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Evaluation of CBC in Different Vaccines Types of COVID-19

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ABSTRACT

In December 2019, Wuhan reported its first cases of pneumonia which called coronavirus disease 2019 (COVID-19), a single-stranded RNA virus. COVID-19 vaccine is a safe way to help the immune system build defenses against COVID-19. The immune system relies on various types of cells, such as Lymphocytes, monocytes, macrophages, and other immune cells to fight infections. The aim of the study is to the assessment of blood parameters in different vaccinated groups of COVID-19 vaccines. We collected 100 samples from individuals that vaccinated with AstraZeneca, Sinopharm, and Pfizer vaccines and unvaccinated (infected), which were divided into four groups, each containing 25 samples, and did a CBC test. The study results indicate that different COVID-19 vaccines and natural immunization result in diverse immune responses in males and females. In males, the Sinopharm vaccine stimulates higher white blood cell count (7.11±0.44s) with a significant difference (*p<0.05*), while the AstraZeneca vaccine triggers greater lymphocyte (LYM%) activation (34.3±0.99) with a significant difference (*p<0.05*) than others covid19 vaccines. Natural immunization leads to increased monocyte (MON%) levels (8.34±0.69) with a significant difference *(p<0.05)* compared to covid19 vaccines in which the Sinopharm vaccine (6.96±0.49) shows significantly lower monocyte activation. The Pfizer and Sinopharm vaccines induce higher granulocyte (GRA%) activation (60.34±1.88 and 60.28±1.63, respectively) with a significant difference *(p<0.05)*, while natural immunization (55.87±3.8) shows lower activation compared to covid19 vaccines with a significant difference *(p<0.05)*. While in females, The AstraZeneca, Sinopharm vaccines, and natural immunization (6.1±0.5, 6.89±0.68, and 6.26±0.52, respectively) had the higher white blood cell (WBC) number with no significant difference*(p>0.05)* among them, while the Pfizer vaccine (5.7±0.36) had the lower WBC with a significant difference (p<0.05). The AstraZeneca vaccine had higher lymphocytes (LYM%) (36.14±1.25) with a significant difference *(p<0.05)*, while the Sinopharm vaccine had significantly lower (29.85±3.62). Natural immunization had a significantly higher MON% (8.11±1.28a) with *(p<0.05)* compared to covid19 vaccines (with no significant difference among them), while the Sinopharm vaccine showed a higher in both GRA% and GRA number (64.38±3.88 and 4.52±0.57, respectively) with a significant difference *(p<0.05)*. In conclusion, the AstraZeneca vaccine elevated the lymphocytes (LYM%) while natural immunization increased (MON%) in both genders. The study also reveals that males and females exhibit varied immune responses to different COVID-19 vaccines and natural immunization, and these variations may be attributed to vaccine composition, mechanisms of action, immune response variability, and timing of the research.

KEYWORDS: COVID-19 , Vaccines , CBC , Natural immunization

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INTRODUCTION

Early in December 2019, Wuhan, the provincial capital of Hubei, reported its first pneumonia cases of unknown cause. The pathogen was discovered to be a new enveloped RNA betacoronavirus2, currently known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which shares evolutionary similarities with SARS-CoV(Guan et al., 2020). It is also called coronavirus disease 2019 (COVID-19), which has killed more than 6 million people worldwide(Cascella et al., 2022). Coronavirus is a member of the family of Coronaviridae، the Nidovirales class (Özdemir, 2020).

Coronaviruses are single-stranded, positive-sense RNA-containing enclosed viruses(Sotomayor et al., 2020).

The genome size of COVID-19 is 29,903 bp (Mittal et al., 2020). Covid19 viral genome encodes four structural proteins (Spike protein (S), Membrane protein (M), 16s Nucleo-capsid protein (N), and Envelope protein (E))and at least sixteen non-structural proteins (nsps)(Sotomayor et al., 2020). Because the S glycoprotein that projects from the viral capsid causes "Corona" spikes, coronaviruses are so named(Mart et al., 2021). SARS-Cov-2 primarily infects lower airways in the beginning and binds to ACE2 on pulmonary epithelial cells via the S1 subunit's receptor-binding domain (RBD)(Jiang et al., 2020).

