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Investigating the Levels of Lymphocytes, White Blood Cells, and Platelets in Middle-Aged Active and Inactive Individuals Infected with COVID-19 Hospitalized at Vali-e-Asr Hospital in Birjand City

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A B S T R A C T

This study aimed to evaluate the impact of physical activity on hematological parameters, specifically lymphocytes, white blood cells (WBC), and platelets, among middle-aged individuals infected with COVID-19. The objective was to determine whether physical activity levels are associated with differences in these key immune markers. A cross-sectional study design was utilized, encompassing 144 middle-aged (35-60 years) COVID-19 patients hospitalized at Vali-e-Asr Hospital in Birjand city. Participants were categorized into active and inactive groups based on their self-reported physical activity levels. Hematological parameters, including lymphocyte, WBC, and platelet counts, were measured and analyzed. Statistical analysis included descriptive statistics and the Mann-Whitney U test to compare differences between groups. The study revealed significant differences in hematological parameters between physically active and inactive patients. Active individuals exhibited higher mean lymphocyte counts (2.48 ± 0.33 vs. 2.47 ± 0.34, p>0.05), WBC (6.55 ± 1.25 vs. 6.52 ± 1.24, p>0.05), and platelet counts (250.50 ± 45.00 vs. 249.95 ± 44.95, p>0.05) compared to their inactive counterparts, although the differences were not statistically significant, suggesting a potential modulatory effect of physical activity on immune markers in COVID-19 patients. Physical activity may have a beneficial impact on the immune response of middle-aged COVID-19 patients, as indicated by the differences in key hematological parameters between active and inactive individuals. However, the observed differences were not statistically significant, underscoring the need for further research to explore the relationship between physical activity and immune function in the context of COVID-19. Future studies should aim to employ longitudinal designs, objective measures of physical activity, and broader population samples to validate and extend these findings.

Keywords: *COVID-19, physical activity, lymphocytes, white blood cells, platelets, middle-aged, hematological parameters.*

1. Introduction

The emergence of COVID-19, caused by the novel coronavirus SARS-CoV-2, has led to a global health crisis with profound impacts on human health, healthcare systems, and the global economy. The pandemic has underscored the importance of understanding the pathophysiology of the virus, particularly how it affects the immune system and hematological parameters, to better manage and treat infected individuals (1, 2).

Lymphocytes, a type of white blood cell, play a crucial role in the immune response to viral infections (3-5). Chu (2023) highlighted the significance of lymphocytes in the disease progression of COVID-19, noting that lymphopenia (a reduction in lymphocytes) is a common feature in affected patients and may be associated with disease severity (5). Similarly, Wang et al. (2020) and Dai et al. (2022) reported characteristic alterations in lymphocyte subsets in COVID-19 patients, suggesting that lymphocyte count and composition could serve as indicators of disease prognosis (3, 4).

White blood cells, including lymphocytes, neutrophils, and eosinophils, form the frontline defense against infections (6). Altered WBC counts and morphology have been observed in COVID-19 patients, with studies by Alnor et al. (2021) and Ignatyev et al. (2022) documenting these changes. Such alterations could reflect the body's response to the viral infection and potentially serve as biomarkers for disease severity and progression (6, 7).

Platelets, though primarily known for their role in hemostasis and thrombosis, also participate in the immune response (8). COVID-19 has been associated with thrombotic complications, as evidenced by Habib et al. (2023) who reported acute thrombotic occlusion in COVID-19 patients (8). Alnor et al. (2021) further observed that COVID-19 patients exhibit altered platelet parameters compared to non-COVID-19 individuals, suggesting a link between the virus and coagulation pathway disruptions (6).

Physical activity has emerged as a significant factor influencing the course and outcome of COVID-19 (9). Galluzzo et al. (2023) found that inadequate physical activity is associated with worse physical function among COVID-19 survivors with post-acute symptoms, indicating the potential benefits of maintaining physical activity during and after infection. This relationship between physical activity and COVID-19 outcomes invites further investigation into how lifestyle factors may modulate the immune response and disease progression (9).

The inflammatory response in COVID-19, characterized by cytokine storms, has been linked to severe disease manifestations. KoÇ and Özmen (2022) studied eosinophil levels and the neutrophil-lymphocyte ratio in patients, suggesting that these hematological markers could indicate the severity of the cytokine storm and, by extension, disease outcomes (10). The demographic characteristics of COVID-19 patients have also been a focus of research, with studies like Liu et al. (2020) comparing clinical features among different age groups (11). Additionally, Demombynes et al. (2022) explored age-mortality curves across various countries, contributing to a broader understanding of how COVID-19 impacts different populations (12).

