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Is Human Immunodeficiency Virus Still Transmissible Through Blood Transfusion in Children with Sickle Cell Anaemia in Jos, Nigeria?

E. U. Ejeliogu[1*], S. N. Okolo[1], S. D. Pam[2], E. S. Okpe[1], C. C. John[1] and M. O. Ochoga[3]

[1]Department of Paediatrics, University of Jos/Jos University Teaching Hospital, Jos, Nigeria.
[2]Department of Paediatrics, Rockhampton Base Hospital, Rockhampton, Australia.
[3]Department of Paediatrics, Benue State University Teaching Hospital, Makurdi, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author EUE designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SNO and SDP supervised the work and reviewed the first draft of the manuscript. Authors ESO and CCJ managed the analyses of the study. Author MOO managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aims: To compare the prevalence of HIV infection amongst transfused and non-transfused children with sickle cell anaemia (SCA) in Jos, Nigeria and explore the factors affecting it.
Study Design: This was a prospective case control study.
Place and Duration of Study: Department of Paediatrics (Sickle Cell Clinic), Jos University Teaching Hospital, Jos, Nigeria, between January 2008 and March 2009.
Methodology: A total of 200 transfused children with SCA (117 males and 83 females) were recruited consecutively and screened for HIV using rapid test kits. A questionnaire was used to ascertain the details of blood transfusion and other relevant clinical information. Two hundred age and sex matched non-transfused children with SCA attending the same clinic were recruited as controls.
Results: The prevalence of HIV infection amongst transfused children with SCA was 2%, compared to 0% in the control group (P=.04). The four HIV positive cases were transfused in private hospitals with blood of unknown screening status. The number of blood transfusions was

**Corresponding author: Email: emekam12@yahoo.com;*

not a significant factor in acquiring HIV infection (P=.78); however remunerative blood donation increased the risk of acquiring HIV through blood transfusion (AOR=6.28; 95% CI (1.82-9.92); P=.01).

Conclusion: HIV is still transmissible through blood transfusion and screening of blood before transfusion is still not completely practiced in Jos, Nigeria. Policies on proper screening of blood before transfusion and voluntary blood donation should therefore be enforced at all levels of healthcare.

Keywords: Sickle cell anaemia; blood transfusion; remunerative blood donation; HIV-transmission; Jos; Nigeria.

1. INTRODUCTION

The Human Immunodeficiency Virus (HIV) has become one of the major social and medical issues of our time since it was discovered. HIV is contributing substantially to the rising child mortality rates in many areas of sub-Saharan Africa, reversing years of hard won gains in child survival [1]. UNAIDS estimated that 3.3 million children <15 years were infected with HIV at the end of 2012 [1]. In Nigeria, 260,000 children were estimated to be living with HIV at the end of 2011 [2].

About 90% of children infected with HIV in Nigeria acquired the infection through mother to child transmission; however blood transfusion remains an important route of HIV transmission in Nigeria, accounting for between 5-15% of cases [3-5]. With the scaling up of prevention of mother-to-child transmission (PMTCT) services across Nigeria, other routes of transmission like blood transfusion may become more important if stringent measures are not put in place to prevent them.

Sickle Cell anaemia (SCA) is one of the important health problems of Nigerian children. The prevalence of the homozygous haemoglobin S among the general population in Nigeria is about 3% [6]. Deoxygenation induced tactoid formation and erythrocyte sickling of haemoglobin S manifests as a lifelong haemolytic anaemia for which blood transfusion is occasionally indicated [7]. In Nigeria, SCA is one of the main indications for blood transfusion, second only to malaria as the main causes of severe anaemia [3]. Patients with SCA may require repeated transfusions and are therefore at the risk of contracting blood-borne infections if the blood units are not properly screened [8].

