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ORIGINAL ARTICLE

Current sickle cell disease management practices in Nigeria

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Background: Although Nigeria has the highest burden of sickle cell disease (SCD) worldwide, there is still variable and poor utilisation of standard-of-care practices for SCD patients in the country.

Methods: This was a questionnaire survey of doctors in some dedicated SCD clinics in Nigeria in order to document the facilities available and common management practices.

Results: There were responses from 18 clinics based in 11 institutions. The number of patients being followed in each centre ranged from 15 to approximately 11 000. All clinics provided malaria prophylaxis and folic acid routinely to their patients. Only eight clinics prescribe penicillin prophylaxis. Eight prescribe hydroxyurea to patients who can afford it when indicated. All of the centres except three have electronic cell counters, but all had access to haemoglobin electrophoresis. Three had high-performance liquid chromatography machines installed but none was being routinely used. One institution had a functioning molecular biology laboratory. There is no official newborn screening programme in the country. All had access to microbiology and chemistry laboratories. Nine institutions had CT, six had MRI and three had transcranial Doppler facilities.

Conclusion: The care available for SCD in Nigeria is still suboptimal and there is an urgent need for concerted effort to tackle the problem, but to make a significant impact on the burden of the disease would require more focus at the primary care level. Some steps to achieving this are outlined.

Keywords: Sickle cell disease, Nigeria, Management, Future projections

Introduction

Sickle cell disease (SCD) is a hereditary disorder in which an individual has inherited two abnormal Hb genes, at least one of which is responsible for the production of sickle Hb (HbS). The most common clinical phenotype is the homozygote, i.e. HbSS, also known as sickle cell anaemia. Compound heterozygotes include HbSC, SD, SO-Arab and Sβthal, which are all collectively (in addition to SS) referred to as SCD. The HbS gene became prevalent in different parts of the world following selective pressure because the heterozygote (HbAS) is protected against some of the deleterious effects of malaria. Therefore, SCD is found at its highest frequencies in parts of the world where malaria is or was endemic. In addition, because of slave trade and recent migrations, it is now found even more widely including in Europe and the USA.[1] Nonetheless, the prevalence is highest in tropical Africa and, indeed, the country with the highest burden is Nigeria where the trait occurs in 25–30% and sickle cell anaemia occurs in approximately 2% of all births.[2]

The most common features of SCD are chronic haemolytic anaemia and recurrent vaso-occlusion. The latter is responsible for the painful crises that characterise the disease. There is also a chronic vasculopathy triggered by free heme resulting in nitric oxide scavenging and upregulation of adhesion molecules in reticulocytes, neutrophils and endothelial cells.[3,4] This is further complicated by a procoagulant state following the activation of platelets.[3,5] There is smooth muscle dystonia and eventual hyperplasia, which contributes to vascular occlusions. This explains the plethora of features and complications seen in SCD.

The major cause of mortality in childhood is overwhelming bacterial infections especially due to encapsulated organisms, principally pneumococcus.[6,7] This is secondary to a variety of immune defects in the disease, the most important of which is splenic dysfunction.[8] Acute chest syndrome,[9] stroke[10,11] and

multiple organ failure[12] are other not uncommon causes of death. In older patients, chronic organ failure, especially renal failure, becomes quite important.[13] Some other distressing, but not necessarily fatal, complications include chronic leg ulcers and avascular bone necrosis typically affecting the femoral heads.[14,15]

Most SCD patients in the developing world, especially those living in rural areas with little access to medical care, die before their 5th birthday. Malaria contributes not only to mortality but also to anaemia and other crises.[16,17] While the lifespan of SCD patients was also quite dismal in the USA prior to the 1970s, there has been a dramatic upturn in the last 30 years such that most patients now live into their 40s and 50s.[18] The main factor responsible for this turnaround is the availability of comprehensive care with newborn screening for early diagnosis,[19] penicillin prophylaxis,[20] pneumococcal vaccination[21,22] and the use of transcranial Doppler (TCD) ultrasound to predict patients at risk of stroke who are then treated on chronic transfusion programmes.[23,24] Use of hydroxyurea, which is effective in reducing the frequency of painful crisis, acute chest syndrome and anaemia, has changed the outlook of the disease both in adults and children.[25,26]

Despite the high burden of SCD in Nigeria, a national policy to combat the disease is still awaiting ratification and many of the new modalities of management are not widely available. In 2010, the Nigerian SCD Network (NSCDN) was established as a co-operating body bringing together Nigerian physicians, non-governmental organisations (NGOs) and other interested bodies both within the country and in the Diaspora. One of the first tasks of the network was a survey to document the available facilities and the prevalent management practices in SCD clinics in the country in order to put the current situation in perspective and to enable planning and rational research projections. Here we present the analysis of this survey and suggest ways of moving forward to improve the care of patients in the country.

