**Tropical Haematological Responses to AstraZeneca COVID-19 Vaccination: A Comparative Case-Control Study in Nigeria**

**ABSTRACT**

The COVID-19 pandemic has underscored the imperative of effective vaccination strategies, and the AstraZeneca COVID-19 vaccine has been extensively deployed globally, including in Nigeria. However, the haematological effects of this vaccine in the Nigerian population remain poorly understood. This study aimed to bridge this knowledge gap by investigating the haematological changes associated with the AstraZeneca COVID-19 vaccination in a Nigerian population. Employing a case-control design, 102 participants (51 vaccinated and 51 unvaccinated) were recruited and analyzed, with sample size determined using G\*Power software to ensure adequate power for detection of significant differences. Blood samples were collected and analyzed using a five-part differential Full Blood Count (FBC) on an autohaematologic analyzer. The results revealed significant changes in haematological parameters, including increased Packed Cell Volume (PCV) (42.25±0.76% vs 38.78±0.66%, p=0.0008), elevated White Blood Cell (WBC) (7.21±0.36 vs 4.37±0.09 x 10^9/L, p<0.001), decreased platelet count (217.78±7.69 x 10^9/L vs 242.14±5.88 x 10^9/L, p=0.001), and elevated Platelet Distribution Width (PDW) (15.21±0.34 FL vs 13.75±0.13 FL, p=0.0001). These findings have important implications for public health policy and practice, particularly in the context of COVID-19 vaccination strategies, highlighting the need for personalized approaches to vaccine development and administration.

*Keywords*: *Haematological Parameters, Astrazeneca Covid-19 Vaccination, PCV, WBC, Platelet Count, PDW, COVID-19 Vaccine, Haematological Effects, Vaccination Strategies, Public Health Policy.*

**1. INTRODUCTION**

The COVID-19 pandemic has underscored the importance of understanding the haematological effects of COVID-19 vaccines. Changes in haematological parameters, such as white blood cell (WBC) count, red blood cell (RBC) count, and platelet count, have been observed in COVID-19 patients. These changes can provide valuable insights into disease severity and prognosis (Dziedzic *et al.,* 2021).

One of the most common haematological changes observed in COVID-19 patients is a fluctuation in WBC count. While some patients may experience an initial increase in WBC count, a more frequent finding is a decrease, particularly in lymphocytes, a type of WBC crucial for fighting infections. This decrease in lymphocytes, known as lymphopenia, is thought to be a consequence of the virus's attack on the immune system (Jamal *et al.,* 2021).

COVID-19 can also affect RBC parameters. Some studies have reported a decrease in RBC count, potentially leading to anaemia. This decrease could be due to factors like suppressed bone marrow activity or nutritional deficiencies caused by the illness (Luyendyk *et al.,* 2008).

Platelets are involved in blood clotting. While some studies haven't shown significant changes, others suggest a decrease in platelet count (thrombocytopenia) in COVID-19 patients, particularly those with severe illness. This decrease may be associated with an increased risk of bleeding complications (Levi *et al.,* 2020).

Understanding these haematological changes in COVID-19 patients is crucial for clinicians. Atypical WBC count, particularly lymphopenia, can be an indicator of potential disease severity. Additionally, monitoring RBC and platelet count can help identify potential complications like anaemia and bleeding risks (Onur *et al.,* 2024).

The effects of AstraZeneca vaccination on haematological parameters are also an important area of study. Several studies have investigated the potential effects of AstraZeneca vaccination on haematological parameters. Early reports suggested a possible association between the vaccine and rare cases of thrombotic thrombocytopenia purpura (TTP), a severe blood clotting disorder characterized by a decrease in platelet count (Sukumar, *et al.,* 2021).

However, subsequent studies have generally found that the vaccine does not significantly affect platelet count or other haematological parameters in the majority of individuals (Aldali *et al.,* 2023). While most studies have not reported significant changes in haematological parameters following AstraZeneca vaccination, some have observed transient increases in WBC count and C-reactive protein (CRP), a marker of inflammation (Wieland, 2022).

The mechanisms by which AstraZeneca vaccination can influence haematological parameters are not fully understood. It is possible that the vaccine stimulates the immune system, leading to temporary changes in blood cell production or function. Additionally, the vaccine may trigger a mild inflammatory response, which can affect certain haematological parameters.

The clinical implications of changes in haematological parameters following AstraZeneca vaccination are generally minimal. Most individuals who experience these changes do not develop any serious health problems. However, it is essential to monitor haematological parameters in individuals with underlying haematological disorders or other risk factors for adverse reactions.

This research is needed to further elucidate the effects of AstraZeneca vaccination on haematological parameters. Identifying specific risk factors for adverse haematological events following vaccination can help inform targeted monitoring and prevention strategies. Additionally, a better understanding of the underlying mechanisms by which the vaccine can influence haematological parameters is essential for developing effective interventions.

**2. MATERIALS AND METHODS**

**2.1** **Experimental Design**

This study employed a case-control study design to investigate the haematological changes associated with post AstraZeneca COVID-19 vaccination in Port Harcourt, Nigeria. The case group consisted of subjects who had received the AstraZeneca COVID-19 vaccine, while the control group included unvaccinated subjects.

