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A comparative analysis of blood-borne infections among sickle cell anemia patients and first-time donors in Gabon

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ABSTRACT

Managing sickle cell disease often requires transfusions, exposing multi-transfused sickle cell patients to a heightened risk of transfusion-transmitted infections. This study aimed to assess the seroprevalence of the human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), and hepatitis C virus (HCV) in multi-transfused sickle cell patients and first-time donors in Libreville. The serological testing for HBsAg, anti-HIV, and anti-HCV antibodies was conducted using commercial enzyme immunoassays and confirmed by the COBAS modular analyzer (Roche Diagnostics). The seroprevalence of HIV, HCV antibodies, and HBsAg was 4%, 10%, and 10%, respectively, in multi-transfused sickle cell patients and 5%, 0%, and 8% in first-time donors. Interestingly, HIV and HBsAg seroprevalence were similar in both groups, indicating that transfusion was not associated with these infections. However, HCV antibody seroprevalence was significantly higher in multi-transfused sickle cell patients than in first-time donors (10% vs. 0%, $p<0.001$). Furthermore, the presence of anti-HCV antibodies in multi-transfused sickle cell patients was significantly associated with the number of donations received (7.20±2.37 vs. 3.96±2.06, $p=0.042$). These findings suggest that while blood transfusion is not a significant risk factor for HIV and HBsAg transmission, it may increase the risk of HCV transmission, particularly in multi-transfused sickle cell patients.

Keywords: HBV, HCV, HIV, Sickle cell, blood donor, Gabon.

INTRODUCTION

Sickle cell anemia (SCA) is a significant health concern globally, particularly in sub-Saharan Africa where it is more prevalent (Tebbi, 2022). The disease is caused by a mutation in the beta-globin gene, which produces abnormal hemoglobin molecules, such as HbS. The homozygous state for HbS (βS/βS) is responsible for the most severe form of SCA, but there are also other combinations of SCA genotypes, including Hb S/β0 thal, Hb S/β+thal, and Hb S/C. These different genotypes result in a spectrum of clinical presentations and severity

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of the disease. The management of SCA patients is challenging and requires a multidisciplinary approach, including regular blood transfusions, hydroxyurea therapy and bone marrow transplantation in selected cases (Tebbi, 2022). Early diagnosis and appropriate management are crucial to improving life quality and reducing the morbidity and mortality associated with this debilitating disease.

Globally, an estimated 4.4 million people have sickle cell disease (GBD, 2015; 2016) with approximately 300,000 infants born with the disorder each year (Chakravorty and Williams, 2015). Sickle Cell Disease (SCD) is particularly prevalent in sub-Saharan Africa (Diallo and Tchernia, 2002; Rees et al., 2010) but is also found in parts of India, the Middle East, the Arabian Peninsula, and among people of African descent living in North and South America and other parts of the world (Tebbi, 2022). In Gabon, a study of 4,068 newborns in urban areas of Libreville revealed a 1.33% βS/βS and 0.14% βS/βc SCD prevalence (Ngasia et al., 2011). In contrast, a high frequency of 21.7% of the sickle cell trait (SCT) was found in the Bantu population (Delicat-Loembet et al., 2014). The most common manifestations of SCD include haemolytic anaemia, intermittent vaso-occlusive crises, and a range of other complications such as acute chest syndrome, splenic sequestration, growth retardation, leg ulcers, and infections (Tantawy et al., 2020 ; Tebbi, 2022). Treatment for SCD typically focuses on preventing and controlling symptoms and complications, with transfusions often required in countries where more innovative treatments, such as hydroxyurea, autologous transplantation, and gene therapy, are not yet available, such as Gabon.

In sub-Saharan Africa, 12.5% of transfused patients are at risk of post-transfusion hepatitis, despite safety measures such as rigorous donor selection and biological qualification of donations through adequate virological testing (Nambei et al., 2016; Ankouane et al., 2016). In Gabon, the residual risk of transmissible transfusion infections (TTIs) among donation recipients was estimated to be 64.7, 207.94, and 534.51 per million donations for HIV, HCV, and HBV, respectively (Rerambiah et al., 2014). This high TTI residual risk places multi-transfused SCA patients at an increased risk of infection with blood-borne pathogens. This study aimed to determine the seroprevalence of HIV, HBV, and HCV in non-transfused subjects (first-time donors) and multi-transfused individuals (steady-state SCA patients) in Libreville, Gabon. This would not only improve the safety of blood transfusions for sickle cell patients in Gabon but also benefit other transfusion-dependent patients worldwide.