In developed countries, several studies reported prevalence rate of 0% in multiply transfused patients with SCA [9-11]. However in sub-Saharan Africa the prevalence rate ranged from 0-33% [12-17]. In Lagos, Nigeria, Olatunji [14] reported a HIV prevalence rate of 6% in transfused adult SCA patients while Mamman [15] reported a rate of 4.1% also in adults in Zaria, Nigeria. George et al. [16] reported a prevalence rate of 4.2% among transfused children with SCA in Port Harcourt, Nigeria while Ogunrinde [17] reported a rate of 1.8% in children in Zaria, Nigeria. This study therefore aimed to compare the prevalence of HIV infection amongst transfused and non-transfused children with SCA in Jos, Nigeria and explore factors affecting it.

2. MATERIALS AND METHODS

2.1 Background of Study Area

Jos, the capital of Plateau state of Nigeria, is located in the north central zone of the country. The Jos University Teaching Hospital is one of the two teaching hospitals in the zone. The population of the state was estimated at 3,206,531 in the 2006 census, with the state capital having a population of approximately 900,000 [18]. Children constitute about 45% of the total population.

The sickle cell clinic, which attends to only sickle cell disease patients, is a unit of the paediatric out-patient department (POPD) of the hospital. The clinic is run every Wednesday of the week. About 650 children with sickle cell disease were being followed up at the clinic as at the time of the study. The average clinic attendance was thirty patients per week.

2.2 Study Design

This was a prospective case-control study.

2.3 Ethical Consideration

Written informed consent was obtained from the parents/guardians. An explanation of the procedure was given to patients ≥6 years of age. Approval for the study was obtained from the Ethical committee of Jos University Teaching Hospital.

2.4 Sample Size

The minimum sample size for the study was determined using the formula [19]:

$$N = \frac{(Z)^2(1-P)(P)}{d^2}$$

Where

N = Minimum sample size
Z = Constant at 95% confidence interval from two table which for two tailed study =1.96.
P = Best estimate of prevalence in the target population expressed as a fraction of 100.
d = Degree of accuracy desired, set at 5% =0.05.

$$N = \frac{(1.96)^2(1-0.15)(0.15)}{0.0025} = 196$$

Two hundred subjects and 200 controls were recruited for the study.

2.5 Study Population

Study population consisted of children aged between 18 months and 18 years attending the sickle cell clinic of Jos University Teaching Hospital (JUTH). Children less than 18 months were excluded from the study because a positive HIV antibody test is not diagnostic of HIV infection in the age group.

2.5.1 Inclusion criteria

The patients that were included in this study followed the inclusion criteria, such as homozygous haemoglobin S, age 18 months to 18 years, written informed consent obtained, history of blood transfusion for subjects, and no history of blood transfusion for controls.

2.6 Patient Selection and Data Collection

Consecutive consenting patients with homozygous SCA within the stated age range attending the sickle cell clinic of the hospital were recruited from January 2008 to March 2009 for the study. Individual pre-test counseling was done for parents. The investigator did the counseling having acquired HIV testing and counselling experience at AIDS Prevention Initiative in Nigeria supported HIV clinic of the hospital. The confidential and voluntary nature of the study was stressed. Parents were told of the available medical care and treatment in the event of a positive result. Post-test counseling was done for parents of those who tested HIV positive.

Personal data, medical and social information were obtained using questionnaire directly administered by the investigators. Details of blood transfusion were obtained. These include number of blood transfusions, where blood transfusion was given, who donated the blood, and whether blood was screened for HIV or not. Details of exposure to other risk factors for transmission of HIV infection were also obtained. Factors explored include history of uvulectomy/tonsillectomy, scarification, where circumcision was done, multiple intramuscular injections outside the hospital, intravenous drug abuse and sexual contact. Physical examination, specifically for anthropometric measurement, scarification marks, sickle cell habitus, and sexual maturity rating was carried out.

Mothers of those who tested positive for HIV were counseled and screened for HIV. Those whose mothers were HIV positive were excluded from the study to exclude mother to child transmission.

