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Haematological Dysfunction as a Predictor of Hepatic Alterations in COVID-19 Patients: A Retrospective Cohort Study

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ABSTRACT

Background: COVID-19 is a multisystemic disease affecting various organs, including the haematological and hepatic systems. Identifying correlations between haematological dysfunction and hepatic alterations may provide valuable insight into predicting disease severity and outcomes in COVID-19 patients.

Aim: This study aimed to investigate whether haematological abnormalities, particularly elevated white blood cell (WBC) counts and inflammatory markers, can serve as predictors of hepatic dysfunction in COVID-19 patients.

Methods: A retrospective cohort study was conducted on 442 hospitalized COVID-19 patients at a tertiary care hospital in Saudi Arabia. Demographic, clinical, and laboratory data were collected, including haematological markers (haemoglobin, WBC, ferritin) and liver function tests (ALT, AST, albumin). Associations between haematological findings and hepatic dysfunction were analysed using chi-square tests, t-tests, and multivariate logistic regression to identify independent predictors of liver dysfunction.

Results: Elevated WBC counts (p=0.027) and ferritin levels (p=0.042) were significantly correlated with higher ALT and AST levels, indicating hepatic dysfunction. Low haemoglobin levels were associated with lower albumin levels (p=0.009) and prolonged prothrombin time (p=0.016), though they were not independent predictors of liver enzyme elevations. Multivariate analysis showed that elevated WBC (AOR=1.095, p=0.027) and ferritin (AOR=1.253, p=0.042) were significant predictors of hepatic dysfunction.

Conclusion: Haematological dysfunction, particularly elevated WBC counts and ferritin levels, is a significant predictor of hepatic alterations in COVID-19 patients. Monitoring these markers can help identify patients at higher risk of liver injury, potentially guiding clinical management and improving outcomes.

Keywords: COVID-19, haematological dysfunction, hepatic dysfunction, WBC, ferritin, liver enzymes

Introduction:

The COVID-19 pandemic has profoundly impacted global health, challenging medical systems and scientific communities to find ways to predict disease severity and outcomes [1]. As the pandemic unfolded, the ability to predict how COVID-19 would affect individual patients became an urgent focus. Understanding which biomarkers could signal the trajectory of the disease is critical for guiding clinical decisions and resource allocation, particularly in overburdened healthcare systems [2]. Among the many clinical features examined, hepatic and haematological indices have emerged as potential predictors of disease progression and outcomes in COVID-19 patients, especially in the context of severe cases [3].

COVID-19, caused by the SARS-CoV-2 virus, primarily affects the respiratory system, but its impact is far from limited to the lungs. As early studies highlighted, COVID-19 is a multisystem disease that can lead to severe complications across various organ systems, including the liver and haematological systems [4]. Patients with severe forms of the disease often present with abnormal liver function tests (LFTs) and haematological disturbances, raising questions about their role in predicting the outcome of COVID-19 [5]. The identification of reliable prognostic biomarkers is crucial in understanding which patients are more likely to develop severe forms of the disease, require intensive care, or succumb to the infection [6].

Liver dysfunction in COVID-19 has been well-documented, with many patients presenting abnormal

liver function tests upon hospital admission. These abnormalities may reflect a direct viral effect on the liver, but they can also be secondary to other factors such as systemic inflammation, drug-induced liver injury, or hypoxia-related damage [7]. A study reported that liver injury, as evidenced by elevated levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), was significantly associated with worse outcomes in COVID-19 patients, particularly in those requiring intensive care [8].

The liver plays a vital role in many physiological processes, including the detoxification of drugs and the regulation of immune responses. Therefore, any damage to the liver, either directly through the viral infection or as part of the systemic inflammatory response associated with severe COVID-19, can contribute to poorer patient outcomes [9]. In particular, patients with underlying liver diseases such as cirrhosis or non-alcoholic fatty liver disease (NAFLD) appear to be at higher risk of developing severe complications from COVID-19 [10]. This highlights the importance of monitoring liver function in patients hospitalized with COVID-19, as early recognition of liver dysfunction could provide valuable insights into the patient's prognosis [11].

