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ORIGINAL ARTICLE

Blood transfusion services for patients with sickle cell disease in Nigeria

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Introduction: Safe, timely red blood cell transfusion saves lives and chronic transfusion therapy (CTT) prevents or limits morbidities such as stroke, therefore improving quality of life of patients with sickle cell disease (SCD).

Methods: This questionnaire-based study assessed the ability of sickle cell centers in Nigeria to provide safe blood to patients with SCD between March and August 2014.

Results: Out of the 73 hospitals contacted, responses were obtained from 31. Twenty four (78%) hospitals were unable to transfuse patients regularly due to blood scarcity. Packed red blood cells were available in 14 (45%), while only one provided leukocyte-depletion. Most centers assessed donor risk and screened for HIV in 30 (97%), hepatitis B in 31(100%) and hepatitis C in 27 (87%) hospitals. Extended phenotyping and alloantibody screening were not available in any center. A quarter of the hospitals could monitor iron overload, but only using serum ferritin. Access to iron chelators was limited and expensive. Seventeen (55%) tertiary hospitals offered CTT by top-up or manual exchange transfusion; previous stroke was the most common indication.

Conclusion: Current efforts of Nigerian public hospitals to provide safe blood and CTT fall short of best practice. Provision of apheresis machines, improvement of voluntary non-remunerated donor drive, screening for red cell antigens and antibodies, and availability of iron chelators would significantly improve SCD care in Nigeria.

Keywords: Blood transfusion, Nigeria, Sickle cell disease

Introduction

Nigeria has the largest sickle cell disease (SCD) prevalence in the world; approximately 2.0% of newborns have the disease with a projected exponential increase in the coming years.[1] The most severe SCD syndrome, homozygous hemoglobin S disease (HbSS) or sickle cell anemia (SCA) is the phenotype in over 90% of Nigerian patients.[2] It is characterized by chronic anemia, recurrent pain and other life-threatening morbidities ultimately involving all organs and tissues of the body.

Availability of safe blood obtained from voluntary, non-remunerated donors, plays a key role in the standard of care of patients with SCD. Indeed, 40–60% of patients with SCA would require blood transfusion in childhood with many receiving multiple transfusions outside of a chronic transfusion program.[3–6] Chronic transfusion therapy (CTT), to keep the proportion of sickle haemoglobin (HbS) below 30% of total, is the standard of care for primary and secondary stroke prevention and management of patients with recurrent episodes of acute chest syndrome or severe painful events. It also improves the patient's quality of life. Peri-operative blood transfusion before major surgery is also frequently indicated to improve outcome.[7,8]

The current population of Nigeria is approximately 167 million. Administratively, there is a federal government and 36 states divided into six geo-political zones (Figure 1) to ensure equitable distribution of resources. The zones are North-West with seven states, North-Central with seven states plus the Federal Capital Territory, while the North-East, South-West, South-South have six states each and South-East has five. In addition, there are 774 local government councils that bring governance close to the people in the states.

Public hospitals in Nigeria are funded by the federal, state or local governments and are accredited and equipped to offer primary health care (local community clinics), secondary at state levels (general hospitals with some specialist care) and tertiary hospitals where the highest level specialty and sub-specialty health services are available. These include Federal Medical Centers and teaching hospitals, which are affiliated with universities. There are 41 federal government-funded tertiary hospitals listed on the Nigerian Federal Ministry of Health website. There are 16 tertiary and 72 secondary hospitals funded by State governments (http://www.listbesthospitals.com/Hospitals-Nigeria/List-Of-Hospitals-In-Nigeria.aspx), making a total of 129 public hospitals in Nigeria. Only hospitals with dedicated sickle cell clinics were invited to participate in the present study.

The current study aims to document the level of care provided in specialist hospitals with dedicated sickle cell clinics in Nigeria, especially their ability to provide safe blood transfusion as part of standard-of-care and to identify associated challenges.

Methods

This was a cross-sectional, questionnaire-based study focusing on the ability of hospitals in Nigeria to transfuse patients with SCD according to best practice when indicated, as well as documenting some of the challenges encountered. A pre-tested questionnaire was circulated by email using addresses from the mailing lists of the Nigerian Society for Haematology and Blood Transfusion, the Paediatric Association of Nigeria as well as the Nigerian Sickle Cell Disease Network. Doctors from 73 hospitals were contacted, of which 31 responded. Reminders were sent at 8-week intervals by e-mail and phone calls or text messages where phone numbers were available. Only hospitals from which responses were received have been included. The participating hospitals were accredited to provide secondary or tertiary level care and had dedicated sickle cell clinics (pediatric, adult or combined). The consultants or physicians in charge of the clinics were urged to fill in the questionnaire. Respondents were also encouraged to consult with their hematology and blood transfusion units where necessary. The study was conducted between March and August 2014. The responses were returned as email attachments to the first author, who entered the data into Statistical Package for Social Sciences version 20 (SPSS, IBM, Armonk, NY, USA) which was used for the analysis.

