Evaluation of Biochemical Test Results in Patients with COVID-19 Infection

Marilena Stamouli, Sofia Kougioumtzidou, Antonia Mourtzikou, Antonia Korre, Georgia Kalliora, Panagiotis Koupourous, Maria Tsesmeli, Vasiliki Mpourtsala, Anastasios Skliris, and Christos Stergiou

ABSTRACT

Background: The current pandemic outbreak of COVID-19 due to SARS-CoV-2 virus, affected the health care systems, health services and economy globally. Moreover, it significantly affected the health of the population worldwide. Mortality and morbidity rates are still increasing. According to WHO, as of September 2021 there have been 224180869 confirmed cases of COVID-19, including 4621173 deaths. USA, India, and Brazil are the three world's worst-hit countries. In Greece the mortality rate is at 3%.

Methods: Study population included 565 patients, who were admitted at the Emergency Department and the Pathology Department of Naval and Veterans Hospital, Athens, Greece, during a period of 3.5 months. Patients’ demographic characteristics, underlying diseases, travel history, symptoms, aetiology of admission and history of contact with confirmed cases were recorded. All patients included to the study were positive for SARS-CoV-2 and characterized as COVID-19 patients. All statistical analyses were conducted using MINITAB 17.

Results: Statistically significant differences in the results of albumin (marginal p-value), urea, creatinine, AST, ALT, and LDH between hospitalized and non-hospitalized patients were detected. Also, we observed statistically significant differences in the results of albumin, urea, creatinine, and ALT, between male and female patients. Moreover, patient age was statistically significant between male and female patients. The Logistic regression model of hospitalization show that statistically significant variables are ALT, LDH, age and gender.

Conclusions: The rapid spreading of the new COVID-19 pandemic due to SARS-CoV-2 increased the need for the measurement of biochemical tests and the evaluation of their correlation with patient hospitalization. Biochemical monitoring of COVID-19 patients is critical for assessing disease severity and progression as well as monitoring therapeutic intervention. Several common biochemical tests have been implicated in COVID-19 infection progression, providing important prognostic information. In the present study we evaluated the test results of albumin, urea, creatinine, AST, ALT, LDH and total bilirubin in patients with COVID-19 infection.

Keywords: biochemical tests, clinical outcomes, COVID-19 infection, hospitalization, liver function parameters, liver injury, SARS-CoV-2.

I. INTRODUCTION

The virus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is responsible for the coronavirus disease 2019 (COVID-19) and was declared a pandemic by the World Health Organization (WHO) in early March 2020 [1], [2]. SARS-CoV-2 is a single-stranded, positive-polarity RNA virus with genome size 26-32kb, presenting extremely infectious abilities [3], [4]. It causes a wide spectrum of symptoms that vary from completely asymptomatic disease to severe infection, such as acute respiratory distress syndrome, complete respiratory failure, multi-organ failure or death. While the disease continues to spread, several clinical and biological studies take place to further understand the infection mechanism and its impact on human tissues and organs. The most suggested infection mechanism of SARS-CoV-2 is through the angiotensin-converting enzyme 2 (ACE2) receptor of human cells which are on several organs, such as the heart, the kidneys, and the liver. The Receptor Binding Domain of the spike protein (S) of the virus binds to ACE2 receptors of human cells as a key-lock mechanism [5]-[9]. Recent reports showed that COVID-19 disease has an impact on liver dysfunction as the...
virus enters in high degree through ACE2 receptors, found abundantly present on cholangiocytes [10]-[12]. This leads to liver injury and several abnormalities on albumin, ALT (Alanine aminotransferase), AST (Aspartate aminotransferase), LDH (Lactate dehydrogenase) and T Bil (total bilirubin) values [9], [13]-[17]. Moreover, kidney is another important target organ for SARS-CoV-2, causing kidney function injury and affecting urea and creatinine levels, since recently has been demonstrated that SARS-CoV-2 can infect podocytes and tubular epithelial cells, which could contribute to the development of renal abnormalities [18]-[20].

The aim of the present study was to measure biochemical tests in patients with COVID-19 infection and to evaluate the correlation of biochemical results with gender and the need for patient hospitalization.