In addition to hepatic indices, haematological parameters such as lymphopenia, thrombocytopenia, and elevated levels of D-dimer have also been associated with worse outcomes in COVID-19 patients [12]. Hematological indices offer insights into the immune response to SARS-CoV-2 infection and the overall systemic inflammation that characterizes severe cases of the disease [13]. Early in the pandemic, studies revealed that lymphopenia, or a reduced number of lymphocytes, was one of the most consistent laboratory findings in severe COVID-19 patients [14]. The depletion of lymphocytes, particularly T cells, suggests an impaired immune response, which may contribute to the progression of the disease and an increased likelihood of developing complications such as acute respiratory distress syndrome (ARDS) [15].

Another significant haematological marker that has been widely studied in COVID-19 patients is D-dimer, a fibrin degradation product. Elevated D-dimer levels are associated with a hypercoagulable state, which has been observed in many patients with severe COVID-19 [16]. This condition increases the risk of thrombotic events, such as pulmonary embolism, deep vein thrombosis, and stroke, all of which contribute to the poor prognosis of critically ill COVID-19 patients [17]. Monitoring D-dimer levels can therefore serve as a valuable tool in predicting which patients are at a higher risk of developing severe complications or succumbing to the disease [18].

Platelet count, another key haematological parameter, has also been shown to be associated with COVID-19 outcomes. Thrombocytopenia, or a low platelet count, has been linked to increased disease severity and higher mortality rates in COVID-19 patients [19]. The mechanisms behind COVID-19-induced thrombocytopenia are not yet fully understood, but it is believed to be related to both viral-induced bone marrow suppression and increased platelet consumption due to systemic inflammation and endothelial damage [19].

Given the multi-organ involvement of COVID-19, it is becoming increasingly clear that no single biomarker is sufficient to predict outcomes reliably. However, hepatic and haematological indices together offer a promising approach to stratifying patients based on their risk of developing severe disease [20]. These indices are relatively easy to obtain through routine blood tests, making them practical tools in both resource-rich and resource-limited settings [21]. Future research is needed to refine the use of these biomarkers in clinical practice, particularly in the context of early interventions that could potentially alter the disease course for high-risk patients.

Methods

Study Design

This was a retrospective, observational study conducted over a six-month period from July 2020 to January 2021. The study coincided with the first peak of COVID-19 infections in Saudi Arabia and aimed to evaluate the relationship between anemia, hepatic enzyme levels, and clinical outcomes (cure rates, morbidities, and mortality) in patients infected with COVID-19. Data were collected from the electronic medical records (EMRs) of hospitalized patients diagnosed with COVID-19. The study followed the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of King Fahad Hospital Al-Ahsa (IRB Registration number: KFHH H-05-HS-065). Given the retrospective design, the requirement for informed consent was waived by the IRB.

Study Setting

The study was conducted at King Fahad Hospital Al-Ahsa, a tertiary care hospital in Saudi Arabia, which served as a key treatment center for COVID-19 patients during the pandemic. The hospital has specialized departments for intensive care, infectious diseases, and

internal medicine, making it well-equipped to handle severe COVID-19 cases and to provide comprehensive care, including laboratory testing and imaging diagnostics, which were crucial for this study.

Study Population

The target population included all adult patients (aged 18 years or older) who were hospitalized at King Fahad Hospital Al-Ahsa during the study period with a confirmed diagnosis of COVID-19, as indicated by a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test for SARS-CoV-2. The inclusion and exclusion criteria were carefully defined to ensure a homogeneous sample of COVID-19 patients without confounding factors related to pre-existing liver conditions.

Inclusion Criteria:

- Patients aged 18 years and older.
- A confirmed diagnosis of COVID-19 based on a positive RT-PCR test.
- Admitted to the hospital for COVID-19 treatment during the study period.
- Availability of complete demographic, clinical, and laboratory data.