Box 1. Characteristics and practices in sickle cell disease (SCD) clinics

Name and location of the clinic
Number of patients currently being followed
Is there an institutional medical records department?
Is there a database of SCD patients and if so, what type?
Is there regular use of the following:
  a) folic acid
  b) malaria prophylaxis
  c) penicillin prophylaxis
  d) hydroxyurea?
Is there use of other medications, including herbal preparations?

Box 2. Facilities available in the sickle cell disease clinics

Electronic cell counter
Hb electrophoresis
high-performance liquid chromatography
Newborn screening
Isoelectric focusing
Microbiology laboratory
Chemistry laboratory
Molecular biology laboratory
CT
MRI
Transcranial Doppler ultrasound

Materials and methods

This was a questionnaire study conducted with the physicians on the mailing list of the NSCDN between January and June 2011. Only doctors who were in charge of dedicated SCD clinics were encouraged to respond. The first part of the questionnaire was devoted to documenting the characteristics of the clinics and their common practices (Box 1), while the second part sought to document the available facilities (Box 2).

Results

There were 18 responses from 11 institutions in the country (8 in university teaching hospitals, 1 in a general hospital, 1 in a federal medical centre and 1 run by an NGO) (Table 1). Three of these institutions are in the northern part of the country and eight are in the south. Most of the teaching hospitals have an adult and a paediatric clinic. Four clinics were mixed, i.e. with both adult and paediatric patients. The number of patients currently being followed in the clinics varied from 15 to ~11 000. All institutions had medical records facilities and most also had some form of database of their SCD patients. All clinics administer folic acid and malaria prophylaxis to their patients; however, only 8 of the 18 clinics prescribed penicillin prophylaxis. More importantly, only four of the eight paediatric clinics use penicillin prophylaxis. Pneumococcal vaccines are not offered routinely in any centre, although some of the paediatric clinics encourage patients who can afford it to obtain it. Only 8 of the 18 clinics prescribe hydroxyurea. Ciklavit is the most commonly prescribed local medicine derived from herbal preparations and it is used in eight clinics. Other preparations occasionally used include omega 3 fatty acids.

Three centres (Federal Medical Centre–Asaba [FMCA], Murtala Mohammed Specialist Hospital [MMSH] and Obafemi Awolowo University Teaching Hospital [OAUTHC–Ile-Ife and Ilesha]) did not have electronic cell counters; all had facilities for Hb electrophoresis, but only three had high-performance liquid chromatography (HPLC) machines installed but not routinely used, and none had isoelectric focusing facilities (Table 2). There was no established newborn screening programme in any of the centres. All had access to microbiology and chemistry laboratories. Only one (University of Nigeria Teaching Hospital [UNTH]) had a functioning molecular biology laboratory with capability for β^S-globin gene haplotyping and α-globin genotyping, while the facilities in Lagos (Lagos University Teaching Hospital [LUTH] and Sickle Cell Foundation [SCF]) were just being installed. Most institutions have access to CT and MRI facilities. TCD is available in three institutions (Ahmadu Bello University Teaching Hospital [ABUTH], LUTH

Table 1. Characteristics of clinics and common practices

No.	Clinic	City	Adult/paediatric	Approx. no. of patients	Medical records (Y/N)	Database (Y/N)	Folic acid (Y/N)	Malaria prophylaxis (Y/N)	Penicillin (Y/N)	Hydroxyurea (Y/N)	Ciklavit
1	ABUTH	Zaria	Adult/paediatric	1150	Y	N	Y	Y	N	Y	N
2	ABUTH	Zaria	Paediatric	1700	Y	Y	Y	Y	Y	N	N
3	AKTH	Kano	Adult	270	Y	Y	Y	Y	Y	Y	N
4	AKTH	Kano	Paediatric	1300	Y	Y	Y	Y	Y	Y	N
5	FMCA	Asaba	Paediatric	100	Y	N	Y	Y	Y	N	Y
6	FMCA	Asaba	Adult	15	Y	Y	Y	Y	N	N	Y
7	LASUTH	Lagos	Adult	2200	Y	Y	Y	Y	N	N	Y
8	LASUTH	Lagos	Paediatric	670	Y	Y	Y	Y	N	N	N
9	LUTH	Lagos	Adult	1000	Y	Y	Y	Y	Y	Y	Y
10	LUTH	Lagos	Paediatric	1500	Y	Y	Y	Y	Y	Y	Y
11	MMSH	Kano	Adult/paediatric	11 000	Y	Y	Y	Y	Y	Y	N
12	OAUTHC	Ile-Ife	Adult	200	Y	Y	Y	Y	N	N	Y
13	OAUTHC	Ilesha	Paediatric	145	Y	Y	Y	Y	N	N	Y
14	SCF	Lagos	Adult/paediatric	270	Y	Y	Y	Y	N	N	Y
15	UCH	Ibadan	Paediatric	500	Y	Y	Y	Y	N	Y	N
16	UCH	Ibadan	Adult	1000	Y	N	Y	Y	N	N	N
17	UNTH	Enugu	Paediatric	350	Y	Y	Y	Y	N	N	N
18	UATH	Abuja	Adult/paediatric	350	Y	Y	Y	Y	Y	Y	N

