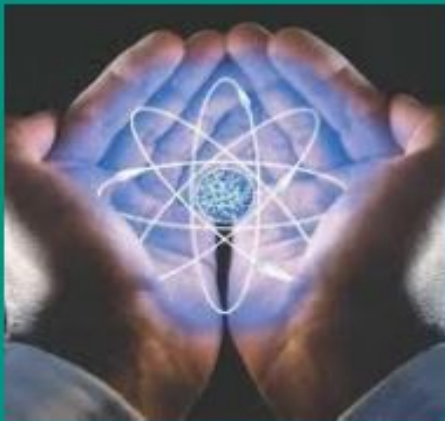


Table Of Content

| | |
|---------------------------------------|---|
| Journal Cover | 2 |
| Author[s] Statement | 3 |
| Editorial Team | 4 |
| Article information | 5 |
| Check this article update (crossmark) | 5 |
| Check this article impact | 5 |
| Cite this article | 5 |
| Title page | 6 |
| Article Title | 6 |
| Author information | 6 |
| Abstract | 6 |
| Article content | 8 |

Academia Open



By Universitas Muhammadiyah Sidoarjo

Originality Statement

The author[s] declare that this article is their own work and to the best of their knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the published of any other published materials, except where due acknowledgement is made in the article. Any contribution made to the research by others, with whom author[s] have work, is explicitly acknowledged in the article.

Conflict of Interest Statement

The author[s] declare that this article was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright Statement

Copyright © Author(s). This article is published under the Creative Commons Attribution (CC BY 4.0) licence. Anyone may reproduce, distribute, translate and create derivative works of this article (for both commercial and non-commercial purposes), subject to full attribution to the original publication and authors. The full terms of this licence may be seen at <http://creativecommons.org/licences/by/4.0/legalcode>

EDITORIAL TEAM

Editor in Chief

Mochammad Tanzil Multazam, Universitas Muhammadiyah Sidoarjo, Indonesia

Managing Editor

Bobur Sobirov, Samarkand Institute of Economics and Service, Uzbekistan

Editors

Fika Megawati, Universitas Muhammadiyah Sidoarjo, Indonesia

Mahardika Darmawan Kusuma Wardana, Universitas Muhammadiyah Sidoarjo, Indonesia

Wiwit Wahyu Wijayanti, Universitas Muhammadiyah Sidoarjo, Indonesia

Farkhod Abdurakhmonov, Silk Road International Tourism University, Uzbekistan

Dr. Hindarto, Universitas Muhammadiyah Sidoarjo, Indonesia

Evi Rinata, Universitas Muhammadiyah Sidoarjo, Indonesia

M Faisal Amir, Universitas Muhammadiyah Sidoarjo, Indonesia

Dr. Hana Catur Wahyuni, Universitas Muhammadiyah Sidoarjo, Indonesia

Complete list of editorial team ([link](#))

Complete list of indexing services for this journal ([link](#))

How to submit to this journal ([link](#))

Article information

Check this article update (crossmark)



Check this article impact (*)



Save this article to Mendeley



(*) Time for indexing process is various, depends on indexing database platform

Hematological Parameters and Liver Function After COVID-19 Vaccination (Simple Population Patients in Ramadi City – Iraq)

*Parameter Hematologi dan Fungsi Hati Setelah Vaksinasi COVID-19
(Populasi Sederhana Pasien di Kota Ramadi - Irak)*

Ridhab Ajeel Jasim , ridhab90@uoanbar.edu.iq, (1)

College of Pure science, University of Anbar, Iraq

Saif Subhi Noori, Saifsubhy89@uoanbar.edu.iq, (0)

College of Pure science, University of Anbar, Iraq

Adeeb Shakir Mahmood , adeebsh88@uoanbar.edu.iq, (0)

College of Pure science, University of Anbar, Iraq

Asmaa Wajeh Jumaa, edw.ah2010n@uoanbar.edu.iq, (0)

College of Education for women, University Of Anbar, Iraq

Fatin Zuher Abd Alkareem, fatin.zuher@uoanbar.edu.iq, (0)

College of Pure science, University of Anbar, Iraq

⁽¹⁾ Corresponding author

Abstract

This study aimed to investigate the influence of COVID-19 vaccination on liver function and blood parameters, specifically Mean Corpuscular Volume (MCV) and Hemoglobin (HGB) levels, among young adults (aged 18-32) in Anbar province. Blood samples from 50 individuals were collected at Ramadi Teaching Hospital, with half of the participants vaccinated and the other half unvaccinated. Results revealed a significant decrease in MCV and HGB levels among the vaccinated group compared to the unvaccinated group. Concurrently, liver function indicators, including Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), and Bilirubin, showed a marked increase in the vaccinated individuals, indicating potential hematological disorders and liver injury. These findings underscore the importance of COVID-19 vaccination while highlighting the need for continued monitoring of liver health and blood parameters in vaccinated individuals to mitigate potential long-term health implications.

