Journal of Gastroenterology Research and Practice

www.jjgastro.com

Short Commentary

Open Access, Volume 4

Severe cases of SARS-CoV-2 in individuals with alcoholic liver disease and cirrhosis: Understanding the impediments to intensive care unit ventilation

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Received: Apr 14, 2024

Accepted: May 03, 2024

Published: May 10, 2024

Archived: www.jjgastro.com

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Abstract

SARS-CoV-2, the causative agent of Severe Acute Respiratory Distress Syndrome (SARS-CoV-2), has instigated a swiftly evolving pandemic since late 2019, characterized by a mortality rate ranging from 0.5% to 3%. The deleterious impact of COVID-19 on the realm of hepatology has become evident, as chronic liver disease has escalated the risk of mortality associated with COVID-19 globally. The constraint on therapeutic interventions may have played a role in contributing to excessive mortality among individuals with pre-existing severe liver disease or alcohol use disorders. The primary aim of this editorial is to delineate the impediments to intensive care unit ventilation in patients with alcoholic liver disease and cirrhosis who are afflicted with severe SARS-CoV-2.

Introduction

The SARS-CoV-2 virus, responsible for severe acute respiratory distress syndrome (SARS-CoV-2), has precipitated a rapidly evolving pandemic since late 2019, with a mortality rate ranging from 0.5% to 3% [1]. Transmission primarily occurs through direct contact via respiratory droplets expelled during speech, coughing, and sneezing, and less frequently through objects contaminated by these droplets [2].

The principal clinical manifestations of COVID-19 include fever and dry cough, with varying degrees of liver impairment observed in several patients presenting gastrointestinal symptoms [3]. Although resolution of acute lung disease is typical, approximately 15% of patients necessitate hospitalization, with 5% requiring admission to intensive care.

The adverse impact of COVID-19 on hepatology is apparent. While patients with liver disease do not seem disproportionately represented among COVID-19 cases, implying that liver disease per se is not a risk factor for SARS-CoV-2 infection [4], the morbidity and mortality associated with COVID-19 are heightened by several concurrent pathologies, including various liver diseases [4].

Early in the epidemic, reported risk factors for severe COVID-19 and mortality included advanced age, male gender, hypertension, obesity, and severe comorbidities [5]. COVID-19 frequently affects the liver, with individuals having underlying chronic liver diseases experiencing elevated rates of hospitalization and mortality [6,7]. Alcohol-induced disorders of the innate and adaptive immune systems may elevate the risk of severe infection in COVID-19 patients. Common underlying medical conditions in alcoholic liver disease patients, such as obesity with metabolic syndrome and chronic kidney disease, can also impact prognosis, serving as risk factors [8]. Notably, two early retrospective studies from China associated metabolic liver disease with progressive COVID-19 [9,10]. A cohort study in the United States linked alcoholic liver disease and hepatocellular carcinoma, but not viral hepatitis, to COVID-19 mortality [11].

Mallet et al.'s study in France revealed that patients with chronic liver disease, including those with decompensated cirrhosis, primary liver cancer, and individuals with alcohol use disorders, faced an increased adjusted risk of COVID-19 death. Surprisingly, they exhibited a reduced, at times negative, adjusted risk for mechanical ventilation during the two pandemic waves in 2020. Chronic liver disease patients were at risk for mechanical ventilation (P<0.001), but not for acute respiratory distress syndrome (P=0.5) [12].

Associations between alcohol use disorders, decompensated cirrhosis, and mechanical ventilation were observed (P<0.001) [12]. The risk of mechanical ventilation was negatively correlated with Covid-19 death for patients with alcohol use disorders, decompensated cirrhosis, or primary liver cancer, unless they underwent liver cancer treatment [adjusted odds-ratio for mechanical ventilation and day-30 mortality 0.78 (95% confidence interval, 0.47-1.49, P=0.472) and 0.79 (95% confidence interval, 0.59-1.05, P=0.109)].

Access to mechanical ventilation was reduced by approximately 25% (OR=0.76) during the first wave for individuals with complicated cirrhosis and alcohol abuse, prompting consideration of therapeutic limitations. Their findings suggest that, despite higher rates of organ failures, chronic liver disease itself marginally contributed to the COVID-19 death toll in France in 2020. Indeed, the results "suggest that limitation of active therapies may have contributed to excess mortality in patients with previous severe liver disease or alcohol use disorders.

Factors leading to restricted availability of mechanical ventilation; an issue pertaining to the therapeutic endeavor

The proposition to admit a patient with cirrhosis to the intensive care unit is frequently met with hesitation from resuscitation practitioners, given the inherent high likelihood of mortality associated with these patients. Ongoing data from the global registry indicate an unfavorable prognosis and increased mortality in individuals with cirrhosis [13-15].

The heightened expression of the ACE-2 enzyme in COVID-19 patients with decompensated cirrhosis may contribute to an elevation in SARS-CoV-2 viral titers [16]. In cirrhotic patients, the reduction of ACE-2 due to SARS-CoV-2-induced internalization may worsen liver fibrosis and portal hypertension, thereby intensifying the severity of the disease. Individuals experiencing hepatocyte necrosis induced by the systemic inflammatory response syndrome or ischemic injury resulting from circulatory or respiratory failure may face an elevated risk of mortality [17].

The prognosis for cirrhotic patients in intensive care is commonly regarded as bleak, and resuscitation practitioners frequently exhibit reluctance to admit them, particularly in the absence of a therapeutic plan for non-abstinent cirrhotic patients. The persisting presence of alcohol intoxication is often perceived as a factor contributing to poor compliance with treatment, potentially influencing the decision to refrain from admitting the patient to the intensive care unit.

Numerous studies have previously identified individuals with liver conditions as being at risk of severe COVID-19. However, the distinctiveness of this particular study lies in establishing a connection between their heightened mortality and a notably reduced access to healthcare. Few hypotheses have been proposed to elucidate these disparities.

According to the European Association for the Study of the Liver (EASL), individuals with liver conditions often encounter a differential treatment paradigm. There persists a degree of stigma surrounding liver disease, rooted in the perception that it is self-inflicted and alcohol-related. This phenomenon predates the advent of COVID-19, as individuals with liver conditions frequently report experiencing disparate treatment compared to others.

Impact of artificial ventilation on mortality

Factors independently correlated with mortality in cirrhotic patients admitted to the intensive care unit include the necessity for mechanical ventilation and the utilization of vasopressors or the presence of shock [18,19]. A comprehensive examination of the literature substantiates the impact of mechanical ventilation on mortality [20,21].

During the 1980s, the imperative for mechanical ventilation was unequivocally linked to a substantial excess mortality rate of approximately 90%. In more recent investigations, the mortality rate for cirrhotic patients requiring mechanical ventilation has somewhat diminished to 50-60% [19,22]. Notably, the presence of respiratory failure is not associated with a surplus in mortality. This apparent reduction in mortality may be attributed to improved patient management or a discerning selection of individuals.

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