Effect of COVID-19 and Its Vaccine: Hematological and Immunological Study of Recovered Individuals Based on Gender

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Abstract

Background: The necessary urgent global response measures were implemented to contain the rapid spread of coronavirus disease 2019 (COVID-19). Vaccination has been the most effective way to combat this pandemic. **Objective:** The aim of the current study was to evaluate the hematological parameters and COVID-19-specific antibodies in a healthy population with different COVID-19 and vaccination backgrounds, taking gender into account. **Materials and Methods:** The study involved 80 healthy adults who were categorized into four groups based on their COVID-19 and vaccination status. The male and female categorization was later added to these groups. Blood samples were collected and analyzed for COVID-19-specific antibodies, IgG and IgM, and complete blood count parameters. The samples were collected in Karbala, Iraq. **Results:** The results showed that the IgG levels of IV and NIV subsets were higher than INV NINV subsets at P value < 0.001. No significant differences were found in white blood cell parameters except for lymphocytes, neutrophils, and their ratio between the four groups. However, when gender was taken into account, few significant differences were observed in white blood cells, lymphocytes, and neutrophils between the groups. The platelet indices showed no significant changes within the individual groups or genders. Red blood cell variables also showed no significant changes between groups, but variations in red blood cells, hematocrit, and hemoglobin were found for each gender-divided group specifically (P value < 0.001). **Conclusion:** The present study concludes that vaccination mimics infection. No changes were observed for most hematological parameters between the four explored subsets. However, the study revealed gender-specific responses to red blood cell counts and other related parameters, reinforcing the importance of complete blood count testing and advocating a deeper exploration into gender-specific responses, especially for patients with specific hematological conditions.

Keywords: COVID-19, hematological tests, sex, vaccines

Introduction

The rapid spread of coronavirus disease 2019 (COVID-19) since its emergence in December 2019[1] has required urgent global response measures. COVID-19, caused by the novel β-coronavirus, SARS-CoV-2,[2,3] presents with symptoms ranging from mild illness to acute respiratory distress syndrome (ARDS), sepsis, and death. Changes in hematological markers have been observed to correlate with disease stage and severity.[4,5] These markers, which include white blood cell and lymphocyte counts, play crucial roles in patient management and can potentially provide insights into prognostic outcomes.[6]

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Vaccination is widely acknowledged as the most effective way to combat this pandemic.[7] Various forms of COVID-19 vaccines have been developed such as inactivated viral particles, mRNA vaccines, and adenoviral-based vaccines.[8-10] While the vaccines have been shown to be effective against COVID-19 infections, there are concerns about their safety, particularly those developed using

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new mRNA technology, which resulted in some vaccine hesitancy.[11]

Previous reports of hematological abnormalities, such as thrombocytopenia and immune thrombocytopenic purpura (ITP) following vector-based or mRNA-based vaccinations[12,13] as well as transient neutropenia post the AstraZeneca vaccine,[14] underline potential impacts on the immune response and the blood system. Given the potentially life-threatening complications that could arise from such abnormalities, it is essential to understand these impacts and estimate the associated risks.[15]

Blood plays a crucial role in the human body as it is intricately connected to various cells and tissues, offering a diverse range of valuable information.[16] The complete blood count (CBC) and the COVID-19-specific antibodies (IgG, IgM) are valuable and rapid tools in the management of this disease and provide a lot of information about the individual health's status. In particular, CBC is used as the most common test in clinical practice especially in many countries with limited resources for patients with COVID-19 or to predict patient recovery.[17,18] It provides essential diagnostic and therapeutic information, with reference intervals (RI) having significant clinical utility.[19,20] However, alterations in these markers have been reported post-recovery from COVID-19, and post-vaccination, potentially impacting pre-established RI.[21-23]

There are few findings that have been published for follow-up studies on hematological changes in patients who recovered from COVID-19 and were vaccinated.[18] Given the context, the aim of this study was to investigate the influence of COVID-19 vaccination and COVID-19 infection on hematological indices. The study was designed to evaluate the hematological parameters and COVID-19-specific antibodies in a healthy population with different COVID-19 and vaccination backgrounds, divided into four distinct groups.

Materials and Methods

Study design

A cross-sectional study was conducted to evaluate the association between the Pfizer COVID-19 vaccine and hematological values in healthy individuals with different COVID-19 and vaccination backgrounds. Healthy adult volunteers who visited the Imam Hussain Hospital, Karbala, Iraq during a period from November 2022 to January 2023 were engaged.

After being agreed to participate, participants were subjected to a detailed interview to collect sociodemographic data and background data on COVID-19 and vaccination, their medical history and other relevant factors. Based on the questionnaire, individuals were first divided into two groups: COVID-19 vaccination and non-COVID-19 vaccination. The two groups were then classified into two further subsets after receiving the results of the COVID-19 antibody titer tests. These four groups of recovered participants from COVID-19 and its vaccines were infected with COVID-19 and vaccinated (IV), infected with COVID-19, non-vaccinated (INV), vaccinated, non-infected COVID-19 (NIV) and non-infected COVID-19 and non-vaccinated (NINV) individuals. Later, these four groups were divided into male and female sets.

