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ORIGINAL ARTICLE

Clinical Features of Sickle Cell Anaemia in Northern Nigerian Children

Caractéristiques Cliniques de l'Anémie Falciforme Chez les Enfants Nigérians du Nord

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ABSTRACT

BACKGROUND**: Sickle cell disease (SCD) is a more common and severe disease in Africa. Nigeria the most populous black nation in Africa has the largest number of sickle cell anaemia (SCA) patients in the world. Borno and Yobe State has the largest number of sickle cell trait in Nigeria with prevalence of 27.9% and 32.6% respectively. Sickle cell anaemia survival to adulthood in Africa was reported to be 10–15% in the first decade of life, with the death rate of about 5% during subsequent decades. Large portion that died have shown no overt chronic organ failure but died during acute episodes of pain, infections, acute chest syndrome, stroke and anaemic crises.**

OBJECTIVE**: To review the morbidity pattern among SCA children in the University of Maiduguri Teaching Hospital, North-Eastern Nigeria.**

METHODS: **This was a retrospective study of SCA patients seen from 1994 to 2003. There were 333 case notes retrieved and reviewed with their age, sex, clinical features at diagnosis and other morbidities documented and analysed.**

RESULTS**: Sickle cell anaemia is commonly diagnosed in infants aged 6–11 months, with hand-foot swelling and jaundice being the commonest symptoms at presentation. Anaemic and vaso-occlusive crises were seen more common in children aged 1–5 years. The over-all morbidity pattern is same in both sexes with diseases such as bronchopneumonia, malaria, osteomyelitis, urinary tract infections, septicaemia and septic arthritis being common. Age has been found to influence morbidity pattern in our studied patients.**

CONCLUSION**: There is need for early diagnosis and counseling, so that mothers or caregivers will be able to assist in prompt identification of these morbidities and to seek for prompt and appropriate treatment in the health facilities. WAJM 2012; 31(2): 81–85.**

Keywords: **Sickle cell anaemia; Clinical features; Children; Northern Nigeria.**

RÉSUMÉ

CONTEXTE: La maladie drépanocytaire est une affection sévère et fréquente en Afrique. Le Nigeria, nation la plus peuplée en Afrique a le plus grand nombre de cas d'anémies drépanocytaires (AD) dans le monde. Les états de Borno et de Yobe ont les plus grandes prévalences de traits drépanocytaires avec des taux respectifs de 27.9% et 32.6%. En cas d'anémie drépanocytaire la survie jusqu'à l'âge adulte a été estimée à 10-15% dans la première décade avec une survie d'environ 5% dans les décades suivantes. Une grande proportion des cas de décès est survenue en l'absence de contexte de défaillance organique chronique mais plutôt dans un contexte de crise douloureuse aigue, d'infections, de syndrome thoracique aigu, d'Accident Vasculaire Cérébral et de crises anémiques.

OBJECTIF: Faire une revue des caractéristiques de la morbidité chez des enfants présentant une AD à l'Hôpital Universitaire de Maiduguri, au Nord Est du Nigeria.

METHODES: Il s'agissait d'une étude rétrospective des patients présentant une AD suivis de 1994 à 2003. Il y'avait 333 dossiers médicaux retrouvés et revus, l'analyse avait porté sur l'âge, le sexe, les caractéristiques cliniques au moment du diagnostic et les autres morbidités documentées**.**

RESULTATS: L'anémie drépanocytaire est fréquemment diagnostiquée chez les enfants âgés de 6 à 11 mois avec comme principaux symptômes un œdème des pieds et des mains et un ictère. Les crises anémiques et vaso-occlusives étaient plus fréquemment retrouvées chez les enfants de 1 à 5 ans. La morbidité avait globalement les mêmes caractéristiques dans les 2 sexes avec généralement la bronchopneumonie, le paludisme, l'ostéomyélite, les infections urinaires, la septicémie et l'arthrite septique. L'âge est apparu comme facteur influant sur la morbidité chez les patients étudiés.

CONCLUSION: Il y'a une nécessité d'un diagnostic précoce et d'un counselling afin que les mères et les soignants soient en mesure d'aider à identifier ces morbidités et orienter les patients vers les structures de soins pour une prise en charge appropriée. **WAJM 2012; 31(2): 81–85.**

Mots clés: Anémie drépanocytaire; Caractéristiques Cliniques; Enfants; Nord du Nigeria.

