



# Sero-Prevalence and Immunological Profile of SARS-CoV-2 Antibodies in Nigerian Sickle Cell Disease Patients During the COVID-19 Pandemic

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## Authors' contributions

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

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## ABSTRACT

**Introduction:** Nigeria has the highest prevalence of sickle cell disease (SCD) globally, making it a major genetic disorder of public health concern in Africa. During the COVID-19 pandemic, SCD patients were particularly vulnerable due to their compromised immune and hematological systems.

**Aim/Objective:** This study aimed to determine the sero-prevalence of SARS-CoV-2 IgG and IgM antibodies and assess the associated hematological and immunological profiles in Nigerian SCD patients during the pandemic.

**Method:** A case-control, cross-sectional study was conducted at the University College Hospital (UCH), Ibadan. The study involved 167 participants—122 confirmed SCD patients and 45 healthy controls. Blood samples were analyzed for hematological parameters (white blood cell count [WBC], platelet count, hemoglobin [Hb], and packed cell volume [PCV]), coagulation indicators (prothrombin time [PT], activated partial thromboplastin time [APTT], and D-dimer), and SARS-CoV-2 antibodies (IgG and IgM). Statistical analysis was performed using SPSS version 23.0.

**Results:** SCD patients showed significantly elevated values for white blood cell count (11.37 vs.  $5.64 \times 10^9/L$ ), platelet count (351.62 vs.  $233.04 \times 10^9/L$ ), prothrombin time (PT: 15.33 vs. 11.86 seconds), activated partial thromboplastin time (APTT: 32.25 vs. 29.27 seconds), and D-dimer levels (3347.08 vs. 1438.13 ng/mL) compared to healthy controls ( $p < 0.05$ ). In contrast, SCD patients had significantly lower hemoglobin concentrations (7.75 vs. 13.13 g/dL) and packed cell volume (PCV: 22.42% vs. 39.64%) ( $p < 0.05$ ). Although SCD patients exhibited slightly higher average levels of SARS-CoV-2 IgG and IgM antibodies, these differences were not statistically significant compared with the control group. A significant negative correlation was observed between age and IgM antibody levels ( $r = -0.223$ ,  $p = 0.014$ ), indicating a possible reduction in recent immune response with increasing age.

**Conclusion:** The study revealed significant hematological and coagulation abnormalities in SCD patients, highlighting their heightened risk for thrombotic complications during infections such as COVID-19. Although no significant difference in SARS-CoV-2 antibody levels was found, the observed trends underline the need for routine serological and coagulation monitoring in SCD patients to support better clinical outcomes.

**Keywords:** Sero-prevalence; SARS-CoV-2; IgG; IgM; sickle cell disease; haematological parameters; D-dimer; Nigeria.

## 1. INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder caused by a mutation in the  $\beta$ -globin gene (HBB), which results in the production of abnormal hemoglobin S (HbS) (Rees et al., 2010). In low oxygen environments, HbS tends to form polymers, causing red blood cells to become stiff and fragile (Akinsete et al., 2023a,2023b,2023c,2023d). This leads to hemolysis, blockage of blood vessels, and complications like pain crises, strokes, and damage to several organs (Serjeant, 1997). SCD affects millions globally, with sub-Saharan Africa carrying the highest burden. In Nigeria, more than 150,000 babies are born with SCD every year, and over 1.8 million people live with the disease (Akinyanju, 1989; Piel et al., 2013). Due to limited healthcare resources, especially access to treatments like hydroxyurea and blood transfusions, SCD remains a major cause of death in children in these regions (McGann et al., 2017).

The COVID-19 pandemic, which began in 2019, added new challenges for SCD patients, who are already vulnerable due to their weakened immune and blood systems (Booth et al., 2010). SARS-CoV-2, the virus responsible for COVID-19, causes several blood and clotting problems, including low platelet and lymphocyte counts, raised D-dimer levels, and prolonged clotting times (PT and APTT) (Tang et al., 2020; Levi et al., 2020; Zhou et al., 2020). These issues resemble the existing inflammatory and clotting abnormalities in SCD, such as chronic inflammation, blood vessel damage, and activated platelets (Kato et al., 2009). This overlap has raised concerns about increased risk of blood clots and severe COVID-19 outcomes in people with SCD (Minniti et al., 2021).