Results

Out of Nigeria's 129 public secondary and tertiary hospitals, 31 hospitals participated in the study. Their geo-political locations and level of healthcare accreditation are shown in Figure 1. The majority (28, 90%), of responding hospitals were tertiary hospitals, while three (10%) were secondary. The North-East zone had the lowest representation with one tertiary hospital (3.2%), while the South-West was the most represented with 10 (32%): three secondary and seven tertiary hospitals.

Although all the hospitals have facilities for whole blood transfusion, only 14 (45%; one secondary and 13 tertiary) provide true packed red blood cells. Washed red cells were available in two tertiary hospitals, and leukocyte-depleted cells in one tertiary hospital. No hospitals provided irradiated blood products. Centrally-administered blood banking services were available in six (19%) of the hospitals in the survey: four in the South-West and two in the North-West zone.

When asked how often they were unable to transfuse a SCD patient because of unavailability of blood, 17 (55%) responded, 1–2 times monthly while seven (23%) had scarcity three or more times monthly. However, the frequency of requests for blood transfusion was not documented. Only one tertiary hospital based in the South-East zone, reported no scarcity of blood for their SCD patients. The practices of the various hospitals in screening potential blood donors clinically and with laboratory tests are shown in Table 1. Most have a risk assessment interview and about half administer a lifestyle questionnaire. Most of the centers screen the donors for HIV (97%), hepatitis B (100%) and hepatitis C (87%). All centers carry out only ABO and Rhesus D cross-matching; facilities for extended phenotyping or screening for alloantibodies were not available. Routine monitoring of patients for iron overload was possible in six of the 25 hospitals (24%) using serum ferritin. There were six non-responders. Liver iron estimation by ferriscan and biopsy were not available in any hospital.

Seventeen (55%) tertiary hospitals offered CTT to adult or pediatric patients with SCD within 2 years preceding the study. However, in 15 (88%), that attempted CTT, the program could not be sustained mainly due to unavailability of blood. The major indications for chronic transfusion included previous stroke in 14 (82%) patients, recurrent acute chest syndrome in seven (41%), high ischemic stroke risk in two (12%), chronic leg ulcer in five (29%) and pulmonary hypertension in one patient (6%).