II. MATERIALS AND METHODS

The population under study consisted of 565 patients, who were admitted at the Emergency Department and the Pathology Department of Naval and Veterans Hospital, Athens, Greece, during a period of 3.5 months. All patients were informed about the study and gave their consent. The study was approved by the Hospital’s Ethics Committee and has been carried out in accordance with Declaration of Helsinki. On admission, patients were asked about travel history, symptoms, contact with confirmed positive COVID-19 cases, and underlying diseases. Data were collected between October 2021 and January 2022. RT-PCR tests for SARS-CoV-2 detection were performed on Cepheid Inc GeneXpert®. Cepheid Inc. has developed an automated molecular test for the qualitative detection of SARS-CoV-2 (CE IVD) based on cartridge technology, in which multiple regions of the viral genome are targeted. The test can provide rapid detection of the current coronavirus SARS-CoV-2 in as soon as 30 minutes for positive results. For Quality Control of the assay, we used both Internal Controls, since each cartridge includes a Sample Processing Control (SPC) and Probe Check Control (PCC), as well as External Controls (AccuPlex™ SARS-CoV-2 Reference Material 0505-0126). Specimens were collected by doctors, stored in viral transport medium or saline, at room temperature (15-05°C) for up to 2 hours, and frozen at -70°C until testing. Controls (AccuPlex™ SARS-CoV-2, Probe Check Control (PCC), as well as External Quality Controls (CE IVD) based on cartridge technology, in which multiple regions of the viral genome are targeted. The test can provide rapid detection of the current coronavirus SARS-CoV-2 in as soon as 30 minutes for positive results. For Quality Control of the assay, we used both Internal Controls, since each cartridge includes a Sample Processing Control (SPC) and Probe Check Control (PCC), as well as External Controls (AccuPlex™ SARS-CoV-2 Reference Material 0505-0126). Specimens were collected by doctors, stored in viral transport medium or saline, at room temperature (15-30°C) for up to 2 hours, and frozen at -70°C until testing.

All statistical analyses were conducted using MINITAB 17. Categorical variables were expressed with frequencies and percentages. All continuous variables were expressed as mean, standard deviation and medians with interquartile ranges. Continuous variables used the Anderson-Darling test to confirm normal distribution. All statistical significance level was presented with 95% confidence intervals and a p-value<0.05 was considered to be statistically significant. Continuous variables were analyzed through ANOVA and multivariate logistic regression models.

III. RESULTS

The population under study consisted of 565 patients, both male (362/565; 64.0%) and female (203/565; 36.0%), aged between 12 and 94 years. Out of them, 428 patients were hospitalized (75.7%), while 137 (24.2%) were not, according to the severance of their symptoms. Descriptive statistics of test results in the population under study are presented in Tables I and II.

| Variable | Gender | N  | Mean | SE Mean | StDev | Minimum | Maximum | Q1    | Median | Q3    | Maximum |
|----------|--------|----|------|--------|-------|---------|---------|-------|--------|-------|---------|
| ALB      | F      | 203 | 3.6524 | 0.0437 | 0.6226 | 1.7000  | 3.3400  | 3.6000 | 4.0000 | 5.3000 |
|          | M      | 362 | 3.8854 | 0.0344 | 0.6543 | 1.9700  | 3.4800  | 3.8100 | 4.3800 | 5.6000 |
| UREA     | F      | 203 | 47.69  | 2.59   | 36.86  | 12.00   | 28.00   | 37.00  | 56.00  | 299.00 |
|          | M      | 362 | 54.02  | 2.58   | 49.15  | 7.00    | 31.00   | 40.00  | 53.00  | 373.00 |
| CREAT    | F      | 203 | 0.9534 | 0.0551 | 0.7854 | 0.3000  | 0.7000  | 0.8000 | 1.0000 | 10.1000 |
|          | M      | 362 | 1.1463 | 0.0382 | 0.7260 | 0.4800  | 0.8375  | 1.0000 | 1.1800 | 7.0000 |
| SGOT     | F      | 203 | 52.30  | 5.37   | 76.55  | 12.00   | 22.00   | 31.00  | 47.00  | 635.00 |
|          | M      | 362 | 52.01  | 4.23   | 80.39  | 5.00    | 24.00   | 35.00  | 55.00  | 1009.00 |
| SGPT     | F      | 203 | 46.75  | 3.75   | 53.38  | 7.00    | 21.00   | 30.00  | 46.00  | 400.00 |
|          | M      | 362 | 63.28  | 4.64   | 88.23  | 9.00    | 26.00   | 39.00  | 71.00  | 1137.00 |
| LDH      | F      | 203 | 371.3  | 20.7   | 294.5  | 119.0   | 216.0   | 299.00 | 413.00 | 2695.00 |
|          | M      | 362 | 356.9  | 16.2   | 307.3  | 89.0    | 199.00  | 269.0  | 413.00 | 3395.00 |
| TBIL     | F      | 203 | 0.7562 | 0.0814 | 1.1600 | 0.1800  | 0.3800  | 0.5200 | 0.7200 | 14.4000 |
|          | M      | 362 | 0.7478 | 0.0318 | 0.6059 | 0.1100  | 0.4100  | 0.5900 | 0.8725 | 7.2600 |
| AGE      | F      | 203 | 60.17  | 1.31   | 18.60  | 16.00   | 48.00   | 61.00  | 74.00  | 94.00  |
|          | M      | 362 | 51.06  | 1.01   | 19.26  | 12.00   | 39.00   | 48.00  | 65.25  | 94.00  |