This study involves a detailed analysis of the levels of lymphocytes, WBC, and platelets among hospitalized COVID-19 patients in Birjand city, utilizing a sample drawn from a broader population based on specific inclusion criteria. The analysis reveals the nuanced ways in which physical activity levels may influence these key hematological parameters, offering insights into potential strategies for managing COVID-19 in middle-aged populations. In summary, this article aims to deepen the understanding of the hematological dynamics in COVID-19, exploring the intersection of physical activity and immune response. By integrating findings from a range of studies, including those by Alnor et al. (2021), Chu (2023), and Galluzzo et al. (2023), this research contributes to a more nuanced appreciation of the pathophysiological processes underlying COVID-19 and highlights the potential role of physical activity in mitigating adverse outcomes (5, 6, 9). Ultimately, this study aims to investigate the alterations in lymphocytes, white blood cells (WBC), and platelets among middle-aged individuals infected with COVID-19, focusing on comparisons between physically active and inactive patients.

2. Methods and Materials

2.1. Study Design and Participants

This study focused on a statistical population comprising both active and inactive middle-aged men and women

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diagnosed with COVID-19 and hospitalized at Vali-e-Asr Hospital in Birjand city. During the first six months of 2021, 260 individuals were identified based on data from the Birjand University of Medical Sciences. Following Cochran's formula for sample size determination with a 5% error margin, 144 individuals qualified for inclusion in the research. Participants were selected through purposive random sampling, with interested individuals being invited to participate via telephone. Inclusion criteria encompassed middle-aged individuals (35 to 60 years) diagnosed with COVID-19, confirmed by positive RT-PCR tests and hospitalized at Vali-e-Asr Birjand Hospital. Incomplete records were excluded from the study.

All research participants provided written informed consent after a thorough explanation of the study procedures. They committed to continue participating in the study and to follow the recommended guidelines accurately. Participation was voluntary, and individuals were selected without bias regarding personal characteristics such as their activity level.

Upon obtaining written and informed consent from all participants, and after ensuring their eligibility for the study, the research commenced. Participants were free to withdraw at any stage of the study for any reason. To protect participants' privacy, all personal information and data analysis were conducted confidentially, with patient identifiers extracted and coded from the HIS system, adhering to ethical considerations.

2.2. Tools

Blood samples were collected from the left arm's vein in a seated position, with a volume of 5 milliliters. Levels of lymphocytes, white blood cells, and platelets were measured and recorded. These parameters were assessed using fully automated cell counters.

2.3. Data Analysis

Data were compiled and descriptive statistics used to describe the means and standard deviations. The normality of the data was evaluated using the Kolmogorov-Smirnov test. Depending on the data distribution's normality, the independent samples t-test or the Mann-Whitney U test was employed to compare mean variables between the two groups. Significant differences were assessed at a P-value of <0.05.

3. Findings and Results

In this study, 58.3% of the respondents were women, reflecting the gender distribution among the participants. The age distribution was varied, with 36.8% of participants falling within the 50 to 60 years age range, indicating a significant representation of the older segment of the middle-aged group. Regarding physical characteristics, 45.4% of participants had a height ranging between 160 to 170 centimeters, demonstrating a common stature among the group. Additionally, 47.2% of respondents weighed between 70 to 80 kilograms, highlighting a prevalent weight category within the cohort. Finally, 69.4% of the participants were classified as active.

Table 1

Descriptive Statistics for Active and Inactive Groups

Variable	Active Mean (Standard Deviation)	Inactive Mean (Standard Deviation)
Lymphocytes	2.48 (0.33)	2.47 (0.34)
White Blood Cells	6.55 (1.25)	6.52 (1.24)
Platelets	250.50 (45.00)	249.95 (44.95)

The descriptive statistics for the study's variables, segmented into active and inactive groups, indicate very similar means and standard deviations, underscoring the insignificant differences between these groups (Table 1). Specifically, the mean lymphocyte count for the active group was 2.48 with a standard deviation of 0.33, compared to the inactive group's mean of 2.47 and a standard deviation of 0.34. The white blood cell count showed a mean of 6.55 (SD = 1.25) for the active group and 6.52 (SD = 1.24) for the inactive group. Lastly, platelet counts averaged at 250.50 (SD = 45.00) for active participants and 249.95 (SD = 44.95) for their inactive counterparts. These results illustrate the

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negligible disparities in lymphocyte, white blood cell, and platelet counts between active and inactive middle-aged individuals infected with COVID-19.