2.7 Specimen Collection and Labeling

Blood samples were collected from each patient by the investigator and a trained assistant from the middle finger after cleansing with 70% alcohol and pricking with a sterile lancet. Each test strip, before application, was labeled using a non-erasable marker with each patient's code number. The antibody test was done in accordance with World Health Organization (WHO) HIV testing algorithm [20] using Determine™ by Abbot Laboratories Japan**,** Unigold™ by Trinity Biotech Plc, Bray, Ireland, and Stat Pack™ by Chembio Diagnostic System INC, New York test kits.

2.8 Statistical Analysis

Data obtained was analyzed using EpiInfo version 3.5.1. Student's t-test was used to compare means of variables while chi-square test was used to test significance of associations. Univariate logistic regression was used to examine the association between the independent variables and outcome with the results expressed as odds ratios (OR) with their 95% Confidence Intervals (CIs). Variables that were associated with HIV infection in the univariate analyses at $P<0.05$ were fit in a multivariate logistic regression model. P value <0.05 was considered significant.

3. RESULTS

Two hundred transfused and two hundred non-transfused children attending the sickle cell clinic were recruited for the study. Out of the 400 patients, 234 (58.5%) were males while 166 (41.5%) were females giving a male female ratio of 1.4:1. The mean age at recruitment was 6.85±4.70 years while the mean age at diagnosis was 15.8±17.8 months for the transfused and 18.0±23.9 months for the non- transfused (*P*=.46). The mean weight was 21.6±9.5kg for the transfused and 18.5±10.5kg for the non-transfused groups (*P*=.03). The mean height was 118.2±24.1cm for the transfused and 107.7±26.9cm for the non-transfused (*P*=.005). The mean number of hospital admission was 2.6±1.8 for the transfused group and 0.8±1.2 for the non-transfused group (*P*<.001). (Table 1) shows the characteristics of the study population.

Table 1. Characteristics of the study population

Characteristic	Total (%)	Transfused	Not transfused	*P* value
Sex				
Male	234 (58.5)	117	117	
Female	166 (41.5)	83	83	
Age				
1-5years	272 (43)			
6-10years	104 (26)			
11-18years	124 (31)			
Mean age at diagnosis(months)	400 (100)	15.8±17.8	18.0±23.9	.46
Mean weight (kg)*	400 (100)	21.6±9.5	18.5±10.5	.03
Mean height (cm)^	400 (100)	118.2±24.1	107.7±26.9	.005
Mean number of hospitalization	400 (100)	2.6±1.8	0.8±1.2	<.001

**kg: kilogram ^cm: centimeter*

The 200 transfused patients received 320 transfusions; 190 (59.4%) were received between the ages of 1-5 years, 108 (33.8%) between the ages of 6-10 years, and 20 (6.2%) at less than 1 year of age. Only 2 transfusions were received after 10 years of age. Out of the 200 transfused patients screened for HIV, 4 (2%) tested positive while no patient in the non transfused group tested positive to HIV (*P*=.04). The number of blood transfusions per subject ranged from 1-5. One hundred and twenty patients were transfused only once while four patients had 5 blood transfusions. Two of the 4 patients that tested positive were transfused only once (*P*=.78). Two hundred and twenty-six (70.6%) transfusions were given in Teaching Hospitals. No transfusion was given in a Primary Health Centre. While only 38 (11.9%) of the transfusions were given in private hospitals, the 4 HIV positive cases were all transfused in private hospitals (*P*<.001).

Out of the 320 transfusions, 302 (94.4%) were donated by voluntary donors while 18 (5.6%) were donated by remunerative donors. Two HIV positive cases were transfused with blood donated voluntarily while the other 2 were transfused with blood donated by remunerative donors (AOR=6.28; 95% CI (1.82-9.92); *P*=.01).

Relatives accounted for the majority of voluntary donors (95%). Other voluntary donors included neighbours (2%), friends (1%) and medical students (1%). Health workers did not donate any blood.