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Abbreviations: HbS, Hemoglobin; **PTB,** Pulmonary tuberculosis; **SCA,** Sickle cell anaemia; **SCD,** Sickle cell disease; **SS,** Homozygous sickle cell; **UTI,** Urinary tract infection;**VOC,** Vaso-oclusive crisis;

INTRODUCTION

Sickle cell anaemia (SCA) occurs in those individuals who are homozygous (SS) for the sickle mutation in the gene for the â-chain of hemoglobin (HbS). It can also occur in a situation where there is co-inheritance of a single HbS gene with the gene for certain other variant such as HbC or beta-thalassaemia.[1] The first African case of sickle cell anaemia (SCA) in literature was a 10 year old boy from Sudan[1] Reports that followed from other parts of Africa indicate that the disease was more severe in this part of the world. There are various reports of survival into adulthood, ranging from 1–20%.[2–4] These has changed significantly with improvement in the health facilities and diagnosis of the disorder to 10–15% in the first decade of life, with death rate of about 5% in the subsequent decade.[5] It has also been reported that 50% of patients with SCA survive beyond 50 years of age.[6] Large portion that died have shown no overt chronic organ failure but died during acute episodes of pain, such as acute chest syndrome, infections, strokes and anaemic crises.[6]

Nigeria the most populous black race in Africa has the largest number of sickle cell anaemia patient in the world.[7] With sickle cell trait highest in the northern Nigeria where it was found in *Kanuri* tribe of Borno state 27.9% and *Bade* tribe 32.6% in Yobe state.[7] It is expected that sickle cell anaemia is very common in this environment. It is known that infections, vaso-occuclsive and anaemic crisis are common manifestations in sickle cell anaemia patients[8]. Vaso-occlusive crisis has been reported to be the commonest cause of hospitalizations among children with SCD.[8–9] There has not been any detailed study of morbidity pattern among sickle cell anaemia children in North-Eastern Nigeria.

SUBJECTS, MATERIALS AND METHODS

The University of Maiduguri Teaching Hospital is situated in Maiduguri, the capital of Borno state in North-Eastern Nigeria. It is a tertiary health facility but function as general and referral hospital. Paediatric department has a special clinic for SCA patients. Patients are usually referred from Paediatric General Out-patient Department and Paediatric Wards of the hospital after the diagnosis of SCA has been established by haemoglobin electrophoresis. The patients attend sickle cell clinic at 4, 6 and 8 weeks interval depending on age, severity of symptoms, and distance from the hospital or town. In special cases appointment for visit can be as short as 1 or 2 weeks if need for closer monitoring, or patients are admitted if warranted by their clinical conditions. Routine medication consists of Folic acid and Proguanil. Case notes of all SCA patients admitted from 1994 to 2003 were retrieved. A total of 362 case notes were registered on the hospital central library computer, of which 333 case notes were retrieved, 29 folders were not seen. All retrieved case notes were reviewed and the following were recorded; age, sex, age at diagnosis, presenting complaints at diagnosis and examination findings at diagnosis. Data analysis was conducted using SPSS software program which provided frequency distribution, percentages, tables, Chi square test and student't' test where applicable.

RESULTS

The age at which diagnosis of SCA was made is presented in Table 1. The commonest age at diagnosis was between 6–11 months in both sexes (31.5%), followed by age 1–5 years (31.2%). Majority of the patients at diagnosis were severely anaemic as seen in Table 2. The main symptoms with which patients presented at the time of diagnosis of SCA are presented in Table 3. Hand and foot swellings was the main symptom at diagnosis in all age groups constituting 197 (38.7%) and was more common in age group 6 – 11 months, followed by jaundice, then paleness (pallor) 16.1% & 13.6% respectively. Jaundice was complaint in children 1 – 4 years constituting 11.2%.

The age and sex distribution of main intercurrent infection are shown in Table 4. Twenty nine percent of the males and 19.7% of the females were treated for pneumonia while 18% of the males and 27% of the females were treated for simple malaria. These were the common intercurent infection observed among these patients. Osteomyelitis was relatively common, 12.6% in males and 15.8% in females. Table 5 shows frequency distribution of anaemic and vasooclusive crisis. Anaemic crisis is commonest in the age group 1– 4 years; and is commoner in males. Vasoocclusive crisis is also commoner in age group 1–4 years, and also 5–9 years. It occurs almost equally in both sexes.

Table 1: Age and Sex Distribution of Patients at Diagnosis

Age	Sex		Total n (%)
	Male n (%)	Female n (%)	
< 6 months	20 (11.3)	13 (8.3)	33 (9.9)
6–11 months	55 (31.1)	50 (32.1)	105 (31.5)
1–4 years	49 (27.7)	55 (35.3)	104 (31.2)
5–9 years	8 (4.5)	7 (4.5)	15 (4.5)
10–14 years	2 (1.1)	5 (3.2)	7 (2.1)
Not known	43 (24.3)	26 (16.7)	69 (20.7)
Total	**177 (100.0)**	**156 (100.0)**	**333 (100.0)**

