The Management and Control of Sickle Cell Disorder

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Introduction

Sickle cell disorder, understandably, concerns millions of Africans. In Nigeria, there is no doubt that the prevalence of the condition is increasing, especially among the urban educated elite and in other communities with access to effective basic health care. There is however, a palpable lack of information and education about the disorder within our communities. This, with the increasing prevalence, has encouraged the growth of myths, misinformation, inappropriate treatment, frustration and stigmatisation. The frustration has kindled the desire in many Africans to ***do something about sickle cell disorder***. What needs to be done often appears to be deceptively easy and it is usually not fully thought out and remains a subject of confusion and of controversy even among doctors and other health care workers. In this regard, one frequently hears talk of eradication of the disorder by enactment of legislation while the wider context of control is invariably overlooked.

In this article, I shall base the information on my experience in Nigeria and discuss some issues pertaining to the management and control of sickle cell disorder in the hope that it would promote better understanding of its complexities and help readers identify credible and productive strategies and solutions.

Definition of Sickle Cell Disorder

The term sickle cell disorder is used in this paper to describe a lifelong ailment arising from the inheritance, from both parents, of sickle haemoglobin (Hb SS) or of Hb S from one parent and another variant pathological haemoglobin such as Hb C (Hb SC) or β thalassaemia (Hb Sβthal) from the other parent. The ailment is characterised by premature breakdown of rigidly sickled red blood cells causing, in the case of Hb SS, constant anaemia and occlusion of small blood vessels, which is believed to lead to pain crises and other manifestations.

Magnitude

Sickle Cell Disorder

In Nigeria, by far the commonest type of sickle cell disorder is the homozygous sickle cell disorder (SS) also known as sickle cell anaemia. Less common types include sickle cell-haemoglobin C disorder (SC), which is fairly common in southwestern Nigeria and the rare sickle cell - β^+ thalassaemia (S β^+thal). As persons with Hb SC and other types have, on average, similar but milder syndromes, the rest of this paper will be based on our experience with the more severe sickle cell anaemia.

About 2 % of all babies born to Nigerian parents have sickle cell anaemia. It is well to note that this prevalence is only at birth and progressively decreases through late childhood, adolescence and adulthood. Two per hundred births translates to over 150,000 births annually of children with sickle cell anaemia. This is very high when compared to the incidence of other serious inherited disorders that are commonly found in other races.

Survival of these babies beyond childhood is largely dependent on their access to good basic health care and as most of these children are born into poor underprivileged families they hardly survive childhood. On the other hand, the survival of those with access to good care at every stage of life is steadily improving.

Sickle Cell Trait

It has been established that about 24% of the entire population of Nigeria or 1 in 4 Nigerian men and women are healthy carriers of the sickle cell trait. The Nigerian population is officially quoted to have risen to about 160 million. Consequently, the population of Nigerians who are healthy carriers of the sickle cell trait (Hb AS) must be about 40 million. This number far exceeds the total population of every other affected African country and indeed of several of them put together. Nigeria, therefore, has the largest sickle cell gene pool in the world.

Distribution

The distribution of indigenous sickle cell disorder coincides with the present or past distribution of *Plasmodium falciparum* malaria. This is because possession of the sickle cell trait (Hb AS) confers a natural protection from malaria deaths. In any unprotected community in Nigeria, many children with Hb AA will succumb to malaria before the age of 5 years. Those with the sickle cell trait will have milder malarial syndromes and survive the infection. Thus, a higher proportion of carriers would live to reproduce and pass on the sickle gene to their offspring. Those who inherit Hb AS are thus better fitted for survival in this environment than those who inherit Hb AA.

