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## Implementing comprehensive health care management for sickle cell disease in an African setting

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**Abstract:** Sickle cell disease is the commonest single gene disease in Africa. Morbidity and mortality from this disease has remained unacceptably high in Africa whereas there has been a marked reduction in the burden of this disease in the developed countries. This reduction was not achieved through the use of sophisticated care such as bone marrow transplant, but through the adoption of a Comprehensive Health Care Management protocol for sickle cell disease. This protocol of care emphasizes prevention of crises through effective management of the disease. In Africa, where sickle cell disease is prevalent, this strategy of care is yet to be globally adopted. In 2003, this protocol of care was adopted at the University of Benin Teaching Hospital, Nigeria and this has contributed to the improved clinical status of children with sickle cell disease in the hos-

pital. The mortality rate among children with sickle cell disease has reduced to 1.3%, requirement for recurrent blood transfusion has reduced to about 2%, and their nutritional status has improved: 75.9% have normal nutritional status while 7% are actually overweight. The frequency of bone pain crisis has reduced to about one in every two years and some of the patients have been crisis-free for as long as five years. Hydroxyurea is not routinely used for our patients so this cannot explain the marked improvement recorded. In conclusion, comprehensive health care, adapted to our setting is a very cheap and effective way of managing sickle cell disease. It can be utilized in all health facilities for the care of children with sickle cell disease and is capable of reducing the morbidity and mortality associated with the disease as well as improving their quality of life.

### Introduction

Sickle cell disease (SCD) is the commonest single gene disease in Africa.<sup>1</sup> About 40 countries in Africa and at least 23 countries of West and Central Africa carry the <sup>s</sup> gene.<sup>2</sup> In Nigeria, 20-25% of the population are carriers of the genetic abnormality,<sup>3</sup> and about 3% of babies are born with the disease<sup>4</sup>. The basic pathology in SCD is the polymerization of haemoglobin following deoxygenation, a process that results in vaso-occlusion, which is the hallmark of the disease<sup>5</sup>. This process results in various forms of complications such as bone pains, abdominal pain, cerebrovascular accidents and priapism, which characterize the disease. In addition, children with SCD are prone to various forms of infections as a result of defective immunity arising from defective splenic functions,<sup>6,7</sup> functional abnormalities of white cells<sup>8</sup> as well as abnormalities of the complement pathway.<sup>9</sup> The mortality rate in SCD has remained high in Africa.<sup>10-13</sup> Bone marrow and stem cells transplant offers the potential for clinical cure in SCD. This modality of treatment is very expensive and thus, not available to a majority of

children with SCD. Therefore, alternative treatment modalities which are effective in reducing the morbidity and mortality associated with SCD as well as improving the quality of life in SCD are highly desirable.

The management of SCD continues to pose a challenge in Africa. Not only does the populace have poor knowledge of the disease,<sup>14</sup> the healthcare providers may also not be familiar with the current concepts in the management of the disease. The management of SCD in most health facilities in Africa largely addresses the complications of SCD rather than the disease itself hence, morbidity and mortality in SCD has remained high. In some developed countries, comprehensive health care was adopted as the strategy for the management of SCD and this has resulted in the reduction of mortality from 16-30% to less than 1% in that setting.<sup>15-18</sup> This method of care, as practised in the developed countries, requires the involvement of several professionals such as the genetic counsellor, paediatric haematologist and the social worker among others. This multi-disciplinary approach offers a holistic form of care to children with

SCD and ideally should be the model of care. In Africa and other developing countries where SCD is prevalent, the form of care described above is not within reach due to dearth of most of the required health professionals. Therefore, there is a need to adapt this form of care for the low-resource settings in Africa where SCD is prevalent. This model of care has been successfully adopted in Cotonou, the Republic of Benin. This resulted in a drastic reduction of morbidity and mortality associated with SCD in the country. In recognition of this adaptation, the World Health Organisation, at the meeting of the Regional Committee for Africa in June 2010, proposed that by 2020, half of the 23-Member States with high prevalence of SCD should have developed and commenced the implementation of a clearly designed National Sickle Cell Control programme within the context of a National Health Strategic Plan. It is also expected that 25% of the countries in the African Region should have adopted the concept of comprehensive health care management by the year 2020.<sup>19</sup> This strategy was adopted by the Sickle Cell Centre at the Republic of Benin in 1993<sup>20</sup> and the University of Benin, Benin City, Nigeria in 2003. In Cotonou, the Republic of Benin where this strategy of care is being utilized, the mortality of SCD dropped to 15.5/ 10000, a value ten times less than the overall Under-Five mortality rate in that country.<sup>21</sup> In Italy where this strategy was also adopted, the morbidities and mortality associated with SCD have reduced.<sup>22</sup>