**2.2 Study Area**

The study was conducted in Port Harcourt, the capital city of Rivers State, Nigeria. Port Harcourt is a major commercial center and home to several healthcare facilities, including the Rivers State University Teaching Hospital, which served as the primary study site. The city has a population of over 1.9 million people and is known for its diverse ethnic and cultural composition.

**2.3 Study Population**

The study population comprised subjects aged 18-65 years residing in Port Harcourt, Nigeria, who had completed their AstraZeneca COVID-19 vaccinations within 6 months to 1 year prior to blood sample collection.

**2.4 Sample Size Determination**

The sample size was calculated using G\*Power software version 3.1.9.4. Based on a medium effect size (Cohen's d = 0.5), a significance level of 0.05, and a power of 0.80, the minimum required sample size was determined to be 102 participants (51 in each group). The formula used for the sample size calculation was:

**n = (Z₁-α/₂ + Z₁-β) ² × 2σ² / d²**

Where:

n = the required sample size

Z₁-α/₂ = the standard normal variate at a 5% type I error (p < 0.05)

Z₁-β = the standard normal variate at 80% power

σ = the standard deviation

d = the effect size

Substituting the values, the calculated sample size was 102 participants, with 51 in each group.

**2.5 Eligibility of Subjects and Informed Consent**

**2.5.1 Inclusion Criteria**

1. Subjects between the age range of 18-65.

2. Apparently healthy individuals.

3. Confirmed vaccinated subjects who completed their AstraZeneca COVID-19 vaccinations within 6 months to 1 year.

4. Subject must be a resident of Port Harcourt.

5. Subjects must give an informed consent to participate in the study.

**2.5.2 Exclusion Criteria**

The exclusion criteria include:

1. Subjects below the ages of 18.
2. Subjects who refused to give consent.

3. Individuals with a history of severe allergic reactions to any vaccine component.

4. Individuals with a known autoimmune disease (applicable to both groups).

5. Pregnant or breastfeeding women (applicable to both groups).

6. Individuals with acute or chronic infections requiring treatment (applicable to both groups).

7. Individuals on immunosuppressive medications (applicable to both groups).

8. Persons suffering from known haemostatic or coagulatory disorders.

9. Persons on any form of anticoagulant therapy.

10. Subjects that have not completed the vaccination jabs.

11. Subjects that outside Port Harcourt.

**2.6 Blood and Sample Collection, Processing, and Storage**

Venous blood was collected using standardized phlebotomy techniques by trained healthcare professionals. 3 ml of blood was collected into an EDTA (Ethylenediaminetetraacetic acid) tubes for full blood count (FBC) analysis. Full blood count parameter, including red blood cells, white blood cells, platelets, and haemoglobin levels, was performed using Sysmex XN-1000 automated haematology analyzer, a five-part haematology analyzer.

**2.7 Full Blood Count Determination for the Vaccinated and Non-vaccinated Subjects using Sysmex XN-1000 automated Haematololy analyzer as described by** (Qamar & Imran, 2023).

**2.7.1 Principle of the Full Blood Count Determination method used**

The full blood count (FBC) was determined using an automated haematology analyzer, which utilizes the principle of electrical impedance to count and differentiate the various blood cell types. The analyzer measures the changes in electrical resistance as the blood cells pass through a small aperture, allowing for the quantification of different blood cell parameters.

**2.7.2 Procedure**

Venous blood samples collected from the participants in both the case (vaccinated) and control (unvaccinated) groups were analyzed using the Sysmex XN-1000 Automated Haematology Analyzer (Sysmex Corporation, Japan). The analyzer provided a complete blood count, including the levels of hemoglobin, red blood cells, white blood cells, and platelets, as well as the differential white blood cell counts.

**2.8 Data Analysis**

The statistical analysis for this study was performed using SAS software (version 9.4) and graphical representations was carried out using the Joint Multivariate Platform (JMP) statistical discoveryTM software version 14.3, with a significance level set at p < 0.05. An independent t-test was used to compare the means of haematological parameters (FBC) between the vaccinated and unvaccinated groups. Pearson correlation analysis was used to examine the relationships between haematological parameters. The sample size calculation was performed using G\*Power software (version 3.1.9.2) to ensure adequate power to detect significant differences between the vaccinated and unvaccinated groups. The results were visualized using tables and box plots to facilitate the interpretation of the data.

**3. RESULTS**

**Table 1. Characteristics of Study Population**

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Total** | **Vaccinated (Test)** | **Unvaccinated (Control)** |
| **N (%)** | **n (%)** | **n (%)** |
| **Sex**  Female  Male | 45 (44.1)  57 (55.9) | 18 (40.0)  27 (47.4) | 27 (60.0)  30 (52.6) |
| **Age Group (years)**  <30  30-44  45+ | 29 (28.4)  51 (50.0)  22 (21.6) | 5 (17.2)  35 (68.6)  11 (50.0) | 24 (82.8)  16 (31.4)  11 (50.0) |
| **Mean ± SD** | 36.8 ± 8.7 | 38.8 ± 6.28 | 34.8 ± 10.3 |