Highlights:

- COVID-19 vaccination in young adults may lead to a significant decrease in Mean Corpuscular Volume (MCV) and Hemoglobin (HGB) levels.
- Liver function indicators such as Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), and Bilirubin exhibit a notable increase in vaccinated individuals.
- Continuous monitoring of liver health and blood parameters is crucial for assessing potential long-term health implications associated with COVID-19 vaccination.

Keywords: COVID-19 Vaccination, Liver Function, Blood Parameters, Young Adults, Anbar Province.

Academia Open

Vol 8 No 2 (2023): December

DOI: 10.21070/acopen.8.2023.7843 . Article type: (Medicine)

Published date: 2023-09-06 00:00:00

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leading to coronavirus disease 2019 (Covid-19) was initially reported in December 2019 in Wuhan, China. 1 SARS-CoV-2 is an extremely contagious and disease-causing virus that has expanded globally and resulted in a global outbreak[1]. While the majority of Covid-19 cases exhibit mild symptoms, the rates of hospitalization and death are notable, particularly among individuals with underlying health conditions[2][3].

As the COVID-19 pandemic continues and new strains of SARS-CoV-2 arise, it is crucial to swiftly create a reliable and secure vaccine for disease control. In recent times, numerous potential vaccines for COVID-19 have emerged, such as protein-based vaccines (Novavax), inactivated vaccines (Sinovac Life Science), viral vector vaccines (Janssen, Oxford-AstraZeneca), and mRNA vaccines (Pfizer/BioNtech, Moderna, CureVac). These vaccines have undergone development, testing, and eventual release into the market[4][5].

Among them, mRNA-based products are novel, yet familiar[6]. mRNA vaccinations administer genetically modified mRNA through lipid nanoparticles that function as transporters. Following injection, the mRNA is converted into desired proteins within the body, leading to a robust immune reaction and a two-shot schedule that provides 95% defense against COVID-19[7].

SARS-CoV-2 vaccines activate the interferon pathway as a component of their mode of operation, giving rise to certain worries about the potential for vaccine-related autoimmunity in vulnerable individuals[8]. Numerous immune-related diseases, either specific to certain organs or affecting the entire body, have indeed been documented following administration of the SARS-CoV-2 vaccine[9]. To the utmost of our understanding, Brill et al[10] documented the initial occurrence of liver harm following the initial administration of the Pfizer-BioNTech vaccine. Subsequent incidents have also been documented[11]. The clinical and histological observations of the majority of patients exhibited similarities to autoimmune hepatitis (AIH)[12]

As more residents are vaccinated, cases of hematological side effects of vaccinations become more pronounced. One of the most serious side effects include thrombocytopenia and thromboembolism due to vaccination. A case of thromboembolism has been reported in a patient with pre-existing thrombocytopenia after vaccination with the Oxford-AstraZeneca vaccine[13]

Another systematic review of 286 patients who experienced any form of thromboembolism after vaccination revealed that a large percentage of patients also experienced thrombocytopenia, high D-dimers, and antiplatelet antibodies[14].

Method

Study Sample :

50 blood samples were collected from the vaccinated patients visiting Ramadi General Hospital in Anbar Governorate, for a period from 6/7/2020 to 1/9/2021, and the blood sample was collected in EDTA Tube for the purpose of conducting (CBC analyzes) , in addition to separating part of the blood by centrifugation to obtain serum for the purpose of conducting liver function analyzes (ALT , ALP and Bilirubin).

C omplete Blood Count :

CBC test results, measured from the blood sample obtained immediately after diagnosis, were compared between the patients and control group .CBC results of the 3rd day In the study, some parameters and ratios such as hemoglobin (HGB) and mean corpuscular volume (MCV) .

Biochemical Analyses :

Serum was utilized for quantifying serum liver enzymes activity which included (ALT and ALP) and bilirubin (total, direct and indirect). Serum ALT activity were measured using a colorimetric kit provided by Randox/ UK. Serum ALP activity was measured using a colorimetric kit provided by BioMerieux/ France. Serum total bilirubin (TB) and direct bilirubin (DB) were measured using a colorimetric kit provided by Biolabo SA/ France. Indirect bilirubin (IB) can be calculated using the following equation:

Indirect Bilirubin (μmol/ L) = Total Bilirubin - Direct Bilirubin.

Statistical Analyses :

In order to compare the mean values of two population , the SPSS statistical program was employed , and T- test was preformed , a P- value of less than (0.05) and (0.01) .

