



Original Article

Assessment of immuno-hematological parameters in Oxford-AstraZeneca vaccinated patients: A demographic comparative analysis

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ABSTRACT

Objectives: Vaccination is pivotal in addressing the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, yet comprehensive documentation of immunological and hematological outcomes, particularly with the Oxford-AstraZeneca vaccine (ChAdOx1) in Nigeria, is lacking. This multicenter study evaluated hematological and immunological correlates in individuals vaccinated with the ChAdOx1 vaccine.

Materials and Methods: The study included 227 adult participants, who were enrolled and categorized based on SARS-CoV-2 infection status (non-infection, recent infection, and past infection) and vaccination phase (baseline, first dose, and second dose). SARS-CoV-2 infection status was confirmed using reverse transcription polymerase chain reaction and serological assays, while immune biomarkers (kidney injury molecule 1 [KIM-1], programmed cell death protein 1 [PD-1], and interleukin-6 [IL-6]) were measured using enzyme-linked immunosorbent assay and enzyme-linked fluorescent assay platforms. Complete blood counts were evaluated using a standard hematology analyzer.

Results: In the Federal Capital Territory (FCT) cohort, white blood cell (WBC), neutrophil counts, and mean corpuscular hemoglobin concentration (MCHC) significantly increased in second-dose vaccines compared to baseline and first-dose categories. Similarly, lymphocyte, monocyte, eosinophil, red blood cell (RBC), mean cell hemoglobin (MCH), and IL-6 levels were persistently higher in the FCT cohort, irrespective of infection or vaccination status, while KIM-1 and PD-1 levels revealed no statistically significant difference between the FCT and Calabar cohorts.

Conclusion: Vaccination with the ChAdOx1 vaccine was associated with immunomodulatory effects, particularly in the FCT cohort, including increased white blood cell (WBC) counts, neutrophils, and mean corpuscular hemoglobin concentration (MCHC), and reduced interleukin-6 (IL-6) and lymphocyte counts, which suggest a favorable immune trajectory following vaccination.

Keywords: Federal capital territory, Hematological profile, Immunological correlates, Severe acute respiratory syndrome coronavirus 2, Vaccination

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INTRODUCTION

The World Health Organization declared coronavirus disease-19 (COVID-19) a global pandemic in January 2020. It has impacted more than 216 countries worldwide. To date, there have been more than 700 million confirmed cases, and 6.9 million deaths attributed to the disease. In Nigeria alone, there have been more than 250 thousand cases and more than 3 thousand deaths.^[1] The virus's initial symptoms resemble the common cold, including fever and throat swelling. However, it can progress to various conditions, such as respiratory, enteric, neurological, and hepatic diseases, acute respiratory distress syndrome (ARDS), acute cardiac injury, and secondary infections.^[2] Elderly patients and those with underlying medical conditions are particularly vulnerable to developing severe respiratory illness, which can be fatal.^[3] The current COVID-19 situation has significantly disrupted healthcare services in Nigeria. Studies have shown an increase in diabetes-related problems during lockdown, leading to a higher rate of cardiovascular complications that can worsen the severity of COVID-19. Given the limited availability of technical resources during this pandemic, optimizing their usage is crucial. Routine blood investigations can serve as valuable markers for disease severity, enabling healthcare professionals to identify high-risk patients more effectively. Early diagnosis is vital due to the rapid onset of ARDS after hospital admission and the high mortality rate associated with COVID-19.^[4]

A standard blood test can diagnose and monitor the condition of a disease. This test provides valuable information about the inflammatory process, including the white blood cell (WBC) count and interleukin-6 (IL-6) concentration, which are inflammatory markers. Moreover, the mean platelet volume can indicate collateral organ damage, such as acute renal or liver failure, as well as the severity of the disease. By analyzing blood test results, physicians can gain insights into the nature of pneumonia and determine its underlying cause.^[5] The complete blood count (CBC), which includes the count of platelets, neutrophils, lymphocytes, and monocytes, serves as a marker for the inflammatory process. Neutrophils play a crucial role in the immune system. Regarding COVID-19-positive patients, the use of circulating biomarkers that represent inflammation and the immune system could serve as prognostic indicators. However, the clinical utility of these biomarkers in terms of disease diagnosis, monitoring, and risk stratification has yet to be extensively explored.^[5]

In the present study, we assessed the hematological and immunological variables of Nigerian COVID-19 patients who were followed up from baseline to vaccination with the AstraZeneca vaccine. These indices may be valuable in establishing more accurate prognoses for managing this disease.

MATERIALS AND METHODS

Study design and setting

A longitudinal, hospital-based study was conducted at the Departments of Hematology and Clinical Chemistry in several study locations in Calabar, Cross River State, and Gwagwalada, FCT-Abuja. The Calabar study locations included the Nigerian Navy Reference Hospital (NNRH) and the Infectious Disease Hospital (IDH), while the Abuja study location was at the University of Abuja Teaching Hospital (UATH). From the venous sample, sequestered blood was used for a complete blood count (CBC) and differentials, and serum was used for determining kidney injury molecule 1 (KIM-1), programmed cell death protein 1 (PD-1), and interleukin-6 (IL-6). Oropharyngeal swabs (OPS) and nasopharyngeal swabs (NPS) were used for viral load determination. Enzyme-linked immunosorbent assay kits were used for quantifying levels of human KIM-1 (Enzo Life Sciences, Inc. [Lausanne, Switzerland]), PD-1 (ThermoFisher Scientific [Vienna, Austria]), IL-6 (DRG International, Inc. [Springfield, USA]), and anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin G (IgG) nucleocapsid protein (NovaTec Immundiagnostica GmbH [Dietzenbach, Germany]). Anti-SARS-CoV-2 IgG receptor binding domain (RBD) spike protein levels were measured using an enzyme-linked fluorescent assay equipment (kit from mini VIDAS machine [bioMérieux SA, USA]). An automated hematology analyzer (Mindray BC-5000 [Shenzhen, China]) was used for CBC and WBC differentials. Blood count indices were assessed using an automated hematology analyzer. Viral loads from participants sampled from OPS and NPS were determined using a magnetic induction cyclor polymerase chain reaction (PCR) and GeneXpert before and after vaccination with the AstraZeneca vaccine (Covishield [Serum Institute of India, India]) for SARS-CoV-2 at the study centers between February and November 2021.