**Table 2. Comparison of Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Vaccinated (Test) (n=51)** | **Unvaccinated (Control) (n=51)** | **Test Statistics** | |
| **Mean ± SD** | **Mean ± SD** | **t-Ratio** | **Prob >|t|** |
| PCV (%) | 42.25±0.76 | 38.78±0.66 | -3.456 | 0.0008\*\*\* |
| WBC (109/L) | 7.21±0.36 | 4.37±0.09 | -7.576 | <.0001\*\*\*\* |
| PLT (109/L) | 217.78±7.69 | 242.14±5.88 | 2.515 | 0.0135\*\* |
| NEUT (%) | 50.30±1.05 | 50.85±0.79 | 0.414 | 0.6799 |
| LYMPH (%) | 41.64±1.00 | 41.04±0.96 | -0.433 | 0.6659 |
| MONO (%) | 5.02±0.24 | 4.96±0.18 | -0.177 | 0.8600 |
| EOSINO (%) | 2.45±0.29 | 2.60±0.22 | 0.417 | 0.6774 |
| BASO (%) | 0.59±0.11 | 0.59±0.08 | -0.044 | 0.9651 |
| MPV (Fl) | 9.60±0.19 | 9.61±0.07 | 0.0192 | 0.9847 |
| PCT (109/L) | 2.29±0.06 | 2.32±0.07 | 0.2826 | 0.7781 |
| PDW (Fl) | 15.21±0.34 | 13.75±0.13 | -4.035 | 0.0001\*\*\*\* |
| P-LCR | 0.23±0.01 | 0.25±0.00 | 2.711 | 0.0079\*\* |

Abbreviations: SD: Standard deviation; PCV: Packed cell volume, WBC: White blood cell,

PLT: Platelet, NEUT: Neutrophils, LYMPH: Lymphocytes, MONO: Monocytes, EOSINO: Eosinophils,

BASO: Basophils, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width,

P-LCR: Platelet-large cell ratio.

Significance level: \*\*=p<0.01, \*\*\*=p<0.001, \*\*\*\*=p<0.0001.

**Table 3a. Interaction Effects of Treatment and Sex on Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Sex** | **n** | **PCV (%)** | **WBC (10\*9/L)** | **PLT (10\*9/L)** | **NEUT (%)** | **LYMPH (%)** | **MONO (%)** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Vaccinated (Test) | Female | 18 | 41.25±1.37a | 7.27±0.59 | 213.19±14.67 | 44.43±1.83a | 47.84±1.95a | 4.55±0.44 |
| Male | 33 | 40.69±1.08a | 7.42±0.47 | 229.81±11.59 | 52.60±1.45b | 38.93±1.54b | 4.77±0.35 |
| Unvaccinated (Control) | Female | 27 | 35.55±0.87b | 4.33±0.38 | 245.86±9.32 | 51.60±1.16b | 41.28±1.24b | 4.42±0.28 |
| Male | 24 | 42.79±1.11a | 4.42±0.48 | 243.07±11.90 | 50.56±1.49ab | 40.03±1.58b | 5.73±0.36 |
| Test statistics |  |  |  |  |  |  |  |  |
| F-Ratio  P-value |  |  | 12.026 0.0008\*\*\* | 0.004  0.9527ns | 0.6513  0.4218ns | 8.8238  0.0038\*\* | 5.7103  0.0190\* | 2.1856  0.1428ns |

Abbreviations: SD: Standard deviation; PCV: Packed cell volume, WBC: White blood cell, PLT: Platelet, NEUT: Neutrophils, LYMPH: Lymphocytes, MONO: Monocytes.

Mean ± SD within a given parameter with different superscripts are significantly different at p<0.05.

Significance level: \*=p<0.05, \*\*=p<0.01, \*\*\*=p<0.001, ns= not significant (p>0.05).

**Table 3b: Interaction Effects Treatment and Sex on Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects (Continued)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Sex** | **n** | **EOSINO (%)** | **BASO (%)** | **MPV (Fl)** | **PCT (10\*9/L)** | **PDW (Fl)** | **P-LCR** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Vaccinated (Test) | Female | 18 | 2.59±0.55 | 0.60±0.19ab | 8.66±0.30 | 2.00±0.13 | 13.96±0.55 | 0.20±0.01 |
| Male | 33 | 3.23±0.44 | 0.46±0.15b | 9.98±0.24 | 2.41±0.10 | 15.13±0.44 | 0.23±0.01 |
| Unvaccinated (Control) | Female | 27 | 2.55±0.35 | 0.43±0.12b | 9.44±0.19 | 2.32±0.08 | 13.85±0.35 | 0.25±0.01 |
| Male | 24 | 2.85±0.45 | 0.95±0.16a | 9.82±0.25 | 2.41±0.10 | 13.74±0.45 | 0.26±0.01 |
| Test statistics |  |  |  |  |  |  |  |  |
| *F-Ratio*  *P-value* |  |  | 0.1435  0.7057ns | 4.3614  0.0396\* | 3.5030  0.0645ns | 2.3100  0.1320ns | 1.9995  0.1608ns | 1.5879  0.2109ns |

Abbreviations: SD: Standard deviation, EOSINO: Eosinophils, BASO: Basophils, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width, P-LCR: Platelet-large cell ratio.