Results and Discussion

Results

The results of the statistical analysis, as shown in Table (1) and Figure (1) (2) , (3), showed that there is a significant increase in the level of (ALT , ALP and Bilirubin) in vaccinated people compared to non-vaccinated people Which indicates the possibility of liver disease now and in the future

| Group | Mean \pm SE | | |
|-------------------|------------------|-------------------|------------------|
| | ALT | ALP | Bili |
| Patients | 65.50 \pm 2.50 | 110.70 \pm 7.13 | 2.03 \pm 0.12 |
| Control | 34.35 \pm 3.22 | 53.90 \pm 3.52 | 0.420 \pm 0.04 |
| T-test | 8.574 * | 16.724 * | 0.264 * |
| * (P \leq 0.05) | | | |

Table 1.

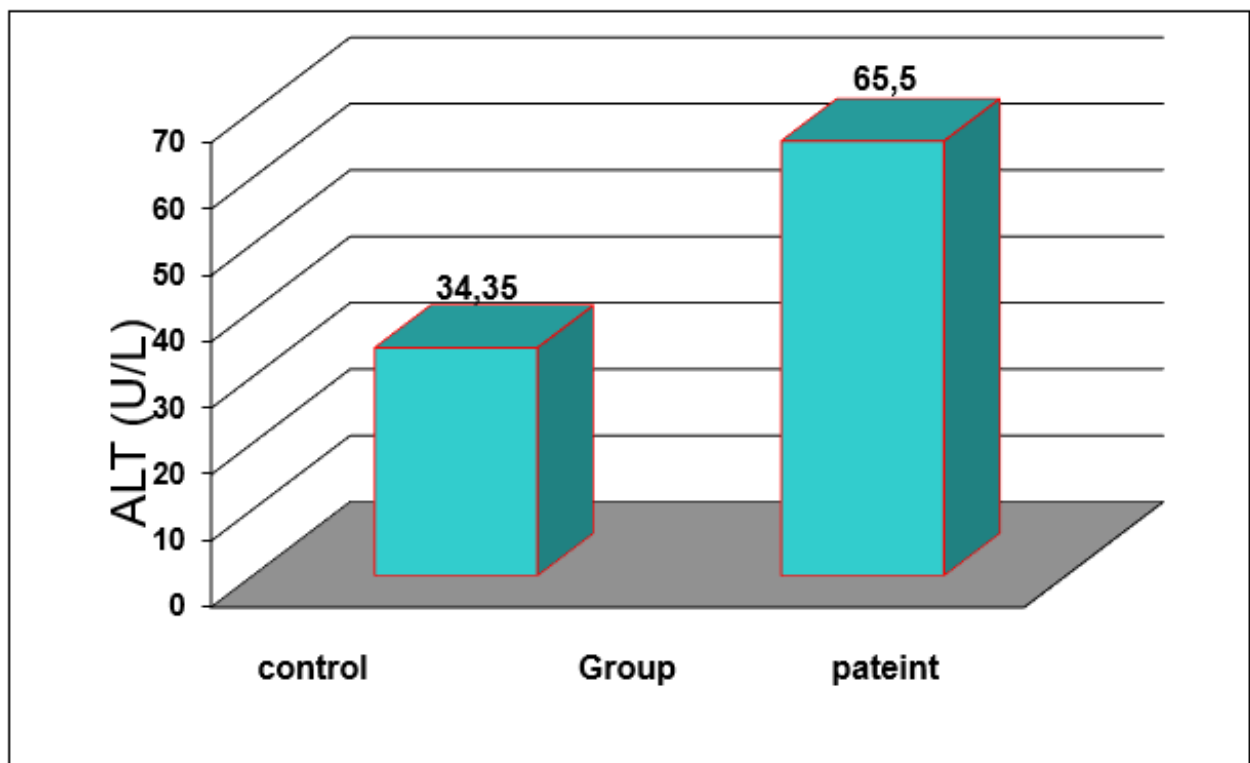


Figure 1. Coparison between pateint and control groups in ALT