Of the 320 blood units transfused, 280 (87.5%) were screened for HIV while 4 (1.3%) were not screened for HIV. It was not known whether the blood was screened for HIV in 36 (11.2%) blood units. Twenty-four of the 36 units with unknown screening status were transfused in private hospitals, 4 in general hospitals and 8 in Mission hospitals. The 4 unscreened blood units were all transfused in private hospitals. The reason for not screening the blood was because they were donated by the fathers of the patients. The four HIV positive cases were transfused with blood of unknown screening status. (Table 2) shows the relationship between different aspects of blood transfusion and HIV status.

Table 2. Relationship between blood transfusion and HIV status

Characteristics	Total (%)	HIV positive	HIV negative	X^2	*P* value
Transfused				4.04	.04
Yes	200 (50)	4	196		
No	200 (50)	0	200		
Number of transfusions				3.1	.78
1	120 (60)	2	118		
2	56 (28)	1	55		
3	12 (6)	0	12		
4	8 (4)	1	7		
5	4 (2)	0	4		
Place of transfusion				31.63	<.001
Teaching hosp	226 (70.6)	0	226		
General hosp	24 (7.5)	0	24		
Mission hosp	32 (10.0)	0	32		
Private hosp	36 (11.9)	4	32		
PHC	0 (0)	0	0		
Source of blood				14.98	.02
Voluntary	302 (94.4)	2	300		
Remunerative	18 (5.6)	2	16		

PHC=primary health centre

There was no significant difference in the prevalence of HIV infection between those who were exposed to other horizontal risk factors of HIV infection and those who were not exposed (Table 3).

In the multivariate analysis, those that received blood from remunerative donors were 6 times more likely to be infected with HIV compared to those that received blood from voluntary donors, AOR (95% CI)=6.28 (1.82-9.92); *P*=.01 (Table 4).

Table 3. Prevalence of HIV infection and other horizontal risk factors

Horizontal risk factor	Total (%)	HIV positive	HIV negative	X^2	*P* value
Uvulectomy				0.1	.63
Yes	244 (60.8)	2	242		
No	156 (39.2)	2	154		
Circumcised at home				0.08	.77
Yes	74 (31.6)	1	73		
No	160 (68.4)	3	157		
Injected outside hospital				1.17	.28
Yes	105 (26.1)	2	103		
No	295 (73.9)	2	293		
Scarification				0.15	.86
Yes	28 (7.0)	0	28		
No	372 (93.0)	4	368		
Sexual contact					
Yes	0	0	0		
No	400	4	396		
Intravenous drug abuse					
Yes	0	0	0		
No	400	4	396		

Table 4. Risk factors for HIV transmission

Risk factor	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Multiple transfusions				
No	1.00 (Ref)		1.00 (Ref)	
Yes	0.66 (0.36-1.73)	.78	0.72 (0.44-1.92)	.32
Remunerative donor				
No	1.00 (Ref)		1.00 (Ref)	
Yes	5.75 (1.74-9.75)	.02	6.28 (1.82-9.92)	.01
Uvulectomy				
No	1.00 (Ref)		1.00 (Ref)	
Yes	0.64 (0.61-6.38)	.63	0.77 (0.76-6.12)	.68
Circumcised at home				
No	1.00 (Ref)		1.00 (Ref)	
Yes	0.72 (0.34-2.90)	.77	0.76 (0.49-2.82)	.84
Injected outside hosp				
No	1.00 (Ref)		1.00 (Ref)	
Yes	2.84 (0.28-3.62)	.28	2.66 (0.31-3.12)	.22
Scarification				
No	1.00 (Ref)		1.00 Ref)	
Yes	0.25 (0.26-1.36)	.86	0.34 (0.11-1.68)	.93

OR=odds ratio CI=confidence interval

4. DISCUSSION

The mean age at diagnosis of SCA was not significantly different between the transfused and non transfused groups. However, the mean number of hospital admission was higher in the transfused group. This is consistent with earlier reports by Mamman [15]. Apart from admissions for blood transfusion, they could also have been admitted for other conditions that could have caused severe anaemia, such as malaria and bacterial infections.