Population

This longitudinal study comprised a total of 227 adult participants from two distinctive study geopolitical zones (Calabar, Cross River State [representing the Southern region] and the Federal Capital Territory [FCT], Abuja [representing the Northern region] of the country) whose samples were screened against SARS-CoV-2 and investigated for hematological, immunological, and biochemical markers. The research participants comprised the active group (COVID-19 screened and confirmed seropositive participants), recovered group (confirmed clearance of SARS-CoV-2 ribonucleic acid [RNA]), first-dose vaccine group (those who had taken the first dose of the AstraZeneca vaccine), second-dose vaccine group (those who had taken the second dose of the

AstraZeneca vaccine), and control group (apparently healthy individual screened COVID-19 seronegative). Participants from these groups were subcategorized as follows: Non-infection group (PCR [negative]/anti-Spike IgG [negative] and/or anti-Nucleocapsid IgG [negative]), past infection group (PCR [negative]/anti-Spike IgG [positive] or/and anti-Nucleocapsid IgG [positive]), and recent infection group (PCR [positive]/anti-Spike IgG [positive] or/and anti-Nucleocapsid IgG [positive]).

Unlike the 69 participants of the Calabar cohort, who were all ultimately recruited, approximately 95.2% (158/166) of participants from the FCT cohort were considered eligible, as the remaining three participants had samples for which the SARS-CoV-2 nucleic acid and/or antibody status could not be determined. This was either due to the participant's refusal to have their samples collected for analysis, based on inconvenience at later stages of the study, an insufficient sample, or invalid results due to inconclusive analysis. Out of 69 participants in the Calabar cohort, 27 were classified as SARS-CoV-2 non-infection baseline, 12 as SARS-CoV-2 recent infection baseline, and 30 as past infection baseline. Out of the 69 participants in the Calabar cohort, 32 participants (46.4%) availed themselves for sampling 3 weeks post-first-dose vaccination, from which: three qualified as non-infection first-dose vaccines, two as recent infection first-dose vaccines, and 27 as past infection first-dose vaccines. Out of 32 participants in the Calabar cohort sampled 3 weeks after the second-dose vaccination, 14 participants (43.8%) were eligible for sampling 3 weeks post-second-dose vaccination, having received a second dose of vaccine. On the other hand, the 158 participants in the FCT cohort were categorized into two groups: 67 as the non-infection baseline and 91 as the recent infection baseline. Out of the 158 participants in the FCT cohort, 128 participants (81%) availed themselves for sampling 3 weeks post-first-dose vaccination, from which: 13 were non-infection first-dose vaccines, 2 were recent infection first-dose vaccines, and 113 were past infection first-dose vaccines. Out of the 128 participants of the FCT cohort sampled 3 weeks after the first-dose vaccination, 106 participants (82.8%) availed themselves for sampling 3 weeks post second-dose vaccination, from which: six were eligible as non-infection second-dose vaccines and 100 as past infection second-dose vaccines. The stratification of study participants was not just based on vaccination status but also on the basis of non-infection, recent infection, and past infection. This finding was in line with the identification of previous and acute infection with SARS-CoV-2 using an immunoglobulin test in Luanda, Angola, by Sebastião and Galangue.^[6]

Infectious disease physicians and nurses from the isolation centers of the UATH, Gwagwalada, FCT-Abuja, the IDH, and the NNRH, Calabar, Cross River State, aided in identifying and recruiting the participants.

Eligibility criteria

Active (recent infection) group

The inclusion criteria for the recent infection group were:

- Participants who have been confirmed positive for COVID-19 using reverse transcription PCR (RT-PCR)
- Participants who were seropositive or seronegative for SARS-CoV-2 IgG RBD Spike and SARS-CoV-2 IgG Nucleocapsid proteins.

On the other hand, the exclusion criterion for the recent infection group involved participants who had been confirmed COVID-19 negative using RT-PCR.

Recovered (past infection) group

The inclusion criteria for the past infection group were as follows:

- Participants with RT-PCR confirmed SARS-CoV-2 RNA clearance in at least two respiratory tract samples collected over 24 h apart
- Participants who were seropositive for SARS-CoV-2 IgG RBD Spike and SARS-CoV-2 IgG Nucleocapsid proteins.

On the other hand, the exclusion criteria for the past infection group were as follows:

- Participants who have been confirmed COVID-19 positive using RT-PCR
- Participants who were seronegative for SARS-CoV-2 IgG RBD Spike and SARS-CoV-2 IgG Nucleocapsid proteins.

The vaccinated group after the first dose

The inclusion criterion for the first-dose vaccination group involved participants who were at least 3 weeks post-vaccination for just the first dose of the AstraZeneca vaccine.

On the other hand, the exclusion criteria for the first-dose vaccination group were as follows:

- Participants who neither received the vaccine nor are <3 weeks post-vaccination for the first dose of the AstraZeneca vaccine
- Participants who received any other vaccine besides the AstraZeneca vaccine.

The vaccinated group after the second dose

The inclusion criteria for the second-dose vaccination group involved participants who were at least 3 weeks post-vaccination for just the second dose of the AstraZeneca vaccine.

On the flip side, the exclusion criteria for the second dose vaccination group were as follows:

- Participants who neither received the vaccine nor are <3 weeks post-vaccination for the second dose of the AstraZeneca vaccine

- b. Participants who received any other vaccine besides the AstraZeneca vaccine.

Control (non-infection) group

The inclusion criteria for the non-infection group involved:

- Participants who have been confirmed COVID-19 negative using RT-PCR
- Participants who are seronegative for SARS-CoV-2 IgG RBD Spike and SARS-CoV-2 IgG Nucleocapsid proteins.

On the flip side, the exclusion criteria for the non-infection group were as follows:

- Participants who have been confirmed COVID-19 positive using RT-PCR and/or seropositive for SARS-CoV-2 IgG
- Participants with any known underlying illness.

Sample collection, preparation, and precautions

Venipuncture was used to collect 7 mL of venous blood from each participant. Three milliliters of blood were dispensed into a K3-Ethylene Diamine Tetraacetic Acid (EDTA) vial to determine the CBC. Four milliliters of blood were dispensed into plain tubes and spun at 3000 rpm for 10 min to extract serum for the determination of SARS-CoV-2 (COVID-19) IgG, KIM-1, PD-1, and IL-6. Nasal and oral swabs were also collected from participants using swabs preserved in their respective viral transport media. Nasal and oropharyngeal specimens were analyzed within 24 h of sampling using the magnetic induction cycler, PCR, and GeneXpert. Personal protective equipment was used to handle and process all the samples. All work surface areas were decontaminated during the protocols, and spills and aerosols were avoided.