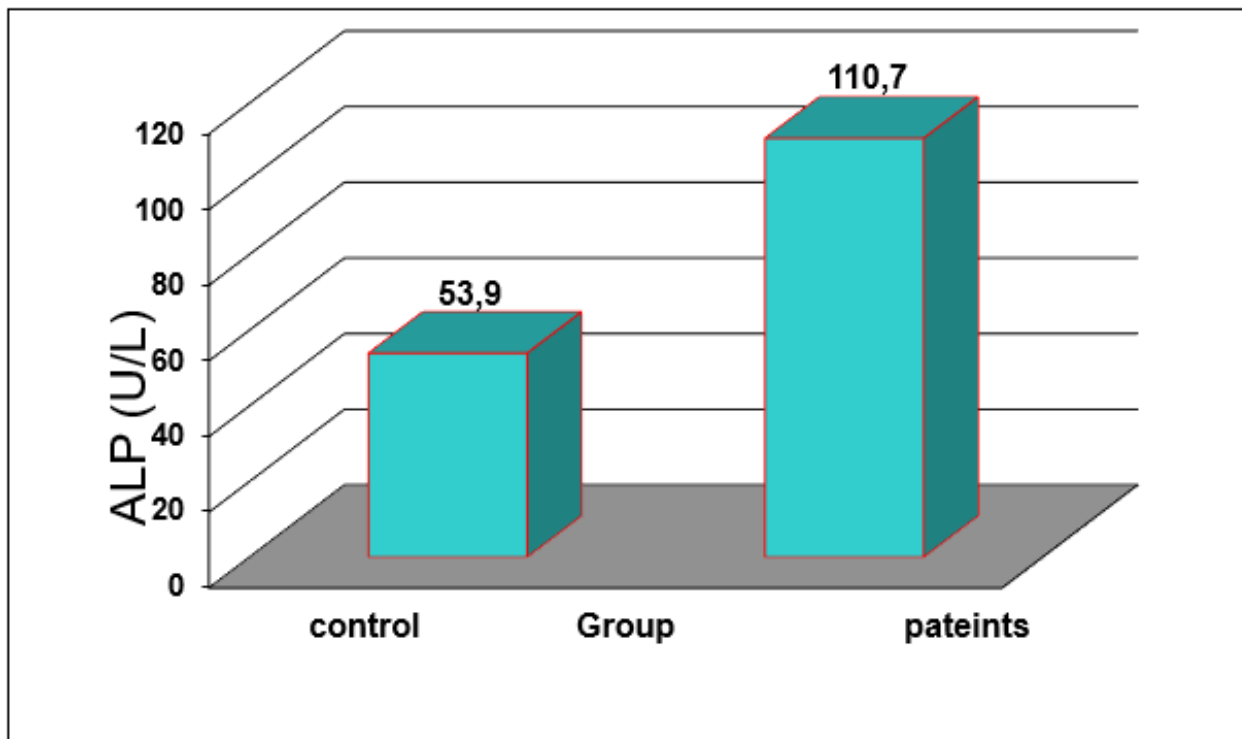


Figure 2. Comparison between pateints and controh groups in ALP

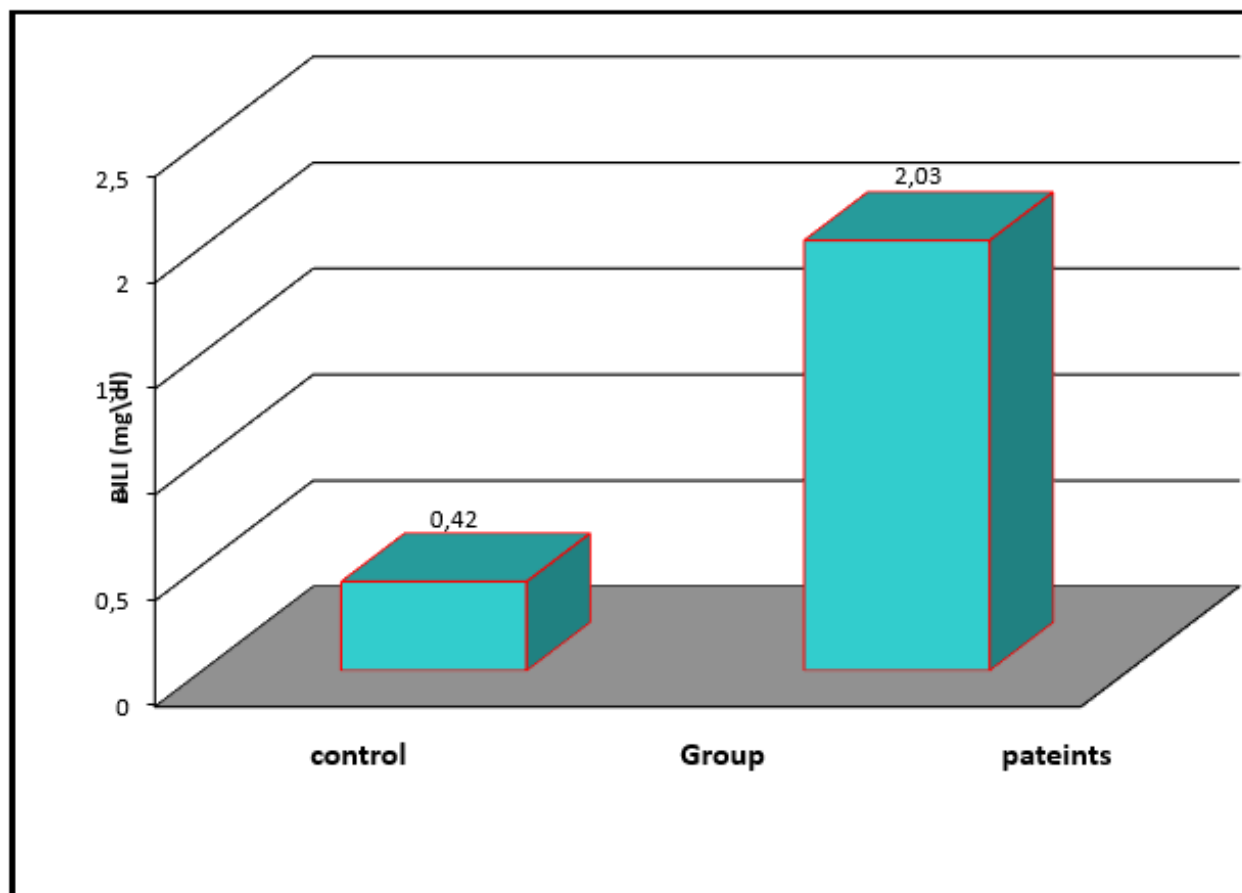


Figure 3. Comparison btween pateints and control groups in BIL

-The results of the statistical analysis of HGB and MCV showed a non-significant decrease as in Table (2), Figure (4) and (5), as the reason is that there was a lack of platelets and the occurrence of blood clots, which led to a decrease in the level of red cell count.

| Group | Mean \pm SE | |
|---|------------------|------------------|
| | HGB | MCV |
| Patients | 12.37 \pm 0.37 | 82.74 \pm 1.19 |
| Control | 13.58 \pm 0.52 | 85.86 \pm 2.36 |
| T-test | 1.107 NS | 5.362 NS |
| P-value | 0.0439 | 0.249 |
| * (P \leq 0.05), NS: Non-Significant. | | |

Table 2.