Conversely, a study of population genetics has shown that the eradication of falciparum malaria, by eliminating the reproductive advantage of Hb AS carriers, predictably leads to a gradual dilution of the S gene pool within a population. Hence, in South Africa and southern Mozambique, both of which lie within the temperate non-malaria zone of sub-Saharan Africa, the S gene frequency is so low that sickle cell anaemia is not perceived there as a problem. Carriers of the trait (Hb AS) do not exceed 0.3% of the Bantu population in these areas in contrast to the much higher prevalence among Bantus in northern Mozambique and in countries lying to the north of the Zambezi River. The 2000-year-old migration of Bantus from western to malaria-free southern Africa is conjectured to have led to the remarkably low S gene frequency among South African Bantus. The same argument is advanced for the lower S gene frequencies in African-Americans (AS 8%) and African -West Indians (AS 10%). Thus, the ultimate control of the S gene within a population is linked to the eradication of malaria in that population. The problem in the affected countries in Africa is that malaria is not being controlled. Professor Luzzatto has estimated that, even if malaria were controlled, it would still take some 300 years for the gene frequency to be reduced by half. As a strategy for reducing the incidence of sickle cell anaemia, it is too slow to be appealing to countries in which sickle cell disorder is a significant public health problem. Undoubtedly, the immediate beneficiaries from control of malaria would be persons affected with sickle cell anaemia whose survival through childhood would be better assured.

Ironically, although carriers of the sickle cell trait can withstand deadly malaria, persons with sickle cell anaemia (Hb SS), for diverse reasons, cannot. They are thus least fitted for survival in the hostile malaria environment. Their survival in Nigeria in appreciable numbers is a relatively recent phenomenon reflecting the improvement in standards of care, including effective prevention and treatment of malaria and other infections. Owing to their peculiar susceptibility to infection in childhood, the survival of children with sickle cell anaemia can be used as a sensitive barometer to assess the effectiveness of the health care programme in any community.

Many Nigerians find it hard to believe that its high prevalence of sickle cell anaemia in many of our communities is a relatively recent phenomenon. It is not fortuitous that despite a much higher incidence in sub-Saharan Africa, the first report of a patient with sickle cell anaemia was that of a 20 year old West Indian student in Chicago in 1910 . Over the next three to four decades, there were many other reports of affected patients in Europe and America but surprisingly few in Africa. In the mid 1940's quite a few reports of a high prevalence of the sickle cell trait emanated from Africa . The low prevalence of sickle cell anaemia in indigenous African became not only paradoxical but also quite puzzling.

This led some workers to believe that sickle cell anaemia was indeed commoner in the African-American than in the indigenous African. In 1950, Dr A B Raper wrote, ***''This essay has been directed to showing that the disease is of more importance to the American Negro than to the African''.*** Although he acknowledged a higher frequency

of sickle cell trait in indigenous Africans he suggested that the admixture of African and Caucasian genes was responsible for the higher incidence of sickle cell anaemia in American Negroes! With hindsight, he was, of course, very wrong.

What he failed to realise was that very many more children with sickle cell anaemia were born in Africa than in America but that very few of the former survived the hostile environment. The true incidence and public health importance of sickle cell anaemia in Nigeria was not widely appreciated until 1956 when the late Professor Mabayoje wrote, " ***sickle cell anaemia is a major disease of west Africa. It is a cause of distress in many families. It therefore deserves much better recognition than it gets at present. It should be treated as a major disease in schools of tropical medicine, textbooks and in all medical schools in tropical Africa."***

Over two decades later, Fleming and co-workers in rural Garki district in Kano State found that although over 2% of all newborn children had sickle cell anaemia, there was no one with sickle cell anaemia in the adolescent or adult population in the community. In fact, except for a nine-year-old child, no person with sickle cell anaemia was older than four years in the entire community of villages. In contrast, obstetricians in urban centres like Lagos and Ibadan had, by the early 1970's, already reported many pregnancies and childbirths in women with sickle cell anaemia. This dichotomy in the survival of rural and urban dwellers clearly illustrates their critical sensitivity to environmental factors. Some years later, Fleming and co-workers were able to observe a

significant improvement in the survival of persons with sickle cell anaemia in the same district following the introduction of anti-malarial measures.