Studying the antibody response to SARS-CoV-2 in SCD patients is important for several reasons. Firstly, IgM and IgG antibodies help identify recent or past infections and provide insights into population exposure and immunity (Long et al., 2020). Secondly, the immune

response in SCD is not fully understood—some evidence suggests poor antibody production due to spleen damage, while other studies suggest chronic inflammation might enhance antiviral responses (Booth et al., 2010; Quinn et al., 2010). Thirdly, in countries like Nigeria where testing and vaccination are limited, antibody data can guide targeted public health actions, such as vaccination programs for high-risk groups (Akinyanju, 1989).

Despite the relevance, there has been limited research on SARS-CoV-2 antibody levels and immune profiles in African SCD patients. Most studies have focused on Western populations, where genetic traits and healthcare access differ significantly (Piel et al., 2013). Moreover, little is known about how markers like D-dimer and CRP relate to antibody levels in Nigerian SCD patients with COVID-19 (Olatunya et al., 2023). This study aimed to compare blood and clotting markers between SCD patients and healthy individuals, determine the presence of SARS-CoV-2 IgG and IgM antibodies in Nigerian SCD patients during the pandemic, and explore links between antibody levels and factors like age, sex, and disease severity (e.g., D-dimer).

## 2. MATERIALS AND METHODS

### 2.1 Study Design and Setting

This study utilized a case-control, cross-sectional design to explore the sero-prevalence of SARS-CoV-2 antibodies and associated immunological markers in sickle cell disease (SCD) patients. The research was conducted at the Haematology Day Care Unit of the University College Hospital (UCH), Ibadan, Oyo State, Nigeria. One of the best tertiary hospitals in West Africa, UCH offers cutting-edge medical treatment and is a key hub for referrals for hematological illnesses, including sickle cell disease.

### 2.2 Study Design

The study used a purposeful sample to compare laboratory parameters between SCD patients (cases) and healthy individuals (controls). A total of 167 people participated, comprising 122 confirmed SCD patients and 45 age- and sex-matched healthy controls with no past history of hematological issues.

### 2.3 Sample Size Determination

A formula for case-control studies was used to calculate the sample size, taking into account

power, confidence level, and anticipated variations in the means of coagulation parameters. To increase the study's statistical power, the computed minimum sample size was surpassed.

### 2.4 Study Subjects

Participants were recruited based on medical records, history of SCD, and consent to participate in the study.

#### 2.4.1 Inclusion criteria

- Confirmed diagnosis of SCD (HbSS or HbSC)
- Age  $\geq 5$  years
- Attendance at UCH Haematology Day Care Unit
- Consent to participate in the study

#### 2.4.2 Exclusion criteria

- History of recent blood transfusion within three months
- Presence of other chronic diseases (e.g., HIV, TB, or cancer)
- Refusal to provide informed consent

### 2.5 Materials and Equipment

The study utilized various laboratory tools and reagents including:

- EDTA and citrate blood collection tubes
- Automated hematology analyzers (Sysmex XN-series)
- ELISA kits for IgG, IgM, CRP, and FDP (validated for SARS-CoV-2 detection)
- Coagulation analyzers for PT, APTT, and D-dimer analysis
- Spectrophotometers and microplate readers
- Personal protective equipment (PPE) for biosafety

### 2.6 Clinical Laboratory Investigation

#### 2.6.1 Sample collection and analysis

Venous blood samples were collected under aseptic conditions. Blood in EDTA tubes was used for full blood count and haematological profiling. Citrated blood samples were used for coagulation studies including PT, APTT, INR, and D-dimer. Plasma was separated and stored

at -20°C for ELISA-based serological testing. IgG and IgM antibody levels were quantified to assess SARS-CoV-2 exposure, and CRP and FDP levels were measured as markers of inflammation and fibrinolysis respectively.

### 2.7 Statistical Analysis

Data were analyzed using SPSS version 23.0. Descriptive statistics such as means and standard deviations were used to summarize the data. Inferential statistics including independent samples t-tests, chi-square tests, and Pearson's correlation coefficient were applied to examine differences and relationships between variables.

A p-value of less than 0.05 was considered statistically significant.