Exclusion Criteria:

- Patients with pre-existing liver diseases or chronic liver function abnormalities, such as chronic hepatitis B or C, autoimmune hepatitis, or alcoholic liver disease.
- Patients with incomplete medical records, particularly those missing key laboratory data such as liver enzymes and haemoglobin levels.
- Patients with comorbidities that could independently affect liver function, including end-stage liver disease, hepatocellular carcinoma, or significant alcohol use.
- Patients with missing laboratory or imaging data related to liver function.

Data Collection

Data were extracted from the hospital's electronic medical record system, which maintained detailed clinical and laboratory information on all hospitalized patients. A pre-designed data collection form was used to ensure consistency and completeness of the data extraction process. The following data were collected for each patient:

- **Demographic data:** Age, gender, and pre-existing comorbidities (e.g., diabetes, hypertension, chronic kidney disease, cardiovascular disease).
- **Clinical data:** Duration of hospitalization, symptoms at admission (e.g., fever, cough, dyspnea), disease severity at admission (mild, moderate, or severe based on WHO criteria), need for intensive care unit (ICU) admission, mechanical ventilation, and clinical outcomes (cure, morbidity, or mortality).
- **Laboratory data:** Hemoglobin levels, liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin. Additional haematological parameters such as platelet count, white blood cell count, lymphocyte count, and D-dimer levels were collected. These laboratory parameters were measured on admission and during the course of the patients' hospital stay.
- **Imaging data:** Radiological findings (chest X-rays and CT scans) were reviewed to assess the extent of lung involvement and any complications related to COVID-19 infection, such as pneumonia or pulmonary embolism.

Study Outcomes

The primary outcomes of interest were the relationship between anemia and hepatic dysfunction with the clinical outcomes of COVID-19 patients, specifically cure rates, morbidity (defined as any complication arising during hospitalization), and mortality. Secondary outcomes included the need for ICU admission and mechanical ventilation, and the length of hospital stay.

Anemia was defined as a haemoglobin concentration of less than 13.0 g/dL in men and less than 12.0 g/dL in women, based on the World Health Organization criteria. Hepatic dysfunction was defined by abnormal liver function tests, with elevated levels of ALT and AST being the primary markers of liver injury.

Statistical Analysis

All collected data were entered into a secure database and analysed using the Statistical Package for the Social Sciences (SPSS) software, version 21 (IBM Corp, Armonk, NY). Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Continuous variables, such as age and laboratory values, were expressed as means ± standard deviations (SD) for normally distributed data, or medians and interquartile ranges (IQR) for non-normally distributed data. Categorical variables, such as gender and comorbidities, were presented as frequencies and percentages.

Comparative analyses were performed to evaluate the relationship between anemia, liver function abnormalities, and patient outcomes. For continuous variables, independent t-tests were used to compare normally distributed data between groups (e.g., survivors vs. non-survivors), while the Mann-Whitney U test was applied for non-normally distributed data. Categorical variables were compared using chi-square tests or Fisher's exact test, as appropriate.

To determine the independent predictors of mortality and morbidity, multivariate logistic regression models were employed. Variables with a p-value of less than 0.05 in univariate analyses were included in the multivariate models. Adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated for each predictor. A p-value of less than 0.05 was considered statistically significant for all analyses.

Ethical Considerations

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB) of King Fahad Hospital Al-Ahsa (IRB Registration number: KFHH H-05-HS-065). Due to the retrospective nature of the study and the use of de-identified patient data, the requirement for informed consent was waived by the IRB. All data were anonymized before analysis to protect patient confidentiality. Data were stored securely, and access was restricted to authorized research personnel only.

Sample Size Calculation

The sample size was determined based on the number of COVID-19 patients admitted to the hospital during the study period who met the inclusion criteria. A total of 442 patients were included in the final analysis. This sample size was considered adequate to detect statistically significant differences between groups and to provide sufficient power for the multivariate regression analysis.

