have an influence on the management and clinical features of liver illnesses in the elderly.

Conclusion

Due to the fact that Acute-onset liver failure (ACLF), is still a relatively common, potentially fatal condition with limited treatment choices, it presents a significant clinical issue. There are currently only supportive measures available as a kind of treatment. On the other hand, ACLF has shown to be a possibly curable consequence of persistent liver disease. This highlights the necessity of a directed therapeutic approach, moving the ACLF downward spiral in the direction of hepatic decompensation. The utilization of hepatic support devices for this particular indication has yielded dismal results; nevertheless, additional research in certain patient subgroups may be necessary. Understanding of the pathogenesis of ACLF has significantly improved in recent years. All of the research has indicated that the three main contributors are (micro)circulatory dysfunction, bacterial translocation from the gut, and innate immunological dysfunction. This has led to the development of many liver disease therapy techniques that have been shown to be effective in in vitro or animal investigations. Nevertheless, there are insufficient human clinical trials, particularly with ACLF. Early diagnosis of ACLF-related condition may be a second line of defense against death from ACLF. For instance, early detection of kidney injury by the use of biomarkers of renal function may be helpful in predicting the development of ACLF in cirrhotic patients faced with acute illness, as the onset of ACLF corresponds with the development of multi-organ failure. It is expected that individuals with ACLF will have higher survival rates if the disease is identified early and treated with a more pathophysiology-guided approach, which will also lessen the necessity for liver transplantation as a last resort.

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