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The burden of human immunodeficiency virus, hepatitis B and C virus infections in patients with sickle cell anemia in Uyo, Nigeria: A hospital based cross-sectional study

Idongesit Samuel Akpan, Asukwo Etim Onukak, Iyanam Victory Edet, Ajayi Oyedele Oyewumi

ABSTRACT

Aims: Blood transfusion is an invaluable therapeutic intervention in sickle cell anemia (SCA) patients' care. Sickle cell anemia patients usually require frequent blood transfusion and are at increased risk of contracting human immunodeficiency virus (HIV), hepatitis B and C virus infections through these transfusions. To determine the seroprevalence of HIV, hepatitis B and C virus infections in patients' with sickle cell anemia and the role of blood transfusion in the transmission of the infections.

Methods: This was a prospective, observational cross-sectional study conducted on adult patients with SCA attending the Haematology Outpatient Clinic of University of Uyo Teaching Hospital, Uyo, from January 1, 2019 through December 31, 2019. Relevant clinical history was obtained from consenting subjects. Blood samples were collected for hemoglobin electrophoresis and viral antigen/antibody screening using ELISA kits. Data were analyzed using Statistical Package for Social Sciences (SPSS) windows version 23.0.

Results: Eight-six patients with SCA participated in the study. Forty (46.5%) of the subjects were male and 63 (73.3%) of the participants were within the age range of 20–29 years. Seventy-five (87.2%) of the subjects had blood transfusion while 11 (12.8%) never received blood transfusion in their entire life. Seroprevalence of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) among the transfused SCA patients in this study was 9.3%, 24.0%, and 18.7% respectively while those not transfused had seroprevalence of 9.1% for HIV and 0% for both HBV and HCV. One (1.2%) of the transfused subjects tested positive for HIV and HCV. There was no statistically significant difference in the seroprevalence of HIV, HBV, and HCV infections in relation to the transfusion status of the subjects (p=0.98, 0.07, and 0.12, respectively).

Conclusion: The proportion of our SCA patients who were HIV, HBV, and HCV positive was considerable. Blood transfusion did not significantly influence the seroprevalence rates of these viral infections. Measures aimed at controlling the infections in the patients and the general population should be scaled up.

Keywords: HBV, HCV, HIV, Sickle cell anemia, Uyo

Idongesit Samuel Akpan[1], Asukwo Etim Onukak[2], Iyanam Victory Edet[3], Ajayi Oyedele Oyewumi[4]

Affiliations: [1]Department of Haematology, University of Uyo/University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria; [2]Department of Internal Medicine, University of Uyo/University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria; [3]Department of Family Medicine, University of Uyo/University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria; [4]Department of Histopathology, University of Uyo/University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria.

Corresponding Author: Idongesit Samuel Akpan, Department of Haematology, University of Uyo/University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria; Email: idongakpan200326@yahoo.com

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INTRODUCTION

Sickle cell anemia (SCA) is an inherited red blood cell (RBC) disorder caused by a single nucleotide substitution (GTG for GAG) in the sixth codon of the beta globin gene on chromosome 11, where glutamic acid is replaced by valine, resulting in the polymerization of hemoglobin (Hb) and formation of HbS, with protean devastating clinical manifestations [1]. Deoxygenation of the HbS results in sickling of the red blood cells making them to be rigid and susceptible to hemolysis, thus anemia ensues [2]. Anemia of varying severity begins in the middle to second half of the first year of post-natal life making blood transfusion an important treatment option during infancy [3].

Sickle cell anemia is principally a genetic disease of Africans, Indians, and Arabs [4]. The incidence of sickle cell anemia in sub-Saharan Africa ranges between 1% and 2% with Nigeria having the largest cohort of patients with the disease [5]. It is estimated that the prevalence of sickle cell trait is as high as 25–30% in West African Countries while 1 in 10 Afro-Caribbeans and 1 in 2 African-Americans have the trait [6–8]. Severe anemia due to hemolysis, acute sequestration and aplastic crises, and multi-organ failure are the common causes of death in individuals with SCA especially in the absence of early diagnosis, proper education of the patients, and their caregivers as well as robust preventive strategies [8]. Therefore, blood transfusion as a supportive modality has become an integral component of the therapeutic interventions in the management of patients with sickle cell anemia. It is useful for optimizing hemoglobin concentration when below steady state, diluting sickle hemoglobin, and suppressing endogenous sickle red cell production [9].