DOI: http://dx.doi.org/10.24018/ejbiomed.2022.1.1.5
Vol 1 | Issue 1 | February 2022
We observed statistically significant differences in the results of albumin (marginal p-value), urea, creatinine, AST, ALT, and LDH between hospitalized and non-hospitalized patients. Moreover, patient age was statistically significant between hospitalized and non-hospitalized patients. The results are presented in Table III:

### Table III: Observed P-values <0.05 for Albumin, AST, ALT, LDH, Urea, Creatinine, and AGE

| Variable   | P-value | Correlation |
|------------|---------|-------------|
| ALBUMIN    | 0.048   | YES         |
| AST        | 0.001   | YES         |
| ALT        | 0.001   | YES         |
| LDH        | 0.001   | YES         |
| TOTAL BILIRUBIN | 0.413 | NO         |
| UREA       | 0.006   | YES         |
| CREATININE | 0.001   | YES         |
| AGE        | 0.001   | YES         |

We performed chi–square test in order to evaluate if gender is statistically significant for hospitalization. We observed that gender is not statistically significant for hospitalization (Table IV).

### Table IV: Chi-Square Test for Association: Gender; HOSP (Rows: Gender Columns: HOSP)

|   | 1  | 2  | All |
|---|----|----|-----|
| F | 58 | 145| 203 |
| M | 79 | 283| 362 |
| All | 137 | 428 | 565 |

Pearson Chi-Square = 3.225; DF = 1; P-Value = 0.073. Likelihood Ratio Chi-Square = 3.177; DF = 1; P-Value = 0.075.

We observed statistically significant differences in the results of albumin, urea, creatinine, and ALT, between male and female patients. Moreover, patient age was statistically significant between male and female patients. The results are presented in Table V:

### Table V: Observed P-values <0.05 for Albumin, Urea, Creatinine, ALT and AGE

| P-value | Correlation |
|---------|-------------|
| ALBUMIN | 0.001 | YES         |
| AST     | 0.051 | NO          |
| ALT     | 0.000 | YES         |
| LDH     | 0.108 | NO          |
| TOTAL BILIRUBIN | 0.090 | NO         |
| UREA    | 0.043 | YES         |
| CREATININE | 0.003 | YES         |
| AGE     | 0.001 | YES         |

A. Logistic Regression of Hospitalization

A logistic regression model was fitted, with response variable the hospitalization (yes, no), numerical variables albumin, urea, creatinine, AST, ALT, LDH, TBIL, patient age and categorical variable gender. Regression was fitted three times, one with all the variables included, one with the method of forward selection and once with the method of backward elimination. In all cases, statistically significant variables are ALT, LDH, age and gender, table 6. The estimated model was the following:

\[ Y' = -2.345 + 0.008032 \text{ALTL} + 0.002647 \text{LDH} + 0.03653 \text{AGE} \]

\[ Y' = -1.639 + 0.008032 \text{ALTL} + 0.002647 \text{LDH} + 0.03653 \text{AGE} \]

### Table VI: Observed P-values <0.05 for ALT, LDH, AGE and Gender after Logistic Regression Model of Hospitalization

| Coefficients | P-value |
|--------------|---------|
| ALT          | 0.006   |
| LDH          | 0.001   |
| AGE          | 0.000   |
| GENDER       | 0.002   |

Fig. 1. Boxplot of age in non-hospitalized (1) and hospitalized patients (2).
The mechanisms for hypoalbuminemia in COVID-19 patients have not been fully explained. According to the literature, it is a result of decreased albumin synthesis in severe COVID-19 cases, but it is also a result of systemic inflammation due to escape of serum albumin into severe COVID-19 cases. Hypoalbuminemia can also indicate a decreased rate of protein synthesis due to liver function impairment. The rapid spreading of the new COVID-19 pandemic due to SARS-CoV-2 increased the need for the measurement of biochemical tests and the evaluation of their correlation with patient hospitalization. Biochemical monitoring of COVID-19 patients is critical for assessing disease severity and progression as well as monitoring therapeutic intervention. Several common biochemical tests have been implicated in COVID-19 infection progression, providing important prognostic information. In the present study, we evaluated the test results of albumin, urea, creatinine, AST, ALT, LDH and total bilirubin in patients with COVID-19 infection.