Ethical considerations

The study was approved by the National Health Research Ethics Committee (Ref. NHREC/01/01/2007-23/11/2020) and the Institutional Health Research Ethical Committee of the University of Calabar Teaching Hospital (Ref. UCTH/HREC/33/102).

Data collection and confidentiality

There were no burdens or anticipated effects on the participants, as efforts were made to minimize perceived risks during the stages of meeting with the participants, receiving written informed consent, collecting specimens, and transporting them.

All information collected from participants in this study was aggregated, and all identifying information was removed. The samples were anonymized with coded numbers. Pretested structured questionnaires were used to obtain

sociodemographic data (age, sex, educational level, and occupational status, and residential setting), knowledge (variables on infection type, symptoms, preventive, and control measures), and attitudes and practices to prevent transmission through person-to-person contact, contact with contaminated surfaces and touching of the eyes, mouth, and nose with contaminated hands.

Statistical analysis

The generated data were systematically analyzed as appropriate for the mean, standard deviation, Pearson correlation analysis, and analysis of variance (ANOVA) in Microsoft Excel, Statistical Package for the Social Sciences software version 18 (California, Inc.), and Prism v9. The results are presented as the mean \pm standard deviation. A two-sided $P \leq 0.05$ was considered to indicate statistical significance for Pearson's correlation analysis, and repeated-measures ANOVA was used to determine the intervariable associations of the various groups.

RESULTS

A total of 227 participants were recruited into this study, involving 69 individuals from Calabar centers and 158 individuals from the FCT location. In the Calabar cohort, the age of participants ranged from 17 to 84 years, with an average of 32.62 ± 12.98 years. In contrast, the ages of the participants in the FCT cohort ranged from 22 to 61 years, with a mean of 40.86 ± 9.24 years.

Sociodemographic comparisons

Tables 1 and 2 reveal a concise breakdown of sociodemographic features for each study site. In the Calabar cohort, both age ($P = 0.023$) and occupation ($P = 0.006$) were significantly associated with vaccination status, suggesting that these factors may influence vaccine uptake and timing. On the other hand, in the FCT cohort, none of the sociodemographic features were significantly associated with vaccination status, revealing a more coherent distribution across subgroups.

Table 3 presents a comparative analysis between the Calabar and FCT cohorts, highlighting regional disparities in the participant profiles. Notably, the FCT cohort comprised a greater proportion of middle-aged adults and employed individuals, whereas the Calabar cohort exhibited a more diverse age distribution and higher representation of students. These dissimilarities in demographic composition between these geographical locations are vital for contextualizing both the immunological and hematological outcomes and may account for the notable differences in vaccine response and infection history across these locations.

Table 1: Sociodemographic features and identification of recent and past infection with SARS-CoV-2 nucleic acid and antibody tests in Calabar

Variables	Indices	Baseline			First-dose vaccine			Second-dose vaccine (Past infection) (n=14) (%)	Test Statistic	
		Non-infection (n=27) (%)	Recent infection (n=12) (%)	Past infection (n=30) (%)	Non-infection (n=3) (%)	Recent infection (n=2) (%)	Past infection (n=27) (%)		Chi-square	P-value
Age (years)	17–35 (young adult)	17 (63)	8 (66.7)	22 (73.3)	3 (100)	1 (50)	23 (85.2)	12 (85.7)	19.015	0.088
	36–55 (mid-age adult)	4 (14.8)	4 (33.3)	6 (20)	0 (0)	1 (50)	4 (14.8)	2 (14.3)		
	>55 (older adult)	6 (22.2)	0 (0)	2 (6.7)	0 (0)	0 (0)	0 (0)	0 (0)		
Gender	Female	8 (29.6)	3 (25)	15 (50)	1 (33.3)	0 (0)	18 (66.7)	9 (64.3)	14.657	0.023*
	Male	19 (70.4)	9 (75)	15 (50)	2 (66.7)	2 (100)	9 (33.3)	5 (35.7)		
Occupation	Employed	9 (33.3)	8 (66.7)	13 (43.3)	3 (100)	2 (100)	22 (81.5)	12 (85.7)	44.749	0.006*
	Unemployed	3 (11.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
	Self-employed	5 (18.5)	2 (16.7)	1 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)		
	Retired/pensioner	2 (7.4)	0 (0)	1 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)		
	Student	8 (29.6)	2 (16.7)	15 (50)	0 (0)	0 (0)	5 (18.5)	2 (14.3)		
BMI (kg/m ²)	Chronic energy deficiency (<18.5)	0 (0)	0 (0)	1 (3.3)	0 (0)	0 (0)	1 (3.7)	0 (0)	36.94	0.425
	Moderate underweight (18.5–20.9)	1 (3.7)	2 (16.7)	6 (20)	0 (0)	0 (0)	3 (11.1)	0 (0)		
	Normal weight (21–24.9)	10 (37)	1 (8.3)	9 (30)	0 (0)	1 (50)	12 (44.4)	6 (42.9)		
	Overweight (25–29.9)	14 (51.9)	7 (58.3)	8 (26.7)	2 (66.7)	1 (50)	7 (25.9)	4 (28.6)		
	Class 1 obesity (30–34.9)	1 (3.7)	2 (16.7)	3 (10)	0 (0)	0 (0)	3 (11.1)	4 (1.6)		
	Class 2 obesity (35–39.9)	1 (3.7)	0 (0)	2 (6.7)	1 (33.3)	0 (0)	1 (3.7)	0 (0)		
	Class 3 obesity (≥40)	0 (0)	0 (0)	1 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)		
Education	Primary	3 (11.1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.7)	0 (0)	12.736	0.389
	Secondary	7 (25.9)	1 (8.3)	5 (16.7)	0 (0)	1 (50)	7 (25.9)	3 (21.4)		
	Tertiary	17 (63)	11 (91.7)	25 (83.3)	3 (100)	1 (50)	19 (70.4)	11 (78.6)		
Marital status	Married	12 (44.4)	5 (41.7)	9 (30)	1 (33.3)	0 (0)	5 (18.5)	2 (14.3)	12.981	0.793
	Single	14 (51.9)	7 (58.3)	20 (66.7)	2 (66.7)	2 (100)	19 (70.4)	11 (78.6)		
	Widowed	1 (3.7)	0 (0)	1 (3.3)	0 (0)	0 (0)	2 (7.4)	1 (7.1)		
	Separated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.7)	0 (0)		
Residential area	Urban	23 (85.2)	8 (66.7)	22 (73.3)	1 (33.3)	1 (50)	20 (74.1)	10 (71.4)	13.681	0.322
	Rural	2 (7.4)	0 (0)	4 (13.3)	0 (0)	0 (0)	4 (14.8)	2 (14.3)		
	Suburb	2 (7.4)	4 (33.3)	4 (13.3)	2 (66.7)	1 (50)	3 (11.1)	2 (14.3)		
Household size	1–4	18 (66.7)	10 (83.3)	18 (60)	2 (66.7)	0 (0)	20 (74.1)	9 (64.3)	9.759	0.637
	5–8	9 (33.3)	2 (16.7)	11 (36.7)	1 (33.3)	2 (100)	7 (25.9)	5 (35.7)		
	≥9	0 (0)	0 (0)	1 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)		

*P<0.05 = Significant, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, BMI: Body mass index.

