ORIGINAL ARTICLE

Seroprevalence of SARS-CoV-2 antibodies among sickle cell patients in Burkina Faso

Séroprévalence des anticorps anti-SRAS-CoV-2 chez les drépanocytaires du Burkina Faso

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Abstract

Introduction:
Like all countries in the world, sub-Saharan Africa has been affected by the COVID-19 pandemic. The socio-economic impact of the crisis has affected the health system, pushing certain health priorities into the background. In sub-Saharan Africa, the disease remains a major problem, with the highest incidence and lethality. It causes severe clinical manifestations and decreased immunity in patients, making them susceptible to significant morbidity and mortality related to COVID-19. The aim of this study was to determine the seroprevalence of SARS-CoV-2 antibodies and the risk factors in sickle cell patients in Burkina Faso.

Patients and methods:
We conducted a cross-sectional study in three sickle cell disease (SCD) reference centers in Ouagadougou from November to December 2021 and one center in Bobo-Dioulasso from July to October 2022. Patients of any age and gender attending these SCD centers were included. Sociodemographic and clinical data were collected from the patient's clinical record; SARS-CoV-2 IgG/IgM screening were performed using rapid diagnostic test.

Results:
A total of 304 patients (151 from Ouagadougou and 153 from Bobo-Dioulasso) with a median age of 12 years and a sex-ratio (M/F) of 0.82 were included. The median age at diagnosis of SCD was 4 years and the acute complications were the main circumstances of diagnosis (83.5%). The majority (55.6%) were SS homozygotes. The overall crude seroprevalence (IgM or IgG) was 57.9%. After adjustment for the sensitivity and specificity of the kit used, the seroprevalence was 69.1% (95% CI [65.5-72.6]). The positivity to SARS-CoV-2 antibodies was 2.51-fold (*p=0.005*), 3.25-fold (*p=0.004*) and 2.85-fold (*p=0.027*) higher in patients aged 10-19, 20-29 and 30-39 years respectively, compared to those under 10 years. History of recurrent vaso-occlusive crises in the last 12 months was also associated with SARS-CoV-2 seropositivity (OR=2.18; 95% CI [1.18-4.05], *p=0.013*).

Conclusion:
SCD patients, like the general population, were affected by the COVID-19 pandemic. Given their relative immunosuppression and comorbidities, it is necessary to promote protective measures against COVID-19, including vaccination, in these patients.

Keywords: Sickle cell disease, COVID-19, Seroprevalence, SARS-CoV-2 antibodies.

Résumé

Introduction:
A l'instar du reste du monde, l'Afrique Sub-Saharienne a été touchée par la COVID-19. L'impact socio-économique a concerné le système de santé, reléguant au second plan certaines priorités de santé. La drépanocytose constitue un problème de santé publique en Afrique, avec l'incidence et la létalité les plus élevées. Elle provoque des manifestations cliniques graves et une diminution de l'immunité chez les patients, les exposant à un risque important de morbidité et de mortalité. Le but de l'étude était de déterminer la séroprévalence et les facteurs de risque des anticorps anti-SRAS-CoV-2 chez les drépanocytaires du Burkina Faso.

Patients et méthodes :
Nous avons mené une étude transversale dans trois centres à Ouagadougou de novembre à décembre 2021 et un centre à Bobo-Dioulasso de juillet à octobre 2022. Les patients de tout âge, deux sexes fréquentant ces centres de référence ont été inclus. Les données sociodémographiques et cliniques ont été recueillies à partir des dossiers cliniques. Le dépistage des anticorps anti-SRAS-CoV-2 a été réalisé à l'aide de tests de diagnostic rapide.