ABUTH: Ahmadu Bello University Teaching Hospital; AKTH: Aminu Kano University Teaching Hospital; FMCA: Federal Medical Centre, Asaba; LASUTH: Lagos State University Teaching Hospital; LUTH: Lagos University Teaching Hospital; MMSH: Murtala Mohammed Specialist Hospital; N: no; OAUTHC: Obafemi Awolowo University Teaching Hospital; SCF: Sickle Cell Foundation; UCH: University College Hospital; UNTH: University of Nigeria Teaching Hospital; UATH: University of Abuja Teaching Hospital; Y: yes.

Table 2. Facilities available in the different clinics/hospitals

No.	Clinic	City	Electronic cell counter	Hb electrophoresis	HPLC	Newborn screening	IEF	Microbiology laboratory	Chemistry laboratory	Molecular biology laboratory	CT	MRI	TCD
1	ABUTH	Zaria	Y	Y	N	N	N	Y	Y	N	Y	Y	Y
2	ABUTH	Zaria	Y	Y	N	N	N	Y	Y	N	Y	Y	Y
3	AKTH	Kano	Y	Y	N	N	N	Y	Y	N	Y	Y	N
4	AKTH	Kano	Y	Y	N	N	N	Y	Y	N	Y	Y	N
5	FMCA	Asaba	N	Y	N	N	N	Y	Y	N	N	N	N
6	FMCA	Asaba	N	Y	N	N	N	Y	Y	N	N	N	N
7	LASUTH	Lagos	Y	Y	N	N	N	Y	Y	N	Y	Y	N
8	LASUTH	Lagos	Y	Y	N	N	N	Y	Y	N	Y	Y	N
9	LUTH	Lagos	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y
10	LUTH	Lagos	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y
11	MMSH	Kano	N	Y	N	N	N	Y	Y	N	N	N	N
12	OAUTHC	Ile-Ife	Y	Y	Y	N	N	Y	Y	N	Y	Y	N
13	OAUTHC	Ilesha	N	Y	N	N	N	Y	Y	N	Y	N	N
14	SCF	Lagos	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
15	UCH	Ibadan	Y	Y	N	N	N	Y	Y	N	Y	Y	Y
16	UCH	Ibadan	Y	Y	N	N	N	Y	Y	N	Y	Y	Y
17	UNTH	Enugu	Y	Y	N	N	N	Y	Y	Y	Y	N	N
18	UATH	Abuja	Y	Y	Y	N	N	Y	Y	N	Y	N	N

ABUTH: Ahmadu Bello University Teaching Hospital; AKTH: Aminu Kano University Teaching Hospital; FMCA: Federal Medical Centre, Asaba; IEF: isoelectric focusing; HPLC, high-performance liquid chromatography; LASUTH: Lagos State University Teaching Hospital; LUTH: Lagos University Teaching Hospital; MMSH: Murtala Mohammed Specialist Hospital; N: no; OAUTHC: Obafemi Awolowo University Teaching Hospital; SCF: Sickle Cell Foundation; TCD: transcranial Doppler; UCH: University College Hospital; UNTH: University of Nigeria Teaching Hospital; UATH: University of Abuja Teaching Hospital; Y: yes.

and University College Hospital [UCH]). The SCF shares imaging facilities, including TCD, with LUTH.

Discussion

The current population of Nigeria is approximately 160 million and administratively there is the federal government at the centre, 36 state governments and 774 local government councils.[27] The structure of healthcare delivery in the country is such that primary care is delivered by the local government, secondary care by the state government and tertiary care by the federal government.[27,28] The latter is through federal medical centres, of which there are 22, generally situated in state capitals depending on need. There are also 22 university teaching hospitals that are generally situated in large urban areas. SCD patients are generally cared for in the secondary and tertiary institutions, but there are few clinics or centres that are dedicated to these patients. The existing ones are often situated in teaching hospitals.