Results

Baseline Characteristics

The baseline characteristics of the 442 COVID-19 patients are summarized in Table 1. The cohort had a mean age of 54.3 years, with a higher proportion of male patients (64.5%). The majority of the patients were Saudi nationals (76.7%). The overall mortality rate was 20.4%, with 90 patients succumbing to the infection. Radiological investigations revealed that 80.8% of the patients had abnormal chest X-rays, suggesting significant respiratory involvement. The median length of hospital stay was 8 days, ranging from 1 to 155 days, indicating variable disease severity and hospitalization needs among the patients.

Table 1: Baseline Characteristics of the Patients (n=442)

Study Variables	**N (%)**
Age (mean ± SD)	54.3 ± 14.9
Gender	
Male	285 (64.5%)
Female	157 (35.5%)
Nationality	
Saudi	339 (76.7%)
Non-Saudi	103 (22.3%)
Prognosis Outcome	
Alive	352 (79.6%)
Deceased	90 (20.4%)
X-ray Findings	
Normal	85 (19.2%)
Abnormal	357 (80.8%)
CT Scan Findings	
Normal	87 (19.7%)
Bilateral ground-glass opacity	12 (2.7%)
More than one type	25 (5.7%)
Not done	318 (71.9%)
Length of Hospital Stay (median, min-max)	8 (1–155) days

Laboratory investigations revealed significant variations in both haematological and hepatic parameters (Table 2). The mean haemoglobin (Hb) level was 12.9 g/dL, with several patients presenting with elevated liver enzyme levels, including ALT and AST. The average WBC count was 7.71 × 10^9/L, indicating the presence of an inflammatory response. Additionally, patients had elevated inflammatory markers such as ferritin (1139.9 ng/mL) and D-dimer (3.27 mg/L), reflecting the systemic effects of COVID-19. These findings indicate that many patients experienced both haematological and hepatic dysfunction during their illness.

Table 2: Laboratory Characteristics of the Patients (n=442)

Parameter	Mean ± SD
Hemoglobin (Hb) (g/dL)	12.9 ± 2.20
Platelets (×10^9/L)	250.7 ± 93.5
White Blood Cells (WBC) (×10^9/L)	7.71 ± 6.76
Lymphocytes (%)	19.8 ± 15.2
Neutrophils (%)	63.2 ± 26.7
ALT (U/L)	60.2 ± 117.0
AST (U/L)	59.0 ± 90.6
Total Bilirubin (µmol/L)	13.0 ± 36.5
Direct Bilirubin (µmol/L)	4.02 ± 6.19
Albumin (g/L)	31.7 ± 6.68
Urea (mmol/L)	7.47 ± 6.95
Creatinine (µmol/L)	131.2 ± 148.7
Ferritin (ng/mL)	1139.9 ± 1367.9
D-dimer (mg/L)	3.27 ± 6.31

The association between haemoglobin levels and hepatic function parameters is shown in Table 3. Patients with lower haemoglobin levels (n=121) had significantly lower albumin levels (p=0.009), reflecting impaired liver function. Additionally, these patients had prolonged prothrombin time (p=0.016) and activated partial thromboplastin time (p=0.018), suggesting coagulation abnormalities, which are often linked to hepatic dysfunction. Although ALT and AST levels were elevated in patients with low haemoglobin, the differences were not statistically significant.

Table 3: Association Between Hemoglobin Level and Hepatic Function Parameters (n=442)

Parameter	Low Hemoglobin (n=121)	Normal Hemoglobin (n=314)	P-value
ALT (U/L)	54.1 ± 140.9	62.6 ± 107.5	0.503
AST (U/L)	63.8 ± 130.7	57.2 ± 69.7	0.498
Albumin (g/L)	30.3 ± 6.88	32.3 ± 6.58	0.009 **
PT (sec)	14.8 ± 10.5	12.5 ± 3.98	0.016 **
PTT (sec)	37.2 ± 15.8	33.5 ± 7.86	0.018 **
Ferritin (ng/mL)	1197.5 ± 1714.4	1081.5 ± 1196.8	0.522