In the last 13 years, the Paediatric Haematology Unit of the University of Benin Teaching Hospital has managed 547 children with sickle cell anaemia (SCA) using the new protocol. Twenty children with SCA died over this period; the majority of the deaths occurred among 13 children referred from other facilities on account of complications of SCA. Seven children in the new protocol died; two from acute chest syndrome, one from liver failure, one from sequestration crisis (died in a private facility) and the rest from sepsis. In the last five years, all the deaths among children in the programme occurred at the Children Emergency Room before the Paediatric Haematology Unit could have an input in their care. The admission rate for sickle cell crises has reduced to an average of one in about two years with some children being crises-free for five years. The transfusion rate has also reduced drastically to less than 2% and the mortality rate amongst our cohort is 1.3% (7/547). Using the Body Mass Index (BMI)-Z scores in a recent nutritional survey of 187 children with SCD, the nutritional status of the children in this programme was similar to that of their peers, with a reduction in the prevalence rate of severe malnutrition to less than 18%. Indeed, 75.9% had normal nutritional status while 7% were overweight. With these achievements, it became necessary to share this method of care so healthcare providers in other parts of the country and beyond, can adopt same and more children with SCD may benefit from its numerous advantages.

### *Management of sickle cell disease*

It is important to stress that the management of SCD is not synonymous with the management of the complications of the disease. Patients with SCD only have chronic anaemia as a constant feature of the disease. While chronic anaemia is the only constant feature of SCD, other morbidities associated with the disease are actually complications of the disease. The aim of managing SCD includes the prevention and early recognition of the complications of the disease. These complications are, usually, the causes of death in SCD.

The concept of Comprehensive Health Care management of SCD is hinged on the following constituent services which are provided by the clinician during clinic visit:<sup>19</sup>

- Parental counselling and education.
- Education on the need for adequate nutrition.
- Education of the need for adequate hydration.
- Early identification of fever and its urgent treatment
- Early identification of a large spleen.
- Use of prophylactic medications like Penicillin V, anti-malarial drugs, Folic acid and Vitamin C.
- Immunization against infections which are common to children with SCD such as *Salmonella*, *Hemophilus influenzae* type b, Pneumococcus and Hepatitis B virus infections.
- Need for regular hospital follow-up.

### *Parental counselling and education*

The knowledge of how sickle cell disease is acquired has remained very poor amongst Africans despite the high prevalence of the disease in this area.<sup>14</sup> Therefore, marriage between carrier individuals persists without inhibition.<sup>14</sup> Usually, it is the presence of the disease in an affected child that brings the carrier status of the parents to fore. Only very few intending couples practice pre-marital screening for SCD particularly where churches insist on screening before marriages are contracted. In situations where couples co-habit and where marriages are contracted according to traditional practices, screening for SCD is usually not done. In counselling couples with a child who has sickle cell disease, they are taught how the child acquired the disease and the effects of the disease on the child are explained to them to enhance a thorough understanding of the pathophysiology of the disease. The aspect of education is very important in an African setting where mothers are usually blamed for the production of "bad children" or witchcraft when families experience childhood deaths attributed to SCD. In addition, the knowledge of the patho-physiology of the disease helps parents to manage the child with SCD better and comply with the protocol of care.<sup>18</sup> The care of the children enrolled into this programme is accomplished in the homes of the affected families rather than in the hospitals, hence, the need for parental education.

### *Adequate nutrition*

Malnutrition is a common problem among African chil-

dren. A lot of African children are stunted due to poor nutritional intake. In Nigeria, 41% of the general population of children are stunted.<sup>24</sup> It is this same setting that has the bulk of children with SCD. Specifically, SCD poses a high nutritional burden on the affected children. The disease is associated with a high metabolic rate because of the bone marrow hyperactivity.<sup>25,26</sup> The life span of the sickled red cell is 10-20 days instead of the 100-120 days for normal haemoglobin. This places a high nutritional demand on the child with SCD. In addition, a child with SCD also requires the same nutrients for his growth and development. This implies that children with SCD on diet similar to that of healthy children are at risk of failure to thrive in early childhood and stunted grow with delayed secondary sexual characteristics later in life. These children are usually thin with asthenic build. With adequate nutrition, children with SCD are able to achieve normal growth and development as their peers with normal haemoglobin. The stigmata of the disease such as prognatism, skull bossing and long thin extremities have been observed to disappear with adequate nutrition. Therefore, caregivers are advised to feed their children frequently with as much as six to eight meals daily using nutritious diets. Non-nutritious meals or snacks should be discouraged and the parents are advised to ensure children go to school with food instead of snacks.