Study cohort or participant characteristics

Participants aged ≥20 were included if they were considered clinically healthy. These were accepted as blood donors and entered into the study groups. The sample size was 80 individuals including 44 women and 36 men distributed into four previous describing groups. The study excluded individuals who had any medical conditions such as high blood pressure, diabetics, or those who had taken any type of medicine within 60 days before the hematological tests. Other specific conditions included history of cancer, recent chemotherapy, radiotherapy, or use of drugs for malignant disease, and immunosuppression within 90 days prior were also excluded. Participants who were smoking and alcoholic habits were excluded.

Blood sample analyses

Blood samples were collected from the elbow veins of each participant. These samples were divided into two tubes: one ethylenediaminetetraacetic acid (EDTA) tube to prevent coagulation and another gel tube.

COVID-19 antibody titer

The gel tubes were used to detect IgG and IgM. The COVID-19 IgG and IgM titers were determined using the mini-VIDAS (BioMérieux, France) assay according to the manufacturer's instructions. All blood samples were analyzed on the hematology autoanalyzer (Sysmex Corporation, Kobe, Japan).

Complete blood count

Blood samples collected in EDTA tubes were analyzed using the Swelab autoanalyzer hematology machine (BOULE, Sweden). This device automatically measured and analyzed various blood parameters, including the absolute white blood cell (WBC, leucocytes), lymphocytes, neutrophils, mixed, and the ratio of lymphocytes and neutrophils (LNR). Their percentiles in addition to the values of platelet count (PLT), mean platelet volume (MPV, fl), and platelet distribution width (PDW) were noted. The red blood cell (RBC, $\times 10^{12}$/L), hemoglobin concentration (Hb, g/dL), hematocrit (HCT, %), mean corpuscular volume (MCV, fL), mean corpuscular hemoglobin (MCH, pg/cell), Mean Corpuscular Hemoglobin Concentration (MCHC, g/dL), RBC distribution width standard deviation (RDW-SD, fL), RBC distribution

width-coefficient of variation (RDW-CV, %) were also recorded. The machine utilized a combination of optical and electrical methods to perform the analysis, with results displayed on a computer screen and subsequently saved for further reference and interpretation.

Ethical approval

The research was conducted in accordance with the tenets of the Helsinki Declaration. Written informed consent was obtained from each participant, ensuring their clear understanding of the study's purpose, potential risks, and benefits. Thus, the participants gave their consent voluntarily, upholding their protection and well-being. The ethical approval was obtained from a local ethics committee that evaluated and approved the study protocol and subject information at the Al-Qasim Green University, College of Biotechnology and Karbala Health Directorate (according to research committee letter 20220180 dated October 30, 2022).

Statistical analysis

The collected data were analyzed using the Statistical JMP®Pro version 16.0.0 (2021, SAS Institute Inc., USA). An analysis of variance (ANOVA) test was performed to identify any significant differences among the means of the four groups. The Tukey HSD (honest significant difference) test was used for pairwise comparison between groups. Results were considered statistically significant when the *P* value was less than 0.05.

Results

The current study included 80 individuals divided into four groups based on COVID-19 and vaccination backgrounds [Table 1]. To ensure an unbiased analysis accounting for age and gender, these factors were considered during data evaluation. Their mean ages differed among the four investigated groups without significant differences. Females accounted for 50% of the infected and vaccinated (IV) group, 70% of the infected and not-vaccinated (INV) group, 45% of the not-infected and vaccinated (NIV) group, and 55% of the not-infected and not-vaccinated (NINV) group. However, a *P* value of 0.431 indicated no significant association between gender and infection/vaccination statuses. The current results of titer tests revealed no statically dramatic differences between IgG of NIV, and IV sub-groups compared to IgG of INV and NINV sets even when gender is taken into account.

The result showed that there were no significant differences in the WBC count and neutrophils (NEU), lymphocytes (LYM), and mixed cell (MXD) percentiles among the four main groups. However, statistically significant differences were found in the NEU, LYM, and NLR parameters where the number of LYMs has the strongest association among the investigated parameters in the CBC test ($P = 0.000$) [Table 2] and considerably lower counts in the NIV and NIV sets compared to the IV group.