Table 4 illustrates the correlation between key haematological markers and liver enzyme levels. Elevated WBC counts were significantly associated with higher ALT levels (p=0.027), suggesting a link between the inflammatory response and hepatic dysfunction. Ferritin, a marker of systemic inflammation, was also correlated with higher liver enzyme levels (p=0.042), indicating that patients with greater inflammatory burden had more significant hepatic involvement. Although platelets and haemoglobin were assessed, they did not show a significant correlation with liver enzyme levels.

Table 4: Correlation Between Hematological Markers and Liver Enzymes (n=442)

Parameter	ALT (p-value)	AST (p-value)

WBC	0.027 **	0.065
Ferritin	0.042 **	0.091
Platelets	0.611	0.378
Hemoglobin	0.503	0.498

Multivariate regression analysis revealed that elevated WBC counts and ferritin levels were independent predictors of hepatic dysfunction, as evidenced by higher liver enzyme levels (Table 5). Specifically, higher WBC counts were associated with increased ALT levels (AOR=1.095; 95% CI=0.901-1.331), and elevated ferritin was associated with greater liver involvement (AOR=1.253; 95% CI=1.015-1.505). However, haemoglobin levels were not found to be an independent predictor of hepatic dysfunction after controlling for other variables.

Table 5: Multivariate Regression Analysis of Predictors of Hepatic Dysfunction (n=442)

Factor	**AOR**	**95% CI**	**P-value**
WBC	1.095	0.901 – 1.331	0.027 **
Ferritin	1.253	1.015 – 1.505	0.042 **
Hemoglobin	0.916	0.700 – 1.198	0.521
Albumin	1.051	0.991 – 1.115	0.098
PT	0.935	0.849 – 1.030	0.171

Discussion

This study aimed to investigate the correlation between haematological findings and hepatic dysfunction in COVID-19 patients, with a specific focus on whether haematological abnormalities could predict hepatic function alterations. The findings demonstrate that certain haematological parameters, particularly elevated white blood cell (WBC) counts and ferritin levels, are strongly associated with liver enzyme elevations in COVID-19 patients. These results suggest that haematological dysfunction is a significant predictor of hepatic alterations, highlighting the multisystemic nature of COVID-19 [12].

The baseline characteristics of the cohort showed a mean age of 54.3 years, with a mortality rate of 20.4%. This is consistent with previous studies that have reported higher mortality rates in older COVID-19 patients, particularly those with underlying comorbidities the study had abnormal chest X-rays, reflecting the severe respiratory involvement typical of COVID-19. The median hospital stay of 8 days also aligns with global data, which indicates prolonged hospitalizations for severe cases [22].

Hematologngs as Predictors of Hepatic Dysfunction

One of the key findings of this study is the significant association between elevated WBC counts and liver enzyme levels (ALT and AST). Elevated WBC levels, which indicate an inflammatory response, were strongly correlated with higher ALT levels, suggesting that systemic inflammation contributes to hepatic dysfunction. This finding is consistent with existing literature that links the "cytokine storm" associated with severe COVID-19 to liver injury [22]. Previous studies have at inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP), are elevated in COVID-19 patients with liver injury [22]. The association between elevated ferritin liver enzyme abnormalities in this study further supports the hypothesis that inflammation plays a crucial role in hepatic dysfunction [25].

Ferritin, an acute-phase reactant, is known to increase significantly in response to inflammation and has been proposed as a marker of severe COVID-19 [26]. In this study, elevated ferritin was significantly with higher ALT levels, corroborating findings from earlier research indicating that patients with severe COVID-19 often exhibit both hyperferritinemia and liver enzyme abnormalities [27]. These findings suggest that monitoring ferritin and WBC leveD-19 patients could help clinicians

identify those at risk for hepatic involvement and potentially worse outcomes [28].

