

Evaluation of liver function (GPT, GOT, ALP) and cardiac isoenzyme (LDH1, LDH2, LDH3, LDH4) in COVID19 patients after recovering

Abeer Ghazi Nazzal¹ and Dr. Ahmmad Ghazi Sabbar²

⁽¹⁾ College of Health & Medical techniques/Medical laboratory techniques dep. and work in Mahmoudia Primary Health Care Sector Baghdad- Iraq.

E-Mail : Abeeralobaidi21@gmail.com

⁽²⁾ College of Health & Medical Techniques/ Medical laboratory techniques dep.

Abstract

The present study was carried out to evaluate liver function and estimate specific cardiac biomarker in 200 subject including 150 recovered Covid-19 Patients and 50 healthy control groups. GOT, GPT, ALP and LDH isoenzyme were estimated using CUSIBIO protocol. While LDH isoenzymes were also estimated using CUSBIO protocol. The data revealed increase levels of liver enzyme GOT, GPT and ALP in recovered patients, while the LDH isoenzyme showed increasing level of LDH2, LDH3, and LDH4 except LDH1 revealed decrease level. We conclude that the dysregulation in liver function and increase of liver enzyme is due to the present the ACE2 as Covid-19 receptors in cholangiocyte of liver. Some LDH iso enzymes are existing in several human organ including lung, kidney and intestine when the Covid-19 attack these members lead to pathophysiological changes in level of some LDH isoenzymes. The study included 200 subjects, 150 recovered patients and 50 healthy control and age from 15-65 years. Was conducted in Baghdad teaching hospital/ Baghdad- Iraq from July to September 2021, all patients had recovered from covid19. The following parameter were evaluated using different protocol (GPT, GOT, ALP) measured by the Automation method, while (LDH1, LDH2, LDH3, LDH4) were measured by the method obtained with CUSBIO.

The results revealed an increased level of both GPT, GOT and ALP in recovered patients in comparison with healthy control. And also (LDH2, LDH3 and LDH4) showed increasing in recovered patients compared with healthy control; while showed decrease in LDH1 of both recovered patients compared healthy control. We conclude that the attack by Covid-19 leads to abnormal changes in biochemical parameters. It concludes that the dysregulation in liver function and increase of liver enzyme is due to the presence of ACE2 as Covid-19 receptors in cholangiocyte of liver. Also the pathophysiological changes in level of some LDL isoenzymes due to it are existing in several human organ including lung, kidney and intestine which are attacked by Covid-19.

Keywords: recovered Covid-19, LDH isoenzymes, liver function, cardiac isoenzyme.

تقييم وظائف الكبد (GPT,GOT,ALP) والانزيمات القلبية (LDH1,LDH2,LDH3,LDH4) في المرضى المتعافين من الإصابة بفيروس كورونا

طالبة الدكتوراه عبير غازي نزال¹ و أ.م.د. أحمد غازي صبار²

الخلاصة

أجريت الدراسة الحالية لتقييم وظائف الكبد وتقدير المؤشر الحيوي القلبي المحدد في 200 شخص بما في ذلك 150 مريضاً متعافياً من Covid-19 و 50 مجموعة سيطرة. تم تقدير GOT و GPT و ALP القلوي باستخدام بروتوكول CUSIBIO. بينما تم تقدير إنزيمات LDH أيضاً باستخدام بروتوكول CUSBIO. كشفت البيانات عن زيادة مستويات إنزيم الكبد GOT و GPT و ALP في المرضى المتعافين، بينما أظهرت أنزيمات LDH أيضاً زيادة كبيرة باستثناء LDH1. نستنتج أن خلل التنظيم في وظائف الكبد وزيادة إنزيم الكبد يرجع إلى وجود ACE2 كمستقبلات لـ Covid-19 في الخلايا الصفراوية في الكبد. بعض إنزيمات LDH الموجودة في العديد من الأعضاء البشرية عند مهاجمة الكوفيد لهذه الأعضاء بما في ذلك الرئة والكلى والأمعاء تؤدي إلى التغيرات الفسلجية المرضية. المرضى المتعافين من كورونا كانوا قد ادخلوا إلى مستشفى بغداد التعليمي / بغداد - العراق من يوليو إلى سبتمبر 2021 ، وقد تعافى جميع المرضى من مرض كوفيد 19 ، وقمنا بقياس