Table 1: Main characteristics of healthy individuals with various COVID-19 and vaccination histories and their immunoglobulins

COVID-19 and vaccination statuses	IV	INV	NIV	NINV	*P* value
Age (years)	32.45 ± 1.84	35.2 ± 2.34	38.85 ± 2.05	31.8 ± 2.38	0.0950
Gender number (%)					
Female	10 (50)	14 (70)	9 (45)	11(55)	0.431
Male	10 (50)	6 (30)	11(55)	9 (45)	
COVID-19 Ab					
IgG	29.84 ± 7.10[a]	14.57 ± 4.04[b]	32.30 ± 7.46[a]	0.31 ± 0.21[c]	<0.001
IgM	0.34 ± 0.26[a]	0.28 ± 0.21[a]	0.37 ± 0.30[a]	0.34 ± 0.28[a]	0.794

IV: infected, vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; NINV: not-infected, not-vaccinated; Age expressed as mean± standard deviation (SD); COVID-19-Ab (IgG and IgM) expressed as mean ± SD

[a,b,c] Statistically significant differences (P ≤ 0.05).

Table 2: Parameters of white blood cells in the different COVID-19 and vaccination backgrounds

COVID-19 and vaccination statuses	IV	INV	NIV	NINV	*P* value
WBC ($\times 10^9$/L)	8.71 ± 0.59a	7.56 ± 0.5a	7.24 ± 0.42a	7.55 ± 0.41a	0.1590
NEU (%)	59.36 ± 1.46	61.65 ± 1.78	59.48 ± 1.87	57.55 ± 1.69	0.4130
LYM (%)	30.79 ± 1.52	27.59 ± 1.65	30.56 ± 1.68	32.15 ± 1.39	0.2190
MXD (%)	9.96 ± 0.54	10.81 ± 0.5	9.96 ± 0.78	11.16 ± 0.7	0.4420
NEU ($\times 10^9$/L)	5.71 ± 0.52a	4.54 ± 0.48ab	3.9 ± 0.28b	4.62 ± 0.25ab	0.0190
LYM ($\times 10^9$/L)	3.01 ± 0.24a	1.91 ± 0.19b	2.1 ± 0.13b	2.35 ± 0.14b	0.0000
MXD ($\times 10^9$/L)	0.89 ± 0.09	0.78 ± 0.06	0.76 ± 0.07	0.8 ± 0.06	0.5650
NLR ratio	1.93 ± 0.14b	3.13 ± 0.51a	1.8 ± 0.16b	2.11 ± 0.18ab	0.0060

NEU: neutrophils, LYM: lymphocytes, MXD: mixed cell, NINV: not-infected, not-vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; IV: infected, vaccinated

The interactions between gender and groups of COVID-19 and vaccination backgrounds revealed variable and statically significant differences in the WBC, NEU, and LYM counts between the studied groups [Figure 1]. The IV-males had statically higher WBCs compared to NINV-females. Furthermore, IV-males had levels of NEU and LYM compared to NIV and INV females. However, there were no significant differences noted among other groups.

Additionally, the PLT parameter was shown to be generally without statistically significant differences ($P > 0.05$) in the IV, NIV, INV, and NINV groups. It is noteworthy that the NINV group had slightly higher PLT counts compared to the other three groups nevertheless no significant distinctions were displayed [Table 3].

The Gender-specific analysis within each group revealed no statistically significant differences for the absolute counts of PLT, MPV, and PDW ($P > 0.05$, [Figure 2]). Notably, NINV- males had higher PLT counts compared to NINV-females, while IV-females exhibited higher PLT counts compared to IV-males. However, both increased levels were not statistically significant.

The red blood cell variables and their indices categorized based on infection and vaccination status showed no