The Need for the Control of Sickle Cell Disorders

The need for control of sickle cell disorder in Nigeria and other tropical African countries is self evident. Molineaux and co-workers in 1979 correctly summarised the situation when they wrote, "***There is no other known inherited disorder present at such high frequency in a large population and of comparable severity as sickle cell anaemia in Africa. With rising standards of living and control of malaria, sickle cell anaemia will become an immense medical, social and economic problem throughout the continent***."

It is also clear that despite the uniformly high incidence of sickle cell disorder, the need for its control cannot be equally felt all over the country. This is because of the remarkably low level of awareness in many communities in which deprivation has ensured a low prevalence of the disorders. Awareness is dependent on recognition of the condition, which in turn is dependent on evident survival of affected persons. In the deprived areas, infant and child mortality rates are high enough to affect virtually all the children who are born with sickle cell anaemia.

Nevertheless, children with sickle cell anaemia only in fact account for a small proportion of infant or childhood deaths in the deprived areas and thus, do not, contrary to popular belief, solely account for the phenomenon of so-called reincarnation of dead children known in Nigerian parlance as Ogbanje (*Igbo*) or Abiku (*Yoruba*). The work of Edelstein

in Anambra State of Nigeria clearly refutes any significant connection between physically branded Ogbanje children and sickle cell disorder. Therefore, the popular stigmatisation of children with sickle cell anaemia as Abiku or Ogbanje is unjustified.

The felt need in the deprived areas is for provision of the basic necessities of life including effective health care. It would therefore be folly to attempt to introduce any specific control programme for sickle cell to these communities before their immediate needs are met. It is only after the basic necessities of life have been provided and the quality of their lives improves that their children with sickle cell and other non-communicable disorders will survive to merit special attention.

Control of Inherited Haemoglobin Disorders

The approach to the control of inherited disorders is necessarily different to that of the control of communicable or acquired disorders. Factors that must be taken into account are listed in table 1

Tested strategies for the control of inherited haemoglobin disorders in countries outside Africa include those listed in table 2.

A control programme, as stated earlier, should be sensitive to the felt needs of the target community. In order to achieve maximum coverage, efficient utilisation of resources and sustainability, it should be integrated into the health care system of the country. The control programme should also be one that would have been pre-tested for efficacy and acceptability. A control programme should gradually decrease and certainly not increase stigmatisation and anxiety, especially of carriers and affected persons within the target population.

Table 1: Factors impacting on the Control of Inherited Haemoglobin Disorders

- Political will
- Land size and terrain of the country
- Total population
- Level of literacy and education
- Severity of the disorder
- Magnitude of the disorder
- The infrastructure – water supply, communication and power supply.
- The quality and coverage of the health care and social welfare services.

Table 2. Strategies for Control of inherited Haemoglobin Disorders

- Accessible and effective treatment of affected persons
- Appropriate education of health care professionals
- Adequate supply of safe blood for transfusion
- Adequate and reliable laboratory diagnostic facilities
- Adequate numbers of trained counsellors
- Prenatal & preconceptual diagnostic programmes.
- Effective community information and education
- Support for research – molecular, clinical and operational
- Constant monitoring and periodic evaluation of programmes.

Every country should develop an appropriate programme guided by strategies already shown to be effective in other countries. There is no doubt that the process of designing and implementing an effective control programme for an inherited condition as prevalent and as complex as sickle cell disorder, in a large and populous country like Nigeria, would be an immense task. It would require meticulous planning, adequate research and efficient mobilisation and co-ordination of resources. It is important to appreciate the enormity of the task right from the outset so that the right attitudes and perspectives are adopted.

Developing a National Control Programme

The sickle cell problem in Nigeria is too immense to be amenable to quick-fix solutions. A frequently canvassed quick-fix 'solution' has been mass Hb genotype screening of the population and prohibition of marriages between couples who both carry the sickle cell trait. The Military Administrator of Oyo State, had, in 1995, proposed a punitive edict aimed at prohibiting such marriages, but the conference of solicitor–generals in Nigeria

thwarted its introduction by declaring that it was unconstitutional and offended the human rights charter to which Nigeria is a signatory.