The Role of Hemoglobin and Coagulation Abnormalities

Interestingly, while patients with low haemoglobin levels exhibited lower albumin levels and prolonged prothrombin time (PT) and partial thromboplastin time (PTT), low haemoglobin was not an independent predictor of liver enzyme elevations in the multivariate analysis [29]. This suggests that anemia in COVID-19 patients may not directly contribute to hepatic dysfunction but could reflect the overall severity of the disease [30]. Anemia is common in critically ill patients and can result from a combination of factors, including inflammation, hypoxia, and nutritional deficiencies [31].

The association between prolonged PT/PTT and low albumin levels in pth low haemoglobin reflects liver dysfunction, as the liver plays a critical role in coagulation factor synthesis and albumin production [32]. However, the lack of a direct association between low haemoglobin and elevated es suggests that other factors, such as systemic inflammation or hypoxia, may be driving hepatic dysfunction in COVID-19 patients [33].

Implications for Clinical Practice

These findings have important clinical implications. First, the strong association between elevated WBC and ferritin levels and liver enzyme abnormalities suggests that haematological parameters can serve as early indicators of hepatic dysfunction in COVID-19 patients. Monitoring these markers could help clinicians identify patients at risk of developing liver injury, allowing for earlier interventions and closer monitoring of hepatic function. Second, while low haemoglobin levels were associated with coagulation abnormalities and hypoalbuminemia, they were not independent predictors of liver enzyme elevations, suggesting that anemia may not be as directly linked to hepatic injury in COVID-19 as inflammation.

Given the complexity of COVID-19 and its multisystemic effects, the identification of early markers of organ dysfunction is critical for improving patient outcomes. This study contributes to the growing body of evidence that suggests a strong link between systemic inflammation and liver injury in COVID-19 patients . Further research is needed to better understand the mechanisms underlying this relationsexplore potential therapeutic strategies aimed at mitigating inflammation and its effects on the liver.

Limitations

There are several limitations to this study. First, the retrospective design limits the ability to establish causal relationships between haematological dysfunction and hepatic alterations. Second, the study was conducted at a single tertiary care hospital, which may limit the generalizability of the findings to other populations or healthcare settings. Additionally, we did not assess the impact of specific treatments, such as antiviral therapy or corticosteroids, on haematological or hepatic outcomes. Future prospective studies are needed to validate these findings and to explore the long-term effects of haematological dysfunction on hepatic function in COVID-19 patients.

Conclusion

In conclusion, this study demonstrates a significant correlation between haematological dysfunction, particularly elevated WBC and ferritin levels, and hepatic alterations in COVID-19 patients. These findings suggest that haematological markers could serve as valuable predictors of liver injury in patients with COVID-19, allowing for early identification of those at risk for worse outcomes. Further research is needed to fully understand the mechanisms linking systemic inflammation to hepatic dysfunction in COVID-19 and to develop targeted interventions for mitigating these effects.

Data availability statement

All data relevant to the study are included in the article.
Ethics **statements**

Patient consent for **publication**

Not applicable.

Ethics approval

All data collected contained no personal health identifiers.
Formal local audit approval was sought and received for data acquisition from King Fahad Hospital Al-Ahsarecords [Registration number – IRB KFHH No. (H-05-HS-065)] .

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Competing interests None declared

References :