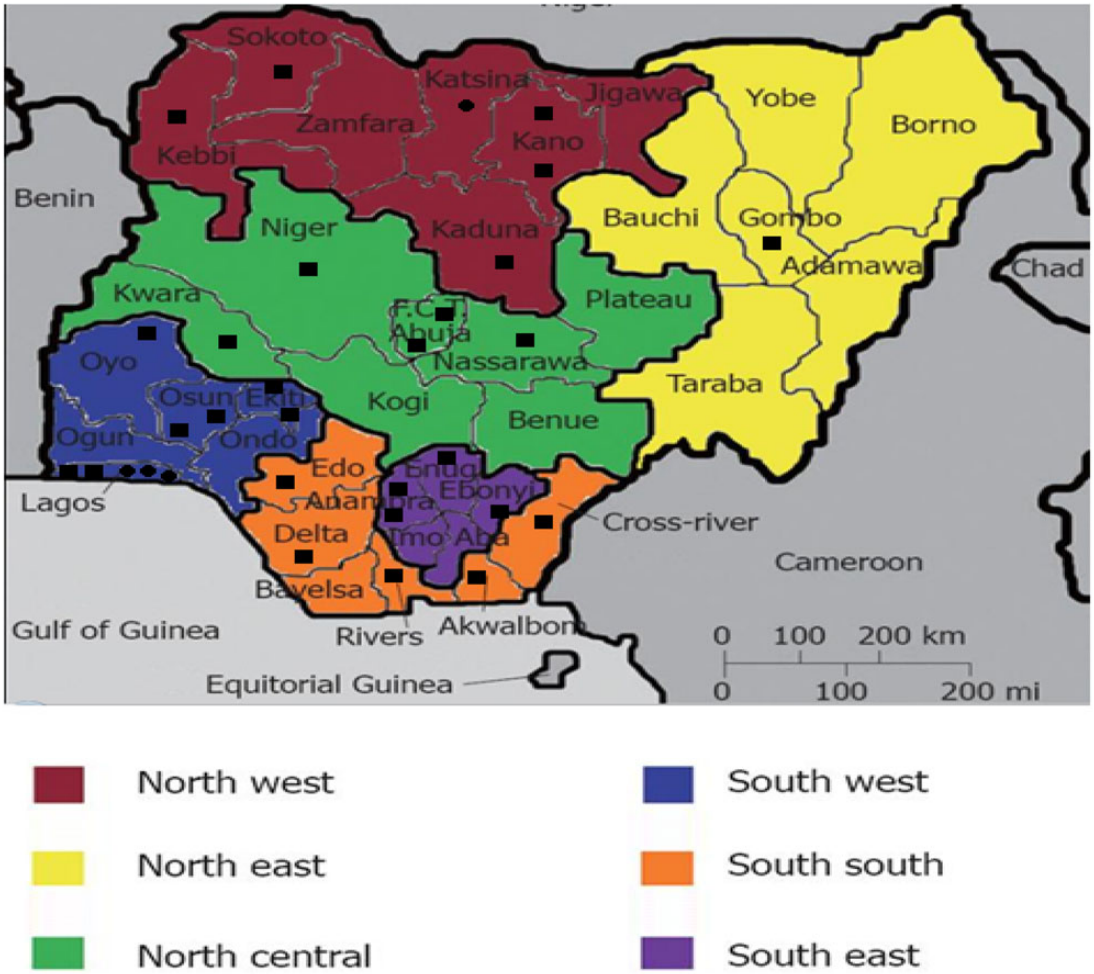

Figure 1. The six geo-political zones of Nigeria. The tertiary centers in the study are shown in black squares while the circles are the secondary centers. F.C.T.: Federal Capital Territory. This figure is available in black and white in print and in color at International Health online.

Table 2 shows the modalities for monitoring patients on CTT. Of the 16 centers that responded to the question on iron status monitoring, only five (31%) measured serum ferritin and none had ferriscan or offered liver biopsy. No center monitored alloantibodies and only one could do Coomb's test. All the 17 centres screen for HIV, hepatitis B and C except for one that did not screen for the latter. Automated exchange transfusion was not available in any center during this study. However a few centers have subsequently acquired this capability. Table 3 shows the most common way that exchange blood transfusions for CTT was performed was manually through large peripheral veins.

Challenges encountered with CTT programs include financial constraint 14 (82%), inadequate blood availability 12 (71%), defaulting patients 12 (71%), delay in procuring blood 11 (65%), transfusion reactions in three patients (18%), death despite chronic transfusion in three (18%), stroke despite transfusion in one patient (6%) and known alloimmunization in two (12%).

The average cost of one unit of blood is ₦4783.33 (about US$24) while only one hospital offers free blood transfusion service. Cost of chelation therapy using manufacturer's recommended age and weight appropriate doses of daily oral Deferasirox (Ansura marketed by Novartis, Mushin, Lagos State, Nigeria) where available ranged from ₦3000.00 (about US$15) in children to ₦80 000.00 (about US$400) in adults, monthly. The difference in cost is probably associated with the dosage and amounts used, although these were not documented. The other costs associated with blood transfusion were not estimated.

Only one tertiary center offers bone marrow transplantation and it is located in the South-South zone of the country. They are unable to provide irradiated blood and do not routinely screen donor blood for syphilis, cytomegalovirus, Epstein Barr virus, human papilloma virus or rubella.

Discussion

There is a good network of dedicated public specialist sickle cell clinics cutting across all geo-political zones in Nigeria. The current survey focuses on the ability of these centers to provide timely and safe red cell transfusion and monitor for common complications, particularly transfusion reactions, alloimmunization, transfusion-transmissible infections and to detect and manage iron overload.

Table 1. Blood donor screening practices

	Responses	Level of care		Total n=31 n (%)
		Secondary n=3	Tertiary n=28	
Routine donor blood screening practices				
Risk assessment by interview	No	0	3	3 (9)
	Yes	4	24	28 (90)
Lifestyle questionnaire	No	1	13	14 (45)
	Yes	3	14	17 (55)
Examination: pallor	No	4	27	31 (100)
	Yes	0	0	0
Blood pressure measurement	No	1	6	7 (23)
	Yes	3	21	24 (77)
Donor screening laboratory test				
PCV/Hb	No	1	1	2 (6)
	Yes	3	26	29 (94)
HIV screening	No	0	1	1 (3)
	Yes	4	26	30 (97)
Hepatitis B screening	No	0	0	0
	Yes	4	27	31 (100)
Hepatitis C screening	No	1	3	4 (13)
	Yes	3	24	27 (87)
Syphilis screening	No	2	11	13 (42)
	Yes	2	16	18 (59)
EBV screening	No	4	27	31 (100)
CMV screening	Yes	0	0	0
	No	4	26	30 (97)
	Yes	0	1	1 (3)
Malaria parasites screening	No	4	26	30 (97)
	Yes	0	1	1 (3)
Rubella screening	No	4	27	31 (100)
	Yes	0	0	0