It is estimated that there are >40 million sickle cell carriers in Nigeria and >150 000 babies are born yearly with the disease. Because of the associated rampant mortality, it is estimated that there are only approximately 1 million surviving past childhood. All of the clinics in the present survey are in tertiary or secondary health institutions, which are expected to provide the best care available to SCD patients. In addition, they should be in the forefront of research into different aspects of the disease. There is therefore a minimum standard that is expected in such centres. They should have facilities including haemoglobin electrophoresis and HPLC to confirm the diagnosis of SCD. They should have capacity (both in terms of personnel and equipment) for diagnosing and treating the commonly associated problems; namely severe anaemia, pain crisis, infections, acute chest syndrome, gallstones, leg ulcers, stroke etc. Therefore, the supportive laboratory and imaging services should be of top quality. Because ischaemic stroke is a major devastating complication, which can be prevented, TCD should be available to identify children at risk.

The present report has highlighted some of the existing deficiencies in the management of SCD in Nigeria. While the numbers of patients covered in this survey is very small compared with the overall burden of the disease, it is nonetheless typical of the care available in tertiary institutions in the country. It is encouraging that all centres prescribe malaria chemoprophylaxis since the infection is the commonest trigger of crises and it is also associated with considerable morbidity and mortality. Penicillin prophylaxis and pneumococcal vaccination are still sparingly used. Initial reports from Nigeria and some other African countries[29–31] had reported a low incidence of invasive pneumococcal disease, but there might have been several confounding factors in those studies, e.g. the patients might have succumbed to overwhelming infections before reaching the hospital, extensive use

of non-prescription antibiotics, suboptimal laboratory isolation techniques and the non-longitudinal nature of the studies.[32,33] Until there is firm evidence to the contrary, it is prudent to assume a high risk for invasive pneumococcal disease and to provide penicillin prophylaxis and pneumococcal vaccines especially to children who are most at risk.

Although questions regarding blood transfusion were not specifically included in this study, discussion with the centres showed that all have blood banks. However, most depend on family or commercial donors for their supplies. This and other factors severely limit the scope of transfusions, and chronic transfusion programmes are not a realistic option even when indicated.

Given the enormous burden of SCD in Nigeria, focusing on tertiary care will probably not make an appreciable impact in improving the overall outcome in terms of control and survival. The more practical strategy would be to tackle the problem at the primary healthcare (PHC) level following a well articulated national policy. It is gratifying that a policy has been formulated in the context of non-communicable diseases in the country and is awaiting ratification. Moreover, a Bill for the Control and Management of Sickle Cell Disease, which provides comprehensive provisions for SCD, was recently presented to the National Assembly.

The care of SCD patients at the PHC level should revolve around the following:

(1) Training: PHC workers should be trained in the aetiology, presentation and common complications of SCD. They should also be able to provide basic genetic counselling to dispel the myths and stigma that surround the disease. Such trained personnel should be available in every PHC clinic.
(2) Awareness and education: massive awareness drives organised with involvement of the media, community/religious leaders, committed advocates from the political class, sports and other celebrities, and key players in the private sector. This should be on an on going basis in each local government area. Learning about SCD should also be incorporated into the primary school curriculum.
(3) Early diagnosis, preferably through universal newborn screening, has to be introduced, with the enrolment of identified patients in a follow-up clinic.
(4) Health surveillance: all patients should be seen in a clinic on a regular basis. They must have access to a minimum level of care, which should include malaria prophylaxis, folic acid supplementation, penicillin prophylaxis and pneumococcal vaccination in children.
(5) Referral to a secondary or tertiary institution as necessary. The latter should focus on providing specialist care, including hydroxyurea therapy when indicated, and screening for patients at risk for stroke using TCD. A reliable blood supply should also be available for acute and chronic needs.

Some practical steps have been taken in the last few years to pursue programmes of SCD control and management. There is now a SCD desk, with a designated officer at the Non-Communicable Diseases Division of the Federal Ministry of Health, that controls SCD-related programmes in the country. There is a commitment to newborn screening and six comprehensive SCD centres have been established in the different geopolitical zones of the country. Informational and educational pamphlets have been prepared for wide distribution. Management protocols and guidelines have also been prepared to ensure uniformity and accepted management of SCD in the country. A national SCD policy has been prepared and should be ratified soon. A Bill for the Control and Management of Sickle Cell Disease was also presented to the National Assembly in 2011, and it is hoped this will eventually become a legislated Act. It should also be mentioned that since the completion of the present study, there have been some improvements in the facilities available and more centres now have TCD, and the use of hydroxyurea and penicillin prophylaxis is more widespread.

It appears that Nigeria is on the cusp of a major resurgence in SCD-related activities but it will take political will and commitment from all arms of government as well as the involvement of international funding agencies and private companies to realise the potential possibilities. There are vast research opportunities and there are many well-trained Nigerian professionals available for translational research and to provide excellent care to patients. The problem of SCD has to be tackled now for Nigeria to have a realistic chance of meeting the WHO Millennium Development Goals.

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