1. Filip R, Gheorghita Puscaselu R, Anchidin-Norocel L, Dimian M, Savage WK. Global Challenges to Public Health Care Systems during the COVID-19 Pandemic: A Review of Pandemic Measures and Problems. *J Pers Med*. 2022;12(8):1295. doi:10.3390/jpm12081295
2. Rizzi M, D'Onghia D, Tonello S, et al. COVID-19 Biomarkers at the Crossroad between Patient Stratification and Targeted Therapy: The Role of Validated and Proposed Parameters. *Int J Mol Sci*. 2022;22(8):7099. doi:10.3390/ijms22087099
3. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of <scp>COVID</scp> -19. *Am J Hematol*. 2020;95(7):834-847. doi:10.1002/ajh.25829
4. Singh A, Zaheer S, Kumar N, Singla T, Ranga S. Covid19, beyond just the lungs: A review of multisystemic involvement by Covid19. *Pathol - Res Pract*. 2021;222:153384. doi:10.1016/j.prp.2021.153384
5. Kariyawasam JC, Jayarajah U, Abeysuriya V, Riza R, Seneviratne SL. Involvement of the Liver in COVID-19: A Systematic Review. *Am J Trop Med Hyg*. 2022;106(4):1026-1041. doi:10.4269/ajtmh.21-1220
6. Baldirà J, Ruiz-Rodríguez JC, Wilson DC, et al. Biomarkers and clinical scores to aid the identification of disease severity and intensive care requirement following activation of an in-hospital sepsis code. *Ann Intensive Care*. 2020;10(1):7. doi:10.1186/s13613-020-0625-5
7. Yu SY, Xie JR, Luo JJ, et al. Liver test abnormalities in asymptomatic and mild COVID-19 patients and their association with viral shedding time. *World J Hepatol*. 2022;14(11):1953-1963. doi:10.4254/wjh.v14.i11.1953
8. Hartl L, Haslinger K, Angerer M, et al. Age-adjusted mortality and predictive value of liver chemistries in a Viennese cohort of <scp>COVID</scp> -19 patients. *Liver Int*. 2022;42(6):1297-1307. doi:10.1111/liv.15274
9. Nardo AD, Schneeweiss-Gleixner M, Bakail M, Dixon ED, Lax SF, Trauner M. Pathophysiological mechanisms of liver injury in COVID-19. *Liver Int*. 2021;41(1):20-32. doi:10.1111/liv.14730
10. Dietrich CG, Geier A, Merle U. Non-alcoholic fatty liver disease and COVID-19: Harmless companions or disease intensifier? *World J Gastroenterol*. 2022;29(2):367-377. doi:10.3748/wjg.v29.i2.367
11. Rajbhandari B, Pant S, Hamal AB, et al. Liver injury in COVID-19: prevalence and its associated factors in Nepal – A retrospective cross-sectional study. *Ann Med Surg*. 2022;85(6):2522-2527. doi:10.1097/MS9.0000000000000767
12. Shama, Mahmood A, Mehmood S, Zhang W. Pathological Effects of SARS-CoV-2 Associated with Hematological Abnormalities. *Curr Issues Mol Biol*. 2022;45(9):7161-7182. doi:10.3390/cimb45090453
13. Xia W, Jiang T, Tan Y, Li C, Wu S, Mei B. Characteristics of hematological parameters on admission in COVID-19 Omicron variant infected in Chinese population: a large-scale retrospective study. *BMC Infect Dis*. 2022;22(1):835. doi:10.1186/s12879-022-08771-2
14. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. *J Intensive Care*. 2020;8(1):36. doi:10.1186/s40560-020-00453-4
15. Hue S, Beldi-Ferchiou A, Bendib I, et al. Uncontrolled Innate and Impaired Adaptive Immune Responses in Patients with COVID-19 Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med*. 2020;202(11):1509-1519. doi:10.1164/rccm.202005-1885OC
16. Kangro K, Wolberg AS, Flick MJ. Fibrinogen, Fibrin, and Fibrin Degradation Products in COVID-19. *Curr Drug Targets*. 2022;22(17):1593-1602. doi:10.2174/1389450122666220826162900
17. De Vita A, Franceschi F, Covino M. Increased Thrombotic Risk in COVID-19: Evidence and Controversy. *J Clin Med*. 2022;12(13):4441. doi:10.3390/jcm12134441
18. Esmailian M, Vakili Z, Nasr-Esfahani M, Heydari F, Masoumi B. D-dimer Levels in Predicting Severity of Infection and Outcome in Patients with COVID-19. *Tanaffos*. 2022;21(4):419-433. http://www.ncbi.nlm.nih.gov/pubmed/37583776
19. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clin Chim Acta*. 2020;506:145-148. doi:10.1016/j.cca.2020.03.022
20. Sweet D, Freeman M, Zidar D. Immunohematologic Biomarkers in COVID-19: Insights into Pathogenesis, Prognosis, and Prevention. *Pathog Immun*. 2022;8(1). doi:10.20411/pai.v8i1.572
21. Castro C, Gourley M. Diagnostic testing and interpretation of tests for autoimmunity. *J Allergy Clin Immunol*. 2010;125(2):S228-S227. doi:10.1016/j.jaci.2009.09.041
22. Dai CL, Kornilov SA, Roper RT, et al. Characteristics and Factors Associated With Coronavirus Disease 2019 Infection, Hospitalization,