MATERIALS AND METHODS

Ethical considerations

This prospective study underwent validation by the management of the CNTS and its ethics committee. Prior to participating, all donors and SCA patients were fully informed about the various tests that would be conducted on their donations and provided their informed consent by signing a consent form. The confidentiality of test results was strictly maintained, and they were disclosed individually to the concerned individuals, their parents, or guardians only after counseling sessions. In the case of minors, their inclusion in the study was contingent upon obtaining permission from their parents or legal guardians. Donors and SCA patients identified as reactive or positive were promptly referred to the appropriate management services for the detected pathologies.

Study site and design

This prospective study was carried out in the Gabonese capital of Libreville in April 2017, encompassing both first-time blood donors from the National Blood Transfusion Centre and sickle cell multi-transfused patients monitored at the Lalala private clinic situated in the 5th district of Libreville.

Recruitment of multi-transfused steady-state SCA patients and first-time blood donors

SCA patients who had undergone a minimum of two transfusions were enlisted from the esteemed Lalala private clinic. Throughout the study duration, this clinic offered comprehensive clinical monitoring to a total of 75 patients with sickle cell disease. However, only fifty (50) individuals in the stationary phase of the disease, who willingly consented to participate in the study, were ultimately recruited.

Donors were recruited during the first two weeks of April 2017. A total of 960 donors were received during this period. However, 48 donors were eliminated during the pre-donation interview. Consequently, only 912 donors remained eligible for the study. Out of these, only 200 donors who matched in terms of age and sex with sickle cell anemia patients were included as controls in this study. The donors were selected based on their medical history and eligibility criteria, which included being voluntary non-remunerated donors (VNRD) or family/replacement donors (FRD), aged between 15 and 65 years, and weighing at least 50 kg. A panel of questions was used to exclude individuals who had received a transfusion, had jaundice or signs of hepatitis, or any other infections, pregnant women, and those who engaged in risky sexual behavior in the six months prior to presenting for blood donation.

Blood collection, ABO, rhesus and hemoglobin determination

During blood collection from both blood donors and sickle cell patients, aseptic techniques were employed to obtain 5 mL of venous blood in EDTA tubes. To determine the ABO and Rhesus phenotypes, monoclonal monospecific antisera including anti-A, anti-B, anti-AB, and anti-D were used. This was performed using either an automated system (QWALYS®3, DIAGAST, France) or a card gel (ID Card, BIO-RAD) based on the manufacturer's instructions. Positive and negative control red cells were utilized, and the Beth-Vincent and Simonin-Michon's tests were carried out as controls. To determine the hemoglobin A and S types, cellulose acetate gel electrophoresis was initially performed, which was then confirmed using capillary electrophoresis with the semi-automatic SEBIA system (SEBIA, Paris, France) as recommended by the manufacturer.

HBV, HCV and HIV serology in blood donors and steady-state sickle-cell patients

Blood samples collected from both blood donors and sickle cell patients were tested for the presence of hepatitis B surface antigen (HBsAg), P24 antigen, anti-HIV-1&2 antibodies, and anti-HCV antibodies and antigens. The tests were performed using commercially available MONOLISA HBsAg Ultra Genscreen, ULTRA HIV Ag-Ab and Monolisa HCV Ag-Ab ULTRA kits from Bio-Rad, Marnes-la-Coquette, France. Any reactive samples were subjected to confirmation tests using the Elecsys HBsAg II, Elecsys HIV combi PT and Elecsys Anti-HCV II kits from Roche Diagnostics, Germany. A sample was considered positive for a particular infection if both the initial and confirmation tests yielded positive results.

Statistical analysis

The data collected was recorded in an Excel spreadsheet and analyzed using the Statistical Package for Social Sciences (SPSS version 20) and EPI-info version 6. The analysis involved Pearson's Chi-square test and Fisher's exact test to compare categorical variables. Differences were considered significant when the p-value was less than 0.05.