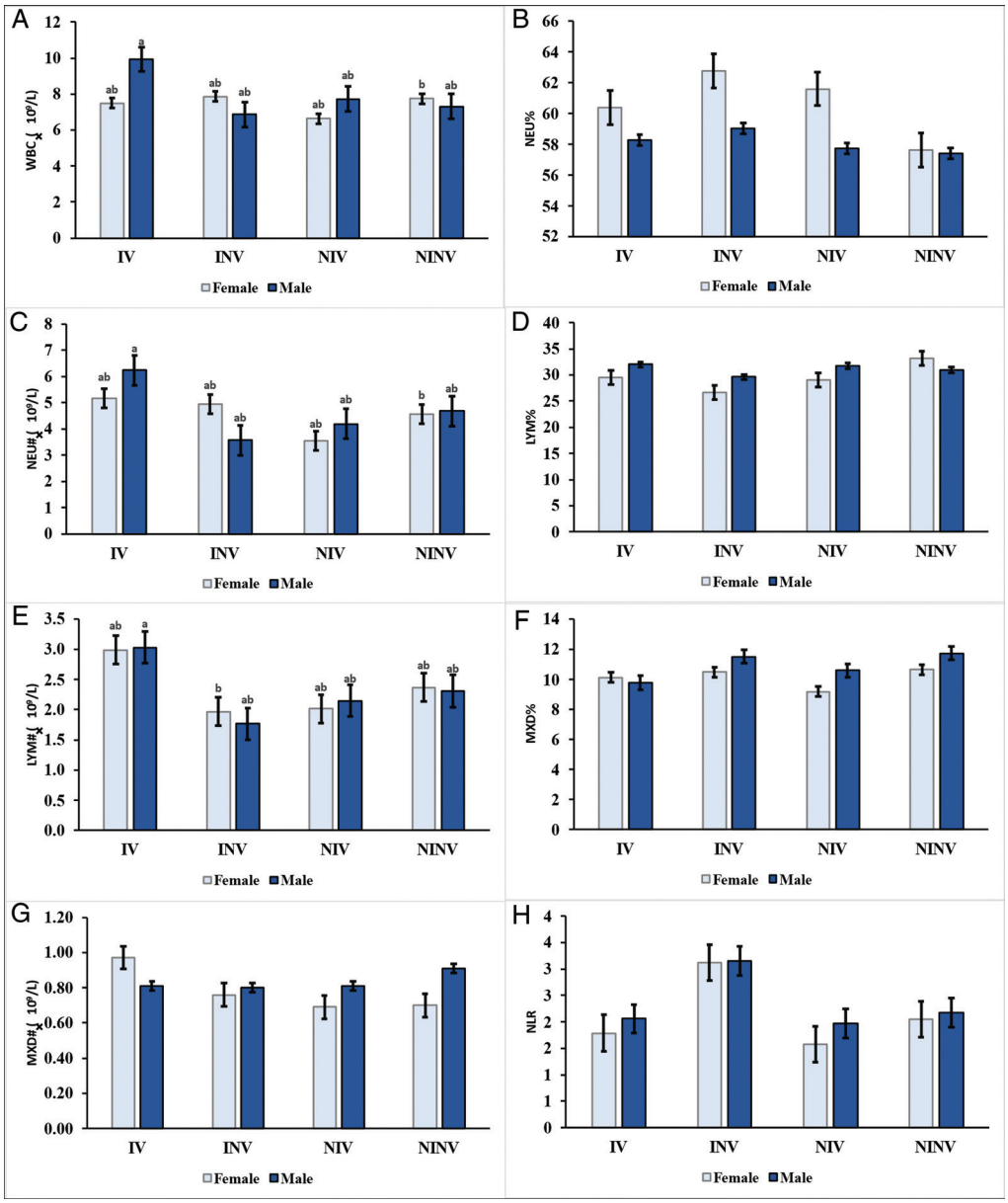

Figure 1: Parameters of white blood cells determined by gender in the different COVID-19 and vaccination backgrounds. NINV: not-infected, not-vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; IV: infected, vaccinated. *The values not connected by any letter and indicated having the same letter (a) is not significantly different or values without letters added indicate that they have the same letter (a) and are not statistically significant

Table 3: Platelet parameters in the different COVID-19 and vaccination backgrounds

COVID-19 and vaccination background	NINV	INV	NIV	IV	*P* value
PLT (103) µL	301.15±13.86	290.8±18.04	250.6±15.11	291.15±10.65	0.0800
MPV	10.13±0.15	10.02±0.25	9.81±0.22	9.87±0.19	0.6770
PDW	13.76±0.34	13.28±0.54	13.26±0.7	13.18±0.53	0.8730

NINV: not-infected, not-vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; IV: infected, vaccinated
The values not connected by any letter indicate there are not significantly different.

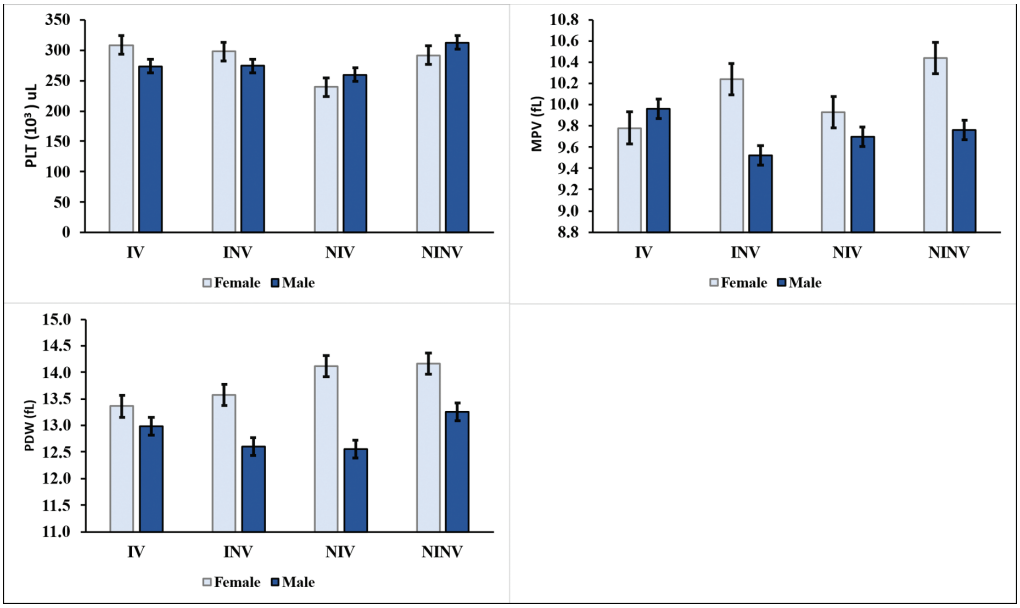

Figure 2: Complete 4 platelet parameters determined by gender with different COVID-19 and vaccination backgrounds. NINV: not-infected, not-vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; and IV: infected, vaccinated. *The values not connected by any letter and indicated having the same letter (a) is not significantly different or values without letters added indicate that they have the same letter (a) and are not statistically significant

