

Evaluation of liver function post COVID –19 recovery

Rajiha M. Hasan¹, Nihad N. Hilal², Abdulhadi M. Jumaa³

¹ Medical Technologist (for pathological analyzes), Kirkuk General Hospital/Iraq

² Professor of chemical pathology, Tikrit University College of Medicine/Iraq

³ Lecturer of Physiology, Tikrit University College of Medicine/Iraq

Email: drnehad76@tu.edu.iq

ABSTRACT

The 2019 novel coronavirus disease (COVID-19) outbreak began in Wuhan, China, in December 2019 and has since spread across the world as a major epidemic. SARS-CoV-2 (severe acute respiratory syndrome coronavirus -2) is the virus that causes this disease. The respiratory system is greatly affected by the Coronavirus, which is the most common. It has been observed that SARS-2 harms many organs of the body. The **aim** of this study was performed to evaluate the concentration of liver function tests post COVID-19 patients' recovery. **Patients and Methods** This cross-sectional controlled study was conducted in Kirkuk city, the study included 60 patients who were selected randomly 2-3 months after recovery from COVID-19 disease, All patients were PCR +ve previously hospitalized with oxygen therapy. The control group consist of 60 persons who were apparently normal with no severe chronic illness. The **result** the level of the studied parameter (ALT, AST, TSB) significantly increases ($p < 0.05$) by mean (17.25), (24,60), (0.57) respectively when compared with control group by mean (13.57), (15.54), (0.445). **Conclusion** the present study revealed a significant difference in the recovery for the ALT, AST, and TSB when compared with healthy group.

Keywords: Alanine aminotransferases: D. Dimer: COVID-19: ACE2.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Corona Virus 2(SARS-CoV-2). The emerging corona virus is a virus encapsulated with a large genome single-stranded RNA genome, 32 kbps insensitive. It is widely spread around the world and has caused significant pressure on the social and impact on human health⁽¹⁾. Study showed that SARS-CoV-2 enters the lungs through the angiotensin-converting enzyme 2 (ACE2) receptor⁽²⁾, which can lead to severe lung fibrosis and consolidation and a significant mortality rate in severe cases⁽³⁾. The presence of SARS-CoV-2 in cholangiocytes could lead to liver damage due to the damage to bile duct cells. Angiotensin-converting enzyme 2 (ACE2) is the key receptor for the entry of SAR's into the cells which expressed in both liver cells and bile duct cells. Infection with COVID-19 can have serious side effects, including lung disease. It causes a systemic condition that affects several organs, possibly leading to serious consequences including mortality and long-term complications.⁽¹⁻⁴⁾

The infection caused by the SARS-CoV-2 virus is predominantly a respiratory disease. However, its adverse effects on other organ systems remain unclear. The most common clinical presentation includes respiratory tract involvement with mild to high fever, shortness of breath, and cough⁽⁵⁾. Liver is one of the largest organs in the body. It has many important metabolic functions. Liver tissue has a relatively large

amount of enzymes activity and alteration of various enzymes in hepatitis.⁽⁶⁾ Post COVID-19 condition is defined as the illness that occurs in people who have a history of probable or confirmed SARS-CoV-2 infection; usually within three months from the onset of COVID-19, with symptoms and effects that last for at least two months. It is difficult to predict how long the post-COVID-19 condition will last for any given patient. There is much to learn about the post-COVID-19 condition, but current research shows that patients can experience lingering symptoms for weeks to months following COVID-19.⁽⁷⁻⁹⁾

Objectives of the study

The objectives of the study were:

To evaluate liver function tests (ALT, AST, TSB) for patients affected previously by moderate to severe covid-19.

2. Materials and Methods

Study design

This is a cross-sectional controlled study was conducted during the period from December 2021 to the end of March 2022 in Kirkuk city, the study included 60 patients who were selected randomly 2-3 months after recovery from COVID-19 disease previously hospitalized with oxygen therapy. The control group consist of 60 persons who were apparently normal with no severe chronic illness. The blood sample was collected from patients and the control group, and interviews were carried out with

them using the questionnaire form. Serum level of ALT, AST, TSB were measured by Cobas C311.

Exclusion criteria

- 1- Chronic liver disease.
- 2- Any medicines that may alter patients finding like steroids, NSAID drugs, and chemotherapy.

Ethical approval

The protocol for this study was approved by the Scientific Committee at Tikrit University – College of Medicine, and the agreement of the attendance to Kirkuk General for collecting the sample from the patients was approved via the Directorate of Kirkuk Health. Each patient was educated about the research, filled out a questionnaire, and signed a consent form to participate in the study.