المؤشرات التالية باستخدام بروتوكول مختلف (GPT ، GOT ، ALP) تم قياسه بطريقة الأتمتة ، بينما (LDH1 ، LDH2 ، LDH3 ، LDH4) بالطريقة التي تم الحصول عليها باستخدام CUSBIO

كشفت النتائج عن زيادة مستوى كل من GPT و GOT و ALP في المرضى المتعافين مقارنةً بمجموعة السيطرة. وكذلك أظهرت (LDH1 ، LDH2 ، LDH3) زيادة في المرضى المتعافين مقارنةً بمجموعة السيطرة. بينما أظهر انخفاضاً في LDH1 لكل من المرضى المتعافين مقارنةً بالسيطرة السليمة. نستنتج أن الإصابة بـ Covid-19 يؤدي إلى تغييرات غير طبيعية في المعلمات البايوكيميائية . خلصت الدراسة إلى أن خلل التنظيم في وظائف الكبد وزيادة إنزيم الكبد يرجع إلى وجود ACE2 كمستقبلات لـ Covid-19 في الخلايا الصفراوية في الكبد. كما أن التغيرات الفيزيولوجية المرضية في مستوى بعض إنزيمات LDL الناتجة عن وجودها في العديد من الأعضاء البشرية بما في ذلك الرئة والكلى والأمعاء التي تهاجمها Covid-19 .

الكلمات المفتاحية : المتعافين من مرض كوفيد 19، إنزيمات القلب ، وظائف الكبد .

Introduction

A novel coronavirus, designated as 2019-nCoV, hit the central Chinese city of Wuhan in late December 2019, and subsequently spread rapidly to all provinces of China and multiple countries[1]. , and multiple organ failure (MOF)[2].

Experimental Many laboratory parameters can be used to determine the severity of the disease and the likelihood of it progressing to more serious conditions like acute respiratory distress syndrome (ARDS).

Subjects: The study included 200 subjects, 150 recovered patients and 50 healthy control and age from 15-65 years. Was conducted in Baghdad teaching hospital/ Baghdad- Iraq from July to September 2021, all patients had recovered from covid19.

Methods

5 ml bloods were taken from the entire subject and the serum, plasma were obtained. The following parameters were evaluated using different protocols (GPT, GOT, ALP) measured by the Automation method, while (LDH1, LDH2, LDH3, LDH4) were measured by the method obtained with CUSBIO.

Statistical analysis

Statistical analysis was done according to percentages to compare between samples using SPSS V.25 computer software.

Results and discussion

The 200 samples were including in the present study, 150 recovered COVID19 patients and other 50 a healthy control. The result in the figure (1) revealed a highly significance difference ($P=0.0001$) between recovered patients and healthy control. The increase (GPT) in plasma, the of recovered patients (47.17) in compare with healthy control (33.62)

By the other hand the result (GOT) in the figure (2) revealed a highly significance difference ($P=0.0001$) and increase level (GOT) between recovered patients (39.58) and healthy control (32.63) .