RESULTS

Sociodemographic characteristics of multi-transfused sickle cell anemia patients and first-time blood donors

In this study, a total of 50 multi-transfused sickle cell patients and 200 first-time blood donors were enrolled. The majority of blood donors (80%) and sickle cell patients (56%) were male, as shown in Table 1. The mean age of sickle cell patients was 15±9

years, while the mean age of first-time blood donors was 28±7 years. The age range of sickle cell patients was 1 to 36 years, and the age range of first-time blood donors was 15 to 65 years. Among sickle cell patients, 50% belonged to the age group 1-14 years, while the remaining 50% were in the age group 15-36 years. Among first-time blood donors, the age group 15-36 years was the most represented, accounting for 78% of the sample.

Blood group analysis revealed that the majority of sickle cell patients had blood group O (60%), and all of them were Rhesus positive. All sickle cell patients had the HbS/S genotype, while HbA/S and HbA/A genotypes were found in 2.5% and 97.5% of first-time blood donors, respectively. The HbA and HbS alleles were in Hardy-Weinberg equilibrium (P=0.856), as presented in Table 1.

Seroprevalence of HBsAg, HCV and HIV in multi-transfused sickle cell patients and first-line blood donors

This study investigated the seroprevalence of HBsAg, HCV and HIV in steady-state SCA patients and first-time blood donors. A total of 50 SCA patients and 200 first-time blood donors were included. SCA patients had a seroprevalence of 10% for HBsAg, 4% for HIV and 10% for HCV, while first-time blood donors had a seroprevalence of 8% for HBsAg, 0% for anti-HCV antibodies, and 5% for anti-HIV antibodies (Table 2 and 3). Anti-HCV antibodies were only found in SCA patients aged 18 or older who had received 4-12 transfusions (Table 3). There was no significant difference in HBsAg and anti-HIV antibodies seroprevalence between multi-transfused SCA patients and first-time blood donors. However, the seroprevalence of anti-HCV antibodies was significantly higher in SCA patients compared to first-time blood donors (10% vs 0%, P=0.001). Among SCA patients, anti-HCV antibodies were associated with the mean number of transfusions received (7.20±3.271 in anti-HCV positive SCA versus 3.96±2.056 in anti-HCV negative SCA patients, p=0.042) (Table 3). Gender and the mean number of blood transfusions received were not associated with the seroprevalence of HBsAg and anti-HIV antibodies in SCA patients.

Table 1: Socioclinical characteristics of multi-transfused sickle cell patients and first-time donors in Libreville.

	Steady-state sickle cell individuals (N=50)		**First-time blood donors (N=200)**	
Characteristics	Number	Percentage	Number	Percentage
Sex				
Male	22	44.0	160	80.0
Female	28	56.0	40	20.0
Age groups (years)				
1-14	25	50.0	-	-
15-36	25	50.0	156	78.0
37-45	-	-	10	5.0
>45	-	-	34	17.0
Blood groups				
O	30	60.0	116	58.0
A	10	20.0	42	21.0
B	9	18.0	36	18.0
AB	1	2.0	6	3.0
Rhesus				

Positive	50	100	194	97.0
Negative	0	0.0	6	3.0
Hemoglobin				
AA	-	-	195	97.5
AS	-	-	5	2.5
SS	50	100.0	0	0.0
HWE	ND		P=0.856	

Table 2: Serological markers in 50 multi-transfused sickle cell patients in Libreville.