Table 4: Erythrocyte parameters assessed in the different COVID-19 and vaccination backgrounds

	NINV	INV	NIV	IV	*P* value
RBC	4.45±0.31	4.73±0.15	5.01±0.2	4.85±0.14	0.2970
HCT	40.16±0.94	38.79±0.88	40.83±0.73	40.11±0.76	0.37
HGB	12.77±0.31	12.51±0.35	13.18±0.3	12.94±0.27	0.474
MCV	78.43±1.08	78.51±1.81	81.03±1.41	81.63±1.29	0.257
MCH	26.13±0.57	26.19±0.92	27.75±0.65	26.87±0.63	0.334
MCHC	33.04±0.28	32.92±0.56	33.47±0.35	32.25±0.32	0.184
RDW-SD	43.43±0.84	43.27±0.96	43.49±0.93	43±0.64	0.978
RDW-CV	13.08±0.31	13.98±0.52	13.03±0.22	13.63±0.45	0.268

NINV: not-infected, not-vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; IV: infected, vaccinated
The values not connected by any letter indicate there are not significantly different.

statistically significant alteration between the groups for any of these blood parameters based on *P* value [Table 4].

The results presented variable correlations between various RBC parameters for categorized groups by infection and vaccination status, as well as gender [Figure 3]. The NIV-male group had a statically higher RBC count compared to the NIV-female group in addition to INV-female, IV-female, and NINV-female groups, whereas IV-male had statically only a higher RBC count compared to the NIV-female [Figure 3A]. Similarly, the percentages of HCT for the IV-male, NIV-male, and NINV- male clusters were significantly greater and different from the IV- female INV-female, and NINV- female [Figure 3B]. Additionally, the values of HGB in NIV-male and IV-male groups were slightly increased compared to INV-male and NINV-male without noteworthy alterations, but their levels were significantly higher than NIV-female

