Malaysian Journal of Social Sciences and Humanities (MJSSH) (e-ISSN : 2504-8562)
2025, Volume 10, Issue 9, e003584
DOI: https://doi.org/10.47405/mjssh.v10i9.3584

RESEARCH ARTICLE

Impact of Non-Alcoholic Fatty Liver Disease on COVID-19 Severity and Healthcare Outcomes: A Systematic Review

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KEYWORDS:
Non-Alcoholic Fatty Liver Disease (NAFLD)
COVID-19 severity
Liver injury
Comorbidities
Immune dysregulation

CITATION:
Mesk Ghulais, AbdulRahman Muthanna, Nurliyana Najwa Md Razip, Hasni Idayu Saidi, Ummi Nadira Daut, Khaled Belal, & Huzwah Khaza'ai. (2025). Impact of Non-Alcoholic Fatty Liver Disease on COVID-19 Severity and Healthcare Outcomes: A Systematic Review. *Malaysian Journal of Social Sciences and Humanities (MJSSH), 10*(9), e003584. https://doi.org/10.47405/mjssh.v10i9.3584

ABSTRACT

The systematic review investigated the association between non-alcoholic fatty liver disease (NAFLD) and COVID-19, focusing on pathophysiology, clinical outcomes, and public health implications. A comprehensive search of EBSCO, Scopus, and PubMed from January 2020 to December 2022 was conducted, following PRISMA guidelines. Included studies involved patients diagnosed with NAFLD or metabolic-associated fatty liver disease (MAFLD) and reported relevant comorbidities and COVID-19 outcomes. Quality was assessed using tools like the Newcastle-Ottawa Scale and AMSTAR-2. The review found that COVID-19 patients with NAFLD often had multiple comorbidities, especially diabetes and cardiovascular disease, which worsened outcomes. NAFLD was linked to higher hospitalization rates (odds ratio ~3.25), longer hospital stays by about two days, increased oxygen supplementation, higher ICU admissions, and a trend toward increased mortality, though mortality significance varied. Liver injury, indicated by elevated ALT and AST levels and hepatic steatosis on imaging, correlated with severe COVID-19. NAFLD patients showed systemic inflammation, immune dysregulation, and coagulation

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abnormalities contributing to disease severity. Ethnic disparities were noted, with certain groups having higher NAFLD prevalence and worse COVID-19 outcomes. These findings reveal challenges for healthcare systems due to increased resource demands and the need for integrated liver function monitoring during COVID-19 care. Overall, NAFLD significantly impacts COVID-19 severity through complex metabolic and immunological pathways, emphasizing the importance of clinical vigilance and multidisciplinary management for this high-risk population.

Contribution/Originality: This study documents the links NAFLD with severe COVID-19 outcomes, driven by metabolic, inflammatory, and immune factors. It highlights increased hospitalization, ICU admission, and ethnic disparities, emphasizing the need for vigilant liver monitoring and multidisciplinary care to improve prognosis and reduce healthcare burdens in affected patients.

1. Introduction

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), represents an extraordinary global health crisis that has profoundly impacted clinical practice and public health worldwide (World Health Organization [WHO], 2020). Characterized primarily by respiratory symptoms, COVID-19 often induces systemic inflammation and multi-organ involvement, with acute respiratory distress syndrome (ARDS) following a cytokine storm being a predominant cause of mortality (Zhang et al., 2020). Importantly, the extent and severity of COVID-19 are influenced by underlying comorbidities, which exacerbate patient outcomes and complicate clinical management (Chen et al., 2021). Among prevalent comorbidities, Non-Alcoholic Fatty Liver Disease (NAFLD), a metabolic condition marked by hepatic fat accumulation unrelated to alcohol use, has emerged as a crucial factor influencing COVID-19 progression (Hussain et al., 2020).

NAFLD is strongly associated with metabolic syndrome components such as obesity, type 2 diabetes mellitus, and hypertension, all of which have consistently been identified as risk factors for severe COVID-19 illness and related complications (Ji et al., 2020). Clinical studies have demonstrated that individuals with NAFLD show increased susceptibility to SARS-CoV-2 infection and a higher likelihood of severe disease manifestations, including increased hospitalization duration, heightened intensive care unit (ICU) admission rates, and elevated mortality risks (Hashemi et al., 2021; Yip et al., 2021). These findings suggest that NAFLD may potentiate COVID-19 severity through complex pathophysiological mechanisms involving hepatic inflammation, immune dysregulation, and systemic metabolic dysfunction, although the precise interplay remains under active investigation (Sharma et al., 2021).