Résultats :
Un total de 304 patients (151 de Ouagadougou et 153 de Bobo-Dioulasso) avec un âge médian de 12 ans et un sex-ratio (H/F) de 0,82 a été inclus. La majorité (55,6%) était homozygote SS. La séroprévalence brute était de 57,9%. Après ajustement en fonction des performances du kit, la séroprévalence était de 69,1% (IC 95% [65,5-72,6]). Comparés aux patients de moins de 10 ans, la séropositivité aux anticorps était 2,51 (*p=0,005*), 3,25 (*p=0,004*) et 2,85 (*p=0,027*) fois plus élevée chez les patients âgés de 10-19 ans, de 20-29 ans et de 30-39 ans. Des antécédents de crises vaso-occlusives au cours de l'année étaient également associés à la séropositivité (OR=2,18; IC 95% [1,18-4,05], *p=0,013*).

Conclusion :
Les patients drépanocytaires ont été affectés la COVID-19. Compte tenu de leur immunodépression relative et de leurs comorbidités, il est nécessaire de promouvoir des mesures de protection contre la COVID-19, y compris la vaccination, chez ces patients.

Mots-clés : Drépanocytose, COVID-19, Séroprévalence, anticorps anti-SRAS-CoV-2.

INTRODUCTION

In late 2019, severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) emerged and caused the COVID-19 pandemic (1). The number of cases increased and spread rapidly worldwide, reaching 663,640,386 confirmed cases and 6,713,093 deaths as of January 20, 2023 (2). Sub-Saharan Africa (SSA) had 9,466,921 confirmed cases and 175,177 deaths as of the same date. Compared to other continents, Africa has fewer cases (2). But these figures do not reflect the magnitude of the pandemic in SSA. Indeed, SSA experienced a low number of tests performed daily at the time of the pandemic. While developed countries had implemented large-scale screening, in Africa, testing was mainly offered to people with symptoms consistent with COVID-19 and to travellers (3). The pandemic has affected various socio-economic conditions in SSA, including the functioning of health services and their use by patients (4). During the pandemic, government efforts focused on managing the effects of the pandemic, pushing certain health priorities into the background (5).
Sickle cell disease (SCD) is a genetic disease of autosomal recessive inheritance due to the presence in red blood cells (RBC) of the abnormal hemoglobin S. According to the World Health Organization (WHO), SCD is a major public health problem worldwide and specifically in SSA (6). Indeed, SSA accounts for 3/4 of the incident cases and the highest case fatality in children under five (6, 7). The *primum movens* of the pathogenesis of SCD is the polymerization of deoxygenated HbS, which induces RBCs sickling and shortening of their life span (hyperhemolysis) and also vascular obstruction phenomena resulting in vaso-occlusive crises (VOCs) and ischemic lesions. The reduction of anti-infectious immunity due to impaired leukocyte function and functional or organic asplenia exposes SCD patients to recurrent infections (8). Thus, SCD patients with these various factors (functional hyposplenism, vasculopathy, and recurrent VOCs) of immune system impairment are in the «high-risk category» for contracting SARS-CoV-2 (9, 10). Due to the dual hypoxemic burden (SCD and COVID-19), they may develop severe clinical manifestations, including acute respiratory distress syndrome, pneumonia, acute chest syndrome (ACS), all of which are leading causes of mortality in SCD patients (11).
Burkina Faso, an intertropical country located in the Lehmann sickle cell belt. The incidence of SCD in Burkina Faso is 1.8 to 1.9%, according to neonatal screening data from certain towns in the country (12, 13). In some hospital studies, the prevalence of SCD ranged from 8.4 to 12.1% (14, 15), and in a community study, it was about 1.4% (14). Like other countries in the West African sub-region, Burkina Faso experienced its first cases of COVID-19 in the middle of the first quarter of 2020. Given the weakness of the healthcare system, the impact of the pandemic in general, and specifically on patients with chronic hematological diseases such as SCD, was a matter of great concern. So, based on a review of the literature available at the time, the *Groupe d'intervention en hématologie (GIH)* and the *Société Burkinabè de Transfusion Sanguine (SBTS)* made recommendations for physicians to ensure continuity and quality of care for these chronic patients (16). However, these recommendations did not include the implementation of a monitoring system such as a specific database. Therefore, there are no specific data on COVID-19 in sickle cell patients in Burkina Faso. The aim of this study was to investigate the cumulative prevalence of SARS-CoV-2 IgM and IgG antibodies in sickle patients active file of cell patients in Ouagadougou and Bobo-Dioulasso, the two cities with the largest SCD in Burkina Faso. The results of this study could be used for better understanding of the extent of COVID-19 in sickle cell patients in Burkina Faso with a view to suggesting protection and management measures.