### 3. RESULTS

The Table 3 showed a strong significant negative correlations between Age and IgM ( $r = -0.223$ ,  $p = 0.014$ ) of test subjects. The table also showed no significant correlation between age and IgG ( $r = 0.128$ ,  $p = 0.159$ ) of test subjects respectively.

The Table 4 showed that there were no significant differences between the SARS-COV-2 (COVID-19 INFECTION) ANTIBODIES (IgM and IgG) of sickle cell patients in relation to their sexes ( $p > 0.05$ ) as shown in Table 3.

**Table 1. Comparison of mean±sdsars-cov-2 (covid-19 infection) antibodies of study subjects (test/cases and control)**

	SICKLE CELL PATIENTS (n=122)	NORMAL PEOPLE/CONTROL (n=45)	t-test	p-value	Remark
<b>Other important parameters</b>	<b>Mean±SD</b>	<b>Mean±SD</b>			
IgM	0.28 ± 0.20	0.24 ± 0.10	1.330	0.185	Not Significant
IgG	0.17 ± 0.03	0.16 ± 0.03	1.118	0.265	Not Significant

\* $p < 0.05$  (i.e. Significant).

**Table 2. Correlation of age with sars-cov-2 (covid-19 infection) antibodies of test subjects (n=122)**

Variables (r values (p values))	Age (Years)	IgM	IgG
Age (Years)	1		
IgM	-0.223 (0.014*)	1	
IgG	0.128 (0.159)	-0.036 (0.692)	1

\* $p < 0.05$  (i.e. Significant).

**Table 3. Relationship between sex and sars-cov-2 (covid-19 infection) antibodies of test subjects (n=122)**

SARS-COV-2 ANTIBODIES	SEX	t-test	p-value	Remark	
	Male (n=64) Mean (±SD)	Female (n=58) Mean (±SD)			
IgM	0.28 ± 0.20	0.28 ± 0.21	0.152	0.879	Not Significant
IgG	0.17 ± 0.02	0.16 ± 0.03	0.259	0.796	Not Significant

\* $p < 0.05$  (i.e. Significant)

**Table 4. Hematological parameters in SCD patients vs controls**

Parameter	SCD Patients (Mean ± SD)	Controls (Mean ± SD)	p-value	Remark
Hemoglobin (Hb) (g/dL)	7.75	13.13	<0.05	Significant
Packed Cell Volume (PCV) (%)	22.42	39.64	<0.05	Significant
White Blood Cell Count ( $\times 10^9/L$ )	11.37	5.64	<0.05	Significant
Platelet Count ( $\times 10^9/L$ )	351.62	233.04	<0.05	Significant

**Table 5. Coagulation parameters in SCD patients vs controls**

Parameter	SCD Patients (Mean ± SD)	Controls (Mean ± SD)	p-value	Remark
Prothrombin Time (PT) (seconds)	15.33	11.86	<0.05	Significant
Activated Partial Thromboplastin Time (APTT) (seconds)	32.25	29.27	<0.05	Significant
International Normalized Ratio (INR)	Not specified	Not specified	0.274	Not Significant
D-dimer (ng/mL)	3347.08	1438.13	<0.05	Significant

#### 4. DISCUSSION

The findings of this study offer critical insights into the hematological, immunological, and coagulation profiles of Nigerian sickle cell disease (SCD) patients during the COVID-19 pandemic. While SARS-CoV-2 IgG and IgM antibody levels did not differ significantly between SCD patients and healthy controls, significant abnormalities were observed in blood and clotting parameters, underscoring the heightened vulnerability of SCD patients during infectious disease outbreaks.

As shown in Table 1, SCD patients had markedly elevated white blood cell (WBC) counts ( $11.37$  vs.  $5.64 \times 10^9/L$ ) and platelet counts ( $351.62$  vs.  $233.04 \times 10^9/L$ ), both of which are consistent with chronic inflammation and immune activation in this population. Additionally, SCD patients exhibited significantly lower hemoglobin (Hb) concentrations ( $7.75$  vs.  $13.13$  g/dL) and packed cell volume (PCV) values ( $22.42\%$  vs.  $39.64\%$ ) compared to controls. These hematologic derangements reflect the hemolytic nature of SCD and the chronic compensatory erythropoiesis seen in these patients (Olatunya et al., 2023; Hebbel, 1997; Valko et al., 2005).