Table 2: Sociodemographic features and identification of recent and past infection with SARS-CoV-2 nucleic acid and antibody tests in FCT

Variables	Indices	Baseline		First-dose vaccine			Second-dose vaccine		Test statistic	
		Non-infection (n=67) (%)	Recent infection (n=91) (%)	Non-infection (n=13) (%)	Recent infection (n=2) (%)	Past infection (n=113) (%)	Non-infection (n=6) (%)	Past infection (n=100) (%)	Chi-square	P-value
Age (years)	17–35 (young adult)	28 (41.8)	28 (30.8)	6 (46.2)	0 (0)	43 (38.1)	2 (33.3)	35 (35)	9.396	0.669
	36–55 (mid-age adult)	36 (53.7)	54 (59.3)	7 (59.3)	2 (100)	60 (53.1)	4 (66.7)	57 (57)		
	>55 (older adult)	3 (4.5)	9 (9.9)	0 (0)	0 (0)	10 (8.8)	0 (0)	8 (8)		
Gender	Female	17 (25.4)	27 (29.7)	5 (38.5)	0 (0)	30 (26.5)	0 (0)	24 (24)	6.63	0.356
	Male	50 (74.6)	64 (70.3)	8 (61.5)	2 (100)	83 (73.5)	6 (100)	76 (76)		
Occupation	Employed	63 (94)	90 (98.9)	11 (84.6)	2 (100)	110 (97.3)	6 (100)	98 (98)	7.525	0.275
	Unemployed	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
	Self-employed	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
	Retired/pensioner	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
	Student	4 (6)	1 (1.1)	2 (15.4)	0 (0)	3 (2.7)	0 (0)	2 (2)		
BMI (kg/m ²)	Chronic energy deficiency (<18.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	15.118	0.917
	Moderate underweight (18.5–20.9)	1 (1.5)	1 (1.1)	0 (0)	0 (0)	2 (1.8)	0 (0)	2 (2)		
	Normal weight (21–24.9)	25 (37.3)	37 (40.7)	5 (38.5)	0 (0)	43 (38.1)	5 (83.3)	30 (30)		
	Overweight (25–29.9)	41 (61.2)	51 (56)	8 (61.5)	2 (100)	66 (58.4)	1 (16.7)	67 (67)		
	Class 1 obesity (30–34.9)	0 (0)	1 (1.1)	0 (0)	0 (0)	1 (0.9)	0 (0)	1 (1)		
	Class 2 obesity (35–39.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
	Class 3 obesity (≥40)	0 (0)	1 (1.1)	0 (0)	0 (0)	1 (0.9)	0 (0)	0 (0)		
Education	Primary	1 (1.5)	1 (1.1)	0 (0)	0 (0)	2 (1.8)	0 (0)	1 (1)	3.335	0.993
	Secondary	2 (3)	4 (4.4)	1 (7.7)	0 (0)	6 (5.3)	0 (0)	7 (7)		
	Tertiary	64 (95.5)	86 (94.5)	12 (92.3)	2 (100)	105 (92.9)	6 (100)	92 (92)		
Marital status	Married	54 (80.6)	80 (87.9)	11 (84.6)	2 (100)	91 (80.5)	5 (83.3)	83 (83)	3.196	0.784
	Single	13 (19.4)	11 (12.1)	2 (15.4)	0 (0)	22 (19.5)	1 (16.7)	17 (17)		
	Widowed	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
	Separated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
Residential area	Urban	63 (94)	86 (94.5)	13 (100)	2 (100)	103 (91.2)	6 (100)	91 (91)	4.961	0.959
	Rural	1 (1.5)	2 (2.2)	0 (0)	0 (0)	4 (3.5)	0 (0)	3 (3)		
	Suburb	3 (4.5)	3 (3.3)	0 (0)	0 (0)	6 (5.3)	0 (0)	6 (6)		
Household size	1–4	65 (97)	86 (94.5)	12 (92.3)	2 (100)	107 (94.7)	6 (100)	94 (94)	3.006	0.996
	5–8	2 (3)	4 (4.4)	1 (7.7)	0 (0)	5 (4.4)	0 (0)	5 (5)		
	≥9	0 (0)	1 (1.1)	0 (0)	0 (0)	1 (0.9)	0 (0)	1 (1)		

P<0.05: Significant. SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, FCT: Federal capital territory, BMI: Body mass index.

Hematological comparisons between the Calabar and FCT cohorts

Tables 4 and 5 indicate the CBC parameters from both Calabar and FCT cohorts. All CBC indices across vaccination

phases (baseline, first dose, and second dose) in the Calabar cohort revealed no significant variation [Table 4]. On the other hand, several hematological indices in the FCT cohort revealed significant variations across vaccination status, which involved WBC count, neutrophils, lymphocytes,

Table 3: Comparative sociodemographic characteristics between Calabar and FCT cohorts based vaccination and infection status