#### *Adequate hydration*

Vaso-occlusive events occur frequently among children with SCD because the sickled red cells cause hyperviscosity of the blood which results in sluggish blood flow. Dehydration worsens this hyperviscosity and the latter reduces the flow velocity and thus, increases the delay time that is critical in polymer formation.<sup>5</sup> Polymers are responsible for vaso-occlusion which is the hallmark of SCD. Most of the morbidities and mortality which characterize SCD result from multiple organ damage following recurrent vaso-occlusive events. Therefore, the prevention of vaso-occlusive events is important in ensuring not only the wellbeing of the SCD child but also the prevention of chronic organ damage and early death. Children with SCD are advised to drink 2-3L /m<sup>2</sup> of water daily. The child is advised to go about with water in order to facilitate adequate water intake and good hydration. Adequate hydration also enhances the urinary excretion of bilirubin resulting from the chronic haemolytic state in SCD. Children with SCD in our programme remain crisis-free for as long as two to five years following adequate water intake. Hydroxyurea, an anti-sickling drug, is not routinely used for the children with SCD enrolled in the programme hence the use of this medication may not explain the observed improvements among our cohorts.

#### *Early identification and treatment of fever*

Fever is regarded as an emergency in a child with SCD as fever may be a flag sign for infections. Infections are common causes of morbidities and mortality among children with SCD since their immune functions are

usually poor.<sup>27</sup> Caregivers should be taught how to detect fever in children using a thermometer or by feel and report to the hospital once the child with SCD is noticed to be febrile. In most parts of Africa, this advice is very pertinent as most caregivers patronize drug vendors for medications when their children are ill. This contributes to delay in seeking appropriate care for the child with SCD. It is important to note that pneumococcal infections have a doubling rate of 30 minutes.<sup>28</sup>

#### *Early identification of a large spleen*

Splenic function among children with SCD is defective as early as the sixth month of life. However, the most life threatening splenic event in SCD is the sequestration crisis.<sup>29</sup> This event results in the pooling of sickled red cells in the spleen with a resultant severe anaemia and severe hypovolaemia or shock. This event can be fatal if it is not promptly identified and appropriately managed with blood transfusion.<sup>29</sup> Caregivers should be taught how to identify a large spleen in a child. In Africa, identifying a large spleen by caregivers is important as its presence has been associated with anaemia and frequent illness. In traditional parlance, scarification marks are made over the abdomen to "treat the spleen". A large number of children with SCD in Nigeria have these scarification marks on their anterior abdominal wall. The caregivers should be taught how to detect a large spleen in their children during bath. The caregivers are advised to take the child to the hospital if they notice an enlarged spleen for thorough evaluation especially to check the packed cell volume.

#### *Use of prophylactic medications*

Drugs routinely given to children with SCD include Folic acid 5 mg daily, Vitamin C and malaria prophylaxis. Folic acid therapy prevents megaloblastic crises as a result of high red cell turnover, Vitamin C functions as anti-oxidant because of the oxidant stress imposed by the red cell hemolysis<sup>30</sup> while malarial prophylaxis is important for children in malaria-endemic region.<sup>17</sup> Malaria not only worsens the anaemia but is also a cause of frequent morbidity. Penicillin V tablet is administered for the prevention of pneumococcal infections.<sup>31,32</sup> For children less than three years, Penicillin V 125 000 IU is administered twice daily while the dose is doubled for children aged between three and five years. The drug is used along with the pneumococcal vaccine.

#### *Immunization for the child with SCD*

Infection is the commonest cause of death in SCD children, especially infections due to encapsulated organisms.<sup>27,28,31,33-35</sup> Therefore, vaccinations against *Haemophilus influenza* type b,<sup>36</sup> pneumococcus<sup>37,38</sup> and *Salmonella* are essential in the care of children with SCD. However, the routine immunization schedules in most African countries do not include these vaccines. Nigeria, for example, has just implemented the use of the *Haemophilus influenza* type b and pneumococcal vaccines for routine immunization. *Salmonella* vaccine

is not included in the routine immunization schedule for children in Nigeria. These bacterial organisms have been proven to be the major causes of infections in children with SCD, hence, there is an urgent need to vaccinate these immune-compromised children to prevent morbidities and mortality associated with infections. These vaccines are routinely used for the children with SCD enrolled into the programme at the University of Benin Teaching Hospital, Benin City. Hepatitis B vaccine was only introduced 12 years ago in Nigeria, hence, children with SCD who are older than 12 years must have missed the vaccines. Therefore, children who are older than 12 years and those aged less than 12 years but who were not vaccinated should be tested for Hepatitis B virus infection and the vaccine should be administered if they are sero-negative.

### Regular hospital follow up

For a disease that has lifelong implications, there is a need for regular hospital follow up. In Africa, most patients with SCD do not attend follow-up care in the hospital setting. Children are only brought for care when they have crises. This attitude may be detrimental to the health of children with SCD because regular follow-up hospital visits may ensure adequate growth and development through growth monitoring and frequent education. This allows for early identification and prompt management of complications. This allows the child with SCD to maintain good health.

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