The COVID-19 vaccine is a safe strategy to assist the immune system to develop defenses against COVID-19(*Understanding COVID-19 Vaccines*, 2021). The globe quickly developed, tested, and deployed several COVID-19 vaccinations, and as a result, 69% of people worldwide have gotten at least one dose of a COVID-19 vaccine (Sarker et al., 2022). The most widely used COVID-19 vaccines were the Pfizer-BioNTech Comirnaty (BNT162b2), AstraZeneca (ChAdOx1S/Covishield), and Sinopharm (BBIBP-CorV)(Sarker et al., 2022).

Similar to infection, vaccination results in the early production of serum IgA, IgM, and IgG antibodies as well as long-lasting memory B-cell and T-cell responses(Sharma & Ravindra, 2022). When exposed to the Spike protein again, T and B cells establish immunological memory of it and will be ready to act(*Immune Response after COVID-19 Vaccination*, n.d.).

The human immune system is a complex network of cells, molecules, and receptors that work together to protect the body from infections, and injuries, and promote healing(Austermann et al., 2022). The immune system relies on different types of lymphocytes, including CD4+ T cells, CD8+ T cells, B cells, monocytes, macrophages, Dendritic cells, Neutrophils, and Natural killer cells, to combat infections(Knoll et al., 2021). These cells are activated by pattern recognition receptors and release pro-inflammatory cytokines such as IL-1, IL-18, IL-33, and IL-6. These cytokines activate natural killer (NK) cells, which are essential for viral defense due to their cytotoxic function and cytokine release, including interferon-gamma, which activates both B and T cells(Ekşioğlu-Demiralp et al., 2022).

During viral infection, Macrophages use pattern recognition receptors to detect danger signals from pathogens or damaged tissue. They then release inflammatory molecules to eliminate pathogens, initiate inflammation, recruit additional immune cells, and promote tissue repair(Knoll et al., 2021). Monocytes are contributing to inflammatory responses, phagocytosis, antigen presentation, and other immune processes. Inflammatory signals can cause peripheral circulating monocytes to migrate into peripheral tissues, where they differentiate into macrophages and dendritic cells(Sayahinouri1 et al., 2023). Neutrophils mainly migrate to the site of infection and utilize respiratory bursts and phagocytosis to combat microorganisms. T and B lymphocytes are key immune mediator cells, but their function is regulated by dendritic cells. Dendritic cells process antigens, express lymphocyte-stimulating molecules on their surface and migrate to lymph nodes, where they secrete cytokines to activate adaptive immune responses(Sayahinouri1 et al., 2023). Natural killer cells are providing rapid responses against pathogens and tumor cells. They present in mucosal and lymphoid tissues and quickly migrate to sites of infection, where they can kill infected or cancerous cells(Sayahinouri1 et al., 2023). Depending on the virus involved, the numbers and subsets of lymphocytes can change. CD8+ T cells are especially effective in eliminating virus-infected cells(Lagadinou et al., 2021). CD4 helper T cells assist in fighting viral infections by activity of cytotoxic T cells and stimulate B cells to produce virus-specific antibodies which then neutralize the virus and help to kill infected cells. Studies in both humans and animals have found that neutrophils are recruited to the site of infection in COVID-19, contributing to lung inflammation. In acute COVID-19 patients, the levels of neutrophils were significantly higher compared to mild and moderate COVID-19 patients who required hospitalization (Rajamanickam et al., 2022).

The aim of the study is to the assessment of blood parameters in different vaccinated groups of COVID-19 vaccines.

MATERIALS AND METHODS

Sample Collection

Between August 1, 2022, and December 1, 2022, we gathered 100 samples from individuals aged 20-55 who were either vaccinated (using AstraZeneca, Sinopharm, or Pfizer vaccines) or unvaccinated (infected). These individuals were divided into four groups, with 25 samples in each group. We collected samples from medical and work staff at Marjan Teaching Hospital, Al-Hilla Teaching Hospital, and Imam Al-Sadiq Hospital, as well as from residential areas in the Babylon province. The personal information we gathered for each individual included their name, age, gender, place of residence, academic background, vaccine type received, history of prior infection, dates of vaccination doses, vaccine symptoms experienced, inoculation duration, smoking habits, pregnancy status for women, any chronic illnesses, infection type, infection period duration, and whether infection occurred before or after vaccination.