Variable	Category	Calabar (69) (%)	FCT (158) (%)	P-value	Significance
Age (years)	17–35 (Young adults)	64	36.7	0.002*	More young adults in Calabar cohort
	36–55 (Middle-aged adults)	16.3	56.3	0.001*	More middle-aged adults in FCT cohort
	>55 (Older adults)	3.5	7.6	0.218	Not significant
Gender	Female	47.8	26.6	0.010*	Greater female participation in Calabar cohort
	Male	52.2	73.4	0.0022*	Greater male participation in FCT cohort
Occupation	Employed	67.0	96.5	<0.001*	Higher employment in FCT cohort
	Student	28	2.5	<0.001*	More students in Calabar cohort
	Others (Unemployed/Retired)	5	<1	0.0044*	More unemployed/retired in Calabar cohort
BMI (kg/m ²)	Normal (21–24.9)	32.5	38.1	0.382	Not significant
	Overweight (25–29.9)	35.3	58.4	0.005*	More overweight in FCT cohort
	Obesity (≥30)	18.5	3.8	0.002*	More obesity in Calabar cohort
Education	Tertiary	77	93	0.004*	More tertiary education in FCT cohort
	Secondary	21	5.7	0.006*	More secondary education in Calabar cohort
	Primary	1.5	1.3	0.912	Not significant
Marital status	Married	30.5	84.1	<0.001*	More married amongst FCT cohort
	Single	63.8	15.5	<0.001*	More singles amongst Calabar cohort
Residential area	Urban	77.8	94.0	0.001*	More urban dwellers in FCT cohort
	Rural/Suburban	22.2	6.0	<0.001*	More rural/suburban dwellers in Calabar cohort
Household size	1–4 members	68	94	<0.001*	Larger household size in FCT cohort
	≥5 members	32	6	<0.001*	Larger household size in Calabar cohort

Results are expressed as percentages, * $P < 0.05$: Significant. FCT: Federal capital territory, BMI: Body mass index.

monocytes, eosinophils, red blood cell (RBC) count, mean cell hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) ($P < 0.05$) [Table 5].

Table 6 reveals a direct comparison of hematological parameters between the Calabar and FCT cohorts, summarizing average values and indicating statistically significant variations. Enrollees of the FCT cohort had significantly higher WBC and neutrophil counts, while the monocyte count, MCH, and MCHC were significantly higher in the Calabar cohort ($P < 0.05$). These variations suggest site-specific immune responses or population characteristics that may have influenced the hematologic findings following vaccination for COVID-19.

Serum immunological indices

Tables 7 and 8 indicate the serum IL-6, KIM-1, and PD-1 indices from both Calabar and FCT cohorts. All immunological indices across vaccination phases (baseline, first dose, and second dose) in the Calabar cohort revealed no significant variation [Table 8]. On the other hand, only IL-6 levels in the FCT cohort indicated a statistically significant variation across vaccination statuses, while no statistically significant changes were observed for KIM-1 and PD-1 values [Table 7].

Immunological comparisons between the Calabar and FCT cohorts

Table 9 presents a comparative analysis of immunological parameters (IL-6, KIM-1, and PD-1) between the Calabar and FCT cohorts, categorized by vaccination and infection status. IL-6 levels were persistently and statistically higher in the FCT cohort compared to those of the Calabar cohort across almost all the vaccination categories for baseline (non-infection, recent infection, and past infection), first dose (non-infection and past infection), and second dose (past infection) groups.

Surprisingly, the first-dose (recent infection) subgroup revealed no statistically significant difference between the two cohorts, implying a potential normalization or suppression effect of IL-6 in this subgroup. These outcomes may indicate regional immunological dissimilarities or differential immune response dynamics following exposure to the SARS-CoV-2 infection and vaccination.

Conversely, KIM-1 and PD-1 values reveal no statistically significant changes between the two cohorts in any subgroup. Although the KIM-1 and PD-1 levels were higher in the Calabar cohort compared to the FCT cohort, the differences were not statistically significant, implying that KIM-1 and

Table 4: Plasma hematological profile of baseline and vaccinated participants in Calabar stratified by non-infection, recent, and past infection status

Variables	Baseline			First-dose vaccine			Second-dose vaccine (Past infection) (n=14)	Test statistic	
	Non-infection (n=27)	Recent infection (n=12)	Past infection (n=30)	Non-infection (n=3)	Recent infection (n=2)	Past infection (n=27)		F-ratio	P-value
WBC count (10 ⁹ /L)	4.98±0.28	4.92±0.33	5.32±0.25	5.21±0.65	6.27±2.22	5.16±0.27	4.55±0.22	0.869	0.378
Neutrophil count (10 ⁹ /L)	2.09±0.15	2.24±0.14	2.01±0.2	2.29±0.4	3.565±2.03	1.93±0.14	1.76±0.12	1.627	0.222
Lymphocyte count (10 ⁹ /L)	2.44±0.19	2.09±0.18	2.7±0.15	2.28±0.13	2.14±0.01	2.68±0.17	2.25±0.11	1.409	0.248
Monocyte count (10 ⁹ /L)	0.30±0.03	0.48±0.08	0.45±0.06	0.5±0.09	0.49±0.15	0.34±0.02	0.41±0.04	2.102	0.126
Eosinophil count (10 ⁹ /L)	0.15±0.02	0.11±0.03	0.15±0.03	0.14±0.07	0.08±0.04	0.21±0.03	0.13±0.03	0.835	0.479
Basophil count (10 ⁹ /L)	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.978	0.384
RBC count (10 ⁹ /L)	4.99±0.24	5.67±0.47	4.96±0.22	4.71±0.27	6.09±1.94	5.30±0.26	4.58±0.13	1.261	0.283
HGB (g/dL)	14.23±0.67	14.93±1.37	13.68±0.42	13.77±0.63	18.05±5.15	14.94±0.84	12.82±0.39	1.210	0.274
HCT (%)	40.81±1.78	42.44±3.56	40.33±1.25	40.10±2.01	50.90±13.80	42.69±2.21	36.59±1.02	1.128	0.287
MCV (fL)	82.49±1.35	75.78±3.30	82.66±1.634	85.17±2.26	84.85±4.35	80.48±0.91	80.14±1.57	1.669	0.212
MCH (pg)	28.68±0.50	26.54±1.26	27.97±0.45	29.27±0.65	30.00±1.10	28.06±0.40	28.03±0.52	1.232	0.301
MCHC (g/dL)	34.76±0.23	34.98±0.36	33.98±0.33	34.37±0.29	35.35±0.45	34.85±0.23	34.97±0.17	1.683	0.199
RDW-CV (%)	13.90±0.26	13.71±0.29	15.92±1.01	13.53±0.90	13.95±1.85	13.86±0.35	12.93±0.31	2.044	0.165
RDW-SD (fL)	44.09±1.08	39.58±1.33	52.00±4.33	44.70±4.03	45.50±3.90	43.02±0.95	39.60±1.05	2.379	0.127
PLT (10 ⁹ /L)	169.9±11.18	180.5±16.16	202.5±11.55	176.3±13.20	140.5±50.50	201.5±11.22	207.6±19.03	1.357	0.260
MPV (fL)	10.66±0.20	10.63±0.17	10.08±0.27	10.50±0.61	9.95±0.75	10.49±0.19	10.51±0.25	1.050	0.368
PDW (fL)	15.93±0.06	15.83±0.11	15.86±0.10	15.90±0.20	16.05±0.15	15.97±0.07	16.00±0.13	0.363	0.764
PCT (%)	1.81±0.12	1.91±0.17	2.05±0.13	1.87±0.24	1.44±0.61	2.11±0.11	2.16±0.19	1.919	0.304

Results are expressed as mean ± standard deviation, *P*<0.05: Significant. WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean cell hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW-CV: Red blood cell distribution width coefficient of variation, RDW-SD: Red blood cell distribution width-standard deviation, PLT: Platelet count, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit.

