Morbidity and mortality pattern of children with sickle cell anaemia in Jos, North Central Nigeria: a single institutional study.

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Abstract

Background: The burden of Non-communicable Diseases (NCDs) in the Tropics is enormous. Sickle Cell Anaemia (SCA) is the most prevalent NCD in Nigerian children. There is a paucity of data on morbidity and mortality pattern of SCA patients in North Central Nigeria.
We determined the morbidity and mortality pattern of children with SCA in a teaching hospital.
Methods: This was a descriptive study of consecutive admissions of children with SCA between January and December 2015, whose parents gave consent. The patients' biodata, age at diagnosis of SCA, admission diagnosis, course of management and outcome were among data collected in a proforma and analysed using descriptive statistics.
Results: Sickle Cell Anaemia accounted for 199 out of 1224 Paediatric admissions (16.8%) during the study period. The mean age at diagnosis of SCA was 23± 8 months, and 70% of the SCA patients were 10 years old or younger. Infections (36.2%), severe anaemia (29.7%) and vaso-occlusive crisis (22.1%) were the commonest indications for admission, while cerebrovascular accidents (30%), severe anaemia (30%) and acute chest syndrome (20%) were the leading causes of mortality.
Conclusion: Institution of Early Infant Diagnosis, Public enlightenment, coupled with staff training and improvement in National Blood Transfusion Services are advocated to reduce the high morbidity and mortality from SCA.

Key words: Sickle Cell Anaemia, Morbidity, Mortality, Comprehensive care.

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Introduction

Following the success of global interventions targeted at communicable diseases over the past 3 decades, Non-Communicable Diseases (NCDs) have assumed prominence as the leading causes of death worldwide, posing a threat to national and global health, and the attainment of the World Health Organization (WHO)'s Sustainable Development Goals.[1-3] Sickle Cell Anaemia (SCA) is a prevalent NCD in most of Africa and Asia.[3,4] With increasing globalization and migration, Western countries of Europe and America now have their own fair share of the burden of Sickle Cell Disease (SCD).

Sickle cell anaemia is caused by a single misspelling in the DNA instruction for haemoglobin, the oxygen-carrying protein in the blood. Affected individuals experience life-long complications including anaemia, infections, stroke, tissue damage, organ failure, intense painful episodes and premature death.[5] These morbidities and the complex treatment needs of people living with SCD often limit their education, career opportunities and quality of life. The pattern and severity of these morbidities vary from one individual to the other and from one environment to another, and are highly influenced by time of diagnosis, early presentation, available therapies and management options.[1,2,5-13]

In many African countries, 10-40% of the population carry the sickle cell gene, resulting in estimated SCD prevalence of at least 2%.[14,15] Over 50% of the 300,000 SCA neonates born annually are born in only three countries: Nigeria, India and DR Congo.[14] Seventy-five percent of these SCA neonates are born in Africa, with Nigeria bearing the highest burden.[14]

The WHO and United Nation, recognizing SCD as a global health problem, have called on countries to take deliberate actions to tackle the disease.[1,2,15] The WHO estimates that 75% of SCA deaths in Africa are preventable with interventions such as early identification by newborn screening and the subsequent provision of comprehensive care. These are largely lacking in most African countries at present. Countries like the US and UK have drastically reduced SCA morbidity and mortality through interventions such as Newborn Screening, prevention of infections and the adoption of a comprehensive care.[5,12,13,15,16]

The health outcomes and treatment inadequacies related to SCD as well as the ever-growing population of SCD children make it a public health problem in Nigeria.

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We can take actions to address the needs of these children only if we know and document the pattern of their problems. There is a paucity of data about morbidity and mortality in children with Sickle Cell Anaemia in North Central Nigeria. The objective of this study therefore was to document the common acute events leading to hospital admissions and the mortality pattern in children with SCA seen in a teaching hospital in Jos, North Central Nigeria. Knowledge of these would influence proactive health care planning, staff training and resource mobilization.