BLOOD SAMPLING

We obtained two milliliters of blood from every sample by applying a tourniquet directly on the skin around the arm to aid in identifying the veins and assist with blood collection. Before collecting the blood, the skin covering the vein was sanitized with 70% ethyl alcohol to minimize the possibility of introducing impurities into the sample. The blood samples were collected in a sterile EDTA tube.

Complete Blood Count (CBC) Test

After blood collection immediately done CBC test by the Human Count 30TS made by a Human company /origin in Germany.

RESULTS

Physiological Parameters

Comparison of Physiological Parameters in Males Between COVID-19 Vaccines and Unvaccinated (infected) People

Table (1) presents a comparison of physiological parameters in males between individuals who received different COVID-19 vaccines and those who were unvaccinated but infected. The results reveal variations in blood cell counts. The white blood cells (WBC) count was highest in individuals who received the Sinopharm vaccine (7.11±0.44), followed by the AstraZeneca vaccine (7.04±0.25) with a significant difference ($p<0.05$) than Pfizer vaccines and unvaccinated (infected) persons in which they had the lower WBC with minimal difference between them (6.71±0.49 and 6.73±0.42, respectively). The least significant difference (LSD) value for WBC was 1.08.

Regarding the percentage of lymphocytes (LYM%), the AstraZeneca vaccine had the highest percentage (34.3±0.99) with a significant difference ($p<0.05$), followed by the unvaccinated infected group (33.05±1.44) and the Sinopharm vaccine (32.58±1.76). The Pfizer vaccine had the lowest percentage (31.81±1.53). The LSD value for LYM% was 3.91.

For the percentage of monocytes (MON%), the unvaccinated infected group had the highest percentage (8.34±0.69) with a significant difference ($p<0.05$), followed by both the AstraZeneca and Pfizer vaccines with no significant difference ($p>0.05$) between them (7.83±0.94 and 7.83±0.67, respectively). The Sinopharm vaccine had the lowest percentage (6.96±0.49). The LSD value for MON% was 1.95.

In terms of the percentage of granulocytes (GRA%), the Pfizer vaccine had the highest percentage (60.34±1.88), followed closely by the Sinopharm vaccine (60.28±1.63) with a significant difference ($p<0.05$) compared to AstraZeneca vaccine (57.86±1.28) and the unvaccinated (infected) person (55.87±3.8) which had the lowest percentage. The LSD value for GRA% was 5.54.

The results also indicate slight differences in the number of lymphocytes (LYM) between COVID-19 vaccines and the unvaccinated infected group. The AstraZeneca vaccine had the highest count (2.37±0.09), followed by the Sinopharm vaccine, the unvaccinated infected group (2.21±0.16), and the Pfizer vaccine with the lowest count (2.06±0.09). These differences were not significant. The LSD value for LYM was 0.39.

The number of monocytes (MON) was highest in the unvaccinated infected group (0.57±0.06) and lowest in the Sinopharm vaccine (0.5±0.06) with a significant difference ($p<0.05$). The AstraZeneca and Pfizer vaccines showed slight differences between them (0.54±0.06 and 0.51±0.05, respectively), with an LSD value for MON of 0.16.

Lastly, the number of granulocytes (GRA) was highest in the Pfizer vaccine (4.14±0.41), followed by the Sinopharm vaccine (4.3±0.29), the AstraZeneca vaccine (4.04±0.19), and the unvaccinated infected group (3.79±0.4), which had the lowest count. There is a significant difference ($p<0.05$) between covid19 vaccines and unvaccinated(infected). The LSD value for GRA was 0.84.