PD-1 levels remained comparable between the two cohorts, irrespective of infection or vaccination status.

DISCUSSION

This longitudinal study was conducted between February and November 2021 and included a total of 227 adult participants from two distinctive study geopolitical zones (Calabar, Cross River State [representing the southern region] and the FCT, Abuja [representing the northern region]). These participants were screened for SARS-CoV-2 infection and categorized based on PCR and antibody data into 3 subgroups (non-infection, recent infection, and past infection). Subsequent evaluations of their immunological and hematological profiles were conducted at baseline,

3 weeks after the first dose, and 3 weeks after the second dose of the Oxford-AstraZeneca vaccine (ChAdOx1).

IL-6 profile and dynamics of immune response

In the present study, the primary focus was on the immunological assessment of serum IL-6 levels, a key proinflammatory cytokine implicated in the pathogenesis of COVID-19. The data revealed statistically increased levels of IL-6 in the FCT cohort, particularly among participants who had recently been exposed to SARS-CoV-2 infection at baseline, compared to their counterparts in the Calabar cohort. These findings align with previous studies that establish the link between elevated levels of IL-6 and acute inflammatory responses in critical cases of SARS-

Table 5: Plasma hematological profile of baseline and vaccinated participants in FCT stratified by non-infection, recent, and past infection status

Variables	Baseline		First-dose vaccine			Second-dose vaccine		Test statistic	
	Non-infection (n=67) (%)	Recent infection (n=91) (%)	Non-infection (n=13)	Recent infection (n=2)	Past infection (n=113)	Non-infection (n=6)	Past infection (n=100)	F-ratio	P-value
WBC count (10 ⁹ /L)	4.92±0.18	5.17±0.18	4.99±0.33	5.55±0.15	5.22±0.12	6.08±0.36	6.06±0.133	6.154	<0.001*
Neutrophil count (10 ⁹ /L)	1.97±0.13	1.91±0.09	2.57±0.29	3.14±0.28	2.73±0.09	3.62±0.13	3.49±0.10	28.10	<0.001*
Lymphocyte count (10 ⁹ /L)	2.41±0.10	2.68±0.11	2.11±0.10	2.02±0.14	2.09±0.03	2.13±0.11	2.36±0.05	6.355	<0.001*
Monocyte count (10 ⁹ /L)	0.40±0.02	0.41±0.02	0.21±0.03	0.23±0.12	0.25±0.02	0.08±0.03	0.15±0.01	17.610	<0.001*
Eosinophil count (10 ⁹ /L)	0.12±0.01	0.14±0.01	0.14±0.01	0.17±0.11	0.15±0.01	0.08±0.03	0.07±0.01	5.746	0.017*
Basophil count (10 ⁹ /L)	0.01±0.00	0.01±0.00	0.00±0.00	0.00±0.00	0.01±0.00	0.00±0.00	0.00±0.00	0.638	0.424
RBC count (10 ⁹ /L)	5.11±0.08	5.07±0.07	5.05±0.14	5.50±0.10	5.21±0.06	5.08±0.27	4.87±0.08	2.611	0.039*
HGB (g/dL)	13.58±0.18	13.62±0.19	13.46±0.26	15.15±0.05	13.87±0.12	14.23±0.22	13.99±0.08	1.382	0.250
HCT (%)	41.58±0.51	41.86±0.51	37.86±3.19	45.50±0.50	41.64±0.38	42.00±0.82	42.01±0.26	1.965	0.146
MCV (fL)	82.46±0.73	83.48±0.70	82.75±2.09	83.75±2.55	82.01±0.91	83.53±1.42	83.99±0.69	0.742	0.535
MCH (pg)	27.06±0.28	27.12±0.37	26.47±0.93	26.85±0.25	27.73±0.35	24.40±0.72	25.60±0.33	4.159	0.003*
MCHC (g/dL)	32.60±0.20	32.69±0.12	31.78±0.41	32.70±0.70	32.36±0.18	32.40±1.00	33.25±0.23	2.740	0.050
PLT (10 ⁹ /L)	256.8±7.06	244.3±7.82	236.9±12.58	281.0±41.00	251.6±6.77	247.5±19.70	231.6±4.91	1.409	0.248

Results are expressed as mean ± standard deviation, *P<0.05: Significant. FCT: Federal capital territory, WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean, corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, PLT: Platelet count.

CoV-2 infection, as well as its relationship with disease severity.^[7]

Following vaccination, the concentration of IL-6 varied based on the history of infection and the dosage of the vaccine. At week 3, after the first dose of ChAdOx1 nCoV-19 (AstraZeneca vaccine), the concentration of IL-6, especially in the non-infected group of the FCT cohort, increased, although not significantly, compared to the baseline concentration (before vaccination). Interestingly, the concentration of this proinflammatory cytokine (IL-6) decreased 3 weeks after the second dose of the AstraZeneca vaccine, particularly in participants with prior exposure to SARS-CoV-2 infection, suggesting a possible modulating effect of vaccination. This trend in the kinetics of IL-6 before and following COVID-19 vaccination agrees with the findings of Heo *et al.*^[8] and Willems *et al.*,^[9] who equally documented fluctuations in IL-6 kinetics following vaccination. However, in a later study,^[9] there was no report of IL-6 kinetic events following the second dose of the vaccine. Despite this trend, the study revealed significantly decreased levels of IL-6 in patients receiving second-dose vaccination combined with

a history of infection compared to baseline levels in patients with a recent infection. The study findings suggest that the sampling period following the first and second vaccination doses may have influenced certain variations in IL-6 levels observed between this recent study and previous studies.^[8,9] Unlike previous works, which involved sampling on day 3 following the first and second doses of the ChAdOx1 nCoV-19 vaccine, the present study involved sampling at week 3 following the first and second doses of the ChAdOx1 nCoV-19 vaccine.