Materials and Methods

This was a descriptive study of all admissions of children into the Emergency Paediatrics Unit and Paediatrics Wards of the Jos University Teaching Hospital (JUTH), Jos over a 1-year period from January to December 2014. JUTH is a 525-bed tertiary referral hospital in North Central Nigeria that serves Plateau State and neighbouring states of Bauchi, Taraba, Adamawa, Nasarawa, Benue, parts of Kaduna and the Federal Capital Teritory (FCT). Approval for this study was obtained from the Institutional Review Ethical Committee of JUTH while informed consent was obtained from the parents (and assent from patients older than 10 years).Included were patients with confirmed HbSS phenotype, while neonatal and Paediatric Surgical admissions were excluded. Otherwise healthy HbSS patients who were admitted transiently for planned blood transfusions for stroke prophylaxis were also excluded.

All patients whose Hb phenotype was not known prior to index admission had this done by cellulose acetate electrophoresis. Patients who had HbSS phenotype were consecutively recruited into the study. Relevant data entered on each patient into the designed proforma included personal biodata, age at diagnosis of SCA, number of previous blood transfusions, admission diagnosis (indication for admission), existing long term sequelae/complication, steady state PCV and outcome of management, among other things. All patients were evaluated and managed in line with their presentation and admission diagnosis according to existing management protocol of the hospital for various conditions. Each patient's data was updated daily up to the last day of admission. Verbal autopsy was used to determine cause of death where appropriate. Data generated were analyzed using descriptive statistics.

Results

During the one-year study period, there were 1,224 paediatric admissions out of which there were 199 (16.8%) patients with SCA. Of the SCA admissions, there were 114 (57%) males and 85 (43%) females (M:F=1.3:1). The ages of the patients ranged from 8 months to 19 years, with a median age of 8 years. Over 70% of the patients were 10 years old or younger (Table 1).

Table 1: Clinical characteristics, morbidity and mortality among children with sickle cell anaemia presenting at the Emergency Paediatric Unit of Jos University Teaching Hospital in 2015.

Variables	Number	%
Age; years (n=199)		
< 1	4	2.0
1 - 5	78	39.2
6 - 10	58	29.2
11 - 15	40	20.1
>15	19	9.5
Males	114	57
Indication for admission (n=199)		
Infections	72	36.2
Severe anaemia	59	29.7
Vaso-occlusive crisis	44	22.1
Cerebrovascular accident	13	6.5
Others*	11	5.5
Common infections leading to admission (n=72)		
Acute osteomyelitis	21	29.2
Acute severe malaria	15	20.8
Pneumonia	13	18.2
Septic arthritis	7	9.7
Urinary tract infection	6	8.3
Pharyngo-tonsilitis	5	6.9
Septicaemia	5	6.9
Complication/Long-term sequelae (n=30)		
Chronic osteomyelitis	12	40.0
Stroke with permanent disability	8	26.7
Avascular necrosis of femoral head	6	20.0
Pathologic fracture	3	10.0
Sickle cell nephropathy	1	3.3
Causes of death (n=10)		
Severe anaemia	3	30
Stroke	3	30
Acute chest syndrome	2	20
Severe malaria	1	10
Septicaemia	1	10

*Others included: Sickle cell nephropathy (2), malignancy (2) and 1 each of rheumatic heart disease, acyanotic congenital heart disease, severe malnutrition, acute asthma, juvenile rheumatoid arthritis, exfoliative dermatitis and diabetes mellitus.

Five (2.5%) of the patients were diagnosed during the index admission. The mean age at diagnosis of SCA was 23.8±5.8 months. Eight percent of the patients were diagnosed in infancy, 41% between 1-4 years, 39% between 5-9 years while 12% were diagnosed at age of 10 years or beyond. Table 1 also shows the indications for admission. Infections (36.2%), severe anaemia (29.7%) and acute painful crisis (22.1%) were the commonest

indications for admission. The common infections leading to admission included acute osteomyelitis (29.2%), acute severe malaria (20.8%) and pneumonia (18.2%) among others. The commonest long term sequelae in these patients were stroke with permanent disability, chronic osteomyelitis and avascular necrosis of the femoral head. Chronic leg ulcers were not seen in our patients.