Table (1): The comparison of Physiological parameters in males between the COVID-19 Vaccine and Unvaccinated(infected) People

Type of vaccine	Parameters						
	WBC	LYM%	MON%	GRA%	LYM	MON	GRA
NI	6.73±0.42	33.05±1.44	8.34±0.69	55.87±3.8	2.21±0.16	0.57±0.06	3.79±0.4
AstraZeneca	7.04±0.25	34.3±0.99	7.83±0.94	57.86±1.28	2.37±0.09	0.54±0.06	4.04±0.19
Sinopharm	7.11±0.44	32.58±1.76	6.96±0.49	60.28±1.63	2.32±0.2	0.5±0.06	4.3±0.29
Pfizer	6.71±0.49	31.81±1.53	7.83±0.67	60.34±1.88	2.06±0.09	0.51±0.05	4.14±0.41
LSD	1.08	3.91	1.95	5.54	0.39	0.16	0.84

Comparison of Physiological Parameters in Females between COVID-19 Vaccine and Unvaccinated(infected) People

Table (2) presents a comparison of physiological parameters in females between different COVID-19 vaccines and unvaccinated individuals who were infected. The Sinopharm vaccine exhibited the highest WBC count (6.89±0.68), followed by the unvaccinated infected group (6.26±0.52), the AstraZeneca vaccine (6.1±0.5) with no significant difference ($p>0.05$) among them, while the Pfizer vaccine had a significantly lower WBC count (5.7±0.36) with ($p<0.05$). The LSD value was 1.65.

Regarding the percentage of lymphocytes (LYM%), the AstraZeneca vaccine had the highest percentage (36.14±1.25) with a significant difference ($p<0.05$), followed by the Pfizer vaccine (33.63±2.55), the unvaccinated (infected) persons (33.57±1.52), and the Sinopharm vaccine with the lowest percentage (29.85±3.62). The LSD value was 7.29.

The percentage of monocytes (MON%) was highest in the unvaccinated (infected) persons (8.11±1.28) with a

significant difference ($p<0.05$) compared to COVID-19 vaccines. Among the vaccines, the Pfizer vaccine had a slightly higher percentage (5.89±0.55) compared to the Sinopharm vaccine (5.75±0.95), while the AstraZeneca vaccine had the lowest percentage (5.02±0.57) with no significant difference ($p>0.05$). The LSD value for MON% was 2.83.

In terms of the percentage of granulocytes (GRA%), the Sinopharm vaccine had the highest percentage (64.38±3.88) with a significant difference ($p<0.05$), followed by the Pfizer vaccine (60.47±2.67), the AstraZeneca vaccine (58.83±1.2), and the unvaccinated (infected) persons with the lowest percentage (58.3±2.07). The LSD value was 8.12.

The number of lymphocytes (LYM) was highest in the AstraZeneca vaccine (2.17±0.14), closely followed by the unvaccinated (infected) persons (2.13±0.13) with slight differences between them but significant difference ($p<0.05$) than Sinopharm vaccine (1.98±0.29) and Pfizer vaccine (1.86±0.13) which is the lower. The LSD value for LYM was 0.55.

The number of monocytes (MON) was highest in the unvaccinated (infected) persons (0.53±0.09), followed by the Sinopharm vaccine (0.39±0.09), the Pfizer vaccine (0.34±0.04), and the AstraZeneca vaccine with the lowest count (0.31±0.04) with no significant difference ($p>0.05$). The LSD value for MON was 0.25.

Lastly, the number of granulocytes (GRA) was highest in the Sinopharm vaccine (4.52±0.57) with a significant difference ($p<0.05$), followed by the AstraZeneca vaccine and the unvaccinated (infected) persons (3.62±0.35 and 3.61±0.32, respectively) with no significant difference ($p>0.05$), while the Pfizer vaccine had the lowest count (3.33±0.42). The LSD value for GRA was 1.31.

Table (2): The comparison of Physiological parameters in Females between the COVID-19 Vaccine and Unvaccinated(infected) People

Type of vaccine	Parameters						
	WBC	LYM%	MON%	GRA%	LYM	MON	GRA
NI	6.26±0.52	33.57±1.52	8.11±1.28[a]	58.3±2.07	2.13±0.13	0.53±0.09	3.61±0.32
AstraZeneca	6.1±0.5	36.14±1.25	5.02±0.57[b]	58.83±1.2	2.17±0.14	0.31±0.04	3.62±0.35
Sinopharm	6.89±0.68	29.85±3.62	5.75±0.95[b]	64.38±3.88	1.98±0.29	0.39±0.09	4.52±0.57
Pfizer	5.7±0.36	33.63±2.55	5.89±0.55[b]	60.47±2.67	1.86±0.13	0.34±0.04	3.33±0.42
LSD	1.65	7.29	2.83	8.12	0.55	0.25	1.31