In the present study, we observed statistically significant differences between male and female patients, as well as between hospitalized and non-hospitalized patients. The serum albumin levels <35 g/L were defined as hypoalbuminemia. Only 188 out of the 565 patients (33.3%) presented elevated albumin levels, while 377 out of 565 patients (66.7%) presented decreased albumin levels.

IV. DISCUSSION

The rapid spreading of the new COVID-19 pandemic due to SARS-CoV-2 increased the need for the measurement of biochemical tests and the evaluation of their correlation with patient hospitalization. Biochemical monitoring of COVID-19 patients is critical for assessing disease severity and progression as well as monitoring therapeutic intervention. Several common biochemical tests have been implicated in COVID-19 infection progression, providing important prognostic information. In the present study, we evaluated the test results of albumin, urea, creatinine, AST, ALT, LDH and total bilirubin in patients with COVID-19 infection.

In the present study, we observed statistically significant differences between male and female patients, as well as between hospitalized and non-hospitalized patients. The serum albumin levels <35 g/L were defined as hypoalbuminemia. Only 188 out of the 565 patients (33.3%) presented elevated albumin levels, while 377 out of 565 patients (66.7%) presented decreased albumin levels.

The mechanisms for hypoalbuminemia in COVID-19 patients have not been fully explained. According to the literature, it is a result of decreased albumin synthesis in severe COVID-19 cases, but it is also a result of systemic inflammation due to escape of serum albumin into severe COVID-19 cases.
interstitial space as a consequence of increased capillary permeability [9], [22], [24], [30].

In the present study we observed elevated AST and ALT levels in 200 patients (35.4%), 485 patients (85.8%) presented elevated LDH levels, 60 patients (10.6%) elevated total bilirubin levels, 161 patients (28.5%) elevated urea levels and 69 patients (12.2%) elevated creatinine levels.

AST and ALT levels are elevated due to liver function impairment as well as to widespread organ damage. The virus affects liver function in various ways. Epithelial cells of the bile duct and liver express ACE2, thus providing an access point for the virus to bind to cholangiocytes and disrupt liver function. Moreover, many medications are used for the treatment of the infection, such as antipryretics, antibiotics, antivirals, and steroids, causing drug-induced liver injury. Systemic inflammatory response is also considered as a potential contributing factor for liver injury. Systemic inflammation causes overproduction of inflammatory cytokines that can injure the liver and other organs [9], [22], [31]-[33].

We observed statistically significant differences in AST and ALT levels between males and females, as well as between hospitalized and non-hospitalized patients. Regression analysis showed that ALT levels are statistically significant for patient hospitalization.

Since LDH is present in lung tissue, it is increased in COVID-19 patients, due to pulmonary injury. Patients with severe infections release elevated amounts of LDH in the circulation, and according to many studies LDH is a predictor of worse outcomes in hospitalized patients. Moreover, LDH levels are elevated in thrombotic microangiopathy, associated with renal failure and myocardial injury, thus reflecting multiple organ failure [31]-[34].

Total bilirubin was found elevated in patients. Statistical analysis showed that total bilirubin is not statistically significant for hospitalization and that there are not statistically significant differences between genders and hospitalized patients.

Urea and creatinine are biomarkers of kidney injury and differ significantly between hospitalized and non-hospitalized patients. We also observed statistically significant differences between males and females. According to the literature hospitalized patients can develop acute kidney damage. European Renal Association European Dialysis and Transplant Association suggested that chronic kidney disease patients hold an increased risk for COVID-19 and related mortality. Kidney disease in COVID-19 patients is attributed to many factors, such as direct effects on kidney tissue, endothelial damage, deposition of immune complexes, and virus-induced cytokines or mediators [9], [35], [36].