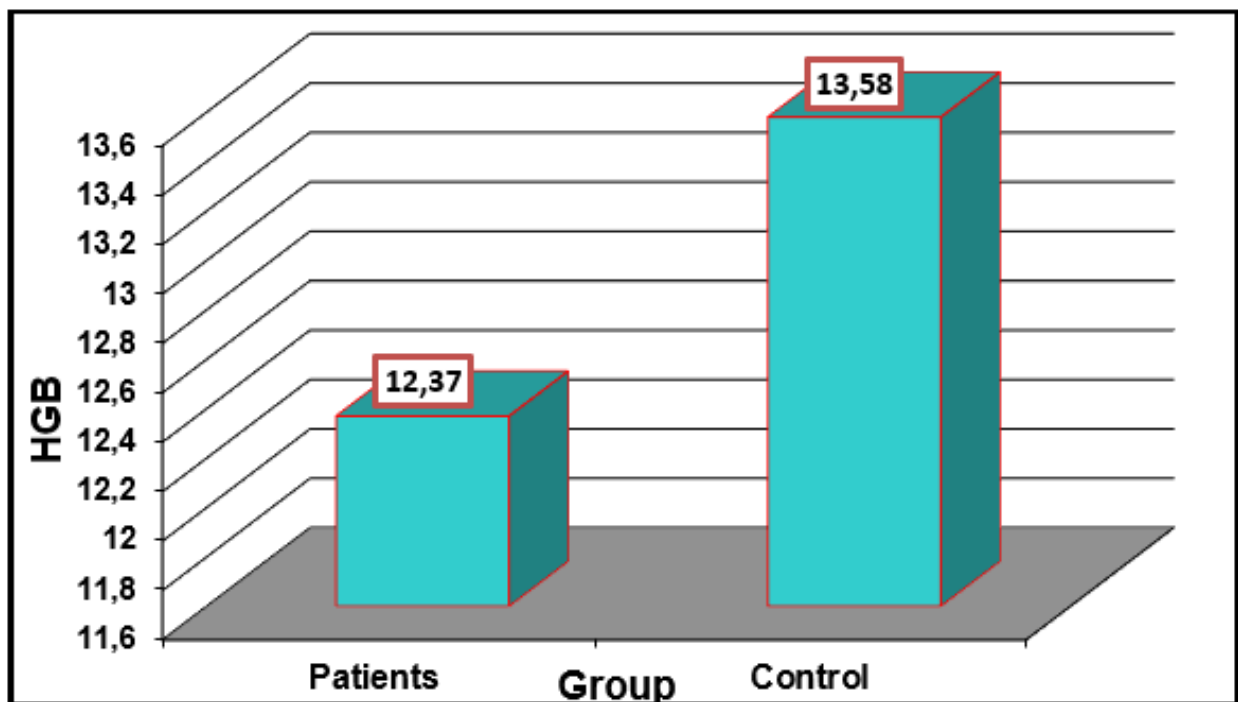


Figure 4. Comparison between patients and control groups in HGB

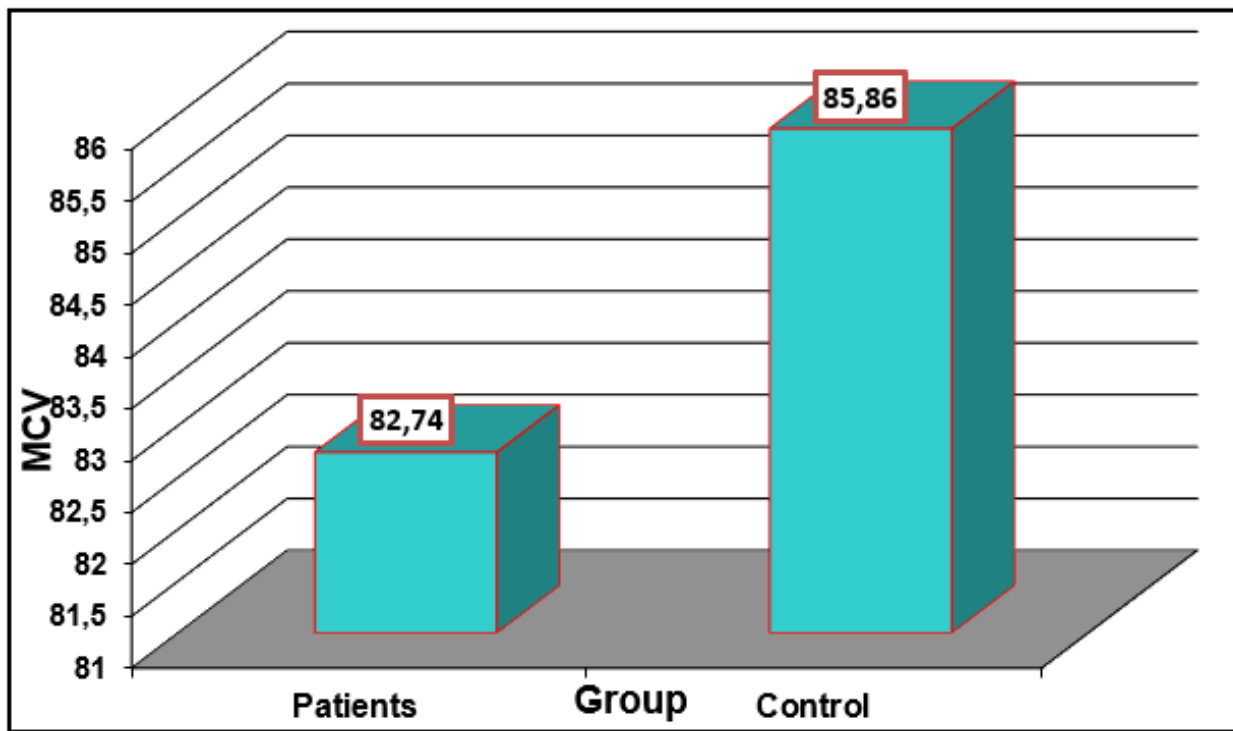


Figure 5. Comparison between patients and control groups in MCV

Discussion

Since the onset of the coronavirus pandemic (COVID-19), the SARS-CoV-2 virus has caused the death of over 6.5 million individuals globally. Nevertheless, the prompt implementation of widespread immunization initiatives leads to significant fatalities, particularly among vulnerable populations like the aged, weak, and those with compromised immune systems[15][16]

In the latter group, solid organ transplant recipients (SOTR) are particularly at risk because underlying causes of organ failure and chronic immunosuppressive burden are associated with reduced immune responses to COVID-19 vaccines, and with an excessive risk of death due to SARS-CoV-2 infection [17][18]

The COVID-19 crisis is considered one of the most significant trials of our era, and its repercussions have also affected mental well-being and can have an adverse effect on mental health. A recent investigation exploring the primary worries linked to the new coronavirus disease (COVID-19) in the Italian population discovered that apprehension regarding potential vaccine outcomes was more prevalent among females and the youth, whereas among the elderly, the most common concern was fear of falling ill and the subsequent consequences. Meanwhile, among young individuals, concern about falling ill and its aftermath (such as isolation) was more widespread[19]

Vaccinations against COVID-19 play a vital role in putting an end to the ongoing global pandemic. Vaccines like Pfizer-BioNTech, Oxford Uni-AstraZeneca, Moderna, Johnson & Johnson, Sinovac-CoronaVac, Covishield, and Sinopharm have been swiftly developed, deemed safe, granted emergency use authorization since the beginning of 2020, and have been widely utilized. As of 1 May 2022, over 5 billion doses of vaccines for severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) have been given worldwide[20].