It is a popular belief that the implementation of this strategy would lead to the eradication of sickle cell disorder in the country. The indications however are that it would not achieve that objective and would, instead, become disruptive and counter-productive. It is a little known fact that, so far, enforced selective mating of couples has never been shown anywhere in the world to have reduced the incidence of any inherited disorder. Attempts to introduce it in Cyprus for the management and control of beta thalassaemia, led to increased anxiety and stigmatisation of affected persons and of carriers of the thalassaemia trait. This in turn led to widespread denial and falsification of haemoglobin genotype results among carriers.

The strategy was therefore abandoned in favour of one comprising optimal treatment of persons living with the disorder, education of members of the public and of health care professionals, screening, counselling and prenatal diagnosis. In practice, the Church in Cyprus no longer threatens not to marry any couples, but only require that they show evidence that they have been educated, screened and counselled. This strategy has led to almost universal awareness and the application in Cyprus of prenatal diagnosis of children expected by parents who both carry the thalassaemia trait. It has been so successful that only 2 of the 71 children diagnosed as having thalassaemia major were born in 1984. It is important to realise that in order to sustain this low birth prevalence of thalassaemia, the strategy has to be continuously applied given the persisting high

prevalence of carriers in the population. The small size and population (670,000) of Cyprus, its excellent infrastructure, its high literacy rate, its excellent and free health and welfare services and the absence of abject poverty on the island have all contributed to the successful outcome. The conditions in Nigeria cannot be more different and one would therefore not expect a similar outcome from application of the same strategy in Nigeria.

Invariably, those who advocate selective mating strategies, have seriously under-estimated the complexity of the problem they intend to address and the resources and skills that would be required. Very little, if any thought is given to the need to have adequate resources and facilities for the accurate laboratory diagnostic screening, the need for public and professional education, expert pre and post screening counselling of the target population and for pre-testing the strategy for efficacy and acceptability in the communities. A common misconception is that genetic counselling means marriage counselling aimed at directing carriers of the trait not to marry each other. This is not one of the objectives of genetic counselling. A cardinal principle is that balanced unbiased information is given and the client is encouraged to make informed decisions on reproductive and other issues. Nigeria has the largest pool of the sickle cell gene in the world and any facile talk of eradication must take this fact into account and also the fact that the magnitude of the sickle cell problem is better determined by the size of the trait carrier population than by the population of persons living with sickle cell anaemia. The former would have at least 20 million S genes while the latter hardly boast of 2 million S genes. In the circumstances, eradication of sickle cell disorder is at best over-optimistic

and would require drastic measures like total and permanent banishment of all carriers to Iceland or somewhere equally distant.

We have to appreciate that, as in war, attainable goals have to be set, the troops (health educators, counsellors and health carers) have to be trained in sufficient numbers, the resources have to be assembled and credible strategies and tactics decided before engagement. It goes without saying that, in the struggle against sickle cell disorder the structures for properly addressing the problem and finding effective and sustainable solutions must first be put in place. Embarking on inadequately planned and tested programmes will be disastrous and would have a good chance of jeopardising or delaying the emergence or success of a future national programme.

The feasibility of control of sickle cell disorder in Africa has, from time to time, engaged the attention of the World Health Organisation. In 1987 the WHO suggested the establishment of four pilot projects for testing the acceptability and effectiveness of certain strategies. In 1994 the WHO went further and recommended that "***In areas where haemoglobin disorders are common special dedicated centres are required, in appropriate numbers and appropriately situated, and with a high degree of autonomy***''. For various reasons including low priority, poor resources, conflict and political instability, the measures recommended have received scant attention in the affected countries. The WHO regularly responds to questions about the absence of programmes for SCD in Africa by stating that African Ministers of Health have never raised sickle cell disorder as a public health priority at their yearly meetings in Geneva. In the meantime

HIV/AIDS has become rampant while malaria and tuberculosis have expanded considerably. Superior professional advocacy is needed to sensitise African governments and the International Aid Agencies to the need to address sickle cell disorder.