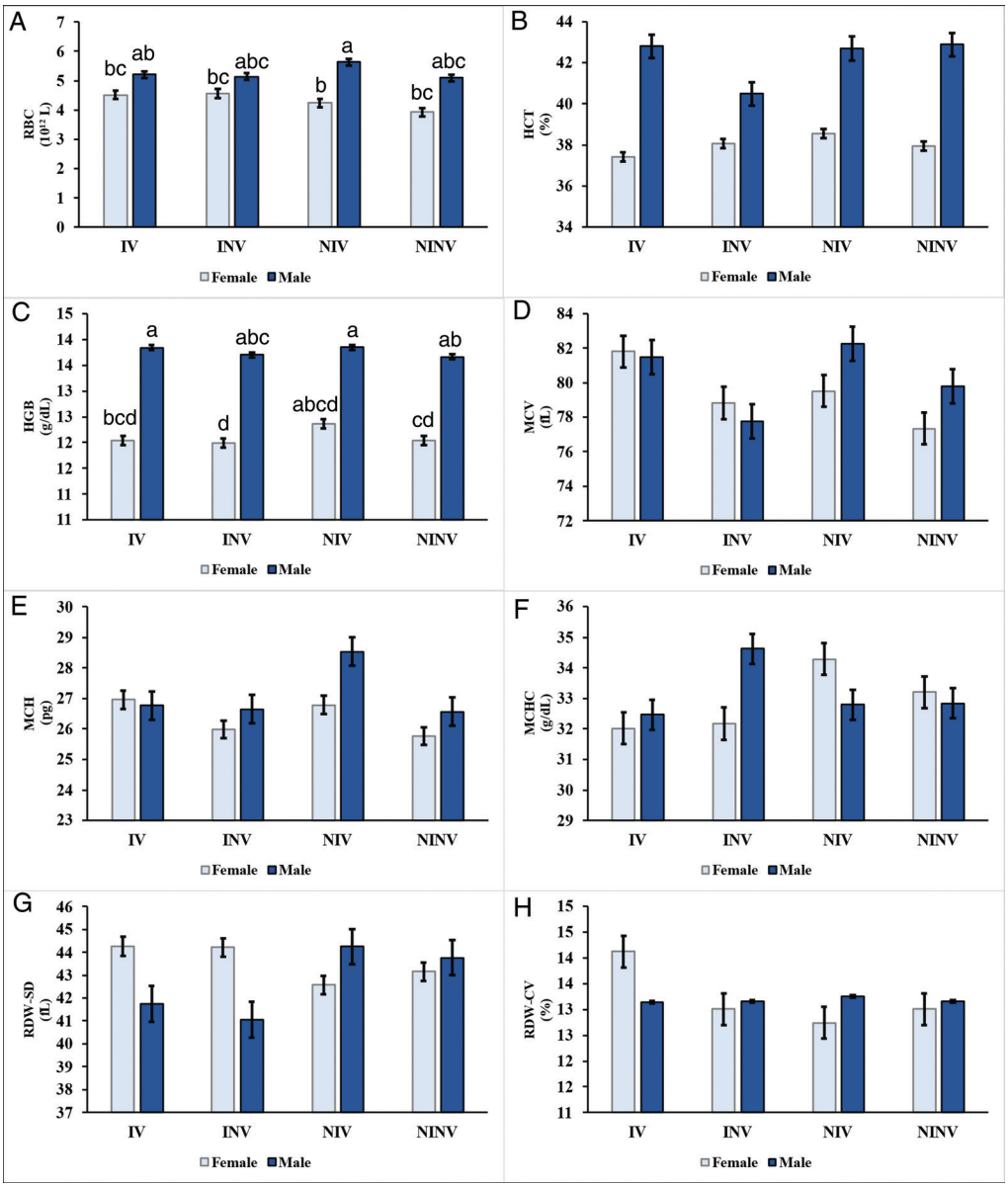

Figure 3: The red blood cell (RBC) variables categorized based on COVID-19 and vaccination backgrounds or the red blood cell variables assessed for different COVID-19 and vaccination backgrounds. NINV: not-infected, not-vaccinated; INV: infected, not-vaccinated; NIV: not-infected, vaccinated; and IV: infected, vaccinated. *The values not connected by any letter and indicate they have the same letter (a) and are not statistically significant

group among IV-female and NINV-female [Figure 3C]. However, the rest RBC parameters do not show strong evidence of statistical significance with respect to group comparisons [Figure 3].

Discussion

In this study, the IgG values of NIV and IV sub-groups were higher than those of INV and NINV subgroups, even when gender was taken into consideration [Table 2]. That is, it is evident that the vaccination mimicked an infection.[24] CBC represents a valuable test providing a wealth of information about an individual's health.[25] It has also been used to determine the RI of CBC in healthy populations with different COVID-19 and vaccination backgrounds.[18] However, to our knowledge, this is the first study in Iraq to examine the impact of COVID-19 infection and vaccination status on individuals after recovery.

Generally, the current results indicated no significant differences in the levels of leukocytes, percentiles of neutrophils, and lymphocytes, and mixed cells were verified with their counts among four groups. Consistent changes in homological profiles in healthy volunteers after vaccination have been reported, similar to changes in COVID-19 patients.[26] The proposed vaccination mimicked infection.[24] The results confirmed the results that WBC parameters can be used to detect the severity of COVID disease and be associated with lung involvement, oxygen requirements, and disease activity.[27,28]

However, changes and statistically significant differences were found in the neutrophil, lymphocyte, and NLR parameters among the current investigated groups. These changes were obvious when gender was also being taken into account. These results agreed with previous observations indicating their stronger correlations among the considered parameters in COVID-19 patients compared to control groups.[29,30] It has been recorded that high levels of leukocytes and neutrophilic count and lower levels of lymphocyte count among severe patients with COVID-19.[27] In the current study, documented lower levels of lymphocytes in the INV group after recovery may be the result of a condition called lymphopenia, which is commonly seen in severe COVID-19 cases.[31] Lymphopenia can be caused by virus attachment or immune injuries from inflammatory mediators.[32] Despite variations in the definition of disease severity across various studies, consistent reductions in lymphocyte subset counts have been observed.[33] Also, not having significant differences between the levels of lymphocyte counts in NIV and INV sets in the presented data indicated that vaccination simulated an infection. Some studies have highlighted hematological abnormalities in vaccinated individuals but concluded that the benefits of vaccination outweighed the risks.[34]

The presented study noticed variable and statically significant changes in the WBC, NEU, and LYM counts between the investigated groups when gender was taken into account [Figure 1]. The higher WBC, NEU, and LYM values of IV-males compared to NINV, NIV, and INV-females respectively in this study may relate to biological variation in the immune system and genetic factors.[35-37]

The present results revealed no statistically significant differences between the four groups: NINV, INV, NIV, and IV for the mean values and standard deviations for the three platelet indices: PLT, MPV, and PDW. Similarly, within each gender group for all three platelet indices, there were no statistically noteworthy alterations as indicated by *P* value greater than 0.05. These findings agreed with Oraibi and Mansour's[38] study who did not find significant differences in platelet counts between vaccinated and unvaccinated individuals. Though, Sing *et al*.[34] identified thrombocytopenia as a hematological abnormality following COVID-19 vaccination concluding the benefits of vaccination outweighed the risks.