Methods (Sampling of blood)

Five ml of blood sample was collected by vein puncture from each subject enrolled in this study. Blood samples were placed into a sterile gel tube, after blood clotting, centrifuged at 3000 rpm for 15 minutes then serum was removed and transferred in to Two Eppendorf tubes which were labeled and kept at -20 C for determination serum level of ALT, AST, TSB, by using Cobas C311 analyzer.

3. Statistical Analysis

All patients signed informed consent to take part in the study, and the study was approved by the ethical committee of Tikrit University, College of Medicine. All data were presented as mean and standard deviation (SD). A P value of less than 0.05 was regarded as significant. Analysis was performed by IBM SPSS Statistics for Windows version 23.0.

4. RESULTS

Table 4.1 Descriptive Statistics					
According to the table (4.1) the (mean±SD) for patients and control were as follows:					
Parameters	Patients		Control		P-Value
	Mean	±SD	Mean	±SD	
ALT (U/L)	17.25	5.89	13.57	3.75	0.02
AST (U/L)	24.61	8.32	15.54	6.044	<0.001
TSB (mg/dl)	0.57	0.19	0.44	0.15	<0.01

- ALT for patients was (17.25±5.89) and for control was (13.57±3.75).
 - AST for patients was (24.60±8.31) and for control was (15.54±6.044).
 - TSB for patients was (0.57±0.19) and for control (0.44±0.15).
- The level of the studied parameter (ALT, AST, TSB significantly increase (p <0.05) by mean (17.25), (24,60), (0.57) respectively when compared with control group by mean (13.57) (15.54), (0.44) respectively.

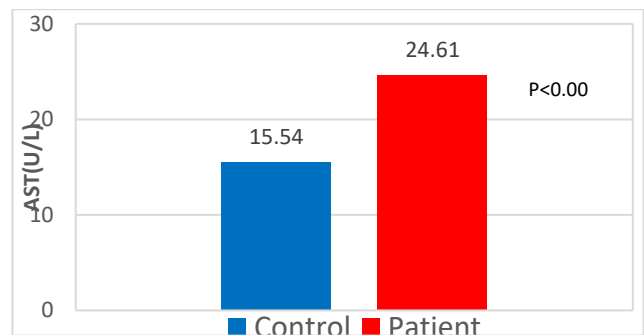


Figure 4.2: mean of AST between patient and control in the study

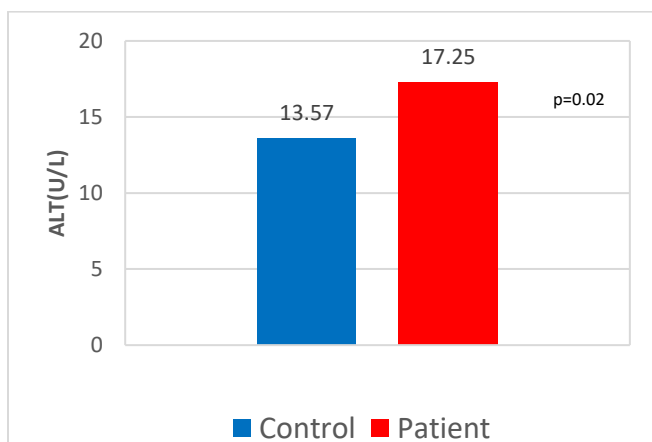


Figure 4.1: mean of ALT between patient and control in the study

The Bar chart shows a significant difference in ALT in patients when compared with the control group.

The Bar chart shows a significant difference in AST in patients when compared with the control group.

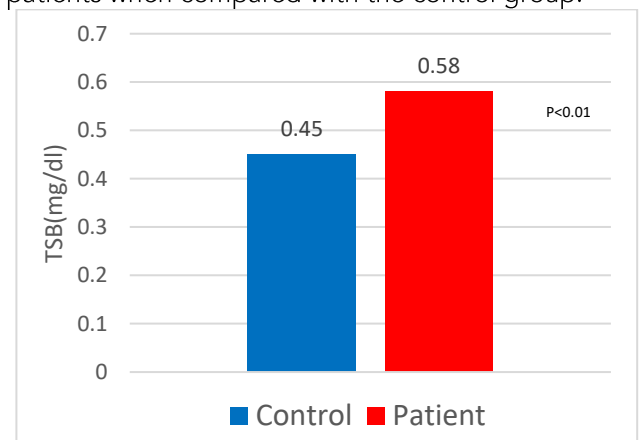


Figure 4.3: mean of TSB between patient and control in the study

The Bar chart shows a significant difference in TSB in patients when compared with the control group.