Liver involvement in COVID-19 is not merely a bystander effect but a significant clinical concern, given the liver's central role in metabolic homeostasis and immune function. SARS-CoV-2 can directly infect liver cells via angiotensin-converting enzyme 2 (ACE2) receptors, particularly cholangiocytes, leading to hepatic inflammation, bile duct dysfunction, and elevated liver enzymes indicative of liver injury (WHO, 2021; Montori, 2023). The presence of NAFLD may prime the liver for increased vulnerability, as

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steatotic livers often exhibit baseline inflammation and compromised regenerative capacity, thereby exacerbating liver injury during COVID-19 (Fan et al., 2020). Elevated markers of liver damage, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), have been correlated with severe COVID-19 phenotypes, longer viral shedding time, and higher mortality rates in this population (Ji et al., 2020; Chen et al., 2021).

From a clinical management perspective, the convergence of NAFLD and COVID-19 presents several challenges. Patients with NAFLD frequently exhibit altered immune responses and impaired hepatic metabolism, which can influence drug pharmacokinetics and increase the risk of adverse drug reactions, particularly when hepatotoxic medications, such as lopinavir/ritonavir, are used in COVID-19 treatment protocols (Zhang et al., 2022). Moreover, metabolic comorbidities common in NAFLD patients, such as obesity and diabetes, further compound risks for poor COVID-19 outcomes, necessitating multidisciplinary approaches for optimized patient care (Hussain et al., 2020). The identification and monitoring of liver function abnormalities during COVID-19 hospitalizations are essential for early intervention and may help reduce morbidity and mortality in this high-risk group.

NAFLD's high global prevalence, estimated to affect about 25% of the population, combined with its frequent underdiagnosis, underscores the need for widespread screening and public health initiatives to address metabolic health broadly (Vrsaljko et al., 2022). In the context of the pandemic, populations with greater NAFLD burden—often correlated with socioeconomic determinants such as lifestyle, diet, and access to healthcare—may experience disproportionately worse COVID-19 outcomes, exacerbating health disparities (Prins & Olinga, 2020). This intersection highlights the urgent imperative for integrated public health strategies that address chronic metabolic diseases alongside infectious threats to mitigate overall disease burden.

This systematic review aims to consolidate current clinical evidence regarding the interaction between COVID-19 and NAFLD, with a focus on elucidating pathophysiological mechanisms, characterizing clinical outcomes, and addressing public health and healthcare system implications. By analyzing data from global populations, especially those with high NAFLD prevalence, this work seeks to inform clinical guidelines and policy decisions for managing patients with overlapping metabolic and infectious disease challenges (Ji et al., 2020; Hashemi et al., 2021). Ultimately, such integrative efforts are critical to improving prognosis, resource allocation, and health equity in the ongoing battle against COVID-19 and its multifaceted complications.

2. Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement Checklist to ensure transparency and reproducibility.

2.1. Search Strategy

A comprehensive literature search was systematically performed across three electronic databases: EBSCO, Scopus, and PubMed, for articles published between January 2020 and December 2022. The search was limited to English-language publications to maintain language consistency. The search terms combined keywords related to COVID-

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19 (e.g., “COVID-19”, “SARS-COV-2”, “COVID-19 mortality”) with liver-related terms (including “NAFLD”, “MAFLD”, “liver injury”, “hepatic steatosis”, “AST/ALT ratio”, “AST Platelet ratio index”). Boolean operators were employed to optimize the search sensitivity and comprehensiveness.

2.2. Study Selection

Two independent reviewers conducted the initial screening by evaluating titles and abstracts against predefined inclusion and exclusion criteria. Eligible studies included epidemiological research and systematic reviews with meta-analyses focusing on NAFLD or MAFLD in patients with COVID-19. These studies were required to report on relevant comorbidities such as hypertension, diabetes, hyperlipidemia, and chronic kidney disease. Disagreements between reviewers were resolved through discussion to reach consensus. For the final screening, the open-source Systematic Review-Accelerator (SR-A) software was utilized to increase screening efficiency and reduce human error.