DISCUSSION

The study results revealed that among males, the Sinopharm vaccine resulted in a higher white blood cell (WBC) count compared to other vaccines and natural immunization. This might be attributed to the specific characteristics and components of the Sinopharm vaccine, which potentially trigger a more robust immune response, leading to increased WBC production. Similarly, the AstraZeneca vaccine exhibited a higher percentage of lymphocytes (LYM%) compared to the Pfizer vaccine, suggesting that the formulation of the AstraZeneca vaccine may enhance lymphocyte activation and proliferation which means it activates the adaptive immune response. On the other hand, natural immunization, which occurs as a result of a previous infection, also showed higher lymphocyte percentages, monocytes (MON%) percentages, and numbers compared to covid19 vaccine, indicating the immune system's response to the infection by activation of both innate and adaptive immune responses to fight the virus. In contrast, the Sinopharm vaccine exhibited lower percentages and counts of monocytes, suggesting a potentially reduced ability to activate this particular immune cell type compared to other vaccines. The AstraZeneca and Pfizer vaccines displayed similar percentages and counts of monocytes, indicating comparable effects on monocyte activation. In terms of granulocytes (GRA%), the Pfizer vaccine demonstrated a higher percentage compared to natural immunization, potentially indicating a more pronounced activation of granulocytes by the vaccine natural infection. The Sinopharm vaccine also showed higher percentages of granulocytes compared to the AstraZeneca vaccine, suggesting differing immune responses elicited by these vaccines. The differences in GRA counts further support these findings, with the Pfizer vaccine exhibiting a higher count and natural immunization displaying a lower count. Overall, the variations in physiological parameters observed among the different vaccines and natural immunization can be attributed to the specific components and formulations of each vaccine, as well as the immune responses triggered by natural infection. Differences in immune response activation can arise due to variations in the composition of vaccines (Jeewandara et al., 2022). These factors influence the activation and proliferation of various immune cells, resulting in variations in blood cell counts and percentages.

The current study also found that WBC count in females was high in the Sinopharm vaccine followed by natural immunization than the AstraZeneca vaccine with a slight difference but lower in the Pfizer vaccine, but all of these not elevated the WBC count as we expected perhaps due to the period in which the research was done, far from the period of vaccination and infection. Also we found that

LYM% was higher in the AstraZeneca vaccine but lower in the Sinopharm vaccine with a significant difference, while both Pfizer vaccine and natural immunization were the percentage closely with slightly differed, with regards to LYM count also high in AstraZeneca vaccine but natural immunization was close to this vaccine with a slight difference while the Sinopharm and Pfizer vaccines were the lower with less difference between them, this may be the AstraZeneca vaccine activated adaptive immune response higher than others. Natural immunization was found to highly elevated the percentage of MON% and MON counts than covid 19 vaccines with significant differences compared to covid19 vaccines, this may be due to the complex immune processes triggered by the actual viral infection, resulting in a more substantial recruitment of monocytes than vaccines. While GRA% and GRA count was highly increased in the Sinopharm vaccine than other vaccines and natural immunization with significant differences. The reasons for the observed variations in physiological parameters among the different vaccines and natural immunization in females might be attributed to several factors like Vaccine Composition which that different COVID-19 vaccines have distinct compositions, including the type of viral vector or technology used. The variations in vaccine composition can result in differences in immune response activation (Jeewandara et al., 2022). For example, the Sinopharm vaccine is an inactivated virus vaccine, which may stimulate a different immune response compared to other vaccines like Pfizer or AstraZeneca, which utilize mRNA or viral vector technology. Another factor Mechanism of vaccine action is that each vaccine has a unique mechanism of action, influencing how it interacts with the immune system. The differences in the activation of specific immune cells, such as lymphocytes (LYM) or monocytes (MON), can be attributed to the specific mechanisms employed by each vaccine to trigger an immune response (Jeewandara et al., 2022). Immune System Variability of Individuals may exhibit variations in their immune responses due to genetic factors, previous exposure to the virus, or underlying health conditions. These factors can influence the way vaccines interact with the immune system and lead to differences in immune cell counts and percentages (Zepeda-cervantes et al., 2022). The timing of the research relative to the vaccination or infection period can also impact the observed results. If the study was conducted during a specific timeframe that was relatively distant from vaccination or infection events, it may affect the immune responses observed in the study participants. The size and characteristics of the study population, such as age, gender, health status, or other demographic factors, can also contribute to the observed differences (Zepeda-cervantes et al., 2022; Yu et al., 2021). These factors may introduce variability and influence the immune response patterns among the different vaccine groups and natural immunization. It's important to note that further research and studies are needed to corroborate these findings and provide a comprehensive understanding of the immune responses elicited by different COVID-19 vaccines and natural immunization.