5. Discussion

Comparison between ALT, AST, and TSB Levels in the Studied Groups

The result of the current study shows significant differences among study groups the ALT, AST, and TSB ($p=0.02$, <0.001 , <0.01), as shown in the table (4-1), (fig.4.1,4.2,4.3) respectively

ALT and AST catalyze the transfer of an amino group from an amino acid to α ketoglutarate. The amino acids are L-alanine and L-aspartate and the reaction products are L-glutamate and either pyruvate or oxaloacetate, respectively. The overall effect is exchange of an amino group and a keto group. Pyridoxal 5'-phosphate serves as a coenzyme in both reactions. According to the findings, all patients had ALT, AST, and TSB levels that were within the upper limit of normal. However, a significant difference was seen between both the recovery group patients' results and that of a healthy control group. We have known that SARS-COV-2 can damage the liver by a different mechanism. Liver damage may be a result of the organ-specific immune response to SARS-CoV-2 or be secondary to hypoxia and systemic inflammation response⁽¹⁰⁻¹⁴⁾

Due to a cellular damage, elevated levels of the enzymes aspartate aminotransferases (AST) and alanine aminotransferases (ALT) have been associated with higher liver function tests.⁽¹⁵⁻¹⁶⁾

Additionally, we observe that the parameters in this study are within the upper limit of the normal range, this is similar to the findings of An Y W et al.⁽¹⁷⁾ who found elevated levels of ALT in COVID-19 survivors for a period of 14 days after discharge, with a gradual return to normality of these parameters within two months. The study conducted in Egypt, on the other hand, demonstrated a persistent elevation of ALT and AST for three months for the resolution of COVID-19⁽¹⁷⁾

Hepatic aminotransferases were shown to be mild to moderately elevated in COVID-19 patients, however, this elevation was not associated with a rise in blood total bilirubin, according to Fan et al.⁽¹⁸⁾ study on the disruption of liver function.

Additionally, Xu et al.⁽¹⁹⁾ observed non-elevated blood bilirubin in COVID-19 patients, despite the high expression of ACE2 in the cholangiocytes as compared to the hepatocytes in the hepatic vascular endothelium.

Although AST is present in the liver but is not specifically associated with liver disease, the current study found that AST levels were higher than ALT levels. ALT and AST are frequently seen in liver and heart cells and have been associated with the severity of the disease.⁽²⁰⁾

According to previous studies, severe patients usually had AST elevations rather than ALT elevations upon admission⁽²¹⁾

6. Conclusions

It was concluded that:

1. The level of (ALT, AST) measured in our study showed a significant difference in recovered patients diagnosed previously with COVID-19 when compared with the control group.
2. The level of (TSB) measured in our study showed a significant difference in recovered patients diagnosed previously with COVID-19 when compared with the control group.

References

1. Wei M, Yang N, Wang F, Zhao G, Gao H, Li Y. Epidemiology of Coronavirus Disease 2019 (COVID-19) Caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Disaster medicine and public health preparedness*. 2020 Dec;14(6):796-804.
2. Rico-Mesa JS, White A, Anderson AS. Outcomes in patients with COVID-19 infection taking ACEI/ARB. *Current cardiology reports*. 2020 May;22(5):1-4.
3. Abbas HA, Alsaade KA, AlMashhdan HA. Study the effect of cyperus rotundus extracted as mouthwash on the corrosion of dental amalgam. *In IOP Conference Series: Materials Science and Engineering* 2019 Jul 1 (Vol. 571, No. 1, p. 012074). IOP Publishing.
4. Zubaida N.M Albarzanji, Thikra Abdullah Mahmood, Entedhar Rifaat Sarhat, Kasim Sakran Abass. Cytokines Storm Of COVID-19 And Multi Systemic Organ Failure: A Review. *Systematic Reviews in Pharmacy*, 2020; 11 (10), 1252-1256. [doi:10.31838/srp.2020.10.179](https://doi.org/10.31838/srp.2020.10.179)
5. Sarhat, E. R.; Zbaar, S. A.; Ahmed, S. E.; Ahmed, T. S.; Sarhat, T. R. Salivary biochemical variables of Liver Function in among Individuals with COVID-19 in Thi-Qar Province. *Egyptian Journal of Chemistry*; 2022;65(6):305-310.
6. AlMashhadani HA. Corrosion protection of pure titanium implant in artificial saliva by electro-polymerization of poly eugenol. *Egyptian Journal of Chemistry*. 2020 Aug 1;63(8):2803-11.
7. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, Wang Z, Li J, Li J, Feng C, Zhang Z. Clinical and biochemical indexes from 2019-to-infected patients linked to viral loads and lung injury. *Science China Life Sciences*. 2020 Mar;63(3):364-74.
8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*. 2020 Mar 28;395(10229):1054-62.
9. Zbaar, S., Sarhat, E., khalaf, S. Association of C-Reactive Protein with Risk of Complications of

diabetic nephropathy. *Egyptian Journal of Chemistry*, 2022; 65(8): 181-186. doi: 10.21608/ejchem.2021.99957.4868.