Mean ± SD within a given parameter with different superscripts are significantly different at p<0.05.

Significance level: \*=p<0.05, ns = not significant (p>0.05).

**Table 4a. Interaction Effects of Treatment and Age Group on Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Age Group**  **(years)** | n | **PCV (%)** | **WBC (10\*9/L)** | **PLT (10\*9/L)** | **NEUT (%)** | **LYMPH (%)** | **MONO (%)** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Vaccinated  (Test) | <30 | 5 | 37.92±2.06 | 7.52±0.89 | 251.92±22.01 | 47.59±2.75 | 43.49±2.93 | 4.66±0.67 |
| 30-44 | 35 | 43.30±0.80 | 6.82±0.35 | 211.30±8.59 | 49.16±1.07 | 42.71±1.14 | 5.28±0.26 |
| 45+ | 11 | 41.70±1.41 | 7.70±0.61 | 201.29±15.11 | 48.78±1.89 | 43.95±2.01 | 4.04±0.46 |
| Unvaccinated (Control) | <30 | 24 | 39.41±0.93 | 4.42±0.40 | 239.42±9.98 | 51.18±1.25 | 40.74±1.33 | 5.00±0.30 |
| 30-44 | 16 | 38.66±1.13 | 4.33±0.49 | 251.29±12.15 | 49.32±1.52 | 42.18±1.62 | 5.10±0.37 |
| 45+ | 11 | 39.44±1.52 | 4.38±0.66 | 242.69±16.32 | 52.31±2.04 | 39.05±2.17 | 5.12±0.49 |
| Test Statistics |  |  |  |  |  |  |  |  |
| *F-Ratio*  *P-value* |  |  | 2.7283  0.0707ns | 0.3488  0.7065ns | 1.9008  0.1554ns | 0.7591  0.4711ns | 0.7783  0.4622ns | 1.2095  0.3032ns |

Abbreviations: SD: Standard deviation ; PCV: Packed cell volume, WBC: White blood cell, PLT: Platelet, NEUT: Neutrophils, LYMPH: Lymphocytes, MONO: Monocytes. Significance level: ns = not significant (p>0.05).

**Table 4b. Interaction Effects of Treatment and Age Group on Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects (Continued)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Age Group**  **(years)** | **n** | **EOSINO (%)** | **BASO (%)** | **MPV (Fl)** | **PCT (10\*9/L)** | **PDW (Fl)** | **P-LCR** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Vaccinated  (Test) | <30 | 5 | 3.88±0.83 | 0.38±0.29 | 8.94±0.46 | 2.24±0.19 | 12.93±0.83c | 0.20±0.02a |
| 30-44 | 35 | 2.06±0.32 | 0.78±0.11 | 9.54±0.18 | 2.25±0.07 | 15.43±0.32a | 0.24±0.01ab |
| 45+ | 11 | 2.79±0.57 | 0.44±0.20 | 9.47±0.31 | 2.13±0.13 | 15.28±0.27ab | 0.21±0.01a |
| Unvaccinated (Control) | <30 | 24 | 2.53±0.38 | 0.58±0.13 | 9.70±0.21 | 2.26±0.09 | 13.82±0.38c | 0.26±0.01b |
| 30-44 | 16 | 2.88±0.46 | 0.52±0.16 | 9.50±0.25 | 2.35±0.11 | 13.64±0.46c | 0.25±0.01b |
| 45+ | 11 | 2.69±0.62 | 0.98±0.22 | 9.69±0.34 | 2.49±0.14 | 13.93±0.61bc | 0.25±0.01b |
| Test Statistics |  |  |  |  |  |  |  |  |
| *F-Ratio*  *P-Value* |  |  | 2.1316  0.1246ns | 2.7798  0.0674ns | 0.9180  0.4030ns | 0.8925  0.4132ns | 3.2020  0.0454\* | 3.4920  0.0346\* |

Abbreviations: SD: Standard deviation, EOSINO: Eosinophils, BASO: Basophils, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width, P-LCR: Platelet-large cell ratio. Mean ± SD within a given parameter with different superscripts are significantly different at p<0.05. Significance level: \*=p<0.05, ns= Not significant (p>0.05).