The inflammatory immune response is vital for activating innate immunity and inducing adaptive immunity after vaccination.^[10,11] IL-6, a proinflammatory cytokine, is produced by several cell types (e.g., macrophages, fibroblasts, T cells, endothelial cells, and monocytes).^[12] The significant targets of IL-6 are B cells, basophils, T cells, neutrophils, and eosinophils. The vital role of IL-6 in acquired immunity is to increase and differentiate B cells into plasma cells; stimulate plasma cells to produce IgG antibodies in addition to other immunoglobulins (e.g., immunoglobulin A, immunoglobulin E, and immunoglobulin M); and enhance

Table 6: Comparative hematological indices between Calabar and FCT cohorts

Variable	Calabar (69)	FCT (158)	P-value	Significance
WBC (10 ⁹ /L)	5.05±0.36	5.57±0.41	0.037*	Higher in FCT cohort
Neutrophil count (10 ⁹ /L)	2.06±0.12	2.92±0.18	<0.001*	Higher in FCT cohort
Lymphocyte count (10 ⁹ /L)	2.41±0.14	2.34±0.09	0.613	Not significant
Monocyte count (10 ⁹ /L)	0.40±0.04	0.26±0.03	0.012*	Higher in Calabar cohort
Eosinophil count (10 ⁹ /L)	0.13±0.02	0.12±0.01	0.428	Not significant
Basophil count (10 ⁹ /L)	0.00±0.00	0.01±0.00	0.392	Not significant
RBC count (10 ¹² /L)	5.03±0.20	5.13±0.11	0.294	Not significant
Hemoglobin (g/dL)	14.04±0.56	13.99±0.26	0.812	Not significant
Hematocrit (%)	40.91±1.43	42.01±0.26	0.089	Not significant
MCV (fL)	80.62±1.87	83.48±0.70	0.063	Not significant
MCH (pg)	28.10±0.46	25.60±0.33	0.006*	Higher in Calabar cohort
MCHC (g/dL)	34.72±0.19	33.25±0.23	0.021*	Higher in Calabar cohort
PCT (10 ⁹ /L)	190.4±14.3	243.4±8.60	0.009*	Higher in FCT cohort
MPV (fL)	10.38±0.22	10.34±0.19	0.734	Not significant
PDW (fL)	15.89±0.10	15.92±0.09	0.693	Not significant
PCT (%)	1.97±0.16	2.03±0.13	0.672	Not significant

Results are expressed as mean ± standard deviation, *P<0.05: Significant. FCT: Federal capital territory, WBC: White blood cell, RBC: Red blood cell, MCV: Mean corpuscular volume, MCH: Mean cell hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, PLT: Platelet count, MPV: Mean platelet volume, PDW: Platelet distribution width.

Table 7: Serum immunological profile of baseline and vaccinated participants in FCT stratified by non-infection, recent, and past infection status

Variables	Baseline		First-dose vaccine			Second-dose vaccine		Test statistic	
	Non-infection (n=67) (%)	Recent infection (n=91) (%)	Non-infection (n=13) (%)	Recent infection (n=2) (%)	Past infection (n=113) (%)	Non-infection (n=6) (%)	Past infection (n=100) (%)	F-ratio	P-value
IL-6 (pg/mL)	630.0±209.8	1130.0±252.7	830.7±343.7	15.7±0.0	637.3±168.8	749.0±135.2	164.1±67.6	3.872	0.001*
KIM-1 (pg/mL)	161.7±73.6	169.5±44.1	148.7±31.88	75.5±0.0	217.4±46.2	146.9±29.6	143.5±27.2	0.388	0.886
PD-1 (pg/mL)	27.5±10.1	14.3±4.6	24.3±17.1	6.7±0.0	24.7±7.4	15.7±7.9	24.6±4.0	0.340	0.914

Results are expressed as mean ± standard deviation, *P<0.05: Significant. FCT: Federal capital territory, IL-6: Interleukin 6, KIM-1: Kidney injury molecule 1, PD-1: Programmed cell death 1.

Table 8: Serum immunological profile of baseline and vaccinated participants in Calabar stratified by non-infection, recent, and past infection status

Variables	Baseline			First-dose vaccine			Second-dose vaccine (Past infection) (n=14) (%)	Test Statistic	
	Non-infection (n=27) (%)	Recent infection (n=12) (%)	Past infection (n=30) (%)	Non-infection (n=3) (%)	Recent infection (n=2) (%)	Past infection (n=27) (%)		F-ratio	P-value
IL-6 (pg/mL)	29.58±20.51	0.00±0.00	73.67±0.00	0.00±0.00	0.00±0.00	0.00±0.00	120.5±0.00	0.607	0.342
KIM-1 (pg/mL)	175.90±33.51	123.40±26.71	128.40±29.16	298.40±253.10	245.70±112.90	188.5±36.29	285.70±83.89	1.418	0.257
PD-1 (pg/mL)	63.43±12.42	55.42±26.99	55.03±9.63	16.40±9.15	7.25±0.25	41.27±11.31	57.89±16.51	0.656	0.560

Results are expressed as mean ± standard deviation, *P<0.05: Significant. IL-6: Interleukin 6, KIM-1: Kidney injury molecule 1, PD-1: Programmed cell death 1.