2.3. Quality Assessment

The methodological quality of the included studies was assessed independently by two reviewers using standardized quality assessment tools appropriate for the study designs, such as the Newcastle-Ottawa Scale (NOS) for observational studies and AMSTAR-2 for systematic reviews and meta-analyses. Studies were evaluated across multiple domains including selection bias, comparability, and outcome assessment. Any discrepancies in quality ratings were resolved by discussion or consultation with a third reviewer.

2.4. Data Extraction

Relevant data were extracted independently by two reviewers using a standardized data extraction form designed to capture essential study characteristics: author information, publication year, study design, population characteristics, details of COVID-19 and liver disease diagnosis, reported comorbidities, outcome measures, and key findings. Extracted data were cross-checked for accuracy and completeness, with disagreements resolved through consensus.

3. Results

3.1. Study selection

The selection process is presented visually in the flow diagram (Figure 1). A total of 2,428 papers were identified from three databases as follows: 472 from PubMed, 1,361 from EBSCO, and 595 from Scopus, covering the period from January 2020 and December 2022. After removing 101 duplicate records, 2,327 titles were screened, leading to the exclusion of 1,276 records that did not meet the criteria. Subsequently, 1,051 abstracts were reviewed, with 979 excluded for failing to meet the inclusion criteria. A total of 72 full-text articles were assessed for eligibility, and 53 were further excluded for not meeting the criteria. Ultimately, 19 studies were included in the review.

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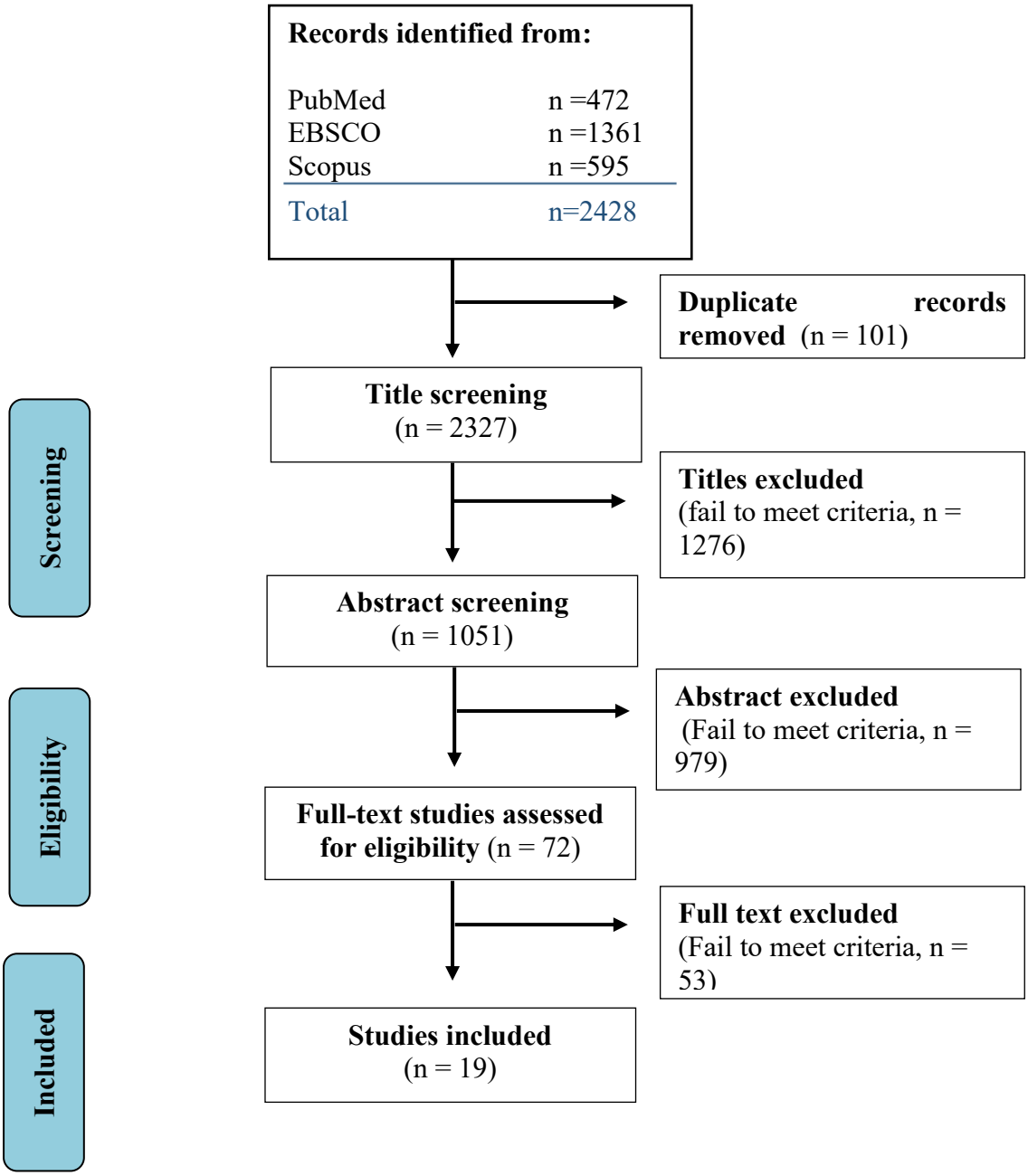
Figure 1: PRISMA flow diagram explaining the methodology to select the eligible studies