10. Entedhar Rifaat Sarhat, Siham Ajmee Wadee, Ban Ismael Sedeeq, Thuraia Rifaat Sarhat. Biochemical and Histological Evaluation of Indomethacin-induced Hepatotoxicity in Rats. *Science Translation Medicine*. 2019. ;12(109):23-35.

11. Sayran Sattar Saleh , Entedhar Rifaat Sarhat .Effects of Ethanolic Moringa Oleifera Extract on Melatonin, Liver and Kidney Function Tests in Alloxan-Induced Diabetic Rats. *Indian Journal of Forensic Medicine & Toxicology*. 2019, 13(4): 1015-1015.

12. Entedhar R. Sarhata, Moayad M. Al Anzy, Takea Shaker Ahmed. Study of oxidant-antioxidant status in cerebrospinal fluid of children with meningitis. *Eurasian Chemical Communications*, 2022, 4(9), 863-869. Link: http://www.echemcom.com/article_148799. Html.

13. E.R Sarhat, S.A. Wadi, B.I. Sedeeq, Th.R. Sarhat and N.A. Study of histopathological and biochemical effect of Punica granatum L. extract on streptozotocin -induced diabetes in rabbits. *Iraqi Journal of Veterinary Sciences*, 2019; 33(2): 189-194. doi: 10.33899/ijvs.2019.125523.1045

14. Entedhar RS, Siham A.W, Ayhan R. M. Effect of Ethanolic Extraction of Moringa oleifera on Paraoxonase and Arylesterase enzyme activity in High Fat Diet-induced Obesity in Rats. *Research J. Pharm. and Tech*. 2018; 11(10): 4601-4.

15. Sarhat E. R, Albarzanji Z. N. M, Pambuk C. I. A. Estimation of Some Interleukins in Cerebrospinal Fluid in Children with Meningitis. *Biomed Pharmacol J* 2019;12(4). Available from: <https://bit.ly/2MAWJXc>.

16. Gan Q, Gong B, Sun M, Cao Z, Zheng Y, Zhang Y, Wen P, Shen Y, Hong L, Hou T, Jia Y. A high percentage of patients recovered from COVID-19 but discharged with abnormal liver function tests. *Frontiers in physiology*. 2021 Mar 17; 12:314.

17. McGrowder DA, Miller F, Anderson Cross M, Anderson-Jackson L, Bryan S, Dilworth L. Abnormal liver biochemistry tests and acute liver injury in COVID-19 patients: Current evidence and potential pathogenesis. *Diseases*. 2021 Sep;9(3):50.

18. AlMashhadani HA, Saleh KA. Electrochemical Deposition of Hydroxyapatite Co-Substituted By Sr/Mg Coating on Ti-6Al-4V ELI Dental Alloy Post-MAO as Anti-Corrosion. *Iraqi Journal of Science*. 2020 Nov 28:2751-61.

19. Gameil MA, Marzouk RE, Elsebaie AH, Rozaik SE. Long-term clinical and biochemical residue after COVID-19 recovery. *Egyptian Liver Journal*. 2021 Dec;11(1):1-8.

20. .An YW, Song S, Li WX, Chen YX, Hu XP, Zhao J, Li ZW, Jiang GY, Wang C, Wang JC, Yuan B. Liver function recovery of COVID-19 patients after discharge, a follow-up study. *International journal of*

medical sciences. 2021;18(1):176.

21. .Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C, Zhang Y, Huang S, Liu Z, Cheng J. Clinical features of COVID-19-related liver functional abnormality. *Clinical Gastroenterology and Hepatology*. 2020 Jun 1;18(7):1561-6.

22. . Xu L, Liu J, Lu M, Yang D, Zheng X. Liver injury during highly pathogenic human coronavirus infections. *Liver international*. 2020 May;40(5):998-1004.

23. . Qin C, Ziwei MP, Tao SY, Ke PC, Shang MM. Dysregulation of immune response in patients with COVID-19 in Wuhan, China; *Clinical Infectious Diseases*; Oxford Academic. *Clinical Infectious Diseases*. 2020.

24. Kadhim MM, AlMashhadani HA, Hashim RD, Khadom AA, Salih KA, Salman AW. Effect of Sr/Mg co-substitution on corrosion resistance properties of hydroxyapatite coated on Ti-6Al-4V dental alloys. *Journal of Physics and Chemistry of Solids*. 2022 Feb 1; 161:110450.

25. .Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *Jama*. 2020 Mar 17;323(11):1061-9.