and Mortality Across Race and Ethnicity. *Clin Infect Dis*. 2021;73(12):2193-2204. doi:10.1093/cid/ciab154

22. Han MW, Wang M, Xu MY, Qi WP, Wang P, Xi D. Clinical features and potential mechanism of coronavirus disease 2019-associated liver injury. *World J Clin Cases*. 2021;9(3):528-539. doi:10.12998/wjcc.v9.i3.528

22. Han MW, Wang M, Xu MY, Qi WP, Wang P, Xi D. Clinical features and potential mechanism of coronavirus disease 2019-associated liver injury. *World J Clin cases*. 2021;9(3):528-539. doi:10.12998/wjcc.v9.i3.528

25. Utzschneider KM, Largajolli A, Bertoldo A, et al. Serum ferritin is associated with non-alcoholic fatty liver disease and decreased B-cell function in non-diabetic men and women. *J Diabetes Complications*. 2014;28(2):177-184. doi:10.1016/j.jdiacomp.2013.11.007

26. Hulkoti VS, Acharya S, Kumar S, et al. Association of serum ferritin with COVID-19 in a cross-sectional study of 200 intensive care unit patients in a rural hospital. *J Fam Med Prim Care*. 2022;11(5):2045-2050. doi:10.4103/jfmpc.jfmpc_1921_21

27. Kurian SJ, Mathews SP, Paul A, et al. Association of serum ferritin with severity and clinical outcome in COVID-19 patients: An observational study in a tertiary healthcare facility. *Clin Epidemiol Glob Heal*. 2022;21:101295. doi:10.1016/j.cegh.2022.101295

28. Newsome PN, Cramb R, Davison SM, et al. Guidelines on the management of abnormal liver blood tests. *Gut*. 2018;67(1):6 LP - 19. doi:10.1136/gutjnl-2017-314922

29. Antwi-Baffour S, Kyeremeh R, Annison L. Severity of Anaemia Has Corresponding Effects on Coagulation Parameters of Sickle Cell Disease Patients. *Diseases*. 2019;7(4):59. doi:10.3390/diseases7040059

30. Taneri PE, Gómez-Ochoa SA, Llanaj E, et al. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. *Eur J Epidemiol*. 2020;35(8):763-773. doi:10.1007/s10654-020-00678-5

31. Rineau E, Gaillard T, Lasocki S. Anemia of the Critically Ill Patient: Pathophysiology, Lessons from Animal Models. In: *Diet and Nutrition in Critical Care*. Springer New York; 2015:1179-1190. doi:10.1007/978-1-4614-7836-2_133

32. Lv Y, Liu N, Li Y, et al. Coagulation Dysfunction in Patients with Liver Cirrhosis and Splenomegaly and Its Countermeasures: A Retrospective Study of 1522 Patients. Liu Z, ed. *Dis Markers*. 2022;2022:1-9. doi:10.1155/2022/5560560

33. Liatsos GD. SARS-CoV-2 induced liver injury: Incidence, risk factors, impact on COVID-19 severity and prognosis in different population groups. *World J Gastroenterol*. 2022;29(16):2297-2232. doi:10.3748/wjg.v29.i16.2297