3.2. Study characteristics

Table 1 shows a comprehensive summary of studies investigating the complex interaction between COVID-19 and NAFLD. These studies employ a variety of methodological approaches including observational clinical data, statistical and multivariate analyses, systematic reviews, meta-analyses, and advanced imaging techniques. Spanning the period from 2020 to 2022, the included research reflects the evolving understanding of this topic throughout different phases of the global pandemic. The patient cohorts represented in these studies come from diverse geographical regions and encompass multiple ethnic groups, thereby enhancing the robustness and generalizability of the findings. Key aspects examined in the review include prevalent comorbidities often seen in COVID-19 patients with NAFLD, such as cardiovascular disease and diabetes mellitus, as well as the frequency and severity of liver

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involvement—ranging from hepatic steatosis observed in imaging to abnormal liver function tests. Clinical outcomes documented include mortality rates, as well as the need for ICU admission and mechanical ventilation. Additionally, the table highlights investigations into fundamental pathophysiological mechanisms underlying this interaction, such as systemic inflammation, immune dysregulation, and coagulopathy. Collectively, these studies offer a multidimensional perspective on how NAFLD influences COVID-19 disease progression and severity, with important implications for clinical management and public health policy.

Table 1: Summary of Studies Investigating Clinical Characteristics, Liver Involvement, Pathophysiological Mechanisms, and Outcomes in COVID-19 Patients with Non-alcoholic Fatty Liver Disease (NAFLD)

Author(s)	Factors/Comorbidities	Tools/Methods	Main Results/Findings
Ji et al. (2020)	Cardiovascular disease, endocrine disorders (diabetes), respiratory diseases, malignant tumors	Systematic review	High prevalence of comorbidities contributing to severity in COVID-19 patients with NAFLD
Nafakhi et al. (2021)	Diabetes mellitus	Statistical analysis (OR calculation)	Diabetes strongly associated with increased mortality risk (OR 2.2, $p < 0.001$)
Jeeyavudeen et al. (2021)	Ethnicity (Black race predominance)	Demographic analysis	Ethnic disparities in NAFLD COVID-19 hospitalizations highlighting socioeconomic/genetic vulnerability
Yip et al. (2021)	Liver injury	Clinical/lab data analysis	Liver injury in 5.1% severe patients; mortality rate associated with liver injury (0.4%, $p < 0.001$)
Du et al. (2022)	Liver illness	Clinical outcome comparison	Liver illness patients had higher mortality (12.4% vs. 7%, $p = 0.018$) and coagulation abnormalities
Sharma et al. (2021)	Pre-existing liver disease	Meta-analysis	Increased death risk from COVID-19 in liver disease patients (RR=2.8, 95% CI 1.9–4.0, $p < 0.001$)
Chang et al. (2022)	NAFLD	Clinical outcome analysis	NAFLD independently predicted ICU admission and mechanical ventilation requirement
Lei et al. (2020)	Hepatic steatosis, liver hypodensity, pericholecystic fat stranding	Imaging (CT scans)	26.09% liver hypodensity, 21.27% pericholecystic fat; liver hypodensity more common in critical cases (58.82%), linked to severe COVID-19
Parlak et al. (2025)	Hepatic steatosis	Imaging (chest CT)	Hepatic steatosis predicted severe disease (OR 3.8, $p < 0.001$)