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China. *N Engl J Med*. 2020 Feb 20;382(8):727-733. doi: 10.1056/NEJMoa2001017.
2. WHO Director-General's opening remarks at the media briefing on COVID-19-11 March 2020. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-
opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020.
3. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Mil Med Res*. 2020 Mar 13;7(1):11. doi:10.1186/s40779-020-00240-0.
4. Mei H, Pond SK, Nekrutkono A. Stepwise Evolution and Exceptional Conservation of ORF1a/b Overlap in Coronaviruses. *Molecular Biology and Evolution*. 2021 December; 38(12):5767–5684. doi:10.1093/molbev/msab265.
5. Sario SE, Periman S. Lessons for COVID-19 Immunity from Other Coronavirus Infections. *Immunity*. 2020;53(3):248-263. doi:10.1016/j.immuni.2020.07.005.
6. Malik YS, Sircar S, Bhat S, Sharun K, Dhamo K, Dadar M, et al. Emerging novel coronavirus (2019-nCoV)-current scenario, evolutionary perspective based on genome analysis and recent developments. *Vet J*. 2020 Dec;440(1):68-76. doi: 10.1016/j.tvjl.2020.1727993.
7. Hoffmann M, Klein-Weber K, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020 Apr 16;181(2):271-280. doi:10.1016/j.cell.2020.02.052.
8. Chen WH, Strych U, Hotzel PJ, and Bottazzi ME. The SARS-CoV-2 vaccine pipeline: An overview. *Curr Trop Med Rep*. 2020 Mar 3;1:4. doi:10.1007/s40475-020-00201-6.
9. McGrowder DA, Miller F, Cross MA, Anderson-Jackson L, Bryan S, Dilworth L. Abnormal Liver Biochemistry Tests and Acute Liver Injury in 2019 COVID-19 Patients: Current Evidence and Potential Pathogenesis. *Diseases*. 2021 Jul 1;9(3):50. doi:10.3390/diseases9030050.PMID: 34287285.
10. Xu L, Liu J, Lu M, Yang D, Zheng X. Liver injury during highly pathogenic human coronavirus infections. *Liver Int*. 2020 May;40(5):998-1004. doi:10.1111/liv.14435.
11. Chai X., Hu L, Zhang Y, Han W, Lu Z, Ke A, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. *BioRxiv*. [Preprint] 2020. Available from: http://doi.org/.
12. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M, COVID-19 and the liver. *J Hepatol*. 2020;73(5):1231-1240. doi:10.1016/j.jhep.2020.06.006.
13. Ridouejo E, Soza A. The liver in times of COVID-19: what hepatologists should know. *Ann Hepatol*. Jul-Aug 2020;19(4):353-358. doi:10.1016/j.ajohep.2020.05.001.
14. Hwaiz R, Merza M, Hamad B, Hamasalih S, Mohammed M, Hama H. Evaluation of hepatic enzymes activities in COVID-19 patients. *Int Immunopharmacol*. 2021 Aug; 97: 107701. doi: 10.1016/j.intimp.2021.107701.
15. Kumar-M P, Mishra S, Isha DK, Shukla I, Choudhury A, Mohindra R, Mandavdhare HS, Dutta U, Sharma V. Coronavirus disease (COVID-19) and the liver: a comprehensive systematic review and meta-analysis. *Hepatol Int*. 2020 Sep;14(5):711-722. doi: 10.1007/s12072-020-10071-9.
16. Zarei M, Bose D, Nouri-Vaskeh M, Tajkinia V, Zand R, Ghasemi M. Long-term side effects and lingering symptoms post COVID-19 recovery. *Rev Med Virol*. 2021 Sep 9:e2289. doi: 10.1002/rmv.2289.
17. Idalsoga A, Ayares G, Arab JP, Diaz LA. COVID-19 and Indirect Liver Injury: A Narrative Synthesis of the Evidence. *J Clin Transl Hepatol*. 2021 Oct 28;9(5):760-768. doi: 10.4121/CTH.2020.00140.
18. Xia T, Zhang W, Xu Y, Wang B, Yuan Z, Wu N, et al. Early kidney injury predicts disease progression in patients with COVID-19: a cohort study. *BMC Infect Dis*. 2021; 21(1):1012. Available from: https://doi.org/10.1186/s12879-021-06576-9.
19. Baywa H, Riaz Y, Ammar M, Farnia S, and Youssaf A. (2020). The Dilemma of Renal Involvement in COVID-19: A Systematic Review. *Cureus*. 2020 Jun 15;12(6):e8632. doi: 10.7759/cureus.8632.
20. Martinez-Rojas MA, Vega-Vega O, and Bobadilla NA. Is the kidney a target of SARS-CoV-2? *Am J Physiol Renal Physiol*. 2020 Jun 1; 318(6): F1454–F1462. doi: 10.1152/ajprenal.00160.2020.
21. https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019.
22. Xu W, Huang C, Fei L, Li Q, and Chen L. Dynamic Changes in Liver Function Tests and Their Correlation with Illness Severity and Mortality in Patients with COVID-19: A Retrospective Cohort Study. *Clin Intersym Aging*. 2021; 16: 675–685. doi:10.2147/CIA.S330362.
23. Hui DS, Azhar EI, Madani TA, Ntomu F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis*. 2020 Feb;91:264-266. doi:10.1016/j.ijid.2020.01.009.
Lippi G, Sanchis-Gomar F, Henr BM. Coronavirus disease 2019 (COVID-19): the portrait of a perfect storm. *Ann Transl Med*. 2020 Apr;8(7):497. doi: 10.21037/atm.2020.03.157.