The mean weight and height were significantly higher in the transfused group. Blood transfusion has a beneficial effect on the growth of children with SCA. Higher haemoglobin levels resulting from transfusion may improve growth by increasing oxygen delivery to tissues and lowering energy expenditure. This is consistent with the study done by Wang [21] which showed that SCA children who received blood transfusions had improved height, weight and Body Mass Index.

HIV was detected in 4 (2%) children in the transfused group while no child in the control group tested positive for HIV. This demonstrates that HIV is still transmissible by blood transfusion in Jos, Nigeria. This is consistent with findings in other studies in sub-Saharan Africa and some parts of the Middle East [14-17,22]. The current prevalence rate of HIV infection in transfused SCA children is lower than the rate reported in some studies done in other localities in Nigeria and other parts of sub-Saharan Africa. Olatunji [14] and Mamman [15] had reported a prevalence rate of 6% and 4.1% in transfused adult SCA patients in Lagos and Zaria respectively. George et al. [16] reported a prevalence rate of 4.2% among transfused children with SCA in Port Harcourt, Nigeria. The rate is however similar to 1.8% reported by Ogunrinde et al. [17] in Zaria, Nigeria. The lower value obtained in this study could be as a result of increasing level of blood screening before transfusion. Previous studies reported HIV screening rate of 50-60% while a screening rate of 87.5% was observed in this study.

Higher numbers of blood transfusion did not increase the risk of HIV infection in this study. This contrasts with the findings of El-Hazmi [22] and Ngo [14] which showed that multiple blood transfusions increase the risk of acquiring HIV infection. The high rate of blood screening observed in this study could have made multiple transfusions safer. Screening of blood before transfusion prevents the transmission of blood-borne infections irrespective of the number of transfusions the person had received.

This study demonstrated a strong relationship between the place where blood transfusion was given and HIV infection. Out of the 320 blood transfusions recorded, 38 (11.9%) were given in private hospitals; however, all the 4 HIV positive cases were transfused in private hospitals. The screening status of blood used in all 4 transfusions is unknown. It is possible that the 4 blood units were not screened for HIV. Adejuyigbe [3] had earlier reported that a lot of blood units transfused in private hospitals in Ife, Nigeria were not screened for HIV. Some private hospitals may also employ untrained personnel or poorly trained laboratory technicians and this could have negative impact on test kit storage and HIV testing procedure. It is also possible that the blood units were donated by HIV infected persons during the window period of HIV seroconversion. As such the presence of HIV could not be detected by the antibody detection kits normally used in blood screening.

Ignorance is a factor that still contributes to the spread of HIV in Sub-Saharan Africa. Although the awareness of the populace on the transmission of HIV through blood transfusion is increasing, a lot of people are still not literate enough to insist that only

properly screened blood is transfused to them and their family members. Because of the prevailing ignorance in our society, the onus lies on health workers who have better awareness of the dangers of transfusing unscreened blood to ensure that only properly screened blood is transfused to patients under their care.

Those who received blood from remunerative donors were significantly more likely to acquire HIV through blood transfusion compared to those that received blood through voluntary donors. Several studies have shown that the prevalence of HIV is higher in remunerative than in voluntary donors and as such there is a greater risk of transmitting HIV infection through remunerative blood donors [23,24].

In an effort to address the risk of blood-transmissible infections through remunerative blood donation, the Regional Strategy for Blood Safety of World Health Organization (WHO) Regional Committee for Africa targeted that by the year 2012 at least 80% of blood donations in member countries would be benevolent, voluntary and non-remunerated [25]. A blood donation and transfusion programme coordinated at national or zonal levels as being advocated by WHO [25] would probably go a long way to ensure adequate availability and improved access to high quality blood and blood products, especially in resource-poor settings.