Table 9: Comparative immunological indices between Calabar and FCT cohorts

Variable	Group	Calabar (69)	FCT (158)	P-value	Significance
IL-6 (pg/mL)	Baseline (non-infection)	29.58±20.51	630.0±209.80	0.001*	Higher in FCT cohort
	Baseline (recent infection)	0.00±0.00	1130.0±252.70	0.001*	Higher in FCT cohort
	Baseline (past infection)	73.67±0.00	637.30±168.80	0.001*	Higher in FCT cohort
	First dose (non-infection)	0.00±0.00	830.70±343.70	0.001*	Higher in Calabar cohort
	First dose (recent infection)	0.00±0.00	15.70±0.00	0.136	Not significant
	First dose (past infection)	0.00±0.00	164.10±67.60	0.018*	Higher in FCT
	Second dose (past infection)	120.50±0.00	749.0±135.20	0.007*	Higher in FCT
KIM-1	Baseline (non-infection)	175.90±33.51	161.70±73.60	0.432	Not significant
	Baseline (recent infection)	123.40±26.71	169.50±44.10	0.298	Not significant
	Baseline (past infection)	128.40±29.16	217.40±46.20	0.109	Not significant
	First dose (non-infection)	298.40±253.10	148.70±31.88	0.238	Not significant
	First dose (recent infection)	245.70±112.90	75.50±0.00	0.068	Not significant
	First dose (past infection)	188.50±36.29	143.50±27.20	0.171	Not significant
	Second dose (past infection)	285.70±83.89	146.90±29.60	0.094	Not significant
PD-1	Baseline (non-infection)	63.43±12.42	27.50±10.10	0.063	Not significant
	Baseline (recent infection)	55.42±26.99	14.30±4.60	0.072	Not significant
	Baseline (past infection)	55.03±9.63	24.70±7.40	0.084	Not significant
	First dose (non-infection)	16.40±9.15	24.30±17.10	0.423	Not significant
	First dose (recent infection)	7.25±0.25	6.70±0.00	0.217	Not significant
	First dose (past infection)	41.27±11.31	24.60±4.00	0.214	Not significant
	Second dose (past infection)	57.89±16.51	15.70±7.90	0.069	Not significant

Results are expressed as mean ± standard deviation, * $P < 0.05$: Significant. FCT: Federal capital territory, IL-6: Interleukin 6, KIM-1: Kidney injury molecule 1, PD-1: Programmed cell death 1.

the activation, differentiation, development, and survival of effector T cells.^[13,14] Elevated systemic concentrations of IL-6 have previously been reported following several types of immunization, including foot and mouth disease vaccination,^[15] diphtheria toxoid vaccination,^[16] Bacillus Calmette-Guérin,^[17] and influenza vaccination.^[18] Farsakoglu *et al.*^[18] revealed the increase in IL-6 production by CD11b+ dendritic cells after influenza vaccination and demonstrated that the secretion of IL-6 was initiated by interferon-gamma synthesis from natural killer (NK) cells. The NK cell response was initially established for a dose of ChAdOx1 nCoV-19^[19], which explains the increased levels of IL-6 following the first dose of the vaccine, as observed in a recent study.

Comparative immune profiles across demographic locations

A comparative assessment of the FCT and Calabar cohorts revealed that IL-6 concentrations were significantly higher in the FCT cohort compared to the Calabar cohort across several stratified groups (baseline, first dose, and second dose), except for the first dose (recent infection) category, where no statistical difference was observed. This implies either demographic variation in immune response or

population-level immunogenetic dissimilarities. On the other hand, KIM-1 and PD-1 revealed no statistically significant differences across cohorts from both regions or vaccination stages, suggesting stable expression regardless of location or history of infection.

Hematological parameters and demographic variation

The present study assessed whether there were connections between alterations in the hematological profile and the vaccination status of participants. The study evaluated specific hematological indices at various periods following vaccination, and variation of these indices was observed across stages of vaccination. However, the FCT cohort revealed statistically significant variations in several hematological profiles following vaccination. Among the profiles, we observed increased WBC and neutrophil counts, and decreased lymphocyte, monocyte, eosinophil, RBC, and mean cell hemoglobin (MCH) levels in the second-dose vaccine groups compared to those in the baseline and first-dose vaccine groups. It is noteworthy that the MCHC was equally significantly altered, which agrees with the reports of Rahman *et al.*,^[20] who identified these biomarkers as predictive of COVID-19 severity in participants.

Direct comparison between both cohorts revealed that participants from FCT had significantly higher WBC and neutrophil counts, while their counterparts from Calabar had significantly higher monocytes, MCH, and MCHC. However, most of the parameter values were within the reference ranges, suggesting that while the values of these indices are biologically vital, they may not always imply clinical pathology.^{ag}

Pathophysiological consequences of hematological trends

The observed hematological changes reflect the systemic immune activation following exposure of the biological system to SARS-CoV-2 and vaccination. Following the invasion of body fluids (blood), SARS-CoV-2 primarily spreads to cells of the liver, lungs, heart, and gastrointestinal tract through viral receptors (i.e., angiotensin-converting enzyme 2). During this phase, systemic inflammation is triggered, which decreases the lymphocyte count and increases neutrophils, while proinflammatory cytokines increase, thereby worsening patient disease outcomes.^[21] Lymphopenia (depleted lymphocytes) is common in patients with acute SARS-CoV-2 infection and worsens as the condition becomes more severe.^[22-24] In addition to increased WBC counts, decreased monocyte, eosinophil, platelet, lymphocyte, and basophil counts are common in the acute phase and severe cases of infection.^[25,26] Previous studies have demonstrated increased peripheral blood neutrophil (neutropenia) counts in SARS-CoV-2-infected patients who needed intensive care unit (ICU) support. Hence, the neutrophil-to-lymphocyte ratio has been proposed to indicate COVID-19 severity.^[27,28] Previous research revealed a significant decrease in platelet count (thrombocytopenia) in hospitalized patients.^[23,24] The severity of COVID-19 has been associated with increased levels of hemoglobin.^[29] A meta-analysis involving the recruitment of 3,377 participants across 21 studies revealed a significant relationship between hematological indices and the severity of COVID-19.^[30] Therefore, abnormal variations in hematological profiles have been associated with COVID-19 severity, extended hospitalization, and ICU support requirements.^[20]

Limitations

First, sample attrition due to loss to follow-up resulted in the partial loss of data from 79.7% (55/69) to 48.1% (76/158) of the Calabar and FCT cohorts, respectively, because they failed to comply by having their samples collected either at baseline, after the first dose or after the second dose of the vaccine. Subsequent follow-up data were collected from the present study.

Second, the exact mechanism of the progressive changes in the hematological profile of the vaccinated population has yet to be adequately explained.

Finally, selection bias may have been introduced since several participants willingly presented themselves for enrollment, and others decided to refrain from participating in the study at any of the first, second, or final sampling steps.

CONCLUSION

This study is among the pioneer research in Nigeria to comprehensively compare immunological and hematological responses to COVID-19 vaccination across several demographic regions. The data highlights vital demographic dissimilarities, especially in IL-6 responses and selected hematological indices, implying the need for localized immune surveillance and potentially targeted vaccination strategies. However, this study emphasizes the clinical importance of IL-6 as a biomarker for SARS-CoV-2 infection and recovery and indicates the applicability of CBC indices in post-vaccination monitoring.

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Ethical approval: The research/study approved by the Institutional Review Board at National Health Research Ethics Committee of Nigeria (NHREC), number NHREC/01/01/2007, dated 23rd November, 2020.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.

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