Hence, recent concerns have arisen regarding the safety, negative impacts, or poisonous aspects associated with the COVID-19 immunization. Negative responses to COVID-19 vaccines are frequently documented, but the majority are not liver-related. Localized discomfort, exhaustion, migraine, and muscle soreness are the foremost prevalent negative effects subsequent to COVID-19 vaccination[21]

Hepatotoxicity is uncommon with all vaccines utilized to prevent COVID-19, but can happen. An increasing body of evidence has suggested that thrombosis of the portal vein, autoimmune liver disease, elevated liver enzymes, and liver damage, among others, may be potential outcomes of COVID-19 vaccines. COVID-19 vaccines are typically given in a 2- or 3-dose series within a short period of time, and the symptoms and indications of the COVID-19 infection overshadow the mild and temporary adverse effects on the liver that arise with some of the vaccines used to prevent COVID-19. Additionally, cases of acute hepatitis, elevated liver enzymes, and liver damage have been reported in patients with moderate and severe COVID-19, in which vaccines did not appear to play a role. Whether the connection between SARS-CoV-2 vaccine and those liver diseases is coincidental or causal is yet to be

clarified[22] [23] [24]

The precise mechanism of liver injury caused by SARS-CoV-2 vaccination is not fully understood. Both types of vaccines (mRNA and viral vector) contain the genetic code for the spike (S) protein of SARS-CoV-2. When the S protein enters the human body, it triggers a strong response from the innate immune system, leading to the activation of cells and the production of proinflammatory cytokines and chemokines. Because the S protein is similar to proteins specific to the liver, an activated immune system may mistakenly target and destroy liver proteins. A recent study demonstrated that antibodies against the SARS-CoV-2 S protein reacted with antigens in human tissues, resulting in significant increases in immune markers associated with autoimmune reactions, such as ANA, anti-actin, and AMA[8] [25]

On the other hand, There are many adverse Hematological Effects of COVID-19 Vaccination within the General Population. Several case sequences have reported hematological abnormalities, including thrombocytopenic purpura (ITP) after vector-based vaccination. The results indicated that the vaccines may trigger an immune response that affects the blood system [26] [27]

Conclusion

The study confirms the case, despite the importance of COVID-19 vaccines, but their effects were clear on many vaccinated people, especially with regard to liver function and blood variables, as the results of this study confirmed a noticeable increase in liver function among those vaccinated with the COVID-19 vaccine, in addition to a decrease in vital blood indicators, which confirms their susceptibility to hepatitis and severe anemia, which negatively affects their health in the future.