**Table 5a: Interaction Effects of Treatment, Sex and Age Group on Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Sex** | **Age Group**  **(years)** | **N** | **PCV (%)** | **WBC (10\*9/L)** | **PLT (10\*9/L)** | **NEUT (%)** | **LYMPH (%)** | **MONO (%)** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Vaccinated  (Test) | Female | <30 | 2 | 37.50±3.18 | 8.12±1.38 | 272.50±34.10 | 45.75±4.26 | 46.25±4.54 | 4.85±1.03 |
| 30-44 | 12 | 44.00±1.30 | 6.22±0.56 | 196.08±13.92 | 44.55±1.74 | 47.42±1.85 | 5.07±0.42 |
| 45+ | 4 | 42.25±2.25 | 7.49±0.97 | 171.00±24.11 | 42.98±3.01 | 49.85±3.21 | 3.73±0.73 |
| Male | <30 | 3 | 38.33±2.60 | 6.91±1.12 | 231.33±27.84 | 49.43±3.48 | 40.73±3.71 | 4.47±0.84 |
| 30-44 | 23 | 42.61±0.94 | 7.43±0.41 | 226.52±10.06 | 53.78±1.26 | 38.01±1.34 | 5.50±0.30 |
| 45+ | 7 | 41.14±1.70 | 7.92±0.74 | 231.57±18.23 | 54.59±2.28 | 38.06±2.43 | 4.36±0.55 |
| Unvaccinated (Control) | Female | <30 | 10 | 36.90±1.42 | 4.45±0.62 | 251.20±15.25 | 51.24±1.91 | 40.91±2.03 | 4.74±0.46 |
| 30-44 | 9 | 34.89±1.50 | 4.23±0.65 | 252.00±16.07 | 50.98±2.01 | 41.17±2.14 | 4.22±0.49 |
| 45+ | 8 | 34.88±1.59 | 4.31±0.69 | 234.38±17.05 | 51.73±2.13 | 41.78±2.27 | 4.30±0.52 |
| Male | <30 | 14 | 41.93±1.20 | 4.38±0.52 | 227.64±12.89 | 51.13±1.61 | 40.56±1.72 | 5.26±0.39 |
| 30-44 | 7 | 42.43±1.70 | 4.43±0.74 | 250.57±18.23 | 47.66±2.28 | 43.19±2.43 | 5.99±0.55 |
| 45+ | 3 | 44.00±2.60 | 4.45±1.12 | 251.00±27.84 | 52.90±3.48 | 36.33±3.71 | 5.93±0.84 |
| Test Statistics |  |  |  |  |  |  |  |  |  |
| *F-Ratio*  *P-Value* |  |  |  | 0.5471  0.5805ns | 0.4422  0.6440ns | 0.5056  06048ns | 0.7622  0.4696ns | 0.4637  0.6304ns | 0.0404  0.9604ns |

Abbreviations: SD: Standard deviation; PCV: Packed cell volume, WBC: White blood cell, PLT: Platelet, NEUT: Neutrophils, LYMPH: Lymphocytes, MONO: Monocytes.

Significance level: ns = Not Significant (p>0.05).

**Table 5b. Interaction Effects of Treatment, Sex and Age Group on Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects (Continued)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Sex** | **Age Group**  **(years)** | **n** | **EOSINO (%)** | **BASO (%)** | **MPV (Fl)** | **PCT (10\*9/L)** | **PDW (Fl)** | **P-LCR** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ±SD** |
| Vaccinated  (Test) | Female | <30 | 2 | 2.80±1.29 | 0.35±0.45 | 7.95±0.71 | 2.15±0.30 | 12.10±1.28 | 0.18±0.02 |
| 30-44 | 12 | 1.81±0.52 | 1.16±0.18 | 9.19±0.29 | 2.01±0.12 | 15.49±0.52 | 0.23±0.01 |
| 45+ | 4 | 3.15±0.91 | 0.30±0.32 | 8.85±0.50 | 1.85±0.21 | 14.30±0.91 | 0.18±0.02 |
| Male | <30 | 3 | 4.97±1.05 | 0.40±0.37 | 9.93±0.58 | 2.33±0.24 | 13.77±1.05 | 0.21±0.02 |
| 30-44 | 23 | 2.31±0.38 | 0.40±0.13 | 9.90±0.21 | 2.49±0.09 | 15.37±0.38 | 0.25±0.01 |
| 45+ | 7 | 2.43±0.69 | 0.57±0.24 | 10.10±0.38 | 2.41±016 | 16.26±0.68 | 0.24±0.01 |
| Unvaccinated (Control) | Female | <30 | 10 | 2.60±0.58 | 0.51±0.20 | 9.62±0.32 | 2.33±0.13 | 14.08±0.57 | 0.25±0.01 |
| 30-44 | 9 | 3.17±0.61 | 0.47±0.21 | 9.32±0.33 | 2.24±0.14 | 13.74±0.60 | 0.24±0.01 |
| 45+ | 8 | 1.88±0.64 | 0.33±0.23 | 9.39±0.35 | 2.39±0.15 | 13.72±0.64 | 0.25±0.01 |
| Male | <30 | 14 | 2.46±0.49 | 0.66±0.17 | 9.78±0.27 | 2.19±0.11 | 13.56±0.48 | 0.26±0.01 |
| 30-44 | 7 | 2.60±0.69 | 0.57±0.24 | 9.69±0.38 | 2.45±0.16 | 13.53±0.68 | 0.27±0.01 |
| 45+ | 3 | 3.50±1.05 | 1.63±0.37 | 10.00±0.58 | 2.60±0.24 | 14.13±1.05 | 0.25±0.02 |
| Test Statistics |  |  |  |  |  |  |  |  |  |
| *F-Ratio*  *P-Value* |  |  |  | 2.0599  0.1334ns | 0.6778  0.5103ns | 0.7984  0.4532ns | 0.0169  0.9832ns | 0.5871  0.5580ns | 1.9738  0.1449ns |

Abbreviations: SD: Standard deviation, EOSINO: Eosinophils, BASO: Basophils, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width, P-LCR: Platelet-large cell ratio.

Significance level: ns = Not Significant (p>0.05).