PATIENTS AND METHODS

Study design, period and settings

It was a cross-sectional study using data collected from November to December 2021 in Ouagadougou, the capital of Burkina Faso and from July to October 2022 in Bobo-Dioulasso, the economic capital. The study was conducted in three health facilities; the *Hôpital Saint Camille de Ouagadougou* (HOSCO), the *Centre hospitalier universitaire Yalgado Ouedraogo* (CHUYO) and the *Centre hospitalier universitaire pédiadrique Charles de Gaulle* (CHUP-CDG) in Ouagadougou. These three hospitals are the main reference centers for SCD management, with HOSCO the most important center (approximatively 4,000 patients registered on the active file). In Bobo-Dioulasso, the study was conducted in the *Centre hospitalier universitaire Sourô Sanou* (CHUSS). The CHUSS is the biggest health facility involved in a pilot newborn screening of SCD program conducted from 2015 to 2019 (13).
The first cases of COVID-19 in Burkina Faso were reported in early March 2020 in Ouagadougou. Bobo-Dioulasso and other regions of the country were gradually affected. By the end of 2022, a cumulative total number of 22,023 confirmed cases and 395 deaths have been recorded nationwide (17). The response to the pandemic focused on barrier measures at the beginning and later, the COVID-19 vaccination introduced on June 2, 2021, for people over 18 years old. It will then be extended to those aged 12 to 18 at the end of 2021 (18). The vaccines available were the two mRNA vaccines from Moderna and Pfizer-BioNTech (single dose vac-

cine regimen), two viral vector-based vaccines from AstraZeneca (two doses vaccine regimen) and Janssen (single dose) and two inactivated viral vaccines from Sinovac and Sinopharm (single dose). Several vaccination campaigns have been launched, but by the end of 2022, 4.3 million of the 21 million population had received at least one dose and 3.3 million were fully vaccinated (19). Apart from any measures on the personal initiative of the attending physicians, no special provision is made for sickle cell patients.

Patients recruitment and data collection

As each patient had an appointment date for their follow-up consultation, they were recruited consecutively at the end of each consultation.

We included sickle cell patients of both genders and all ages followed at the above-mentioned centers on a non-probability basis. As each patient had an appointment date for their follow-up, they were recruited consecutively at the end of each consultation. Data concerning sociodemographic (age, sex, residence), clinical and biological characteristics (age and circumstances of diagnosis, frequency and type of acute complications, chronic complications, SCD phenotype and complete blood count parameters) were collected from clinical records or during face-to-face interviews.

For each patient included, a 5 mL venous blood sample was collected on EDTA (ethylene-diamine-treta-acetic acid) tube and transported to the hematology laboratory in a container with ice-packs. The samples were centrifuged within 6 hours after collection at 2500 rpm for 5 minutes and the plasma was aliquoted into two vials (for antibody screening and quality control, where applicable) and stored at -40°C until serological testing for SARS-CoV-2 antibodies screening.