Transfusion of blood and blood components is however fraught with risk of contracting transfusion transmissible infections (TTIs) such as human immunodeficiency virus, hepatitis B virus and hepatitis C virus infections amongst others [6, 10]. Recent data suggest that transmission of these viral infections still poses a daunting challenge to transfusion safety in Nigeria [6, 11]. The risk of acquiring the TTIs is therefore a matter of utmost public health significance particularly in resource poor settings with profound technical, economic, and infrastructural constraints [10]. Several workers have reported higher prevalence rates of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus infections in SCA patients than the general population [3, 5, 6, 10, 11].

The national prevalence of HIV infection in Nigeria is estimated to be 1.4% and blood transfusion is thought to account for about 10% of HIV transmission [12]. The role of blood transfusion in the transmission of HIV in SCA patients has been documented in studies conducted within and outside the country [6, 10, 13, 14].

Globally, studies have also indicated the increased risk of transfusion-related acquisition of HBV and HCV Infections in sickle cell anemia patients [15–18]. Nigeria, with an estimated population of 190 million people has a hepatitis B seroprevalence rate of 8.1% and hepatitis C prevalence of 1.1% [19]. The prevalence of these viral infections among the general population and SCA patients in Nigeria vary widely depending on the population being considered [6, 10, 11].

Due to absence of data on the prevalence of HIV, HBV, and HCV infections among SCA patients in our environment, we sought to determine the burden of these common transfusion transmissible viral infections in adult SCA patients attending the Haematology Outpatient Clinic of University of Uyo Teaching Hospital, Uyo, Nigeria. The study also investigated the role of blood transfusion in the transmission of the infections. It is our belief that this will serve as the framework for the monitoring of our patients against long-term complications of these infections such as chronic liver disease, hepatocellular carcinoma, and AIDs-related lymphomas among others as well as form the basis for evaluating the effectiveness of the donor screening methods and safety protocols employed in blood transfusion services in our environment.

MATERIALS AND METHODS

This prospective descriptive cross-sectional study was conducted at the Haematology Outpatient Clinic (HOPC) of University of Uyo Teaching Hospital (UUTH), Uyo, between January, 2019 and December, 2019. University of Uyo Teaching Hospital is a tertiary referral health facility in the South-South region of Nigeria that provides specialized healthcare services to residents of Uyo and its environs. Ethical approval was obtained from the Human Research Ethical Committee of UUTH. Written informed consent was obtained from all the participants after explaining to them the objectives, scope, and methodology of the study with the right to decline at any point in the study without any repercussions. The patients recruited were aged twenty (20) years and above. Those who did not understand the nature of the study, refused consent, were aged below 20 years, had other hematological conditions or had been previously immunized with anti-hepatitis B vaccine were excluded from the study.

Relevant information such as age, sex, level of education, occupation, hepatitis B vaccination status, history, and frequency of blood transfusion were obtained from all consenting subjects. 5 mL of blood was collected from each subject by venipuncture, with 2 mL being put into an EDTA (ethylenediaminetetraacetic acid) specimen bottle for hemoglobin electrophoresis using the cellulose acetate method to determine their hemoglobin phenotype. The remaining 3 mL of blood

collected into a plain bottle and allowed to clot was centrifuged at 5000 rpm for 5 minutes to obtain serum which was stored at 20°C until analysis. Solid base wet enzyme linked immunosorbent assay (ELISA) kits from Assaypro, St. Charles, United States was used to screen for HIV I & II antigen-antibody, HBV surface antigen, and HCV antigen-antibody. The methodology spelt out in the information inserts supplied with the kits was strictly adhered to and each test kit had positive and negative controls to ensure accuracy and precision.

Data obtained were analyzed using Statistical Package for Social Sciences (SPSS) windows version 23.0 (SPSS Inc; Chicago, IL, USA) and presented in tables. The comparisons were carried out with Chi-square test as appropriate and the statistical significance was set at p-value < 0.05.

RESULTS

Eight-six (86) patients with SCA were studied. Forty (46.5%) were males while 46 (53.5%) were females giving a male: female ratio of 1:1.2 (Table 1). The mean age of participants was 28.2±7.9 years with an age range of 20–59 years. Majority (79.1%) of the participants were unmarried and 73.3% were aged between 20 and 29 years.

History of blood transfusion was recorded in 75 (87.2%) of the subjects while 11 (12.8%) were never transfused. Amongst the subjects transfused, 36 (48.0%) were males and 39 (52.0%) were females. All (100%) the transfused subjects were able to recall the number of units they received at different times ranging from 1 to 20 units with a mean number of units of 10.4±3.6 (Table 2).