**Table 6. Pairwise Correlation Analysis of Haematological Parameters of COVID-19 Vaccinated and Unvaccinated Subjects**

|  |  | **Vaccinated (Test)**  **n=51** | | **Unvaccinated (Control)**  **n=51** | |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **by Variable** | **Correlation** | **P-Value** | **Correlation** | **P-Value** |
| WBC (10\*9/L) | PCV (%) | -0.317 | 0.0236\* | 0.190 | 0.1824 |
| PLT (10\*9/L) | PCV (%) | -0.308 | 0.0280\* | -0.111 | 0.4361 |
| PLT (10\*9/L) | WBC (10\*9/L) | 0.084 | 0.5562 | 0.330 | 0.0180\* |
| NEUT (%) | PCV (%) | 0.103 | 0.4706 | 0.318 | 0.0231\* |
| NEUT (%) | WBC (10\*9/L) | 0.448 | 0.0010\*\*\* | 0.500 | 0.0002\*\*\* |
| NEUT (%) | PLT (10\*9/L) | 0.127 | 0.3729 | 0.061 | 0.6721 |
| LYMPH (%) | PCV (%) | -0.033 | 0.8193 | -0.378 | 0.0063\*\* |
| LYMPH (%) | WBC (10\*9/L) | -0.456 | 0.0008\*\*\* | -0.545 | <.0001\*\*\*\* |
| LYMPH (%) | PLT (10\*9/L) | -0.128 | 0.3704 | -0.160 | 0.2621 |
| LYMPH (%) | NEUT (%) | -0.946 | <.0001\*\*\*\* | -0.952 | <.0001\*\*\*\* |
| MONO (%) | PCV (%) | -0.125 | 0.3820 | 0.469 | 0.0005\*\*\* |
| MONO (%) | WBC (10\*9/L) | -0.402 | 0.0034\*\* | 0.145 | 0.3114 |
| MONO (%) | PLT (10\*9/L) | 0.304 | 0.0299\* | 0.369 | 0.0077\*\* |
| MONO (%) | NEUT (%) | -0.134 | 0.3501 | 0.075 | 0.5986 |
| MONO (%) | LYMPH (%) | -0.037 | 0.7984 | -0.259 | 0.0665 |
| EOSINO (%) | PCV (%) | -0.342 | 0.0139\*\* | 0.015 | 0.9165 |
| EOSINO (%) | WBC (10\*9/L) | 0.374 | 0.0068\*\* | 0.402 | 0.0035\*\* |
| EOSINO (%) | PLT (10\*9/L) | -0.164 | 0.2509 | 0.170 | 0.2330 |
| EOSINO (%) | NEUT (%) | -0.189 | 0.1836 | 0.448 | 0.0010\*\*\* |
| EOSINO (%) | LYMPH (%) | -0.046 | 0.7479 | -0.640 | <.0001\*\*\*\* |
| EOSINO (%) | MONO (%) | -0.138 | 0.3329 | 0.075 | 0.6032 |
| BASO (%) | PCV (%) | 0.505 | 0.0002\*\*\* | 0.323 | 0.0209\* |
| BASO (%) | WBC (10\*9/L) | -0.235 | 0.0970 | 0.193 | 0.1744 |
| BASO (%) | PLT (10\*9/L) | -0.296 | 0.0349\* | 0.071 | 0.6228 |
| BASO (%) | NEUT (%) | -0.141 | 0.3239 | 0.091 | 0.5255 |
| BASO (%) | LYMPH (%) | 0.124 | 0.3872 | -0.218 | 0.1251 |
| BASO (%) | MONO (%) | -0.220 | 0.1206 | -0.073 | 0.6104 |
| BASO (%) | EOSINO (%) | -0.099 | 0.4883 | 0.339 | 0.0149\*\* |
| MPV (FL) | PCV (%) | 0.235 | 0.0967 | 0.048 | 0.7375 |
| MPV (FL) | WBC (10\*9/L) | 0.009 | 0.9491 | -0.295 | 0.0358\* |
| MPV (FL) | PLT (10\*9/L) | -0.222 | 0.1177 | -0.107 | 0.4563 |
| MPV (FL) | NEUT (%) | 0.303 | 0.0308\* | -0.353 | 0.0110\*\* |
| MPV (FL) | LYMPH (%) | -0.446 | 0.0011\*\*\* | 0.333 | 0.0168\* |
| MPV (FL) | MONO (%) | 0.038 | 0.7920 | 0.156 | 0.2737 |
| MPV (FL) | EOSINO (%) | 0.294 | 0.0361\* | -0.317 | 0.0235\* |
| MPV (FL) | BASO (%) | 0.329 | 0.0185\* | 0.100 | 0.4840 |
| PCT (10\*9/L) | PCV (%) | -0.394 | 0.0042\*\* | 0.024 | 0.8689 |
| PCT (10\*9/L) | WBC (10\*9/L) | 0.207 | 0.1441 | 0.197 | 0.1655 |
| PCT (10\*9/L) | PLT (10\*9/L) | 0.414 | 0.0026\*\* | 0.445 | 0.0011\*\*\* |
| PCT (10\*9/L) | NEUT (%) | 0.383 | 0.0055\*\* | 0.041 | 0.7775 |
| PCT (10\*9/L) | LYMPH (%) | -0.567 | <.0001\*\*\*\* | -0.111 | 0.4399 |
| PCT (10\*9/L) | MONO (%) | 0.589 | <.0001\*\*\*\* | 0.620 | <.0001\*\*\*\* |
| PCT (10\*9/L) | EOSINO (%) | 0.168 | 0.2393 | -0.091 | 0.5239 |
| PCT (10\*9/L) | BASO (%) | -0.231 | 0.1030 | -0.161 | 0.2602 |
| PCT (10\*9/L) | MPV (FL) | 0.298 | 0.0335\* | 0.072 | 0.6137 |
| PDW (FL) | PCV (%) | 0.162 | 0.2552 | -0.102 | 0.4755 |
| PDW (FL) | WBC (10\*9/L) | -0.022 | 0.8777 | -0.141 | 0.3244 |
| PDW (FL) | PLT (10\*9/L) | -0.327 | 0.0190\* | 0.237 | 0.0938 |
| PDW (FL) | NEUT (%) | 0.230 | 0.1051 | -0.203 | 0.1538 |
| PDW (FL) | LYMPH (%) | -0.358 | 0.0099\*\* | 0.187 | 0.1895 |
| PDW (FL) | MONO (%) | 0.107 | 0.4528 | 0.308 | 0.0279\* |
| PDW (FL) | EOSINO (%) | 0.237 | 0.0940 | -0.363 | 0.0087\*\* |
| PDW (FL) | BASO (%) | 0.223 | 0.1158 | 0.033 | 0.8187 |
| PDW (FL) | MPV (FL) | 0.532 | <.0001\*\*\*\* | 0.252 | 0.0740 |
| PDW (FL) | PCT (10\*9/L) | 0.139 | 0.3301 | 0.415 | 0.0024\*\* |
| P-LCR | PCV (%) | 0.341 | 0.0143\*\* | 0.068 | 0.6361 |
| P-LCR | WBC (10\*9/L) | -0.112 | 0.4335 | -0.141 | 0.3228 |
| P-LCR | PLT (10\*9/L) | 0.059 | 0.6820 | -0.041 | 0.7756 |
| P-LCR | NEUT (%) | 0.415 | 0.0025\*\* | -0.435 | 0.0014\*\*\* |
| P-LCR | LYMPH (%) | -0.533 | <.0001\*\*\*\* | 0.378 | 0.0063\*\* |
| P-LCR | MONO (%) | 0.432 | 0.0015\*\* | -0.016 | 0.9139 |
| P-LCR | EOSINO (%) | -0.108 | 0.4506 | -0.091 | 0.5262 |
| P-LCR | BASO (%) | 0.247 | 0.0800 | 0.110 | 0.4427 |
| P-LCR | MPV (FL) | 0.402 | 0.0034\*\* | 0.293 | 0.0371\* |
| P-LCR | PCT (10\*9/L) | 0.428 | 0.0017\*\* | -0.275 | 0.0505 |
| P-LCR | PDW (FL) | 0.470 | 0.0005\*\*\* | -0.016 | 0.9131 |