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Kumar et al. (2020)	Elevated liver enzymes, systemic inflammation	Lab biomarker analysis	NAFLD patients had elevated ALT, AST, and CRP indicating pro-inflammatory state increasing COVID-19 severity
Jafarzadeh et al. (2021)	Lymphopenia, immune dysfunction, liver injury	Immune and clinical labs	Lymphopenia independently associated with liver injury linking immune dysfunction to hepatic damage
Robea et al. (2023)	Coagulopathy	Clinical coagulation parameters	Coagulopathy associated with poorer prognosis and organ failure, worsened by NAFLD's metabolic/inflammatory effects
Lazarus et al. (2022)	Obesity	Epidemiological analysis	Obesity identified as a modifiable risk factor linked to NAFLD contributing to severe COVID-19 outcomes

3.3. Clinical Characteristics and Comorbidities in COVID-19 Patients with NAFLD

The studies included in this systematic review consistently identified a high prevalence of comorbid conditions among COVID-19 patients with underlying NAFLD, which appear to contribute significantly to disease severity and clinical outcomes. Ji et al. (2020) reported that cardiovascular disease, endocrine disorders including diabetes mellitus, respiratory diseases, and malignant tumors were common among COVID-19 patients, underscoring the multifactorial health burden in this population. Notably, Nafakhi et al. (2021) demonstrated that diabetes mellitus was strongly associated with increased mortality risk (odds ratio [OR] 2.2, $p < 0.001$), aligning with the understanding that metabolic comorbidities compound COVID-19 severity. The ethnic distribution of NAFLD in COVID-19 hospitalizations also reflected disparities, with Jeeyavudeen et al. (2021) identifying a predominance of black race, suggesting potential socioeconomic and genetic factors influencing vulnerability. These comorbidities and demographic characteristics provide a critical foundation for understanding how NAFLD intersects with COVID-19 morbidity and help contextualize subsequent findings regarding clinical outcomes and pathophysiological changes.

3.4. Liver Involvement and Clinical Outcomes in COVID-19 Patients with NAFLD

The interaction between COVID-19 and liver pathology, particularly in patients with NAFLD, was a prominent theme in the reviewed studies, demonstrating significant implications for clinical outcomes. Multiple studies consistently reported that liver injury and elevated liver enzymes were common among COVID-19 patients, with severity correlating to worse prognosis. Yip et al., (2021) found that 5.1% of severe COVID-19 patients sustained liver injury, accompanied by a notably high mortality rate of 0.4% ($p < 0.001$), highlighting liver involvement as a critical factor in disease progression. Similarly, Du et al. (2022) identified that patients with liver illness experienced significantly higher mortality rates (12.4% vs. 7%, $p = 0.018$), along with coagulation abnormalities, which further complicate the clinical course. Meta-analytic evidence by Sharma et al. (2021) reinforces these findings, showing that pre-existing liver disease increases the risk of death from COVID-19 (relative risk = 2.8; 95% confidence interval, 1.9–4.0; $p < 0.001$). In addition to mortality, Chang et al. (2022) demonstrated that NAFLD independently predicted ICU admission and the need for

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mechanical ventilation, underscoring the impact of hepatic comorbidity on healthcare resource utilization. Moreover, Imaging studies have also shown notable hepatic steatosis in COVID-19 patients. Lei et al. (2020) found that 26.09% of patients exhibited liver hypodensity and 21.27% had pericholecystic fat stranding. Liver hypodensity was observed more commonly in critical cases (58.82%), and fatty liver was linked to more severe COVID-19 symptoms. Parlak et al. (2025) further supported this by showing hepatic steatosis on chest CT scans predicted severe disease (OR 3.8, $p < 0.001$). Collectively, these data confirm that liver involvement in COVID-19, compounded by NAFLD, contributes to worse clinical outcomes, emphasizing the need for routine liver assessment and careful management in this high-risk group.