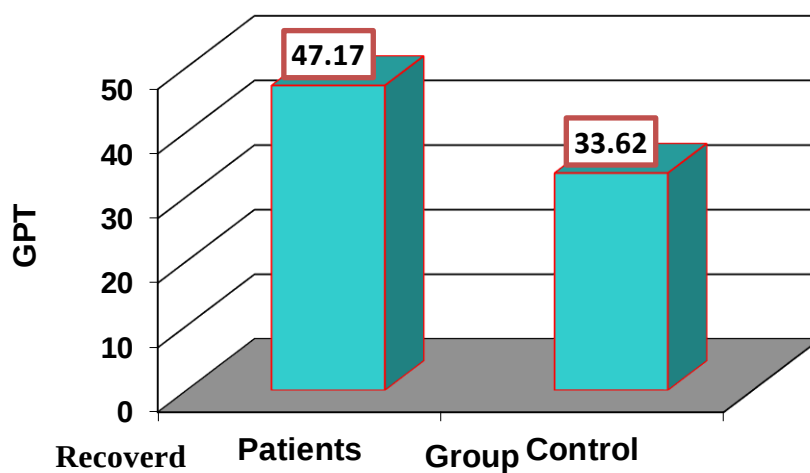


Fig. (1): Comparison between patients and control in GPT

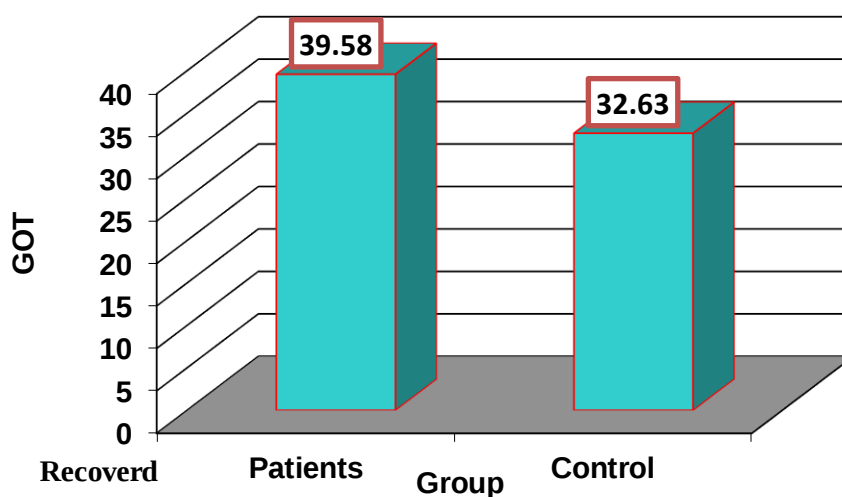


Fig. (2): Comparison between patients and control in GOT

Although alanine aminotransferase (ALT/GPT) and (AST/ GOT) are a helpful screening tool which are an effective modality to detect hepatic dysfunction and heart [3].

The mechanisms underlying liver impairment in covid-19 as a result of direct viral infection of hepatocytes immune-related injury (cytokines storm) which can lead to the damage of the liver cells and myocardial injury and also due to drug hepatotoxicity. There is also suggestion that the virus may bind to cholangiocytes through the ACE2 receptor to dysregulate the liver function [4,5] elevated of (GPT) associated drug-induced liver injury and injury during hospitalization [6]. The result in the figure (3) revealed a highly significance difference ($P=0.0001$) between a recovered patients (426.46) and healthy control (100.35).

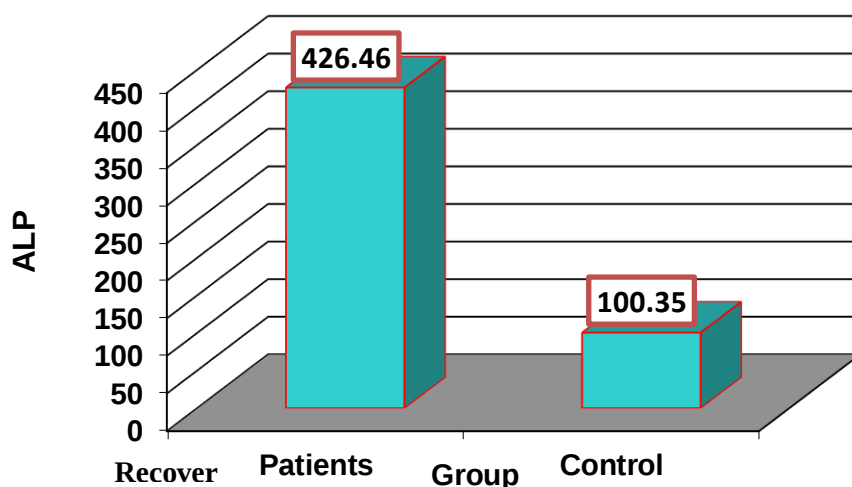


Fig. (3): Comparison between patients and control in ALP

Alkaline phosphatase is an enzyme found in all tissues in the human body but is mostly concentrated in the liver, bones, gallbladder [7]. The direct viral infection or a serious infection as well as from immune interactions, led to cell damage and release more alkaline phosphates which is a gate-keeper of innate immune system [8,9] and life style. The high number of ACE2 receptors on the surface of the cholangiocytes in the liver, cause increasing the incidence of covid-19 infection and so that leading to attack and dysregulation of the liver function [10,5].