The number of blood units donated by voluntary donors in this study (94%) was significantly higher than in other studies [3,23]. This difference could have resulted from better public awareness on the transmission of HIV and other infections through blood transfusion and as such individuals will prefer to donate blood to their sick relatives. Some hospitals like JUTH have adopted a policy of collecting blood only from voluntary donors but this is not the case in all hospitals in Jos. The extended and closely-knit family system as practiced in most parts of Africa usually rallies people around a sick relative making it more likely that a relative will donate blood when necessary. This closely-knit family system is demonstrated by the observation that relatives donated 95% of the 302 blood units donated voluntarily.

Blood is still not universally screened in Jos, Nigeria. Four units of blood were unscreened while the screening status of 36 units was not known. The 4 unscreened blood units were transfused in private hospitals. They were not screened on the basis that they were donated by the fathers of the patients. Though the recipients of the unscreened blood units were HIV negative, they could have been infected with other blood-borne infections. Relatives should therefore insist that all blood irrespective of who the donor is should be screened before being transfused to their patients. Adejuyigbe [3] reported that one HIV positive child was infected through an unscreened blood he received from his father.

No relationship was established between HIV infection and the other horizontal risk factors such as uvulectomy/tonsillectomy, circumcision at home, multiple intramuscular injections outside the hospital, and scarification. Despite the large number of patients who were exposed to unsterilized instruments for various procedures in this study, increased risk of acquiring HIV infection was not established. This contrasts with the reports of Singh [26] and Gisselquist [27] which showed that the use of unsterilized instruments increased the risk of acquiring HIV infection. This may be partly explained on the basis of the short life span of HIV outside the human tissue. Transfer of body fluids through contaminated instruments contributes to the percutaneous transmission of HIV especially if the interval between procedures is short. However it is possible that if there is a long period between procedures, HIV may not survive long enough to infect another person especially if the body fluid has dried up. The process of cleaning, washing and holding the instruments over fire, which is

commonly practiced, will also reduce the possibility of transmitting HIV infection through the percutaneous route.

In this study there was no single case of intravenous drug abuse or sexual activity either voluntary or as sexual abuse. Meel [28] had reported a high incidence of child sexual abuse in South Africa. Slap [29] had reported that 50% of adolescents in Nigeria have had a sexual debut by 16 years of age. This difference could be as a result of non-disclosure by some parents and patients. Also, sexual maturity is delayed in SCA patients [21] and this could delay the onset of voluntary sexual activity. In this study 46.7% of males aged 14 years and above and 45.5% of females aged 13 years and above had delayed puberty.

Harmful cultural practices such as uvulectomy and scarification are still rampant in Jos, Nigeria. In this study, it was observed that about 65% of the children had uvulectomy and/or scarification. Peters [30] had reported a serious HIV related risk inherent in harmful cultural practices of Nigerian traditional healers. Though the prevalence of HIV was not higher in this group of patients, other microorganisms could have been transmitted through the procedure. They are also prone to sepsis, tetanus and complications of haemorrhage. Such practices should therefore be discouraged since they add no medical advantage to life even if they were done in sterile conditions.

This study has a limitation. The power of the study could have been increased by using 4 controls for 1 case; we however used 1 control for 1 case.

5. CONCLUSION

The prevalence rate of HIV infection in transfused children with SCA in Jos, Nigeria was 2% in this study. The four HIV positive cases were transfused in private hospitals. Those that received blood from remunerative donors were 6 times more likely to acquire HIV through blood transfusion compared to those that received blood from voluntary donors. Screening of blood before transfusion is not yet universally practiced in Jos, Nigeria. We therefore recommend that policies on proper screening of blood before transfusion and voluntary blood donation should be sustained, intensified and enforced at all levels of healthcare.

CONSENT

Written informed consent was obtained from the parents/guardians before any patient was recruited for the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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