Eight (9.3%) of the study subjects were seropositive to HIV while 78 (90.7%) were HIV negative. Hepatitis B

Table 1: Sociodemographic characteristics of the study subjects and seroprevalence of HIV, HBV, and HCV infections

Socio-demographic Factors	Number screened (n=86)	Prevalence (%) HIV	HBsAg	HCV
Age (years)				
20–29	63	5(7.9)	9(14.3)	7(11.1)
30–39	16	2(12.5)	6(37.5)	4(25)
40–49	5	1(20)	2(40)	2(40)
≥50	2	0(0)	1(50)	1(50)
p-value		**0.58**	**0.05**	**0.05**
Gender				
Male	40	6(15)	6(15)	5(12.5)
Female	46	2(4.3)	12(26.1)	9(19.6)
p-value		**0.14**	**0.21**	**0.38**
Education level				
No formal education	2	1(50)	0(0)	0(0)
Primary education	6	1(16.7)	1(16.7)	0(0)
Secondary education	62	5(8.1)	12(19.4)	13(21.0)
Post-secondary education	16	1(6.3)	5(31.3)	1(6.3)
p-value		**0.2**	**0.75**	**0.44**
Occupation				
Students	52	7(13.5)	15(28.8)	12(23.1)
Civil servants	9	0(0)	3(33.3)	1(11.1)
Artisans	7	1(14.3)	0(0)	0(0)
Traders	8	0(0)	0(0)	0(0)
Jobless	10	0(0)	0(0)	2(20)
p-value		**0.6**	**0.05**	**0.45**
Marital status				
Single	68	8(11.8)	17(25)	14(20.6)
Married	12	0(0)	1(8.3)	0(0)
Divorced	5	0(0)	0(0)	0(0)
Widowed	1	0(0)	0(0)	0(0)
p-value		**0.78**	**0.44**	**0.31**

HIV: Human immunodeficiency virus; HBsAg: Hepatitis B surface antigen; HCV: Hepatitis C virus.

surface antigen was detected in 18 (20.9%) of the subjects while 68 (79.1%) were HBsAg negative. Antibodies to hepatitis C virus were detected in 14 (16.3%) of the subjects while 72 (83.7%) tested negative for the antibodies (Table 2).

Human immunodeficiency virus antibodies were detected in seven (9.3%) of the transfused subjects while only one (9.1%) subject who was not transfused had HIV antibodies in his serum. Hepatitis B surface antigen and antibodies to hepatitis C virus were detected in 18 (24.0%) and 18 (18.7%) of the transfused subjects, respectively. HBV and HCV markers were not detected in the sera of those who were not transfused (Table 3). One (1.2%) of the transfused subject tested positive for HIV antibodies and HBsAg. There was no statistically significant difference in the seroprevalence of the transfusion transmissible viral infections in relation to transfusion status of the study subjects, p-values 0.98, 0.07, and 0.12 for HIV, HBV, and HCV respectively (not included in Table 3).

Table 2: Transfusion status of the study subjects and seroprevalence of HIV, HBV, and HCV infections

Transfusion status	Negative n (%)	Positive n (%)	Total	p-value
HIV				
Transfused	68(90.7)	7(9.3)	75	0.98
Not transfused	10(90.9)	1(9.1)	11	
HBsAg				
Transfused	57(76.0)	18(24.0)	75	0.07
Not transfused	11(100.0)	0(0)	11	
HCV				
Transfused	61(81.3)	14(18.7)	75	0.12
Not transfused	11(100.0)	0(0)	11	

Table 3: Blood transfusion rate and seroprevalence of HBsAg and hepatitis C virus

No. of units	HIV		HBsAg		HCV	
	Negative	Positive	Negative	Positive	Negative	Positive
0	10(91)	1(9.1)	11(100)	0(0)	11(100)	0(0)
1–3	5(100)	0(0)	5(100)	0(0)	5(100)	0(0)
>3	63(90)	7(10)	52(74.3)	18(25.7)	56(80)	14(20)

DISCUSSION

Patients with SCA are generally prone to several systemic complications necessitating blood transfusion owing to the sickling and chronic hemolytic phenomena associated with the disease. They are therefore at risk of contracting transfusion transmissible infections such as human immunodeficiency virus, hepatitis B and hepatitis C virus infections from the multiple blood transfusions they often receive for their medical care. The risk for acquisition of these transfusion-related infections vary from one setting to the other due to a number of factors like the level of knowledge of the TTIs and their associated risk factors, availability of facilities for effective screening of blood and blood products, properly trained laboratory personnel, as well as existing blood transfusion policies and practices [10].