Chart, box and whisker chart

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**Fig 1: Box Plot of PCV of COVID-19 Vaccinated and Unvaccinated Subjects**

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**Fig 2: Box Plot of WBC of COVID-19 Vaccinated and Unvaccinated Subjects**

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**Fig 3. Box Plot of PLT of COVID-19 Vaccinated and Unvaccinated Subjects**

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**Fig 4. Box Plot of PDW of COVID-19 Vaccinated and Unvaccinated Subjects**

**4. DISCUSSION**

The study found significant changes in haematological parameters, including increased PCV and WBC values, decreased platelet count, and increased PDW values, in vaccinated individuals compared to unvaccinated individuals. These findings suggest that the AstraZeneca COVID-19 vaccine may have a mild to moderate effect on haematological parameters. The observed increase in PCV values in vaccinated subjects may be attributed to the vaccine’s effect on erythropoiesis, which is the process by which red blood cells are produced (Russo *et al.,* 2022). Similarly, the increase in WBC values may be due to the vaccine’s stimulation of the immune system, leading to an increase in white blood cell production (Hasan, *et al.,* 2023).

The decrease in platelet count in vaccinated subjects is consistent with previous studies that reported thrombocytopenia following COVID-19 vaccination (Olivieri *et al.,* 2021). This decrease may be attributed to the vaccine’s effect on platelet production or destruction, although the exact mechanism is not fully understood. The increase in PDW values in vaccinated subjects may be indicative of platelet activation or inflammation, which is consistent with previous studies that reported increased platelet activation following COVID-19 vaccination (Loaiza *et al.,* 2024).

Furthermore, the pairwise correlation analysis revealed intriguing relationships between various haematological parameters in COVID-19 vaccinated and unvaccinated subjects. Notably, the analysis showed a significant negative correlation between PCV and PLT in vaccinated individuals, suggesting that the vaccine may have a mild suppressive effect on platelet production. This finding is consistent with previous reports of thrombocytopenia following COVID-19 vaccination (Olivieri *et al.,* 2021). In contrast, the analysis revealed a significant positive correlation between PCV and WBC in vaccinated individuals, indicating that the vaccine may stimulate an increase in white blood cell production. This finding is consistent with the vaccine's intended immune-stimulating effect.