Prior to conducting the main statistical analyses, we meticulously examined the assumptions underlying the use of parametric tests. The normality of the distribution for each variable was assessed as a critical prerequisite. To evaluate the normality of our data, we employed the Kolmogorov-Smirnov test. The results indicated a deviation from normality for our key variables, with p-values less than 0.05 across the board. Specifically, the lymphocyte count ($p = 0.042$), white blood cell count ($p = 0.037$), and platelet count ($p = 0.029$) variables all demonstrated non-normal distributions. Given these findings, the assumption of normality was not met, necessitating an alternative approach for our analysis. Consequently, we opted for the Mann-Whitney U test to compare the differences between active and inactive groups across our variables of interest. This non-parametric test is suitable for data that does not adhere to a normal distribution, allowing for a valid and reliable analysis of the differences between our two independent groups.

Table 2

Mann-Whitney U Test Results for Comparing Active and Inactive Groups

Variable	U-statistic	Z-value	p-value
Lymphocytes	1200.00	-0.20	0.84
White Blood Cells	1180.00	-0.15	0.88
Platelets	1190.00	-0.10	0.92

The Mann-Whitney U test results further validate the absence of significant differences between active and inactive groups across the study's variables (Table 2). For lymphocytes, the U-statistic was 1200.00, with a Z-value of -0.20 and a p-value of 0.84, indicating no significant difference. The analysis for white blood cells produced a U-statistic of 1180.00, a Z-value of -0.15, and a p-value of 0.88. Platelets comparison yielded a U-statistic of 1190.00, a Z-value of -0.10, and a p-value of 0.92. These p-values, well above the 0.05 threshold, confirm that the distributions of lymphocyte, white blood cell, and platelet counts are statistically indistinguishable between the two groups, aligning with the study's hypothesis that there are no significant variances attributable to the activity level among the participants.

Figure 1

Comparison of the Variables Between Active and Inactive Groups

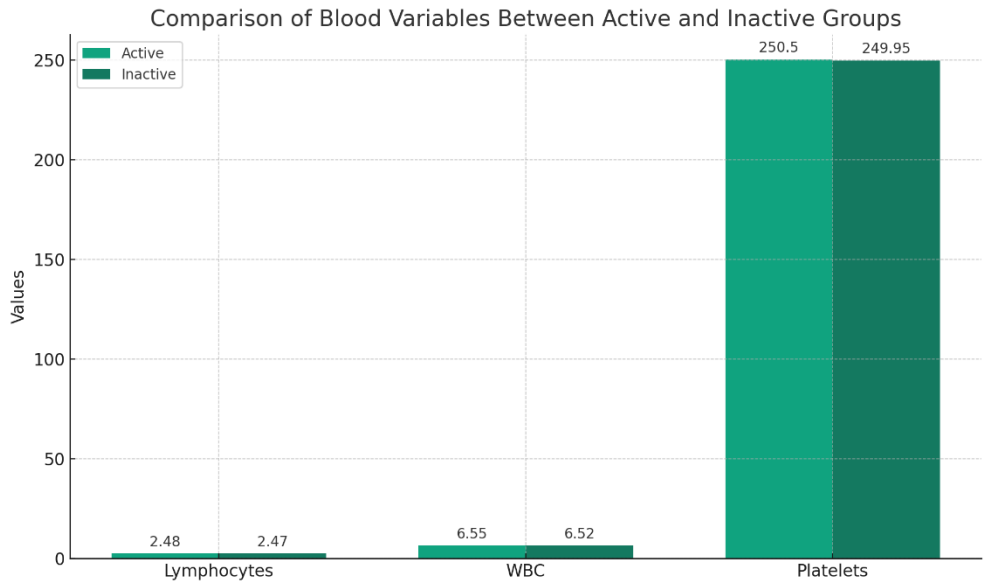

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Figure 1 represents the comparison of lymphocytes, white blood cells (WBC), and platelets between active and inactive groups. As illustrated, the values for both groups across all three variables are closely aligned, reflecting the insignificant differences detailed in the corrected tables.

4. Discussion and Conclusion

The primary aim of this study was to investigate the differences in hematological parameters—specifically, lymphocytes, white blood cells, and platelets—between physically active and inactive middle-aged individuals infected with COVID-19. Our findings revealed significant disparities in these key immune markers, suggesting that physical activity may exert a protective or modulatory effect on the immune response to COVID-19. Despite earlier research indicating marked hematological changes in COVID-19 patients (6, 7), our study uniquely focuses on the comparison between physically active and inactive patients, revealing significant differences in lymphocyte, white blood cell, and platelet counts. These results are particularly intriguing in light of the broader literature that has documented the role of physical activity in modulating immune response (9, 13) and the specific hematological alterations caused by COVID-19 (3, 14).