Coagulation parameters, detailed in Table 2, further illustrated the hypercoagulable state characteristic of SCD. Patients had significantly prolonged prothrombin time (PT:  $15.33$  vs.  $11.86$  seconds) and activated partial thromboplastin time (APTT:  $32.25$  vs.  $29.27$  seconds), along with markedly elevated D-dimer levels ( $3347.08$  vs.  $1438.13$  ng/mL). These findings support previous reports indicating that individuals with SCD are at increased risk for coagulation abnormalities, which can be exacerbated by infections such as COVID-19 (Tang et al., 2020; Al-Ani et al., 2020; Zhou et al., 2020). While international normalized ratio (INR) values showed no significant difference ( $p = 0.274$ ), the overall profile clearly reflects a predisposition to thrombotic complications (Kato et al., 2009).

Although SARS-CoV-2 IgM and IgG levels were slightly higher in SCD patients (IgM:  $0.28$  vs.  $0.24$ ; IgG:  $0.17$  vs.  $0.16$ ), these differences were not statistically significant, indicating a generally preserved humoral immune response despite the underlying disease. This observation is notable, considering the immune compromise commonly associated with SCD due to functional asplenia and chronic inflammation (Booth et al., 2010; Long et al., 2020).

Furthermore, a significant inverse correlation was found between age and IgM antibody levels ( $r = -0.223$ ,  $p = 0.014$ ), suggesting that younger individuals may mount a more robust recent antibody response compared to older patients. This aligns with broader immunological literature indicating age-related declines in primary immune responses (Long et al., 2020; Levin et al., 2021).

Despite the valuable insights provided, this study has limitations. Being cross-sectional in design, it cannot capture the dynamics of antibody waning or temporal patterns of infection. Additionally, as a single-center study conducted at University College Hospital, Ibadan, generalizability to the broader Nigerian SCD population may be limited. Data on prior COVID-19 infection history and vaccination status were also incomplete.

Nevertheless, the consistent abnormalities observed across hematological and coagulation markers in this cohort point to the critical need for regular laboratory monitoring of SCD patients, especially during infectious disease outbreaks. Routine evaluation of parameters such as WBC, platelet count, PT, APTT, and D-dimer may aid in the early identification and management of thrombotic risks (Kato et al., 2009; Olatunya et al., 2023). These findings emphasize the importance of integrating hematologic surveillance into pandemic preparedness and clinical management protocols for SCD patients.

## 5. CONCLUSION

This study established that SCD patients had significantly elevated white blood cell and platelet counts, prolonged PT and APTT, and higher D-dimer levels, along with lower hemoglobin and PCV values compared to healthy controls. These findings confirm the presence of underlying hematologic and coagulation disturbances in SCD patients that could be exacerbated during infections like COVID-19. Although SARS-CoV-2 antibody levels (IgG and IgM) were not significantly different, the data affirm the importance of routine hematological and coagulation monitoring for early detection and management of complications in this high-risk group.

## 6. RECOMMENDATIONS

We firmly believe that routine coagulation monitoring, such as D-dimer, PT, and APTT testing, should be incorporated into standard clinical care protocols for sickle cell disease patients, especially during infectious disease outbreaks, in order to enable early detection and treatment of thrombotic complications. In order to increase the identification of infection symptoms and thrombotic warning signs, healthcare practitioners should prioritize this susceptible population for targeted immunization initiatives and improved preventive care measures. At the same time, they should undertake extensive patient education programs. Furthermore, we advise that specific clinical guidelines be created that integrate these hematological monitoring techniques into the frameworks now in place for the management of sickle cell disease.

Additionally, there is a critical need for longitudinal research to evaluate long-term immune responses and optimize protective interventions for this high-risk group, with the ultimate goal of improving health outcomes during public health emergencies.

## CONSENT AND ETHICAL APPROVAL

Ethical approval for this study was obtained from the UCH Institutional Review Board. All participants or their legal guardians signed informed consent forms. Confidentiality and anonymity of participant information were strictly maintained throughout the research process in accordance with the Declaration of Helsinki.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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