The proportion of SCA patients who tested positive to HIV in this study was 9.3%. This figure was high compared to the finding of the 2020 sentinel survey which put the HIV prevalence in the general population of Akwa Ibom State at 2.8% [20]. It was also higher than similar studies carried out in Tanzania (1.8%), Cameroon (5.6%), and Togo (5.0%), countries endemic for HIV [21–23]. Our rate was however lower than the 11.3% reported by Tshilolo et al. in Democratic Republic of Congo [14]. It is of interest to note that the observed lower rates in studies conducted in Tanzania, Cameroon, and Togo could partly be due to the variation in the age of the study participants which included both children and adults when compared to the present study where only adults were recruited. Hence, the high rate in our study could have resulted from other modes of transmission of the viral infection common in adults such as unprotected sexual intercourse with multiple high-risk partners, intravenous drug abuse, use of unsterilized instruments for scarification, tattoing, and blood rituals. There is also the likelihood that our adult SCA patients may have received larger number of blood transfusion in the course of their illness. Several researchers have reported lower prevalence rates of the TTIs in children compared to adults [6, 13, 15, 17, 18]. Moreover, the difference in findings may be connected with the seroprevalence of the viral infections among the general population in the different countries.

Gender wise, male patients were more infected by HIV than their female counterparts, 15.0% and 4.3%

respectively. This finding was comparable with that of Mwanaut et al. in a cohort of polytransfused adult SCA patients in Kinshasa, Democratic Republic Congo [24]. They documented a prevalence of 10.9% in males and 6.9% in females. However, other workers have reported higher prevalence of HIV infection in females than males [25, 26]. The latter observation is in agreement with epidemiological data in Akwa Ibom State which show that more women are infected by HIV than men [19].

In the current study, seven out of eight of the HIV positive patients had a history of blood transfusion while the remaining one subject did not receive blood transfusion although this was not statistically significant. Most of the transfusions took place in private health facilities. It is rather unfortunate that the HIV seroprevalence rate in this study is still striking as that reported among blood donors in our institution a couple of years ago [27]. The frequency of unsafe blood transfusion should have reduced markedly with increasing public enlightenment, improved blood screening techniques and stringent regulations governing the use of blood and blood products. Possible reasons for this appalling situation include the limitation of some screening methods to detect the virus during the "window period" when the donors may be falsely negative for the offending antigens or antibodies being screened for, poor donor selection criteria, and/or laboratory errors during screening. Sadly, this presages ominous implications for our healthcare delivery system.

The finding of 20.9% seroprevalence for HBsAg observed in this study is a reflection of the hyper-endemicity of hepatitis in Nigeria as well as the whole of sub-Saharan Africa [10, 19, 28]. The prevalence of HCV across different regions of Nigeria varies [19]. Jibrin et al. [29] in Sokoto reported a prevalence of 17.3% and in Ile-Ife, South-Western Nigeria, Bolarinwa et al. [30] recorded a prevalence of 2.4% among SCA patients and 2.2% in controls. A prevalence of 20.2% among SCA patients was reported in Togo by Segbena et al., [23] but in Jos, Angyo et al. [31] obtained a high prevalence of 22.6%. Another study in Benin, by Abiodun et al. [32] documented a much higher prevalence of 39.2% in SCA children and 19.3% in controls. The higher figures recorded in our series and comparable studies may be partly attributed to the high sensitivity of the ELISA method used and also the variation in rates of hepatitis B virus transmission in different regions.

In relation to blood transfusion, those transfused had a seroprevalence of 24% for HBsAg while those that never received blood transfusion had no seroprevalence. There was no significant difference between the transfused and non-transfused ($p>0.05$). However, this observation seemed to have underpinned the increased risk of acquiring the hepatitis B infection through blood transfusion.

The seroprevalence of HBsAg in females compared to that in males was higher in this study which was consistent with findings in previous studies in Nigeria [29, 33, 34]. Contrary to these observations, several authors within and outside our country have reported higher prevalence among males [27, 35–39]. The plausible explanation for our finding is not known but may be related to the number of female patients that participated in this study or due to risky behavioral practices common among females such as ear or nose piercing, indiscriminate use of eye lashes, or other direct contact with mucous membranes of eyes, mouth, or skin for cosmetic gratification.