3.5. Pathophysiological Mechanisms Linking NAFLD and COVID-19 Severity

The interplay between NAFLD and COVID-19 severity is underpinned by several pathophysiological mechanisms that exacerbate disease progression. Studies consistently indicate that patients with NAFLD exhibit heightened systemic inflammation, immune dysregulation, and coagulopathy, all of which contribute to adverse outcomes in COVID-19. Kumar et al. (2020) reported that NAFLD patients presented with significantly elevated liver enzymes—ALT and AST—alongside increased levels of C-reactive protein, a marker of systemic inflammation, suggesting a pro-inflammatory state that may amplify COVID-19 severity. Furthermore, Jafarzadeh et al. (2021) found that lymphopenia, a hallmark of immune dysfunction in COVID-19, was independently associated with liver injury, linking impaired immune response to hepatic damage. Coagulopathic abnormalities, highlighted by Robea et al. (2023), have also been implicated in poorer prognosis and organ failure, with NAFLD potentially exacerbating these coagulation disturbances due to its metabolic and inflammatory milieu. The cumulative effect of these mechanisms may promote a cycle of hepatic and systemic injury, heightening the risk for more severe respiratory compromise, multi-organ dysfunction, and death. This pathophysiological synergy underscores the importance of early identification and targeted management strategies to mitigate the compounded risks faced by COVID-19 patients with NAFLD.

3.6. Public Health and Healthcare System Implications of COVID-19 in Patients with NAFLD

The convergence of COVID-19 and NAFLD presents substantial challenges for public health and healthcare systems globally, underscoring the urgency for tailored strategies to address this high-risk population. The reviewed studies elucidate that the high prevalence of metabolic comorbidities, such as diabetes and cardiovascular disease, alongside liver dysfunction, contributes to increased healthcare resource utilization, including higher rates of ICU admissions and mechanical ventilation (Chang et al., 2022). This amplified burden strains critical care capacities, particularly in regions with already limited healthcare infrastructure. Jeeyavudeen et al. (2021) highlighted notable ethnic disparities in NAFLD prevalence among hospitalized COVID-19 patients, emphasizing the need for culturally sensitive and equitable healthcare interventions targeting vulnerable groups, such as Hispanic populations disproportionately affected. Furthermore, the documented high rates of liver injury and associated mortality (Yip et al., 2021; Du et al., 2022) call for integrating liver function monitoring into COVID-19 management protocols, which necessitates additional training, diagnostic resources, and interdisciplinary collaboration. From a public health perspective, these findings advocate for intensified screening and preventive measures addressing modifiable risk

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factors linked to NAFLD, such as obesity (Lazarus et al., 2022), to mitigate severe COVID-19 outcomes. Policymakers must prioritize resource allocation and develop guidelines supporting early identification, risk stratification, and comprehensive care for COVID-19 patients with NAFLD to reduce morbidity and mortality, while alleviating systemic healthcare pressures.

4. Discussion

This systematic review consolidates growing clinical evidence that patients with NAFLD represent a uniquely vulnerable subgroup during the COVID-19 pandemic, characterized by a convergence of metabolic, inflammatory, and hepatic pathological processes that intensify disease severity. The predominance of metabolic comorbidities such as DM and CVD among COVID-19 patients with NAFLD, consistently highlighted across multiple studies (Ji et al., 2020; Nafakhi et al., 2021), corroborates the notion that NAFLD exists within the broader context of metabolic syndrome, which itself is a known risk factor for adverse COVID-19 outcomes. This clustering of comorbidities complicates clinical management and underscores the necessity for integrated approaches targeting metabolic health as part of COVID-19 mitigation strategies.

Liver involvement in COVID-19, particularly among those with pre-existing NAFLD, emerges as a critical driver of poor prognosis, evidenced by elevated liver enzymes, hepatic steatosis, and increased mortality rates (Yip et al., 2021; Du et al., 2022; Lei et al., 2020). The augmented risk of liver injury and dysfunction may reflect both direct viral effects and an exacerbation of underlying chronic hepatic inflammation that predisposes patients to multi-organ failure. These findings align with meta-analytic evidence showing significantly increased mortality associated with liver disease in COVID-19 (Sharma et al., 2021), stressing the importance of early identification and rigorous monitoring of liver function throughout clinical care pathways for COVID-19 patients.

At a mechanistic level, this review highlights that systemic inflammation, immune dysregulation, and coagulopathy interplay to amplify COVID-19 severity in NAFLD patients (Kumar et al., 2021; Jafarzadeh et al., 2021; Robea et al., 2023). Elevated inflammatory biomarkers and deranged immune cell profiles likely perpetuate hepatic injury and propagate systemic complications such as thrombosis and respiratory failure. This complex pathophysiology suggests potential therapeutic targets that merit further investigation, including modulation of inflammatory cascades and correction of coagulopathic states, to improve patient outcomes. Additionally, the immune impairments documented emphasize the need for vaccine prioritization and tailored clinical interventions for patients with fatty liver disease.