Patient's ID	Sex	Age (years)	Number of blood transfusion received	HBsAg	HCV	HIV
LA1	F	1	2	-	-	-
LA2	F	3	3	-	-	-
LA3	M	7	2	-	-	-
LA4	F	8	2	-	-	-
LA5	M	9	3	-	-	-
LA6	M	4	2	-	-	-
LA7	F	5	2	-	-	-
LA8	M	6	2	-	-	-
LA9	F	10	4	-	-	-
LA10	M	11	3	-	-	-
LA11	F	13	2	-	-	-
LA12	M	2	3	-	-	-
LA13	F	4	2	-	-	-
LA14	M	11	2	-	-	-
LA15	M	14	4	-	-	-
LA16	F	15	3	+	-	-
LA17	M	18	4	-	+	-
LA18	F	16	4	-	-	-
LA19	M	17	3	+	-	-
LA20	F	19	3	-	-	-
LA21	F	23	9	-	-	-
LA22	M	21	2	-	-	+
LA23	F	17	5	-	-	-
LA24	M	16	3	-	-	-
LA25	F	30	4	-	-	-
LA26	M	29	5	+	-	-
LA27	F	31	7	-	-	-
LA28	F	20	6	-	+	-
LA29	F	25	8	-	-	+
LA30	F	36	12	-	+	-
LA31	M	5	2	-	-	-
LA32	M	10	3	-	-	-
LA33	M	14	5	-	-	-
LA34	F	4	2	-	-	-
LA35	F	8	4	-	-	-
LA36	M	7	6	-	-	-

LA37	F	12	3	-	-	-
LA38	F	11	5	-	-	-
LA39	M	13	3	-	-	-
LA40	F	9	5	-	-	-
LA41	M	15	10	-	-	-
LA42	F	16	8	-	-	-
LA43	M	18	4	+	-	-
LA44	M	17	6	-	-	-
LA45	F	20	3	+	-	-
LA46	M	25	5	-	+	-
LA47	M	31	7	-	-	-
LA48	F	19	5	-	-	-
LA49	F	26	3	-	-	-
LA50	M	35	9	-	+	-

Table 3: Comparison of serological markers between multi-transfused sickle cell patients and first-time donors in Libreville in 2017.

		HBsAg positive		**Anti-HCV positive**		**Anti-HIV positive**	
Characteristics	N	N (%)	P-value	N (%)	P-value	N (%)	P-value
Patients' categories							
SCD patients	50	5 (10.0)	0.677	5 (10.0)	<0.001	2 (4.0)	0.778
First-time blood donors	200	16 (8.0)		0 (0.0)		10 (5.0)	
SCD patients Sex							
Male	22	3 (13.6)	0.499	3 (13.6)	0.499	1 (4.5)	0.867
Female	28	2 (7.1)		2 (7.1)		1 (3.6)	
SCD patients' Blood transfusion received	50	HBsAg+	HBsAg-	Anti-HCV+	Anti-HCV-	Anti-HIV+	Anti-HIV-
Mean±SD		3.60±0.894	4.36±2.479	7.20±3.271	3.96±2.056	5.00±4.243	4.25±2.338
P-value		0.109		**0.042**		0.317	

DISCUSSION

This study analyzed the seroprevalence of transmissible transfusion infections in sickle cell disease (SCD) patients who have been multiple transfused and first-time blood donors in Libreville. The gender ratio between SCA patients was similar to the SCA population in Gabonese rural areas (Mombo et al., 2019), and a vast majority of the first-time donors were males due to several reasons such as anemia, pregnancy, breastfeeding, menstruation and low body weight observed in women (Danic and Bigey, 2009). The average age of SCA patients was 15 ± 9 years, and first-time donors were 28 ± 7 years, which is also seen in other SCA patient populations in Koula-Moutou, Gabon (Mombo et al., 2019). This is a result of their lower life

expectancy compared to individuals without SCA, even with advancements in their treatment (Lee et al., 2019). Most blood groups in the multi-transfused SCA patients and first-time blood donors were O and rhesus positive (60% and 100%, respectively). This corresponds with previous research that determined these blood groups being the most common in the Gabonese population (Ngassaki-Yoka et al., 2018). All multiple-transfused steady-state SCA patients had the HbS/S sickle cell genotype and 2.5% of the first-time donors were sickle cell trait (SCT) carriers. The existence of SCT among blood donors can be credited to both the absence of their exclusion from donating and the unawareness of their hemoglobin status and the risk they present to SCA patients receiving their donations (Fenomanana et al., 2020). Additionally, the younger mean age of the SCA patients demonstrates their shorter life expectancy compared to non-SCA individuals, further indicating the importance of treating this life-threatening condition.