Rapid diagnostic test kit

The kit used was the COVID-19 IgM/IgG Rapid test Cassette® kit, lot N° 2008293, Ref: GCCOV-402a (Zhejiang Orient Gene Biotech CO., Ltd; Zhejiang, China). This is a lateral flow immunochromatographic test using anti-human IgM antibodies (IgM test line), anti-human IgG antibodies (IgG test line) and anti-rabbit IgG antibodies (C control line) fixed on nitrocellulose. Each cassette has one well for the sample to be tested and another one for the reagent buffer. The biological sample well contains recombinant SARS-CoV-2 antigens consisting of the receptor binding domain (RBD) of spike protein, coated with a colorimetric conjugate that changes color with the buffer. The SARS-CoV-2 IgG and/or IgM antibodies form an antibody-antigen that migrates by capillary action into the nitrocellulose. When it encounters the corresponding coated antibody (IgG or IgM test line), the complex binds to the antibody and the conjugate turns red, indicating a positive test. The intrinsic performance of the tests claimed by the manufacturer, based on tests performed on whole blood from symptomatic patients with positive RT-PCR and convalescent patients, was 87.9% (for IgM) / 97.2% (for IgG) of sensitivity and 100% of specificity for IgG and IgM (20). In Burkina Faso, a performance evaluation of the same kit in comparison (gold-standard) with Wantai Bio-Pharm IgM/IgG ELISA® kit (Beijing Wantai biological and pharmacy Enterprise co, Ltd, Beijing, China), conducted using plasma collected independently of the history of SARS-CoV-2 infection in individuals prior to the introduction of COVID-19 vaccination, has shown 51.6/97.4% sensitivity/specificity and 95.3/66.8% positive/negative predictive values (21).

Sample testing

Anti-SRAS-CoV-2 antibodies were tested on thawed patient plasma in a 37°C water bath for 20-30 minutes. Samples were tested immediately after thawing according to the reagent manufacturer's recommendations. Samples were tested immediately after thawing according to the reagent manufacturer's recommendations. Testing was performed in batches of 10 samples to avoid prolonged exposure to room temperature.

In practice, the device pack of the pocket kit was opened and labelled with the patient identification code. A volume of 10 µL of plasma was pipetted into the biological sample well and two drops (approximately 60 µL) of dilution buffer (10mM PBS buffer) into the appropriate well. Migration occurred by capillary action and the results were read after 10 minutes, stopwatch in hand. The test is valid only if the control line (C) appears red; if it does not, the test is repeated with another cassette. The presence of anti-SARS-CoV-2 IgM or anti-SARS-CoV-2 IgG is indicated by a red test line in zones M or G respectively. If both lines turn red in addition to the control line, anti-SARS-CoV-2 IgM and anti-SARS-CoV-2 IgG are present. If only the control line (C) is red, the sample is negative.

Statistical analysis

The data collected were entered on Epi-Info 7.2.5.0 (CDC, Atlanta, GA, USA) and exported into STATA/SE version 15.1 (College Station, TX: StataCorp LLC) for analysis. Frequencies and proportions were used to describe categorical variables and means with the standard deviation or median with the 1st (Q1) and 3rd (Q3) quartiles for quantitative variables.

Due to the uncertainties related to the results of serological tests for COVID-19, it is recommended to adjust the seroprevalences using the intrinsic performances resulting from the evaluations of the tests in a context similar to that of the study (22, 23). Therefore, the crude seroprevalences are adjusted according to the kit performances found in Burkina Faso (21), using the following formula: (23). Chi-square or Fischer exact and ANOVA tests as appropriated and Odd-ratio were used in univari-

ate and multivariate logistic regression for statistical comparisons at the significant threshold $p < 0.05$.

Ethical considerations

In the absence of an institutional ethics committee in the hospitals concerned, authorizations were obtained from the administrative department and the quality of care and patient safety department. Signed informed consent was obtained from study participants or their parents or guardians for children under 18 years. Data were analyzed anonymously and kept confidential.