Also the Inflammation of the gallbladder via direct / in direct of virus leading to dysregulation of the gallbladder function reflects increase level ALP. Because ACE2 located in gallbladder cells[11]. Increase alkaline phosphates most often associated with epidemiological characteristics and the side effects of drugs may be one of the primary causes of liver damage [12]. The result in the figure (4) revealed a highly significance difference ($P=0.0108$) between recovered patients (772.85) and healthy control (964.31).

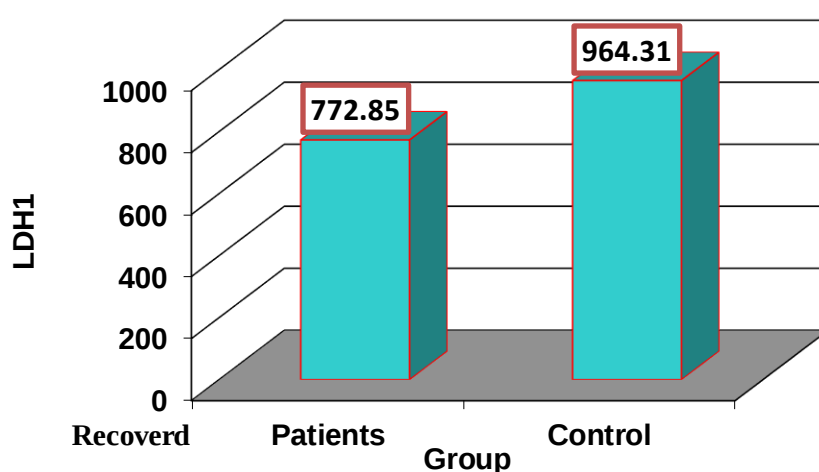


Fig. (4): Comparison between patients and control in LDH1

Lactate Dehydrogenase (LDH-1) Isoenzymes in cardiomyocytes [13], these explain why the concentration of this isoenzymes in heart tissue more than in blood. It required for further study to interpretation the present results. The data in the figure (5) revealed a highly significance difference ($P=0.1339$) between recovered patients (508.08) and healthy control (77.93).

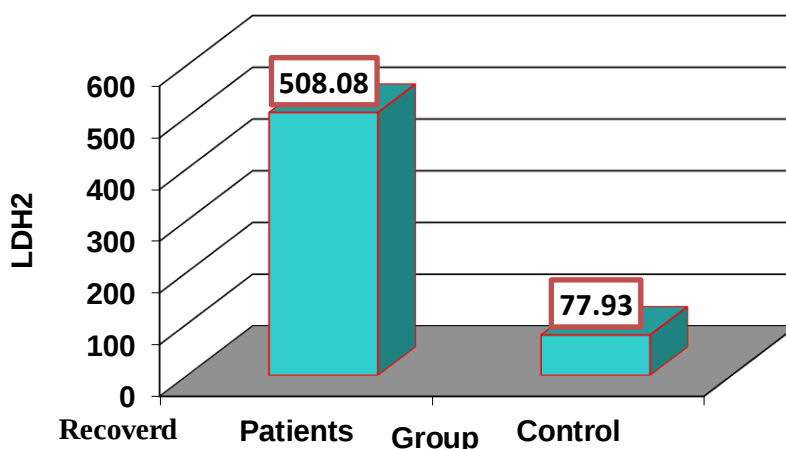


Fig. (5): Comparison between patients and control in LDH2

These results is linked to Immunity cytokine-mediated tissue damage and LDH2 release, it has proposed that Covid-19 causes direct liver injury as well as from immune interactions involving intrahepatic cytotoxic T cells and Kupffer cells, based on the findings suggested that either there a strong correlation between LDH and lung damage as well as disease severity, or that the myocardial and liver injury [14,15].

The result in the figure (6) revealed a highly significance difference ($P=0.1339$) recovered patients (38.73) as healthy control (36.47).