Vaso-occlusive crisis was much commoner in males than females (30 males vs 14 females, $X^2=5.62$, p=0.009). Stroke and avascular necrosis of femoral head were seen more commonly above 10 years of age (10.3±4.7 years vs 7.5±4.8 years, and 14.1±1.7 years vs 7.5±4.7 years; T=2.03, p=0.044 and T=3.455, p=0.0007 respectively).Severe anaemia had no sex preponderance (31 males vs 28 females; $X^2=0.24$,p=0.315). The steady state PCV of the cohort ranged from 18% to 31%, with a median of 24%. Fifty percent of the patients had had two or more blood transfusions in the past.

The total mortality in patients presenting to the Emergency Paediatric Unit during the study period was 110 out of which there were 10 (9%) SCA deaths. Deaths were due to severe anaemia (30%), stroke (30%), severe malaria (10%), acute chest syndrome (20%) and septicemia (10%). The three patients that died of severe anaemia presented late; two died before blood was made available while the third died while on blood transfusion (death not related to transfusion reaction). The deaths from stroke were a 19 year old girl who was presenting to us for the first time, a 17 year old boy who had poor adherence to follow up and a 13 year old girl who had a second stroke and who was not adherent to chronic transfusion program. The two patients who died of acute chest syndrome (a 15 years old male and a 10 years old female) presented with severe generalized painful crisis that progressed to the acute chest syndrome and death. The child that died of severe malaria (an 8- year old male) had multiple organ dysfunction, while the 5- year old that died of septicaemia had hyperpyrexia with no identifiable specific focus of infection.

Discussion

The prevalence of SCA among hospital admissions in our environment is high. Majority of cases are diagnosed around the second and third years of life. Despite early onset of symptoms such as dactylitis, anaemia often requiring blood transfusions, jaundice and intercurrent infections, diagnosis is delayed as many of these patients may have been receiving symptomatic treatment in peripheral hospitals without a specific diagnosis being established. This finding is similar to the report by Akodu and colleagues from Lagos where the peak age of diagnosis was 27months.[17] Akodu et al attributed the delay in diagnosis to low socio-economic status; this coupled with a relatively low level of awareness among the populace may seem to be the case in our setting.[17]

SCA accounted for as high as 17% of all paediatric admissions (excluding neonatal admissions) and 9% of deaths in the year under review, with severe anaemia, VOC and infections being responsible for most of these admissions. This pattern is similar to reports from Enugu, South East Nigeria, Port-Harcourt,South South Nigeria, Kuwait, and India, but contrasts with reports from Britain, where VOC accounted for over 90% of admissions of SCA children.[6-8,10,17-19] Conditions like malaria and infections which contribute significantly to anaemia are uncommon in Britain, while weather conditions there may favour recurrent VOC. Most blood transfusions among SCA patients in London were planned transfusions for stroke prevention.[6,7] Both severe anaemia and planned transfusions were common indications for blood transfusion in our centre. Half of the SCA pts in our study had received at least 2 blood transfusions in the past. This is in line with an earlier finding from this centre which showed that SCA was the commonest indication for blood transfusion among children in Jos, Nigeria. [20] Most of these transfusions were emergency transfusions for severe anaemia in contrast to the planned transfusions for stroke prevention in London and elsewhere; and some died before blood could be made available. [6,7] There is therefore an urgent need to improve National Blood Transfusion Services centres to make screened blood readily available if anaemia-related deaths are to be averted.