RESULTS

A total of 304 patients were included with a median age of 12 years (IQR: 5; 22.5), 54.9% of whom were females (i.e. sex-ratio M/F of 0.82) and 91.1% were from urban areas. The median age at diagnosis of SCD was 4 years (IQR: 1.2; 9). The main circumstance of diagnostic was VOCs (83.5%). The majority of patients (55.6%) were homozygous HbSS (Table 1). Hyperleukocytosis and thrombocytosis were noted in 64.3% and 53.9% of patients respectively. Overall seropositivity (IgM or IgG antibodies to SARS-CoV-2) were found in 176 patients (i.e., 57.9% of crude prevalence). IgG antibodies alone (recovery phase or vaccinated subject) were found in 156 patients, IgM and IgG combined (early recovery phase) in 17 patients and IgM alone (recent infection) in 3 cases. After adjustment to the sensitivity and specificity of test used calculated, the overall adjusted seropositivity was 69.1%; 95% CI [65.5-72.6]. Compared to children under 10 years, young children and adolescents aged 10-19 years (OR = 2.51; 95% CI [1.32-4.80]; *p = 0.005*), young adults aged 20-29 years (OR = 3.25; 95% CI [1.47-7.18]; *p = 0.004*) and 30-39 years (OR = 2.85; 95% CI [1.13-7.24]); *p = 0.027*) presented significant high seroprevalences of SARS-CoV-2, 75.4% (95% CI [66.0-81.7]), 78.3% (95% CI [68.7-86.0]) and 74.6% (95% CI [63.1-84.1]) respectively (Table 2). Patients who reported VOCs in the past 12 months had an odd of 2.18 (95% CI [1.18-4.05]; *p = 0.013*) of having anti-SARS-CoV-2 antibodies compared to those who had no acute complications. As shown in Table 2, there no association between the positivity to anti-SARS-CoV-2 antibodies and patients' gender, hemoglobin phenotype and the presence of SCD chronic complications.

Table 1: Baseline characteristics of sickle cell patients, Burkina Faso (N = 304)

Characteristics	Total (n, % Col)	Ouagadougou (n, % Row)	Bobo-Dioulasso (n, % Row)	p-value
Sex				0.496
Male	137 (45.1)	71 (51.8)	66 (48.2)	
Female	167 (54.9)	80 (47.9)	87 (52.1)	
Age in years, median [Q1 - Q3)	12 [5 - 22.5)	17 [10 - 30)	7 [4 - 19)	< 0.001
Age groups in years				< 0.001
< 10	127 (41.8)	36 (28.3)	91 (71.7)	
[10-19)	78 (25.7)	54 (69.2)	24 (30.8)	
[20-29)	44 (14.5)	23 (52.3)	23 (52.3)	
[30-39)	33 (10.9)	23 (69.7)	10 (30.3)	
≥ 40	22 (7.2)	15 (68.2)	7 (31.8)	
Age at diagnosis of SCD, median [Q1 - Q3)	4 [1.2 - 9)	5 [3 - 12)	3 [1 - 6)	< 0.001
Diagnosis circumstances				< 0.001
Incidental	13 (4.3)	4 (30.8)	9 (69.2)	
Sickle cell crisis	254 (83.5)	147 (57.9)	107 (42.1)	
Newborn screening	23 (7.6)	0 (0.0)	23 (100)	
Parents at risk	14 (4.6)	0 (0.0)	14 (100)	
Crisis episodes per year, median [Q1 - Q3)	2 [1 - 3)	2 [1 - 4)	1 [0 - 3)	0.001
Hemoglobin phenotype				0.004
$S\beta^+$-thalassemia	3 (1.0)	3 (100)	0 (0.0)	
$S\beta^0$-thalassemia	6 (2.0)	1 (16.7)	5 (83.3)	
SC	126 (41.4)	52 (41.3)	74 (58.7)	
SS	169 (55.6)	95 (56.2)	74 (43.8)	
Positivity to SARS-CoV-2 antibodies				0.406
Yes	176 (57.9)	91 (51.7)	85 (48.3)	
No	128 (42.1)	60 (46.9)	68 (53.1)	

Col: Column; Q1 :1st quartile; Q3 : 3th quartile ; SCD: Sickle cell disease

Table 2: Crude and adjusted prevalences and risk factors of SARS-C-oV-2 antibodies in sickle cell patients, Ouagadougou, Burkina Faso (N = 304)