CONCLUSION

In conclusion, there are observed differences in immune responses between males and females regarding various COVID-19 vaccines and natural immunization. The AstraZeneca vaccine has been found to increase lymphocyte (LYM%) levels, while natural immunization leads to higher levels of monocytes (MON%) in both genders. In the case of the Sinopharm vaccine, it appears to stimulate a higher white blood cell count in males, while showing greater activation of granulocytes in females. Conversely, the Pfizer vaccine demonstrates higher granulocyte activation in males. These variations can be attributed to factors such as vaccine composition, mechanisms of action, variability in immune responses, and the timing of the research. However, further research is necessary to validate these findings and develop a comprehensive understanding of immune responses to different vaccines and natural immunization.

REFERENCE

I. Austermann, J., Roth, J., & Barczyk-Kahlert, K. (2022). The Good and the Bad: Monocytes' and Macrophages' Diverse Functions in Inflammation. *Cells*, *11*(12). https://doi.org/10.3390/cells11121979

II. Cascella, M., Rajnik, M., Aleem, A., Dulebohn, S. C., & Di Napoli, R. (2022). Features, evaluation, and treatment of coronavirus (COVID-19). *Statpearls [Internet]*.

III. Ekşioğlu-Demiralp, E., Alan, S., Sili, U., Bakan, D., Ocak, İ., Yürekli, R., Alpay, N., Görçin, S., & Yıldız, A. (2022). Peripheral innate and adaptive immune cells during COVID-19: Functional neutrophils, pro-inflammatory monocytes, and half-dead lymphocytes. *Cytometry Part B - Clinical Cytometry*, *102*(2), 153–167. https://doi.org/10.1002/cyto.b.22042

IV. Guan, W., Ni, Z., Hu, Y., Liang, W., Ou, C., He, J., Liu, L., Shan, H., Lei, C., Hui, D. S. C., Du, B., Li, L., Zeng, G., Yuen, K.-Y., Chen, R., Tang, C., Wang, T., Chen, P., Xiang, J., … Zhong, N. (2020). Clinical Characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicine*, *382*(18), 1708–1720. https://doi.org/10.1056/nejmoa2002032

V. *Immune response after COVID-19 vaccination*. (n.d.). 19.

VI. Jeewandara, C., Aberathna, I. S., Pushpakumara, P. D., Kamaladasa, A., Guruge, D., Wijesinghe, A., Gunasekera, B., Ramu, S. T., Kuruppu, H., Ranasinghe, T., Dayarathna, S., Dissanayake, O.,

Gamalath, N., Ekanayake, D., Jayamali, J., Jayathilaka, D., Dissanayake, M., Jayadas, T. T., Mudunkotuwa, A., … Malavige, G. N. (2022). Persistence of immune responses to the Sinopharm/BBIBP-CorV vaccine. *Immunity, Inflammation and Disease*, *10*(6), 1–11. https://doi.org/10.1002/iid3.621

VII. Jiang, F., Deng, L., Zhang, L., Cai, Y., Cheung, C. W., & Xia, Z. (2020). Review of the clinical characteristics o)f coronavirus disease 2019 (COVID-19. *Journal of General Internal Medicine*, *35*(5), 1545–1549.