The red blood cell variables and their indices categorized based on infection and vaccination status showed there were no significant alterations between the groups for any of the clinical hematological parameters based on the *P* value in the presented data [Table 4]. These findings agreed with others who compared RBC variables between healthy and infected individuals.[39]

Nevertheless, various alterations were detected in blood parameters for each group divided by gender specifically for RBC, HCT, and HGB [Figure 3]. Variable responding in females was documented in this study such as a decrease in RBC of NIV, HCT of IV, and HGB of IV levels during infections or vaccinations [Figure 3]. These dichotomies might be due to differences in male and female biology.[40] Changes in red blood cell and hemoglobin levels and the red blood cell (RBC) membrane homeostasis at the protein and lipid levels during SARS-CoV-2 infection leading to affective of its capacity to carry and deliver oxygen to tissues[39] might also be suggested to explain different responses between female and male. Thus, changes in various blood parameters such as hemoglobin concentration and ferritin levels could be indicative of an inflammatory response or altered iron metabolism due to infection with SARS-CoV-2.[41] Varying side consequences between women and men after vaccination have been reported in the past, for example, with the human papillomavirus (HPV) vaccine.[40] However, few studies informed these effects during infection and vaccination or after recovered individuals with different infection and vaccination backgrounds.

In conclusion, the study demonstrated that IgG values were higher in vaccinated groups, suggesting vaccination mimics infection. Though no significant differences were found in most hematological parameters among the groups, there were significant differences in neutrophil-to-lymphocyte ratio parameters, especially when considering gender. These findings reaffirm existing observations of correlations between these parameters in COVID-19 patients. No significant alterations were found for platelet indices among groups or within each gender group. However, variable responses, specifically for red blood cell count, hematocrit, and hemoglobin levels, were identified when considering gender. The study substantiates the value of CBC testing and highlights the need for further research to understand gender-specific responses.

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Nil.

Conflicts of interest
There are no conflicts of interest.

Informed consent statement
Informed consent has been obtained from all individuals included in this study.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England) 2020;395:497-506.
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, *et al*; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-33.