Furthermore, the prevalence of HIV among multiple-transfused SCA patients was 4% and 5% among first-time donors, in line with studies conducted in Togo and the Central African Republic, which reported a prevalence of 5% and 6% respectively (Segbena et al., 2005; Gody et al., 2014). A study in the Democratic Republic of Congo (DRC), however, recorded a higher seroprevalence of 11.3% (Tshilolo et al., 2007). The HIV seroprevalence found in SCA patients was higher than the 1% recorded in Mali (Diarra et al., 2013). There was no significant difference between multi-transfused SCA patients and first-time donors (Table 3). Additionally, the number of transfusions received by SCA patients did not seem to be linked to HIV infection. This could be attributed to the thorough screening of the virus conducted when qualifying donations in Gabon, effectively reducing the risk of its transmission via transfusion. A study by Morar et al., (2016) suggested transfusion was responsible for only 0 to 1.1% of new HIV cases in SSA. Moreover, the seroprevalence of hepatitis B surface antigen (HBsAg) was found to be 10% in SCA patients and 8% in first-time blood donors, respectively, which is similar to the 10% reported in the DRC among multi-transfused SCA patients (Tshilolo et al., 2007). However, lower seroprevalences of 1.6%, 3%, and 6.48% have been reported in other studies in Sub-Saharan Africa (Batina Agasa et al., 2010; Diarra et al., 2013; Sack et al., 2013). The HBsAg seroprevalence was not significantly different between the two populations, nor was it associated with the sex or mean number of blood transfusions received by SCA patients. This is consistent with the findings of a previous report that did not find a connection between HBsAg and blood transfusion in SCA patients (Akpa et al., 2022).

Hepatitis C virus (HCV) infection is a grave complication for transfusion therapy in SCA patients who received transfusions before the implementation of serological tests for detecting infection in blood donors in 1990 (Maffei et al., 2020). The seroprevalence of anti-HCV antibodies was significantly higher in sickle cell patients (10%) than first-time donors (0%), with a higher seroprevalence of 19.7% reported in the Republic of Congo among multiple-transfused sickle cell patients (Dokekias et al., 2003). In this study, seropositivity was found to be linked with the number of transfusions received; indeed, the mean number of transfusions received by seropositive patients (7.20±3.27) was significantly greater than that of seronegative patients (3.96±2.06). The findings suggest that transfusion is one of the most likely routes of HCV infection acquisition, which is consistent with results from other studies that have identified a connection between blood transfusion and HCV infection in multi-transfused SCA patients in both Sub-Saharan Africa and the Middle East (Sack et al., 2013; Alkinda et al., 2019). Older age, illegal drug use, increasing red blood cell transfusions, >3 pain crises in the previous year and geographic location were all identified as factors associated with increased odds of HCV reactivity (Blatyta et al., 2020). This could be attributed to the fact that these patients would likely have received more

lifetime red blood cell transfusions, increasing their risk of HCV infection.

About 10-20% of sickle cell patients are estimated to have chronic HCV infection (Maffei et al., 2020), while they are frequently exposed to a heightened risk of iron overload and hemosiderosis due to the multiple transfusions needed to manage the sickling crisis and anemia, which can lead to severe liver-related morbidity and mortality (Moon et al., 2017). This study has certain limitations, including the relatively small population size and the failure to confirm anti-HCV serology via molecular tests that would help to differentiate between those who have been cured of hepatitis C and those with an active infection.

Conclusion

The present investigation suggests that the rates of HIV and HBsAg (hepatitis B surface antigen) are similar in both multi-transfused sickle cell patients and first-time blood donors in Libreville. However, there was a higher prevalence of HCV (hepatitis C virus) in multi-transfused sickle cell patients, indicating a possible association between blood transfusion and HCV transmission. It also suggests that introducing viral genomic diagnosis in HCV screening for blood donations in Gabon could help reduce the risk of transmission through blood transfusions in sickle cell patients. This approach could allow for more accurate identification of HCV infections and therefore improve the safety of blood transfusions in Gabon. Overall, these findings highlight the importance of ongoing efforts to improve the safety of blood transfusions, particularly in populations that are at a higher risk of blood-borne infections, such as sickle cell patients who require frequent transfusions.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

CB and JMNN designed the study. Laboratory analyses were carried out by JMEM, SP and SMMB. Data analysis was carried out by CB and TNM. CB, JMEM, BMN, JMNN and LEM wrote the manuscript. All the authors have read and approved the final version of the manuscript.

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