Cerebrovascular Accident (CVA) was not only common but was also a leading cause of death among our patients. It was uncommon in reports from elsewhere, and in Kuwait splenic sequestration and Acute Chest Syndrome (ACS) were more commonly seen. [1-3,7, 8] Even though ACS was uncommon in our setting, when it did occur it was often fatal. There is therefore a need for a high index of suspicion if early and appropriate interventions are to be instituted to prevent death. In the United States of America Incentive Spirometry has been used effectively in combination with analgesics to prevent progression of painful crisis to acute chest syndrome and subsequent mortality.[21]

Infections, severe anaemia and painful crisis were the commonest indications for admission in this study. This is similar to findings elsewhere, but the relative importance varies widely. [8,10,18,19] In Enugu South Eastern Nigeria, even though infections were also the commonest reason for admission, VOC was quite uncommon.[10,18] In Kuwait VOC was the commonest indication for admission, with acute splenic sequestration and acute chest syndrome being relatively common.[8] In India infections and severe anaemia played greater roles than VOC.[19] The relatively high rate of

stroke among our patients contrasts with findings from these centres where stroke was hardly seen. These findings may reflect level of care, environmental differences and inherent patient factors.

Vaso-occlusive crisis (VOC) was significantly more common among the male than female patients in our study. This may be explained by the fact that male children are generally more active and engage in more vigorous play or exercise (often in extremes of weather), than their female counterparts; and this often triggers VOC. Since severe VOC is a common indication for hospital admission among our patients, knowledge and availability of appropriate pain relief drugs should be enhanced, and pt-controlled analgesia put into effective practice if these pts are to be maintained as pain-free as possible. However, this has to be carefully moderated to avoid abuse and over use of these strong analgesics. A greater reliance on patient-reported outcomes and the development of a standardized pain score would ensure that patients' pain is effectively and adequately controlled in good time. George and co-workers in Port-Harcourt [22] have shown the efficacy of a drug, Nicosan, in reducing frequency and severity of painful crisis as well as hospital admissions among SCA patients. When fully developed, this drug would offer a lot of promise for SCA pts and their families.

Leg ulcers which were common in East Africa[11] were not seen in our study. This may be related to environmental changes and habits. The finding of avascular necrosis of head of femur, chronic osteomyelitis and CVA with long term impairment of movement contrasts with reports from elsewhere.[8-10] The increasing number of children with SCA related CVA underscores the need for TCD USS and chronic transfusion programs for selected predisposed patients. However, most of our centres in Nigeria still lack facilities for regular TCD, and our National Blood Transfusion Services centres are often overstretched. Also many centres in Nigeria are still not routinely using Hydroxyurea probably due to inability to monitor its therapy due to laboratory costs. Accessibility and affordability to these vital facilities/agents would drastically reduce SCA-related morbidity and mortality in our environment. The routine use of TCD, HU therapy and chronic transfusion in the US, UK and parts of Brazil has drastically reduced morbidity, mortality and long term sequelae in children with SCA in these countries.[5,12,13,24]

The mean steady state PCV of our pts of 24% is less than what obtains in the USA, but higher than the finding from South Africa.[2, 5] The average PCV of children in the USA is higher than PCVs in developing countries, and this may explain the same trend among SCA pts, often related to differences in standard of living in the 2 different societies. The fact that most SCA patients in the US are on HU would also help to maintain a high HbF level, reduced sickling and haemolysis, and a steady state PCV at a higher level than our setting where only a minority of patients are on HU.[5,13]

Among the infections, acute severe malaria was relatively common, and also contributed to mortality. This is similar to findings in Port-Harcourt and Enugu where malaria played major roles in morbidity.[9, 18] This is despite the fact that these patients are routinely given Proguanil for malaria prophylaxis. There is enough reason to believe that Proguanil may no longer be an effective chemoprophylactic agent for malaria. A recent study in our centre demonstrated that monthly Sulphadoxine-Pyrimethamine combination was cheaper and more efficacious than daily proguanil in reducing the prevalence of asymptomatic malaria parasitemia, clinical malaria attacks and sickle cell crises.[23] An obvious recommendation would therefore be to change to Sulphadoxine-pyrimethamine combination for malaria chemoprophylaxis in these patients.