3. Abed TA, Chabuck Z. The interrelationship between diabetes mellitus and COVID-19. Med J Babylon 2022;19:1-4.
4. Attaway AH, Scheraga RG, Bhimraj A, Biehl M, Hatipoğlu U. Severe COVID-19 pneumonia: Pathogenesis and clinical management. BMJ 2021;372:n436.
5. Khasbak HSM, Al-Janabi HS, Kadhim MJ. Evaluation of CBC in different vaccines types of COVID-19. Int J Pharm Bio Med Sci 2023;3:381-6.
6. Wu Z, McGoogan JM. 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 2020;323:1239-42.
7. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, *et al*. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: A randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis 2021;21:181-92.
8. Mulligan MJ, Lyke KE, Kitchin N, Absalon J, Gurtman A, Lockhart S, *et al*. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. Nature 2020;586:589-93.
9. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, *et al*; Oxford COVID Vaccine Trial Group. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): A single-blind, randomised, controlled, phase 2/3 trial. The Lancet 2020;396:1979-93.
10. Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF, *et al*. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: A randomised, double-blind, placebo-controlled, phase 1/2 trial. Lancet Infect Dis 2021;21:39-51.
11. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, *et al*. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: An observational study using national surveillance data. Lancet (London, England) 2021;397:1819-29.
12. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med 2021;384:2092-101.
13. Scully M, Singh D, Lown R, Poles A, Solomon T, Levi M, *et al*. Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. N Engl J Med 2021;384:2202-11.
14. Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S, Belij-Rammerstorfer S, *et al*; Oxford COVID Vaccine Trial Group. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: A preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet (London, England) 2020;396:467-78.
15. Lee E-J, Cines DB, Gernsheimer T, Kessler C, Michel M, Tarantino MD, *et al*. Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. Am J Hematol 2021;96:534-7.
16. Rijnberg FM, Hazekamp MG, Wentzel JJ, De Koning PJ, Westenberg JJ, Jongbloed MR, *et al*. Energetics of blood flow in cardiovascular disease: Concept and clinical implications of adverse energetics in patients with a Fontan circulation. Circulation 2018;137:2393-407.
17. Wang F, Nie J, Wang H, Zhao Q, Xiong Y, Deng L, *et al*. Characteristics of peripheral lymphocyte subs*et al*teration in COVID-19 pneumonia. J Infect Dis 2020;221:1762-9.
18. Mendieta-Gutiérrez C, Chávez-González S, Rodríguez-Romero BI, Sánchez-Garrido JA, Figueroa-Gómez A, Licona-Vela JB, *et al*. Establishment of reference intervals for complete blood count in times of COVID-19 and vaccination. Biochem Medica 2023;33:020701.
19. Harris EK, Boyd JC. Statistical bases of reference values in laboratory medicine. CRC Press; 1995.
20. Clinical and Laboratory Standards Institute. Defining, establishing and verifying reference intervals in the clinical laboratory: Approved guideline. 3rd ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
21. Mohiuddin Chowdhury ATM, Karim MR, Ali MA, Islam J, Li Y, He S. Clinical characteristics and the long-term post-recovery manifestations of the COVID-19 patients—A prospective multicenter cross-sectional study. Frontiers in medicine 2021;8:663670.
22. Pereira-Roche N, Roblejo-Balbuena H, Marín-Padrón LC, Izaguirre-Rodríguez R, Sotomayor-Lugo F, Zúñiga-Rosales Y, *et al*. Hematological Alterations in Patients Recovered from SARS-CoV-2 Infection in Havana, Cuba. MEDICC Rev 2022;24:7-14.
23. Al-Ali D, Elshafeey A, Mushannen M, Kawas H, Shafiq A, Mhaimeed N, *et al*. Cardiovascular and haematological events post COVID-19 vaccination: A systematic review. J Cell Mol Med 2022;26:636-53.
24. Liu J, Wang J, Xu J, Xia H, Wang Y, Zhang C, *et al*. Comprehensive investigations revealed consistent pathophysiological alterations after vaccination with COVID-19 vaccines. Cell Discov 2021;7:1-15.
25. Agnello L, Giglio RV, Bivona G, Scazzone C, Gambino CM, Iacona A, *et al*. The value of a complete blood count (CBC) for sepsis diagnosis and prognosis diagnostics 2021;11:1881. doi:10.3390/diagnostics11101881.
26. Zhang H, Cao X, Kong M, Mao X, Huang L, He P, *et al*. Clinical and hematological characteristics of 88 patients with COVID-19. Int J Lab Hematol 2020;42:780-7.
27. Elshazli RM, Toraih EA, Elgaml A, El-Mowafy M, El-Mesery M, Amin MN, *et al*. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: A meta-analysis of 6320 patients. PLoS One 2020;15:e0238160.
28. Mao J, Dai R, Du R-C, Zhu Y, Shui L-P, Luo X-H. Hematologic changes predict clinical outcome in recovered patients with COVID-19. Ann Hematol 2021;100:675-89.
29. Chuan Q, Luoqi Z, Ziwei H, Shuoqi Z, Sheng Y, Yu T, *et al*. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis 2020;10.
30. Rostami-Far Z, Rahmani K, Mansouri K, Erfan MBK, Shaveisi-Zadeh F, Nikkhoo B. Complete blood count as an indicator of COVID-19 disease severity. J Clin Res Paramed Sci 2022;11.
31. Chen J, Pan Y, Li G, Xu W, Zhang L, Yuan S, *et al*. Distinguishing between COVID-19 and influenza during the early stages by measurement of peripheral blood parameters. J Med Virol 2021;93:1029-37.
32. Li T, Qiu Z, Zhang L, Han Y, He W, Liu Z, *et al*. Significant changes of peripheral T lymphocyte subsets in patients with severe acute respiratory syndrome. J Infect Dis 2004;189:648-51.
33. Huang W, Berube J, McNamara M, Saksena S, Hartman M, Arshad T, *et al*. Lymphocyte subset counts in COVID-19 patients: A meta-analysis. Cytometry A 2020;97:772-6.
34. Sing C-W, Tang CTL, Chui CSL, Fan M, Lai FTT, Li X, *et al*. COVID-19 vaccines and risks of hematological abnormalities: Nested case–Control and self-controlled case series study. Am J Hematol 2022;97:470-80.
35. Bwire GM. Coronavirus: Why men are more vulnerable to COVID-19 than women? SN Compr Clin Med 2020;2:874-6.
36. Zhong R, Chen L, Zhang Q, Li B, Qiu Y, Wang W, *et al*. Which factors, smoking, drinking alcohol, betel quid chewing, or underlying diseases, are more likely to influence the severity of COVID-19? Front Physiol 2021;11:623498.
37. Tareq AA, Hameed NM, Abdulshaheed TS. Impact of lymphopenia on COVID-19 infection severity. Med J Babylon 2022;19:99.
38. Oraibi SM, Mansour RH. Study of some blood indicators for non-infected with COVID-19 virus and those vaccinated with Pfizer, AstraZeneca and Sinopharm in Babil Governorate. Int J Health Sci 2022;6:6644-9.
39. Thomas T, Stefanoni D, Dzieciatkowska M, Issaian A, Nemkov T, Hill RC, *et al*. Evidence of structural protein damage and membrane lipid remodeling in red blood cells from COVID-19 patients. J Proteome Res 2020;19:4455-69.
40. Yazdani AN, DeMarco N, Patel P, Abdi A, Velpuri P, Agrawal DK, *et al*. Adverse hematological effects of COVID-19 vaccination and pathomechanisms of low acquired immunity in patients with hematological malignancies. Vaccines 2023;11:662.
41. Berzuini A, Bianco C, Paccapelo C, Bertolini F, Gregato G, Cattaneo A, *et al*. Red cell–bound antibodies and transfusion requirements in hospitalized patients with COVID-19. Blood 2020;136:766-8. doi:10.1182/blood.2020006695.