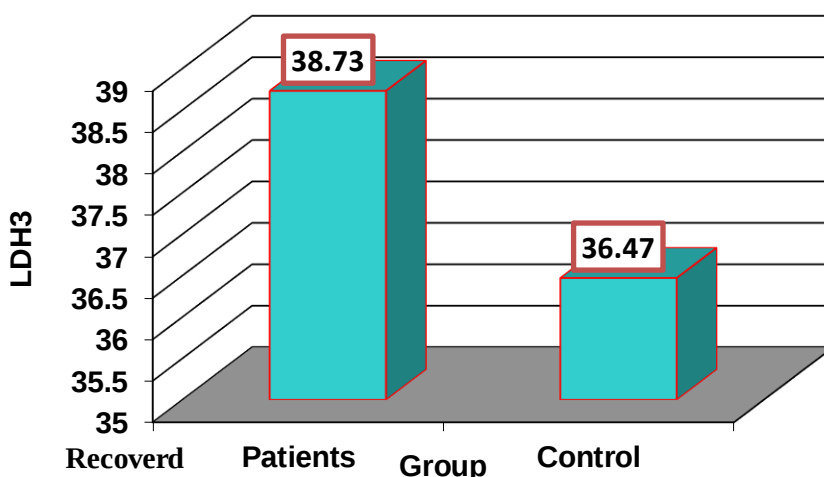


Fig. (6): Comparison between patients and control in LDH3

These findings are a reaction to pathophysiological alterations, and the majority of pathways linked to covid-19 may induce lung fibrosis and damage. Both direct and indirect pathogenic effects of viral infection may cause pulmonary harm. Inflammatory infiltrates are abundant in the lung tissues, showing that tissue damage caused by covid-19 infection is inflammatory [16] The result in the figure (7) revealed a highly significance difference ($P=0.0001$) between recovered patients (246.68) as healthy control (216.39).

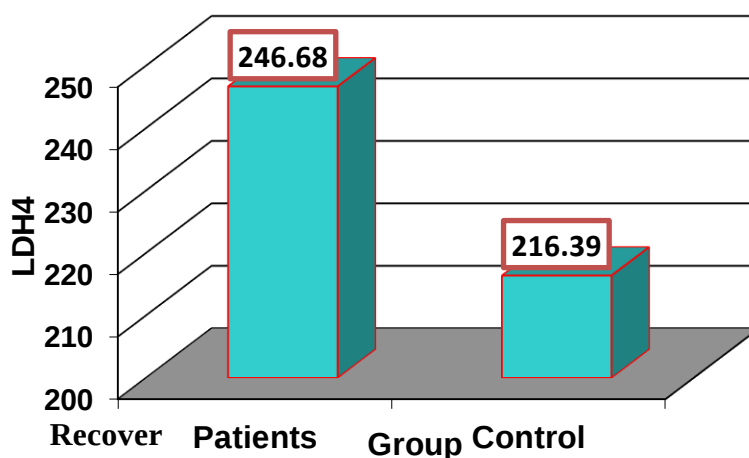


Fig. (7): Comparison between patients and control in LDH4

LDH4 levels in the blood are abnormally high. The covid-19 virus has been identified in a variety of human organs, including the lungs, kidneys, intestines, and pancreas [17]. Pancreatic dysfunction may be linked to covid-19 infection by direct invasion of pancreatic cells or secondary tissue damage produced by the systemic inflammatory immunological response, which may result in increased cytokine levels (e.g., interleukin-6, IL-6) and a "cytokine storm." Furthermore, the production of proinflammatory cytokines by covid-19 infection of the neighboring exocrine pancreas can cause islet cell damage [18].

The covid-19 induced kidney damage is expected to be multifactorial, directly it can infect the kidney podocytes and proximal tubular cells and based on an angiotensin-converting enzyme 2 (ACE2) pathways it can lead to acute tubular necrosis, protein leakage in Bowman's capsule, collapsing glomerulopathy [19].

The covid-19 driven dysregulation of the immune responses including cytokine storm, organ interactions, endothelial dysfunction, hypercoagulability are other potential mechanisms of pathophysiology of kidney injury lead to increase LDH-4.

Conclusion

It concludes that the dysregulation in liver function and increase of liver enzyme is due to the present the ACE2 as COVID19 receptors in cholangiocyte of liver. Also the pathophysiological changes in level of some LDL isoenzymes due to it are existing in several human organ including lung, kidney and intestine which are attack by COVID19.

