



## **IMMUNOLOGICAL MECHANISMS IN NAFLD**

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**Abstract:** The pandemics of coronavirus affliction 2019 (COVID-19) and non-alcoholic fatty liver disease (NAFLD) coexist. High-magnified liver assistance examinations are patronised in COVID-19 and hawthorn consequence liver destruction in NAFLD, preexisting liver destruction from NAFLD hawthorn consequence the progression of COVID-19. On the other hand the prognostication appropriateness of this interaction, though, is unclear. Corpulence is a jeopardy factor for the formal propinquity of NAFLD extremely as a terrible progression of COVID-19. Squadron studies communicate self-contradictory consequences with reference to the consequence of NAFLD formal propinquity on COVID-19 unwellness severity. awe-inspiring molecular similarities of cytokine pathways in both diseases, including postacute sequelae of COVID-19, indicate characteristic pathways for long-standing low-activity inflammation. This another look testament summarise existing collections with reference to the interplay of both afflictions and compare notes accomplishable contrivances of the consequence of individual affliction on the other.

**Key words:** COVID-19, inflammation, NAFLD, cytokine, liver disease.

NAFLD is a noncommunicable affliction whose widespread spread out diffuse upon be contingent on people's lifestyle, exceptionally dietetical habits, COVID-19 has an discriminating progression outstanding to its individualism as an transmissible disease. This show the way to undulations of communication that chalk up prompted widespread hygiene countermeasures to incorporate the infection, exceptionally in the yesteryear 2 second childhood (2020 and 2021). Lockdowns chalk up occurred in numerous nations to confine the mobility of general public and in this manner anticipate the spread out diffuse of the coronavirus[1,2]. The disagreeable isolation and lockdown magnitudes in the yesteryear 2 second childhood underneath the bounteous infective preceding modifications had substantial sociological and intellectual effects. in this manner in augmentation to the orchestrate viral consequences of COVID-19 on the liver, thither are furthermore allusive consequences on the liver or liver disease, which hawthorn amuse oneself an far-reaching impersonation in the extremely exploitation of these diseases. As COVID-19 buoy all the more consideration renewed lockdowns and isolation magnitudes in the looked toward for case history when bounteous deadly modifications originate contrariwise or outstanding to freshly rising transmissible diseases, much consequences should furthermore be sculptured and appropriated into explanation in the future. Numerous studies have indicated that a notable proportion of COVID-19 patients admitted to hospitals have underlying conditions such as hypertension, type 2 diabetes mellitus (T2DM), and cardiovascular disease (CVD), which may increase the risk of mortality from the virus[3]. Non-alcoholic fatty liver disease (NAFLD) is a multifaceted disorder characterized by the pathological accumulation of fat in hepatocytes, occurring in the absence of significant alcohol consumption, is closely associated with T2DM and CVD[4,5]. The diagnosis of NAFLD typically involves a comprehensive evaluation, including imaging modalities such as ultrasound, computed tomography (CT), or magnetic resonance imaging, alongside liver biopsies for histological confirmation[6]. The

escalating global burden of obesity has substantially fueled the increasing prevalence and incidence rates of NAFLD. Presently, NAFLD stands as one of the most common chronic liver diseases globally, affecting approximately 30% of the world's population. Recent medical research has placed considerable emphasis on investigating the association between NAFLD/metabolic-associated fatty liver disease (MAFLD) and COVID-19. A growing body of evidence indicates that individuals with NAFLD face an elevated risk of experiencing severe manifestations of COVID-19, resulting in poorer clinical prognosis[7]. This systematic review expands the discussion by examining the effects of NAFLD on COVID-19 patients, addressing a significant gap in existing literature. It has been established that NAFLD patients have background low-activity inflammation. This phenomenon is maintained by the activation of stellate cells and cytokine production by Kupffer cells, with IL-1 $\beta$ , TNF- $\alpha$ , interferon- $\gamma$ , IL-6, and reactive oxygen species serving as characteristic pro-inflammatory markers in the disease, ultimately inducing fibrotic changes[6]. Interestingly, during the acute response of COVID-19 infection, similar inflammatory cytokines and markers are raised, potentially responsible for the worsening of clinical markers in NAFLD patients[5]. The elevated immune response in such patients may chronically persist as sequelae, explaining the slower recovery duration and readmission rates observed among the studies. Thus, low-activity inflammation of NAFLD is assumed to be amplified during the acute-phase response of COVID-19 infection, highlighting the interaction of the two diseases at a molecular level. Several clinical implications may be inferred from our systematic review's results and literature search. Despite the independent association of mortality with concomitant NAFLD and COVID-19 illness; the worsened in-hospital outcomes remain significant nonetheless. In light of this, hospitalists are encouraged to provide greater care to patients with liver dysfunction, especially NAFLD or MAFLD. Additionally, the potential for drug-drug interactions or drug toxicities presents a notable challenge in the management of such patients[7]. Thus, clinicians are advised to exercise vigilance with respect to monitoring liver function tests and drug dosages to avoid the risk of developing hepatotoxicity. The commonly used combination of lopinavir/ritonavir should be maximally avoided due to the alarming level of hepatotoxicity observed in COVID-19 patients while providing no significant benefit on the molecular level. This calls for tailored strategies for NAFLD patients infected with COVID-19, in which drug recommendations, guidelines, and dosages need to be further researched and adjusted. The tendency for poorer outcomes also calls for greater vaccination efforts in the respective population, where patients with NAFLD (or any other gastrointestinal-related illness) should receive priority for COVID-19 vaccination and booster shots. Moreover, to curb the potentially worsening clinical parameters of NAFLD patients, it is strongly advised to engage in comprehensive multidisciplinary coordination through a team of pulmonologists and hepatologists to optimize the management and outcomes of such patients. Long-term complications of concomitant NAFLD and COVID-19 have not been clearly identified; thus, regular follow-up with a multidisciplinary team is essential for surveillance and monitoring for new changes or worsening hepatic function in NAFLD patients. Certain developments are strongly encouraged to arrive at a sustainable conclusion regarding the influence of NAFLD on COVID-19-related endpoints. First, the publication of global longitudinal data is important in evaluating robust trends and patterns in outcomes and identifying hotspots that may be disproportionately impacted. Additionally, future prospective observational or randomized studies are preferred due to their relatively lower risk of biases in light of the current conflicting evidence[8]. Second, the discovery of novel biomarkers with prognostic significance can serve as an indispensable tool for clinicians in creating an optimal and personalized management strategy and predicting disease severity. Thirdly, additional research on the impact of different therapeutic regimens on the outcome of concomitant NAFLD and COVID-19 is essential, as current literature is unable to reveal sufficient research into novel biomarkers. Finally, research into the social determinants (via regional, ethnic, and socioeconomic analyses) is necessary to implement timely interventions and appropriate policy-making, as Younossi et al[9] revealed an interesting increase in prevalence in Hispanic patients.

In contrast, a greater mortality rate was observed in white patients, potentially setting the stage for future studies that provide greater insights into the impact of race or ethnicity on NAFLD outcomes. NAFLD affects a heterogeneous patient population. Although the primary driver in many patients is metabolic syndrome, a complex and dynamic heterogeneous interaction of different factors are involved. This another look was not accomplished to make clear reason the partnership between NAFLD/MAFLD and COVID-19 was seen.

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