The overall prevalence of HCV in our study was 16.3% while those transfused had a prevalence of 18.7% compared to none among those not transfused. These rates were at variance with the national prevalence of 0.4–14.7% and what has been reported among SCA patients elsewhere in the country [10, 11, 19, 30]. Also, unlike reports from most studies reviewed [11, 15, 16, 23, 39], the prevalence of HCV in our work was higher among females than males. The difference in reported findings in these studies could be multifactorial from population demographics, traditional practices like circumcision, tribal or scarification rituals with re-used or unsterilized instruments, and perilous social behavior to testing methods used. It is equally pertinent to posit that due to the suboptimal immune surveillance in SCA, the patients are susceptible to a wide array of infections [8].

The age of contracting the viral transfusion transmissible infections is an important determinant of prevalence rates [2, 8, 16]. In the present study, the infections were detected with highest prevalence among subjects aged between 20 and 29 years. This finding was in consonance with the findings of Jatau et al. [6] and Bolarinwa et al. [30] who recorded the highest prevalence rates among patients within the same age bracket. The reason for our observation may be due to the fact that majority of the study subjects fell into this age group. It is also likely that increased sexual activity during this period could be responsible.

Distribution of the subjects based on the level of education showed that most of the patients were educated up to secondary school level followed by tertiary and primary levels of education in that order while the least number had no formal education. The largest groups of respondents were students, the unemployed and civil servants, this occupational spectrum mirrors the setting of our hospital; it is situated in a commercial town where these categories of persons constitute a considerable proportion of the patients' population. The risk of contracting HIV, HBV and HCV infections has been documented to be higher in occupations that involve people of lower educational attainment, particularly those who move around a great deal in the course of their work [40–42]. Our study showed that students had the highest prevalence rates across all the TTIs while the prevalence was markedly low in other occupational groups (Table 1). This observation was in keeping with other reports [43, 44]. The reason for this finding is not far-fetched. Studies have shown that education plays a significant role in influencing SCA patients' healthcare seeking behavior. Education provides the knowledge

and information needed for the effective management and coping with SCA and its complications [45, 46]. Our educated subjects were more likely to be better informed about SCA, its management and outcome and the need to seek medical care whenever the need arose. This may have accounted for the increased number of students with SCA in our series.

The unmarried subjects had higher prevalence of the HIV, HBV, and HCV infections compared with the married subjects, while none of the widowed or divorced respondents tested positive for any of the infections. Unprotected sex, especially if it involves multiple sexual partners, is known to be a means of transmission of these viral infections and unmarried status may provide a veritable avenue for unprotected sex which could increase the chances of exposure and transmission of the infections. However, statistical significant association was not established between marital status and HIV, HBV, and HCV positive status despite the fact that significant population of the participants (79.1%) were unmarried ($p>0.05$). This was similar to findings from elsewhere [6, 21]. This seems to buttress the fact that blood transfusion may be the most important risk factor for the acquisition of these viral infections in the patients. Conversely in a study among pregnant women, married subjects were reported to have a higher prevalence of these infections compared with single subjects also possibly substantiating the role of sexual transmission of the infections particularly if the partners engage in indiscriminate extramarital amorous affairs [38].

The strength of this study was that it was the first study from our locality on the seroprevalence of HIV, HBV, and HCV infections among SCA patients. However, it is possible that being a hospital-based study it may have underestimated the burden of the infections in our environment because some of the SCA patients do not access care in our institution. Given that these infections are also transmissible via other means such as through sexual exposure or sharing of sharps, these factors are potential confounders that could have contributed to some of the study findings as was explored in the link between marital status of the subjects and the prevalence of these infections. Another limitation of the study is in the sample size which was small especially during comparison of data between the SCA patients that were transfused and those that were not. There is need for a larger community-based cohort study to better assess the impact of blood transfusion on HIV, HBV, and HCV infections among SCA patients.

CONCLUSION

The study has highlighted the burden of HIV, HBV, and HCV infections among SCA patients in our environment. Although there was no significant relationship between the seroprevalence of these infections and the blood transfusion status of the subjects, there is still need for conscientious effort in implementing all preventive measures against the infections by ensuring robust blood transfusion safety protocols. Routine vaccination against HBV and HCV and antiviral medications for all three infections when necessary should be available and affordable for all SCA patients and the general population to reduce the prevalence of the infections. We advocate that a large community-based study be conducted in our locality for the purpose of validating our findings.

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Author Contributions

Idongesit Samuel Akpan – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Asukwo Etim Onukak – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Iyanam Victory Edet – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ajayi Oyedele Oyewumi – Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.