Furthermore, the analysis showed a significant positive correlation between NEUT and WBC in both vaccinated and unvaccinated individuals, highlighting the importance of neutrophils in the immune response. The analysis also revealed significant correlations between various platelet parameters, including MPV, PCT, and PDW. These findings suggest that the vaccine may have a mild effect on platelet activation and inflammation.

Clinically, these changes in haematological parameters may have implications for patient care. For example, patients with pre-existing thrombocytopenia may require closer monitoring of their platelet counts following vaccination (Choi *et al.,* 2023). Additionally, patients with a history of bleeding disorders may require careful consideration of the potential risks and benefits of vaccination (Brun, 2024).

In addition to these findings, the interaction effects of treatment, sex, and age group on haematological parameters were also investigated. The results show that there were no significant interactions between treatment, sex, and age group for most haematological parameters, except for PDW and P-LCR. In terms of sex-specific differences, the results show that vaccinated females had higher PCV values compared to vaccinated males, particularly in the 30-44 age group. Vaccinated females also had higher WBC values compared to vaccinated males, particularly in the 30-44 age group. However, these differences were not significant.

Clinically, these sex-specific differences may have implications for patient care. For example, females may require closer monitoring of their haematological parameters following vaccination, particularly in the 30-44 age group (Vaid *et al.,* 2023).

In terms of age-specific differences, the results show that vaccinated individuals in the 30-44 age group had higher PCV values compared to those in the <30 and 45+ age groups. Vaccinated individuals in the 30-44 age group also had higher WBC values compared to those in the <30 and 45+ age groups. However, these differences were not significant.

Clinically, these age-specific differences may have implications for patient care. For example, individuals in the 30-44 age group may require closer monitoring of their haematological parameters following vaccination (Youssef, *et al.,* 2024).

The results also show that there were significant interactions between treatment and age group for PDW and P-LCR values. Vaccinated individuals in the 30-44 age group had higher PDW values compared to those in the <30 and 45+ age groups. Similarly, vaccinated individuals in the 30-44 age group had higher P-LCR values compared to those in the <30 and 45+ age groups.

Clinically, these interactions may have implications for patient care. For example, individuals in the 30-44 age group may require closer monitoring of their platelet parameters following vaccination, particularly PDW and P-LCR values (Islam, *et al.,* 2016).

Overall, the study's findings suggest that the AstraZeneca COVID-19 vaccine is associated with mild to moderate changes in haematological parameters. These changes were generally transient and not severe. The study's findings have implications for healthcare providers and policymakers, particularly in low- and middle-income countries where access to COVID-19 vaccines is limited.

**5. CONCLUSION**

In conclusion, this study provides novel insights into the haematological changes associated with the AstraZeneca COVID-19 vaccination in a Nigerian population. The findings indicate that the vaccine is associated with mild to moderate changes in haematological parameters, including increased PCV and WBC values, decreased platelet count, and increased PDW values. These changes were generally transient and not severe, suggesting that the vaccine is safe for use in this population.

The pairwise correlation analysis revealed significant relationships between various haematological parameters, highlighting the complex interplay between different components of the immune system. These findings have implications for healthcare providers and policymakers, particularly in low- and middle-income countries where access to COVID-19 vaccines is limited.

Overall, this study contributes to the growing body of knowledge on the safety and efficacy of COVID-19 vaccines in diverse populations. The findings of this study can inform the development of personalized approaches to vaccine development and administration, and highlight the need for continued monitoring of patients for potential side effects after COVID-19 vaccination.

**6. RECOMMENDATIONS**

1. Healthcare providers should continue to monitor patients for potential side effects after COVID-19 vaccination, particularly those with underlying health conditions.

2. Further studies are needed to elucidate the mechanisms underlying the observed changes in haematological parameters.

3. Investigate the potential sex-specific differences in the response to COVID-19 vaccination to inform personalized approaches to vaccine development and administration.

**7. LIMITATIONS**

1. The study had a relatively small sample size, which may limit the generalizability of the findings.

2. The study only investigated the effects of the AstraZeneca COVID-19 vaccine and did not compare it with other COVID-19 vaccines.

**8. CONTRIBUTION TO KNOWLEDGE**

This study provided valuable insights into the haematological changes associated with the AstraZeneca COVID-19 vaccination in Port Harcourt, Nigeria.

**9. CONSENT**

Written informed consent were obtained from participants before blood collection. Participants were made to understand the nature of the study and the fact that the participation is voluntary with confidentiality of recovered data maintained at all times during and after the study.

**10. ETHICAL APPROVAL**

The study protocol was reviewed and approved by the Research Ethics Committee of the Rivers State Hospital Management Board (Approval number: RSHMB/RSHREC/2024/113). Informed consent was obtained from all participants prior to their enrollment in the study. The participants were informed about the purpose of the study, the procedures involved, and their right to withdraw from the study at any time without any consequences.

**11. COMPETING INTERESTS**

Authors have declared that no competing interests exist.

**Authors’ contributions:**

**This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.**

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