Under the circumstances, non-governmental sickle cell associations have emerged in several African countries and on May 10th 1996, eight of them, including the Federation of Sickle Cell Clubs of Nigeria (FESCCON), formed an international organisation known as **Federation des Associations de Lutte Contre la Depranocytose en Afrique (FALDA**) in deference to the French speaking members who form the majority. A literal English translation is the **Federation of Associations combating sickle cell disorder in Africa.** The membership now comprises 13 national associations from Benin, Burkina Faso, Cameroon, Chad, Cote d'Ivoire, Congo *(Brazzaville)*, Ghana, Guinea *(Conakry)*, Mali, Niger, Nigeria, Senegal and Togo. The formation of this continental body is an exciting prospect, which, hopefully, should ensure that the governments in the affected countries are sensitised to the magnitude of the problem and to the need to commit appropriate resources to it. FALDA has designated May 10th of every year as the "African Sickle Cell Day" and is still hoping that WHO will recognise this date.

Suggested Way Forward

Sickle cell disorder presents a special challenge to Africans and to Nigerians in particular as it affects virtually every extended family. If nothing else, national pride demands that we squarely accept its challenge and demonstrate our ability to plan effectively for the future of our children. Sickle cell is not going to go away unless a concerted effort is

made to combat this trait. Any national programme of this magnitude will certainly generate organisational skills and insights which will be valuable in the execution of other health care initiatives.

Sickle cell is not a hopeless condition. Research in the last two decades, has shown enough promise to suggest that many of the problems can be significantly reduced. In the last few years, the judicious use of a drug named hydroxyurea has reduced the frequency and severity of pain crises. Pneumococcal vaccination and daily oral penicillin, especially in children, have proven effective in preventing lethal pneumococcal infections. In Lagos, we have demonstrated that attentive holistic care including counselling and prompt supply of prescribed medication can drastically reduce hospital admissions, blood transfusions and death rates.

Recently, bone marrow (stem cell) transplantation has been used to cure sickle cell anaemia. Although this is a landmark treatment, its rigorous pre-conditions and expense make it, for now, unattainable to all but a few fortunate patients. In this regard, the other stem cell transplantation using blood from the umbilical cords of newborn babies is more promising. A cure through **gene therapy** is a promise on the horizon, requiring several more years of intensive research before this therapy will be available.

The way forward may be two fold. First is for all health authorities and institutions to adopt, as soon as possible, the simple measures that have been shown to be effective in the management of sickle cell disorder. These include those listed in table 3.

Table 3. Measures Effective in the Management of Sickle Cell Disorder.

- Establishing special sickle cell clinics
- Organising continuing education on SCD for health workers
- Continual training in counselling on SCD
- Employing trained counsellors
- Establishing prenatal diagnosis programmes
- Allocating funds to make these services affordable to all persons with SCD
- Monitoring and periodically evaluating outcomes

Second, a National Sickle Cell Centre must be developed to facilitate the development of a rational, effective, co-ordinated and sustainable national control programme, which will be integrated with the National Health Service. The Centre would appoint a National Sickle Cell Working Group comprising experts in various relevant disciplines who will collate and analyse essential data, identify research priorities and collaborate with national health planners and international organisations in designing, monitoring and evaluating a national control programme. The Sickle Cell Foundation Nigeria, a non-governmental organisation, is already developing what it hopes will be a world class National Sickle Cell Centre, from donations from the public and private sectors in Nigeria.

The Centre will accommodate essential workers and equipment; serve as a reference diagnostic laboratory, as well as a forum for relevant discussion, research and training of personnel. With the local wealth of clinical material, a functional Sickle Cell Centre should attract foreign scientific interest and funding, stimulate research into all aspects of sickle cell disorder and encourage local participation and contribution to knowledge.

Its development is behind schedule because of shortage of funds but in the words of Bernadette Modell, professor of community genetics in the University of London, the proposed Centre, '***marks the first serious attempt to come to grips with this long-standing African health problem, and is an important development for Africa'***.

Readers who would like to contribute to this effort should contact our office

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