Even though most cases of SCA are diagnosed relatively early, morbidity and long term sequelae are hardly ever prevented largely due to low level of awareness by caregivers resulting in late presentation; poor facilities in our centres and sub-optimal care. Like most other centres in Nigeria, we still lack facilities for Transcranial Doppler Ultrasound scan to predict those patients at risk for stroke. We routinely placed those patients whose parents consented to hypertransfusion program on long term blood transfusions after a first stroke to prevent recurrence. Most of the deaths due to stroke could have been prevented if regular follow up and monitoring for stroke recurrence were effective. Chronic osteomyelitis was the commonest long term complication among our patients. Many of these presented late, while others may have been managed earlier as vaso-occlusive crisis resulting in delayed diagnosis.

Sickle cell anaemia accounting for nearly 10% mortality in our centre is a cause for great concern. This is similar to the 8.5% mortality reported from Enugu, South East Nigeria; and underlines the need for more public enlightenment to ensure early presentation, while promoting emergency readiness at the centre to appropriately tackle severe anaemia, stroke and the ACS which were the major causes of mortality.[10] This would mean easy and quick access to screened blood among other things. This study has shown that if we prevent CVA and its recurrence, promptly identify and address severe anaemia and infections in these patients, most deaths would be averted.

Over 70% of our patients were 10 years or younger. This is similar to the report from Port-Harcourt by

George and Opara.[9] This means that we have a relatively young population of SCA patients, implying that most of them die early. This low life expectancy for these children is a clarion call for us all to sit up and improve the care of these patients to increase their life expectancy. Akinyanju and co-workers in their study observed that those SCA patients given a holistic care had lower morbidity and mortality, and a better quality of life.[25]

Most clinical interventions for people with sickle cell anaemia have focused on tertiary preventive measures such as therapy to ameliorate anaemia, reduce the frequency of pain crises or prevent stroke recurrences. We can reduce the prevalence of SCA in our society through health education, premarital counseling and screening, while morbidity and mortality from this condition can be reduced to the barest minimum through protective measures as recommended by the WHO.[1,2,5] Early neonatal diagnosis would allow provision of simple protective measures, including information for the parents, penicillin prophylaxis and anti-malarial treatment, all giving a better quality of life for the affected children. Long term event-free survival of people with sickle cell anaemia has been demonstrated in societies where newborn and community screening for sickle cell disease is routinely practiced.[16,26] While looking forward to the time that New Born Screening will become universal in Nigeria, we advocate routine screening of all children who present for other ailments to improve pick-up rate and initiate care early to prevent long term sequelae and early death. To reduce Sickle Cell Anaemia-related morbidity and mortality, neonatal screening or early infant screening program must be initiated as part of a comprehensive medical care program.[15,16] Such newborn screening program will identify children with SCA to allow early medical interventions, thereby preventing development of SCA-related complications and reducing morbidity and mortality.

A lot of our children with sickle cell anaemia still depend on blood transfusion to either correct anaemia or prevent stroke recurrences. Improvement of medical facilities and most especially National Blood Transfusion Services centres would be key to their survival and enjoyment of good quality of life.

Conclusion

SCA and associated morbidity and mortality is prevalent in our hospital. Deliberate policy on early diagnosis through inclusion of Hb genotyping for all infants would improve pick-up rate and subsequent care to reduce SCA related morbidity and mortality. Since blood transfusion is key to survival, efforts to improve blood banks and encourage voluntary blood donations across states in the country should be made and sustained. The need for continued counseling and public enlightenment on prevention and care of SCA cannot be overemphasized. The recent inclusion of Pneumococcal vaccine (PVC 10) in the routine childhood immunization program in Nigeria may have implications for the survival of the SCA child.

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