Conflict of Interest

The authors hereby declare no conflict of interest.

Consent for publication

The authors declare that the work has consent for publication.

Funding support

The authors declare that they have no funding support for this study.

Ethical Considerations

The study was approved by the institutional ethical committee.

Reference

1. Han Q, Lin Q, Jin S, You L. Coronavirus 2019-nCoV: A brief perspective from the front line. *J Infect.* 2020;80(4):373–7.
2. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin Chem Lab Med.* 2020;58(7):1131–4.
3. Lala V, Goyal A, Bansal P, Minter DA. Liver function tests. *StatPearls [Internet].* 2020.
4. Feng G, Zheng KI, Yan Q-Q, Rios RS, Targher G, Byrne CD, et al. COVID-19 and liver dysfunction: current insights and emergent therapeutic strategies. *J Clin Transl Hepatol.* 2020;8(1):18.
5. 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.* 2020.
6. Clark R, Waters B, Stanfill AG. Elevated liver function tests in COVID-19: Causes, clinical evidence, and potential treatments. *Nurse Pract.* 2021;46(1):21.
7. Kim J-H, Lee HS, Park H-M, Lee Y-J. Serum alkaline phosphatase level is positively associated with metabolic syndrome: A nationwide population-based study. *Clin Chim Acta.* 2020;500:189–94.
8. Chandrupatla DMSH, Molthoff CFM, Ritsema WIGR, Vos R, Elshof E, Matsuyama T, et al. Prophylactic and therapeutic activity of alkaline phosphatase in arthritic rats: single-agent effects of alkaline phosphatase and synergistic effects in combination with methotrexate. *Transl Res.* 2018;199:24–38.
9. Jackson EK, Cheng D, Ritov VB, Mi Z. Alkaline Phosphatase Activity Is a Key Determinant of Vascular Responsiveness to Norepinephrine. *Hypertension.* 2020;76(4):1308–18.
10. Shang J, Wan Y, Luo C, Ye G, Geng Q, Auerbach A, et al. Cell entry mechanisms of SARS-CoV-2. *Proc Natl Acad Sci.* 2020;117(21):11727–34.
11. Zong H, Yin B, Zhou H, Cai D, Ma B, Xiang Y. Loss of angiotensin-converting enzyme 2 promotes growth of gallbladder cancer. *Tumor Biol.* 2015;36(7):5171–7.

12. Hashemi N, Viveiros K, Redd WD, Zhou JC, McCarty TR, Bazarbashi AN, et al. Impact of chronic liver disease on outcomes of hospitalized patients with COVID-19: A multicentre United States experience. *Liver Int.* 2020;40(10):2515–21.
13. Klein R, Nagy O, Tóthová C, Chovanová F. Clinical and diagnostic significance of lactate dehydrogenase and its isoenzymes in animals. *Vet Med Int.* 2020;2020.
14. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: little cause for concern. *lancet Gastroenterol Hepatol.* 2020;5(6):529.
15. Han Y, Zhang H, Mu S, Wei W, Jin C, Tong C, et al. Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. *Aging (Albany NY).* 2020;12(12):11245.
16. Geng Y-J, Wei Z-Y, Qian H-Y, Huang J, Lodato R, Castriotta RJ. Pathophysiological characteristics and therapeutic approaches for pulmonary injury and cardiovascular complications of coronavirus disease 2019. *Cardiovasc Pathol.* 2020;47:107228.
17. Ding P, Song B, Liu X, Fang X, Cai H, Zhang D, et al. Elevated pancreatic enzymes in ICU patients with COVID-19 in Wuhan, China: a retrospective study. *Front Med.* 2021;1345.
18. Lazartigues E, Qadir MMF, Mauvais-Jarvis F. Endocrine significance of SARS-CoV-2's reliance on ACE2. *Endocrinology.* 2020;161(9):bqaa108.
19. Ahmadian E, Hosseiniyan Khatibi SM, Razi Soofiyani S, Abediazar S, Shoja MM, Ardalan M, et al. Covid-19 and kidney injury: Pathophysiology and molecular mechanisms. *Rev Med Virol.* 2021;31(3):e2176.