The public health implications of the intersection between NAFLD and COVID-19 are substantial. The disproportionate burden borne by ethnic minority groups, such as Hispanic populations who exhibit higher NAFLD prevalence among hospitalized patients (Jeeyavudeen et al., 2021), accentuates longstanding health disparities that the pandemic has exacerbated. This calls for culturally and socioeconomically sensitive public health policies, enhanced screening programs, and community-based preventive measures focused on lifestyle modification and metabolic health optimization to prevent severe COVID-19 outcomes in vulnerable populations. Health systems must also anticipate and address the increased demand for intensive care resources posed by this high-risk group (Chang et al., 2022).

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While this review advances understanding of COVID-19 and NAFLD interplay, several limitations warrant consideration. The heterogeneity of included studies—in population demographics, methodologies, and outcome measures—may introduce bias and limits direct comparability. Additionally, most studies were observational and retrospective, restricting causal inferences. Future longitudinal and mechanistic studies are required to clarify the temporal relationships and biological pathways underpinning NAFLD's impact on COVID-19, and to validate targeted therapeutic and preventive interventions. Furthermore, exploring the influence of emerging SARS-CoV-2 variants and vaccination status in this patient population remains an important area for ongoing research.

This systematic review is subject to several limitations that should be acknowledged. First, the included studies exhibited significant heterogeneity in study design, patient populations, definitions of NAFLD, and outcome measures, limiting the comparability and synthesis of findings. Many studies were observational and retrospective in nature, which inherently restricts the ability to establish causal relationships between NAFLD and COVID-19 severity or outcomes. Additionally, variations in diagnostic criteria for liver injury and inconsistent use of imaging or biomarkers across studies may have introduced measurement bias. The evolving nature of the COVID-19 pandemic, including different viral variants, treatment protocols, and vaccination statuses during study periods, further complicates the interpretation and applicability of results to current clinical contexts. Finally, there is a paucity of data addressing long-term outcomes post-COVID-19 in patients with NAFLD, representing a critical gap for future research.

Despite these limitations, this systematic review provides valuable contributions to the understanding of the interface between COVID-19 and NAFLD. The comprehensive approach, incorporating diverse study types—ranging from clinical observations and epidemiological analyses to meta-analyses and imaging studies—strengthens the robustness of the conclusions drawn. Inclusion of multiple geographic populations enhances generalizability and captures ethnic and socioeconomic disparities relevant to global health. The focus on both pathophysiological mechanisms and clinical outcomes offers a multidimensional perspective that integrates molecular, clinical, and public health insights. Moreover, the use of rigorous methodological standards for study selection and a detailed analysis of liver-specific parameters uniquely highlights the clinical importance of hepatic involvement in COVID-19 among patients with NAFLD.

5. Conclusion

In conclusion, the consolidated clinical evidence highlights that NAFLD significantly influences the course and outcomes of COVID-19 through a complex interplay of metabolic, inflammatory, and immunological factors. Patients with NAFLD frequently present with multiple comorbidities such as diabetes and cardiovascular disease, which synergistically increase vulnerability to severe COVID-19 manifestations, including higher rates of liver injury, ICU admission, and mortality. The reviewed studies demonstrate that liver involvement, marked by elevated enzymes and hepatic steatosis, is both a common and prognostically important feature in this population. Underlying pathophysiological mechanisms such as systemic inflammation, immune dysregulation, and coagulopathy appear to mediate these adverse outcomes, suggesting potential therapeutic targets. Moreover, the disproportionate impact on certain ethnic groups and the consequent strain on healthcare systems elucidate critical public health challenges that demand comprehensive prevention, screening, and management strategies tailored to patients with NAFLD. These findings underscore the necessity for heightened clinical

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vigilance and interdisciplinary approaches to improve prognosis and mitigate the burden of COVID-19 in this high-risk group.

Ethics Approval and Consent to Participate

Ethical approval for this study was obtained from the Ethics and Research Committee of King Fahad Hospital, Hofuf, Al Ahsa, Kingdom of Saudi Arabia (reference number IRB-H-05-HS-065).

Acknowledgement

This review was made possible by the Universiti Putra Malaysia (UPM) Library, which provided access to the necessary articles and databases for the completion of the review.

Funding

This study received no funding.

Conflict of Interest

The authors declare no conflict of Interest.

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