References

1. C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, et al., "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China," *Lancet*, 2020, pp. 497-506.
2. Z. Wu and J.M. McGoogan, "Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72,314 cases from the Chinese Center for Disease Control and Prevention," *JAMA*, vol. 323, no. 13, pp. 1239-1242, 2020.
3. C. Efe, R. Dhanasekaran, C. Lammert, B. Ebik, F. Higuera-de la Tijera, C. Aloman, et al., "Outcome of COVID-19 in patients with autoimmune hepatitis: an international multicenter study," *Hepatology*, vol. 73, pp. 2099-2109, 2021.
4. O. Sharma, A.A. Sultan, H. Ding, and C.R. Triggler, "A Review of the Progress and Challenges of Developing a Vaccine for COVID-19," *Front. Immunol.*, vol. 11, p. 585354, 2020.
5. T. Fiolet, Y. Kherabi, C.J. MacDonald, J. Ghosn, and N. Peiffer-Smadja, "Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: A narrative review," *Clin. Microbiol. Infect.*, vol. 28, pp. 221-202, 2021.
6. J.A. Wolff, R.W. Malone, P. Williams, W. Chong, G. Acsadi, A. Jani, et al., "Direct gene transfer into mouse muscle in vivo," *Science*, vol. 247, Pt 1, pp. 1465-1468, 1990.
7. F.P. Polack, S.J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al., "Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine," *N. Engl. J. Med.*, vol. 383, pp. 2603-2615, 2020.
8. J.R. Tejero and D.L. Farber, "COVID-19 vaccines: modes of immune activation and future challenges," *Nat Rev Immunol.*, vol. 21, pp. 195-197, 2021.
9. Y. Chen, Z. Xu, P. Wang, X.M. Li, Z.W. Shuai, D.Q. Ye, et al., "New-onset autoimmune phenomena post COVID-19 vaccination," *Immunology*, vol. 165, pp. 386-401, 2021.
10. F. Bril, S. Al Daffal, M. Dean, and D.M. Fetting, "Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: causality or casualty?," *J Hepatol*, vol. 75, pp. 222-224, 2021.
11. H. Shroff, S.K. Satapathy, J.M. Crawford, N.J. Todd, and L.B. VanWagner, "Liver injury following SARS-CoV-2 vaccination: a multicenter case series," *J Hepatol*, vol. 76, pp. 211-214, 2022.
12. Z. Cao, H. Gui, Z. Sheng, H. Xin, and Q. Xie, "Letter to the editor: exacerbation of autoimmune hepatitis after COVID-19 vaccination," *Hepatology*, vol. 75, pp. 757-759, 2022.
13. A. Mauriello, M. Scimeca, I. Amelio, R. Massoud, A. Novelli, F. Di Lorenzo, et al., "Thromboembolism after COVID-19 vaccine in patients with preexisting thrombocytopenia," *Cell Death Dis.*, vol. 12, p. 762, 2021.
14. A. Mani and V. Ojha, "Thromboembolism after COVID-19 Vaccination: A Systematic Review of Such Events in 286 Patients," *Ann. Vasc. Surg.*, vol. 84, pp. 12-20.e11, 2022.
15. J.S. Tregoning, K.E. Flight, S.L. Higham, Z. Wang, and B.F. Pierce, "Progress of the COVID-19 vaccine effort: Viruses, vaccines and variants versus efficacy, effectiveness and escape," *Nat. Rev. Immunol.*, vol. 21, pp. 626-636, 2021.
16. M. Cascella, M. Rajnik, A. Aleem, S.C. Dulebohn, and R. Di Napoli, "Features, Evaluation, and Treatment of Coronavirus (COVID-19)," *StatPearls Publishing: Treasure Island, FL, USA*, 2022.
17. B.J. Boyarsky, W.A. Werbel, A.A. Avery, A.A. Tobian, A.B. Massie, D.L. Segev, et al., "Antibody response to 2-dose SARS-COV-2 mRNA vaccine series in solid organ transplant recipients," *JAMA*, vol. 325, pp.

- 2204-2206, 2021.
18. Y. Azzi, R. Bartash, J. Scalea, P. Loarte-Campos, and E. Akalin, "COVID-19 and solid organ transplantation: A review article," *Transplantation*, vol. 105, pp. 37-55, 2021.
 19. B. Barchielli, C. Cricenti, F. Gallè, E.A. Sabella, F. Liguori, G. Da Molin, et al., "Climate Changes, Natural Resources Depletion, COVID-19 Pandemic, and Russian-Ukrainian War: What Is the Impact on Habits Change and Mental Health?," *Int. J. Environ. Res. Public Health*, vol. 19, p. 11929, 2022.
 20. World Health Organization, "COVID-19 vaccination dashboard 2022," [Online]. Available: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines>.
 21. A.F. Hernandez, D. Calina, K. Poulas, A.O. Docea, and A.M. Tsatsakis, "Safety of COVID-19 vaccines administered in the EU: Should we be concerned?," *Toxicol Rep.*, vol. 8, pp. 871-879, 2021.
 22. H. Shroff, S.K. Satapathy, J.M. Crawford, N.J. Todd, and L.B. VanWagner, "Liver injury following SARS-CoV-2 vaccination: a multicenter case series," *J Hepatol*, vol. 76, no. 1, pp. 211-214, 2022.
 23. A. Al Mutair, S. Alhumaid, W.N. Alhuqbani, A.R.Z. Zaidi, S. Alkoraisi, M.F. Al-Subaie, A.M. AlHindi, A.K. Abogosh, A.K. Alrasheed, A.A. Alsharafi, et al., "Clinical, epidemiological, and laboratory characteristics of mild-to-moderate COVID-19 patients in Saudi Arabia: an observational cohort study," *Eur J Med Res.*, vol. 25, no. 1, pp. 1-8, 2020.
 24. S. Alhumaid, A. Al Mutair, Z. Al Alawi, K. Al Salman, N. Al Dossary, A. Omar, M. Alismail, A.M. Al Ghazal, M.B. Jubarah, and A. Al SH, "Clinical features and prognostic factors of intensive and non-intensive COVID-19 patients: an experience cohort from Alahsa, Saudi Arabia," *Eur J Med Res.*, vol. 26, no. 1, pp. 1-13, 2021.
 25. A. Vojdani and D. Kharrazian, "Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases," *Clin Immunol.*, vol. 217, p. 108480, 2020.
 26. O. Tarawneh and H. Tarawneh, "Immune thrombocytopenia in a 22-year old post Covid-19 vaccine," *Am J Hematol.*, 2021.
 27. E.J. Lee, D.B. Cines, T. Gernsheimer, et al., "Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination," *Am J Hematol.*, 2021.