VIII. Knoll, R., Schultze, J. L., & Schulte-Schrepping, J. (2021). Monocytes and Macrophages in COVID-19. *Frontiers in Immunology*, *12*(July), 1–12. https://doi.org/10.3389/fimmu.2021.720109

IX. Lagadinou, M., Zareifopoulos, N., Gkentzi, D., Sampsonas, F., Kostopoulou, E., Marangos, M., & Solomou, E. (2021). Alterations in lymphocyte subsets and monocytes in patients diagnosed with SARS-CoV-2 pneumonia: A mini-review of the literature. *European Review for Medical and Pharmacological Sciences*, *25*(15), 057–5062. https://doi.org/10.26355/eurrev_202108_26463

X. Mart, D., Aguirre-sampieri, S., Sampieri, A., & Vaca, L. (2021). *SARS-CoV-2 Vaccines Based on the Spike Glycoprotein and Implications of New Viral Variants*. *12*(July). https://doi.org/10.3389/fimmu.2021.701501

XI. Mittal, A., Manjunath, K., Ranjan, R. K., Kaushik, S., Kumar, S., & Verma, V. (2020). COVID-19 pandemic: Insights into structure, function, and hACE2 receptor recognition by SARS-CoV-2. *PLoS Pathogens*, *16*(8), e1008762. https://doi.org/10.1371/journal.ppat.1008762

XII. Özdemir, Ö. (2020). Coronavirus Disease 2019 (COVID-19): Diagnosis and Management (narrative review). *Erciyes Medical Journal*. https://doi.org/10.14744/etd.2020.99836

XIII. Rajamanickam, A., Pavan Kumar, N., Nancy P, A., Selvaraj, N., Munisankar, S., Mariam Renji, R., V, V., Murhekar, M., Wesley Vivian Thangaraj, J., Santhosh Kumar, M., Girish Kumar, C., Bhatnagar, T., Ponnaiah, M., Sabarinathan, R., Saravanakumar, V., & Babu, S. (2022). Dynamic Changes in Neutrophil Counts and Neutrophil Granular Protein Levels in Convalescent COVID-19 Patients. *Archives of Clinical and Biomedical Research*, *06*(02), 378–389. https://doi.org/10.26502/acbr.50170253

XIV. Sarker, P., Akhtar, E., Kuddusi, R. U., Alam, M. M., Haq, M. A., Hosen, M. B., Chanda, B. C., Haque, F., Alam, M., Razzaque, A., Rahman, M., Ahmed, F., Kibria, M. G., Islam, M. Z., Ahmed, S., & Raqib, R. (2022). Comparison of the Immune Responses to COVID-19 Vaccines in Bangladeshi Population. *Vaccines*, *10*(9), 1–12. https://doi.org/10.3390/vaccines10091498

XV. Sayahinouri1, M., Firouz, S. M., Sadrabadi3, A. E., Masoudnia5, M., Abdolahi5, M., Jafarzadeh, F., Nouripour, M., Mirzazadeh, S., Zangeneh, N., Jalili, A., & Aghdami, N. (2023). Functionality of immune cells in COVID-19 infection: development of cell-based therapeutics. *BioImpacts*, 149–166. https://doi.org/10.15171/bi.2014.008

XVI. Sharma, B. R., & Ravindra, P. V. (2022). *Immune responses to SARS-CoV-2 infection and COVID-19 vaccines*. 648–664. https://doi.org/10.37349/ei.2022.00074

XVII. Sotomayor, F., Corbacho, J. M., Valiente, A., Benítez, Y., & Viera, T. (2020). Aspectos generales sobre la estructura del coronavirus del síndrome respiratorio agudo grave 2 (SARS-CoV-2). *Revista Cubana de Investigaciones Biomédicas*, *30*(3), 3–10. http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0864-03002020000300025

XVIII. *Understanding COVID-19 Vaccines*. (2021).

XIX. Yu, C., Littleton, S., Giroux, N. S., Mathew, R., Ding, S., Kalnitsky, J., Yang, Y., Petzold, E., Chung, H. A., Rivera, G. O., Rotstein, T., Xi, R., Ko, E. R., Tsalik, E. L., Sempowski, G. D., Denny, T. N., Burke, T. W., McClain, M. T., Woods, C. W., … Saban, D. R. (2021). Mucosal-associated invariant T-cell responses differ by sex in COVID-19. *Med*, *2*(6), 755-772.e5. https://doi.org/10.1016/j.medj.2021.04.008

XX. Zepeda-cervantes, J., Mart, D., Ram, O., Tecalco-cruz, Á. C., Alavez-p, S., Vaca, L., & Sarmiento-silva, R. E. (2022). *Implications of the Immune Polymorphisms of the Host and the Genetic Variability of SARS-CoV-2 in the Development of COVID-19*.