CMV: cytomegalovirus; EBV: Epstein-Barr virus; HPV: human papilloma virus; PCV: packed cell volume.

The best-practice guidelines recommend that blood transfusion given to patients with SCD should be leukocyte-depleted red blood cells, antigen-matched for Cc, Ee, K or other antigens for which antibodies are found in the recipient. In addition, such transfusions should be with blood devoid of HbS as much as possible.[9,10]

WHO guidelines for blood donation and safety recommend a centrally/nationally coordinated blood transfusion service that can provide sufficient, suitable and timely amounts of blood from voluntary, non-remunerated donors rather than family or commercial donors.[11] Donors should be screened for fitness to donate and for epidemiologically-relevant, transfusion-transmissible disease.

Hospitals providing blood transfusion through centrally-coordinated blood banking regulatory systems are in the minority in this survey with most administering transfusions at their discretion. Most centers also depend on commercial or family donors. Hence it is not surprising that they often experience blood scarcity. Previous studies have reported inadequate donor blood resulting in predominant use of family/replacement donors and commercial donors in the developing world.[12,13]

Other than ABO and Rh D cross-matching, there was no screening for other red cell antigens or alloantibodies in any of the hospitals in the study. Only one tertiary center routinely performs Coomb's test on patients on chronic transfusion. A recent study by Ugwu et al.[14] showed 9.3% prevalence of alloimmunization among Nigerian multi-transfused adults with SCA. But more importantly, the majority (87.5%) of the alloantibodies were against the red cell antigens that are not routinely screened: Rh antigens that are non-D (E, C and e antigens); then Kell, Duffy, Kp, Js and Lutheran antigens, while only 12.5% were against the routinely screened Rh-D antigens.[13] Nickle et al. found that among multi-transfused American SCA patients, the rate of alloimmunization was 29% with anti-E, K, and C among the most commonly detected alloantibodies.[15]

Inability of our hospitals to produce leukocyte-depleted packed red cells raises concerns for safety from diverse transfusion reactions. Moreover, packed red cells could be produced by less than

Table 2. Routine monitoring of chronically transfused patients

	Response, n=17	Frequency (%)
Ability to detect iron overload[a]		
Serum ferritin	No	11 (69)
	Yes	5 (31)
Liver iron by biopsy	No	16 (100)
	Yes	0
Liver iron by Ferriscan[b]	No	16 (100)
	Yes	0
Detection of alloimmunizations		
Red cell antigen	No	17 (100)
	Yes	0
Red cell antibodies	No	17 (100)
	Yes	0
Coomb's test	No	15 (94)
	Yes	1 (6)
Detection of bloodborne infections		
Blood film for malaria parasites	No	17 (100)
	Yes	0
HIV	No	0
	Yes	17 (100)
Hepatitis B	No	0
	Yes	17 (100)
Hepatitis C	No	1 (6)
	Yes	16 (94)
Efficacy of chronic transfusion		
Percentage haemoglobin S	No	13 (76)
	Yes	4 (24)
Steady state PCV	No	0 (0)
	Yes	17 (100)
Reticulocyte count	No	10 (59)
	Yes	7 (41)

PCV: packed cell volume.
[a]One hospital gave no data for iron overload and Coomb's test;
[b]Ferriscan® Lifescan Pharma Pvt. Ltd, Chennai, India.

Table 3. Use of exchange transfusion and type of venous access

Variable n=17	Response	n (Frequency, %)
Exchange blood transfusion	No	2 (12)
	Yes	15 (88)
Type of exchange blood transfusion	Manual	16 (94)
	No response	1 (6)
Type of venous access	Large peripheral vein	16 (94)
	Central vein	0
	No response	1 (6)

half of all hospitals surveyed and about half of the hospitals offering CTT, implying that the efficacy of transfusions is currently suboptimal in these hospitals. Reducing the proportion of HbS to less than 30% as recommended for chronic transfusion, would require more transfusions with whole blood, hence increasing the risk of transfusion reactions, infections and iron overload.