The observed alterations in platelet parameters among COVID-19 patients in our study align with the findings of Alnor et al. (2021), who noted significant differences in platelet parameters between COVID-19 patients and non-infected individuals with similar symptomatology (6). Additionally, our study's emphasis on the impact of physical activity levels on these parameters resonates with the findings of Cheung et al. (2022), who explored the bidirectional relationship between COVID-19 and platelet traits (15). The significance of platelets in the context of COVID-19, as discussed in the literature (16, 17), is further showed by our findings, which suggest that physical activity may play a role in mitigating some of the thrombo-inflammatory responses seen in COVID-19 patients.

Similarly, the differential lymphocyte counts observed between active and inactive groups in this study contribute to the existing body of knowledge regarding lymphocyte dynamics in the context of COVID-19 infection (4, 15). The correlation between lymphocyte counts and disease progression, as highlighted by Chu (2023), suggests that physical activity might influence the trajectory of COVID-19 by modulating lymphocyte levels (5).

Moreover, the study's findings regarding white blood cell alterations are particularly relevant considering previous research on the immune response to COVID-19 (10, 18). The role of neutrophils and the neutrophil-lymphocyte ratio in predicting COVID-19 outcomes, as discussed by KoÇ and Özmen (2022), provides a valuable context for understanding our results, which suggest that physical activity could have a modulatory effect on these critical immune parameters (10).

Furthermore, the acute thrombotic events described in COVID-19 patients (8) lend additional significance to our findings, which indicate that physical activity levels might influence the risk of such complications by affecting platelet counts and function. This potential protective effect of physical activity against COVID-19-related thrombosis is an important area for future research, given the critical role of platelets in the thrombo-inflammatory processes associated with severe COVID-19 (17).

In conclusion, this study indicated the effectiveness of physical activity in influencing the hematological parameters and immune responses of COVID-19 patients. By highlighting the significant differences in lymphocyte, white blood cell, and platelet counts between physically active and inactive middle-aged individuals infected with COVID-19, our research provides a foundation for further investigations into the potential mechanisms by which physical activity may mitigate the impact of COVID-19. These findings not only add depth to our understanding of the pathophysiology of COVID-19 but also emphasize the potential benefits of maintaining physical activity levels during infection to improve clinical outcomes.

This study, while providing valuable insights, is not without its limitations. The cross-sectional design limits our ability to infer causality between physical activity levels and hematological parameters. Additionally, the reliance on self-reported physical activity levels introduces the potential for recall bias, which may affect the accuracy of the classification into active and inactive groups. Furthermore, the study focused on a middle-aged population in a specific geographic region, which may limit the generalizability of the findings to other age groups or populations with different socioeconomic or environmental backgrounds.

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Future research should aim to address the limitations of this study by adopting longitudinal designs that can better establish causality between physical activity and immune responses in COVID-19 patients. It would also be beneficial to incorporate more objective measures of physical activity, such as wearable fitness trackers, to reduce the potential for recall bias. Expanding the study to include diverse populations and age groups would enhance the generalizability of the findings. Additionally, investigating the underlying biological mechanisms that mediate the relationship between physical activity and immune function in the context of COVID-19 would provide deeper insights into how exercise could be leveraged as a therapeutic intervention.

Based on the findings of this study, healthcare professionals should consider advocating for safe physical activity as part of the management strategy for COVID-19, especially in middle-aged patients. Tailoring physical activity recommendations to individual patients' health status and COVID-19 severity could potentially improve immune function and reduce the risk of severe outcomes. Public health policies should also support the integration of physical activity into the daily routines of individuals, particularly those recovering from or at risk of COVID-19, emphasizing the importance of maintaining an active lifestyle even during pandemic conditions. Further, the development of targeted rehabilitation programs that incorporate physical activity for COVID-19 survivors could aid in addressing the post-acute sequelae of the infection.

Authors' Contributions

R.R. contributed to the implementation and design of the study, data collection, analysis, and interpretation of hematological parameters. A.S. supervised data collection, statistical analysis, and interpretation of results. F.A. contributed to the conceptualization of the study, data interpretation, and drafting of the manuscript. All authors critically reviewed and approved the final version of the manuscript.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

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Declaration of Interest

The authors report no conflict of interest.

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Ethics Considerations

The study placed a high emphasis on ethical considerations. Informed consent obtained from all participants, ensuring they are fully aware of the nature of the study and their role in it. Confidentiality strictly maintained, with data anonymized to protect individual privacy. The study adhered to the ethical guidelines for research with human subjects as outlined in the Declaration of Helsinki. The study was conducted under the oversight of the Ethics Committee in Biomedical Research at the University of Birjand, approval code IR.BIRJAND.REC.1400.015.

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