Risk factors	Total n (%)	Crude prevalence n (%)	Adjusted prevalence [95% CI)	Odd ratio [95% CI)	p-value
Overall	304 (100)	176 (57.9)	69.1 [65.5-72.6)	-	-
Study area					
Ouagadougou	151 (49.7)	91 (60.3)	70.6 [65.5-75.5)	Reference	-
Bobo Dioulasso	153 (50.3)	85 (55.5)	67.7 [62.6-72.7)	1.75 [0.93-3.29)	0.084
Sex					
Male	137 (45.1)	75 (54.7)	67.2 [61.8-72.4)	Reference	-
Female	167 (54.9)	101 (60.5)	70.8 [65.9-75.4)	1.16 [0.70-1.91)	0.571
Age groups (in years)					
< 10	127 (41.8)	56 (44.1)	60.6 [55.1-66.2)	Reference	-
10 – 19	78 (25.6)	53 (67.9)	75.4 [66.0-81.7)	2.51 [1.32-4.80)	0.005
20 – 29	44 (14.5)	32 (72.7)	78.3 [68.7-86.0)	3.25 [1.47-7.18)	0.004
30 – 39	33 (10.8)	22 (66.7)	74.6 [63.1-84.1)	2.85 [1.13-7.24)	0.027
≥ 40	22 (7.2)	13 (59.1)	69.9 [55.7-82.4)	2.16 [0.79-5.93)	0.133
Hemoglobin phenotype					
SS	169 (55.6)	99 (58.6)	69.6 [64.7-74.2)	Reference	-
SC	126 (41.4)	70 (55.5)	67.7 [62.0-73.2)	0.85 [0.51-1.44)	0.557
Sβ-thalassemia [a]	9 (3.0)	7 (77.8)	81.5 [58.0-93.6)	1.76 [0.33-9.30)	0.505
Acute crisis in last 12 months					
None	127 (41.8)	63 (49.6)	64.0 [58.4-69.6)	Reference	-
Acute anemia	14 (4.6)	8 (57.1)	68.6 [51.1-84.3)	1.35 [0.41-4.40)	0.617
Infections	12 (3.9)	5 (41.7)	59.1 [42.6-81.8)	0.93 [0.26-3.35)	0.918
VOCs [b]	147 (48.3)	97 (66.0)	74.2 [69.0-78.9)	2.18 [1.18-4.05)	0.013
Other [c]	4 (1.3)	3 (75.0)	79.8 [45.2-94.9)	3.75 [0.34-41.55)	0.282
Chronic complications					
No	275 (90.5)	158 (57.4)	68.8 [65.1-72.6)	Reference	-
Yes	29 (9.5)	18 (62.1)	71.8 [59.5-82.4)	0.84 [0.34-2.03)	0.693

[a] : Sβ°-thalassemia + Sβ+-thalassemia ; [b] : Vaso-occlusive crises ; [c] : Acute chest syndrome + Priapism + stroke

DISCUSSION

The objective of our study was to investigate the cumulative prevalence of SARS-CoV-2 IgM and IgG antibodies in sickle cell patients in Ouagadougou and Bobo-Dioulasso.