The more units of blood received, the greater the risk of bloodborne infections. HIV, hepatitis B and C were tested for almost universally but it is important to note that donors and chronically transfused patients were not routinely screened for syphilis in all centers currently offering CTT. Falciparum malaria is endemic in Nigeria and poses a significant threat of morbidity and mortality to people living with SCD. However, no hospital screened donor blood for malaria parasites. While it is encouraging that no cases of hepatitis B or HIV were detected among transfused patients in the present study, transfused Congolese SCD patients showed a prevalence of 10% and 11.3% seropositivity for hepatitis B and HIV respectively.[16] Because of the same concern, efforts are being made to limit transfusions among Indian SCD patients.[17] Two previous studies from Nigeria did not report a significant difference in the prevalence of HCV antibodies in transfused and non-transfused SCA patients.[18,19]

Since the first stroke risk assessment study on children with SCD in Ibadan, Nigeria,[20] the need for stroke risk assessment and prevention has been of interest in the country. However, most parents are reluctant to accept chronic transfusion for their children. Hence many Nigerian practitioners have no option but to explore the more acceptable alternative of hydroxyurea, whose efficacy is still under scrutiny but appears promising in lowering transcranial Doppler velocities in patients with SCD.[21,22]

Automated exchange red blood cell transfusion is considered superior to top-up or simple transfusions in the administration of CTT in preventing iron overload, reducing HbS concentration and in keeping blood viscosity at a safe level.[23,24] Among the hospitals that currently offer CTT in this study, two employ top-up transfusion while others offer exchange blood transfusion manually via large peripheral veins. Since the conclusion of this study, 11 centers have received donations of apheresis machines, which would make provision of CTT more practical and optimal.

Chronically-transfused SCD patients accumulate non-transferrin bound iron in the liver, necessitating monitoring their liver iron concentration (LIC).[24,25] The only available parameter for this in the present study is serum ferritin, which is an acute phase reactant, and is not as reliable as MRI technique (Ferriscan® Lifescan Pharma Pvt. Ltd, Chennai, India) for liver biopsy. In addition, iron chelation is either not available or it is very expensive. Only one pharmaceutical company, Novartis, distributes oral Deferasirox for iron chelation. Its high cost in addition to other associated expenses and the unavailability of apheresis machines makes the use of CTT, as standard care, difficult to achieve at the moment. Other persistent challenges including inconsistent power supply, unavailability, the risk of transfusion-transmissible infections and transfusion reactions further limit our hospitals' ability to deliver safe CTT.

Limitations

The participants in this study were contacted using mailing lists compiled from conference attendance and may have excluded potential participants who had not recently attended the conferences organized by the relevant professional bodies, hence limiting our reach. Although 31 out of 129 (24.0%) public secondary and tertiary hospitals participated in the survey, a record was

not created of hospitals that were ineligible because they did not have dedicated sickle cell clinics. The study therefore does not have sufficient information to estimate the proportion of the country's sickle cell clinics that responded to the questionnaire. We are unable to judge the degree to which blood is unavailable for transfusion as the questionnaire was not designed to capture the total number of requests for transfusions for all indications. No estimate could be made of the cost of routine phenotyping and alloantibody monitoring as no hospital provided these services routinely, but the cost is likely high.

Conclusions

Efforts of Nigerian hospitals to provide exchange transfusion for CTT are commendable but currently fall short of best practice. Issues such as availability of adequate, safe blood require improvement of voluntary, non-remunerated donor drives and possibly have an exclusive donor pool for sickle cell patients free of charge from a centrally administered blood banking service. Provision of apheresis machines by the government or through North-South partnerships and improved screening for transfusion transmissible infections, red cell antigens and their antibodies would improve the services significantly. Local manufacture and subsidy of iron chelation agents would improve access greatly. Hydroxyurea may be the most accessible option as CTT may be unsustainable and is associated with considerable potential dangers.

Authors'contributions: IND contributed to the design of the study, and led the analysis and first draft of the paper. SBA, SAA, SA, OA, TA, AA, NAA, AA, AA, JA, SA, AB, BB, OE, IE, IG, AG, AH, GUK, OAL, CM, AJM, AM, MN, OEN, DN, FO, CO, RO, OSO, OO, HO, NIU, AUM, SA, AU, EU and BWJ all participated in the design and testing of the questionnaire before gathering the data, critically reviewing and contributing to the manuscript and reviewing the final draft. ADA contributed to the design, analysis and preparation of the manuscript. IND and ADA are the guarantors of the paper.

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