Del Zompo F, De Siena M, Ianiri G, Gasbarrini A, Pompili M, Ponziani FR. Prevalence of liver injury and correlation with clinical outcomes in patients with COVID-19: systematic review with meta-analysis. *Eur Rev Med Pharmacol Sci*. 2020 Dec;24(24):13072-13088. doi: 10.26355/eurrev_202012_24215.

Wang Q, Zhao H, Liu LG, Wang YB, Zhang T, Li MH, Xu YL, Gao GJ, Xiong HF, Fan Y, Cao Y, Ding R, Wang JJ, Cheng C, Xie W. Pattern of liver injury in adult patients with COVID-19: a retrospective analysis of 105 patients. *Mil Med Res*. 2020 Jun 7;7(1):28. doi: 10.1186/s40779-020-00256-6.

Huang H, Chen S, Li H, Zhou XL, Dai Y, Wu J, Zhang J, Shao L, Yan R, Wang M, Wang J, Tu Y, Ge M. The association between markers of liver injury and clinical outcomes in patients with COVID-19 in Wuhan. *Aliment Pharmacol Ther*. 2020 Sep;52(6):1051-1059. doi: 10.1111/apt.15962.

Hundt MA, Deng Y, Ciarleglio MM, Nathanson MH, Lim JK. Abnormal Liver Tests in COVID-19: A Retrospective Observational Cohort Study of 1,827 Patients in a Major U.S. Hospital Network. *Hepatology*. 2020 Oct;72(4):1169-1176. doi: 10.1002/hep.31487.

Zeng QL, Yu ZJ, Ji F, Li GM, Zhang GF, Xu JH, Lin WB, Zhang GQ, Li GT, Cui GL, Wang FS. Dynamic changes in liver function parameters in patients with coronavirus disease 2019: a multicentre, retrospective study. *BMC Infect Dis*. 2021 Aug 16;21(1):818. doi: 10.1186/s12879-021-06572-z.

Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, et al. Hypoalbuminemia predicts the outcome of Covid-19 independent of age and co-morbidity. *J Med Virol*. 2020 Oct;92(10):2152–2158. doi:10.1002/jmv.26003.

Portincasa P, Krawczyk M, Machill A, Lammert F, Ciaula AD. Hepatic consequences of COVID-19 infection. Lapping or biting? *J Clin Transl Hepatol*. 2020 Mar 28;8(1):18-24. doi: 10.14218/JCTH.2020.00018.

Clark R, Waters B, and Stanfi AG. Elevated liver function tests in COVID-19: Causes, clinical evidence, and potential treatments. *Nurse Pract*. 2021 Jan; 46(1): 21–26. doi: 10.1097/01.NPR.0000722316.63824.19.

Xiang H-X, Fei J, Xiang Y, Xu Z, Zheng L, LIX-Y, et al. Renal dysfunction and prognosis of COVID-19 patients: a hospital-based retrospective cohort study. *BMJ Infectious Diseases*. 2021 Feb; 21:158. Available from: https://doi.org/10.1186/s12879-021-05861-x.

Kim S-G, Sung HH. Status of Kidney Function in Hospitalised COVID-19 Patients in the Southern Gyeonggi Province, South Korea. *Korean J Clin Lab Sci*. 2021Sept 30;53(3):208-216. Available from: https://doi.org/10.15324/kjcls.2021.53.3.208.