The adjusted overall seroprevalence (IgG or IgM antibodies SARS-CoV-2) was 69.1% (95% CI [65.5-72.6]). Only three patients had IgM antibodies and were assumed to have acute SARS-CoV-2 infection at the time of sample collection in our study. However, no RT-PCR tests were performed to confirm this hypothesis. This level of cumulative immunity indicates that since its onset in Burkina Faso in March 2020, the COVID-19 infection spreads very rapidly in the general population, but also in sickle cell patients. This progression has been facilitated by the non-acceptance and non-compliance with the barrier measures decreed by the government (24, 25). Initially, the reality of the disease was denied, discredited, and presented as a disease affecting only the rich. This has affected the public's acceptability of barrier measures and other public health interventions (e.g. vaccination), and consequently their effectiveness (26). At the end of November 2020 (eight months after the start of the epidemic in Burkina Faso), a study conducted among people living with HIV, showed a seroprevalence of 18% (27). Three months later, in February-March 2021, SARS-CoV-2 seroprevalence was estimated to be 35.7%, meaning a nearly 100% increase (28). In the same vein, a nationwide study conducted in October 2021, during the Omicron wave, among 6,592 individuals aged 5 years and older from the 13 administrative regions of Burkina Faso, noted a seroprevalence of 89.8% (95% CI [86.6-92.2]) (unpublished data). Given that there were no specific protective measures for sickle cell patients apart from the generic advice given to all, it is easy to accept that, irrespective of socio-demographic characteristics, the dynamics of the progression of infection were the same in this population of sickle cell patients. Such overall sero-

prevalences, consisting mainly of IgG antibodies, contrasts with the official data which reported a cumulative number of 16,672 confirmed cases (based on PCR and antigenic tests) and 296 deaths (case-fatality ratio of 1.8%) at national level, at the time of collection of our study samples in Ouagadougou (December 2021) (29). In October 2022, the cumulative number of confirmed cases reported by the national surveillance system was 21,883, including 395 deaths (i.e. a difference of 5,211 confirmed cases and only 99 deaths in 10 months) (30). However, virus sequencing data showed that it was the Omicron variant, described as more contagious, that was circulating at the time (31).

In addition to the hypothesis that the virus has spread widely, with a large number of symptomatic and non-symptomatic cases (not supported by solid data from large-scale RT-PCR tests), these high seroprevalences could be due to biases related to the frequent cross-reactions observed with COVID-19 RDTs and to post-vaccination antibodies not discriminated against by the test used (based on a recombinant antigen of the RBD of Spike Protein). However, even if we do not have data on the vaccination status of our study population, it is unlikely that vaccination had a significant impact given the poor success it had in our country. Indeed, vaccination was introduced in early June 2021 only for people over 18 years old initially and extended to people over 12 years old from December 2021 (18). Only 4.5% of the population had received at least one dose in December 2021 (18) and 19.7% a year later in December 2022 (19). Less than 20,000 doses (0.4% of the total number of doses administered) had been received by children in December 2022 (19). The complete vaccination coverage rate was 2.9% in December 2021 and 15% in December 2022 (32), despite multiple immunization intensification campaigns (18). These rates were far from the goal of 70% vaccination coverage to be achieved by all countries by mid-2022 (33).

The adjusted prevalence was 70.6% (95% CI [65.5-75.5]) in Ouagadougou and 67.7% (95% CI [62.6-72.7]) in Bobo-Dioulasso with a non-significant odd ratio difference (*p=0.084*). These results are difficult to interpret because the samples were not collected in the two cities at the same time as described in the study methodology. Nevertheless, we surprisingly noted that the prevalence of SARS-CoV-2 in Bobo-Dioulasso was lower than in Ouagadougou 10 to 12 months earlier. Ouagadougou was the epicenter of the pandemic in Burkina Faso. The first cases were detected there in March 2020; Bobo was affected later. In a seroprevalence study we conducted among blood donors aged 18 to 60 years in April 2022, we noted a significantly higher seroprevalence in Ouagadougou (92.2%; 95% CI [91.1-93.0]) compared to Bobo-Dioulasso (88.8%; 95% CI [87.0-90.3]) (unpublished data). However, the most plausible explanation could be related to patients' age. Indeed, the median age of patients from Bobo-Dioulasso was 10 years lower than the median age of patients from Ouagadougou (Table 1). Many findings suggest an increase in seroprevalence with age due to an increased risk of exposure to the virus with age (frequent human contact in schools and workplaces) (34–36) . Moreover, the predominance of the local innate immune response instead of the humoral response in children has been suggested to explain the low presence of circulating antibodies in children and adolescents (37).

There are scarce relevant data about the susceptibility of sickle cell patients to SARS-CoV-2 infection. Most of the available data are from narrative reviews, case series and not from robust randomized studies. Furthermore, while it is expected that the sickle cell subjects, because of their relative immunosuppression, would be more susceptible to any infection, including COVID-19, there is no scientific data to support such an assumption. However, other immunosuppressed situations such as HIV infection, appear to have nearly a ¼ increased susceptibility to SARS-CoV-2 infection (38). In our study, we found that patients having had recurrent VOCs, in the 12 last months, had 2.18 odds of having SARS-CoV-2 antibodies compared with those without acute complications. The triggers for these VOCs are not known, so it is difficult to speculate on this association. However, according to some results of observational studies that suggest a significant association between SCD and high morbidity in COVID-19 (39–41), it is plausible to think that symptomatic SARS-CoV-2 infection (as any other infection) could potentially be a trigger for sickle cell crises. According to Alkindi *et al*., the frequency of VOCs is 0.5 times higher in sickle cell patients with COVID-19 (39). Painful and acute chest syndrome due to SCD had a relative risk of hospitalization of 1.6 to 2.15 and relative risk of 1.76 to 3.67 for severe COVID-19 infection in children. Painful and renal failure were identified in adults as factors associated to hospitalizations and/or severity of COVID-19 infection (40). In another study, Minniti *et al*. made similar findings. However, they could not conclude that mortality was significantly higher in SCD, despite a case fatality of 10% versus 3% in the general population (41). As in some previous studies (41, 42), our study did not find association between hemoglobin phenotype and morbidity or mortality in COVID-19. However, as a precautionary measure, preventive measures against COVID-19, including vaccination, should be taken in sickle cell patients.

In our study, we found an association between patients' age and the seroprevalence of SARS-CoV-2 antibodies (Table 2). In general population, age is pointed of as a most common susceptibility factors to SARS-CoV-2, with greater susceptibility in older children, adolescents,

and adults than in children under 10 years and persons over 55 years of age (35, 36). This can be explained by the mode of transmission of the virus. People in these age groups are most exposed through close human contact at school or in the workplace.

This is the first study that evaluates the extend of COVID-19 in sickle cell patients in our country. It provides data that will contribute to the understanding of the COVID-19 pandemic dynamic in Burkina Faso. However, our study has some limitations. Indeed, this was an intra-hospital study centered on Ouagadougou and Bobo Dioulasso. Even though these two cities combine the main sickle cell treatment centers, they are far from representing the whole country, especially in terms of the epidemiology of COVID-19. Our results cannot therefore be generalized. The samples from the two towns were taken at different times (at least 10 months apart), which represents a very long delay in the dynamics of the COVID-19 pandemic marked by numerous waves of viral variants of different infectivity and severity. In addition, the population of sickle cell patients of Ouagadougou was significantly different from that of Bobo in terms of age and hemoglobin profile among others. So, the prevalence in the two cities cannot be compared. Finally, we screened SARS-CoV-2 antibodies using a IgM/IgG RDT with the possibility of false negative or positive results due to cross-reactions or poor technical operations (handling and interpretation errors (43). In addition, the test used does not make it possible to discriminate between natural antibodies and post-vaccination antibodies.

CONCLUSION

Our study suggest that a significant proportion of sickle cell patients have been in contact with the SARS-CoV-2. History of VOCs and age were the factors associated with this seropositivity to SARS-CoV-2 antibodies. Taking into account the data in the literature that showing that SCD organic complications have a negative impact on COVID-19 prognosis, it is important to actively consider COVID-19 prevention measures, including vaccination, in sickle cell patients.

Conflict of interest

The authors declare no conflicts of interest.

Author contributions

SS, KE, KN designed the study. SS, KD, NM and TC collected the data, that were analyzed by SS, SAG, HYE, OHG, DEA, NK. SS wrote the manuscript draft. All authors commented and revised the draft of manuscript. The final draft was approved by all the authors before submission for publication.

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