Table 2: Distribution of Patients by Haematocrit at Diagnosis

Haematocrit (%)	Cases n (%)
≤10	44(13.2)
11 – 15	58(17.4)
16 – 20	92(27.6)
21 – 25	81(24.4)
26 – 29	46(13.8)
≥30	12(3.6)
Total	**333(100.0)**

Table 3: Age Distribution of Main Symptoms at Diagnosis

Age	Main Symptoms at Diagnosis* n (%†)							
	HF	FV	CG	AP	BP	JD	PL	DU
<6 months	28 (40.6)	11(15.9)	2 (2.9)	4 (5.8)	4 (5.8)	12(17.4)	8 (11.6)	–
6–11 months	86 (43.0)	16 (8.0)	13(6.5)	14 (7.0)	13 (6.5)	27(13.5)	29 (14.5)	2 (1.0)
1–4 years	79 (38.3)	18 (8.7)	13(6.3)	23(11.2)	14 (6.8)	31(15.0)	27 (13.1)	1 (0.5)
5–9 years	3 (15.0)	2 (10.0)	–	1 (5.0)	5 (25.0)	6 (30.0)	3 (15.0)	–
10–14 years	1 (7.1)	2 (14.2)	1 (7.1)	–	2 (14.2)	6 (42.9)	2 (14.2)	–
Total	**197(38.7)**	**49 (9.6)**	**29(5.7)**	**42 (8.3)**	**38 (7.5)**	**82(16.1)**	**69 (13.6)**	**3 (0.6)**

AP, *Abdominal pain;* ***BP,*** *Bone pain;* ***CG,*** *Cough;* ***DU,*** *Dysuria;* ***FV,*** *Fever;* ***HF,*** *Hand/foot swelling;* ***JD,*** *Jaundice;* ***PL,*** *Pallor;* ****,*** *some patients had more than one main symptom at diagnosis;* †*, the denominator for the percentages were the total number of patients in each age group studied.*

Table 4: Age and Sex Distribution of Main Intercurrent Infection

Age and Sex		Main Intercurrent Infection*									
		SM	OM	SA	BP	UI	CL	SM	CM	TF	MG
< 6 months	M	3	6	4	4	1	2	1	–	–	–
	F	1	4	3	3	1	–	4	–	–	–
6 – 11 months	M	9	7	8	26	3	1	11	–	1	1
	F	8	11	2	12	2	3	18	1	1	–
1 – 4 years	M	5	7	3	15	5	4	15	1	1	2
	F	2	9	5	13	2	4	16	2	-	1
5 – 9 years	M	–	1	1	3	–	3	3	–	2	–
	F	1	–	1	1	–	4	2	1	1	1
10 – 14 years	M	–	–	–	1	1	6	–	–	–	–
	F	–	–	–	1	–	9	1	–	1	–
Total		**29**	**45**	**27**	**79**	**15**	**36**	**71**	**05**	**7**	**5**

B, *Bronchopneumonia;* ***CL,*** *Cellulitis;* ***CM,*** *Complicated (severe) malaria;* ***MG,*** *Meningitis;* ***OM,*** *Osteomyelitis;* ***SA,*** *Septic arthritis;* ***SM,*** *Septicaemia;* ***SM,*** *Simple malaria;* ***TF,*** *Typhoid fever;* ***UTI,*** *Urinary tract infection;* ****,*** *Some patients did not have infection documented at time of review.*

Table 5: Age and Sex Distribution of Anaemic and Vasoocclusive Crises

Age	Type of Crises*			
	Anaemic crises		Vaso-oclusive crises	
	Male n (%)	Female n (%)	Male n (%)	Female n (%)
<6 months	2 (1.3)	2 (1.3)	5 (2.0)	–
6 – 11 months	11 (7.3)	11 (7.3)	14 (5.6)	9 (3.6)
1 – 4 years	34 (22.5)	22 (14.6)	51 (20.2)	40 (15.9)
5 – 9 years	26 (17.2)	20 (13.2)	44 (17.5)	45 (17.9)
10 – 14 years	16 (10.6)	7 (4.6)	20 (7.9)	24 (9.5)
Total	**89 (37.9)**	**62 (34.4)**	**134 (60.1)**	**118 (65.6)**

****,*** *Not all patients had crises; some had more than one crisis while some were admitted because of infections.*

DISCUSSION

The patients in this review suffered mainly from pains, fever, cough and jaundice. This has been reported from many parts of the world; including Nigeria, where Kaine[10] found respiratory tract infections, fever, and pain crisis as main causes of morbidity in children with SCA. Though Ugandan study[11] dwell much on extend of the homozygous sickle cell (SS) in the East African region, still highlight malarial fever as the commonest cause of morbidity/mortality among these children. Despite the fact that Najwa *et al*[9] reported sickle cell disease (SCD) having a milder course among the Kuwaiti

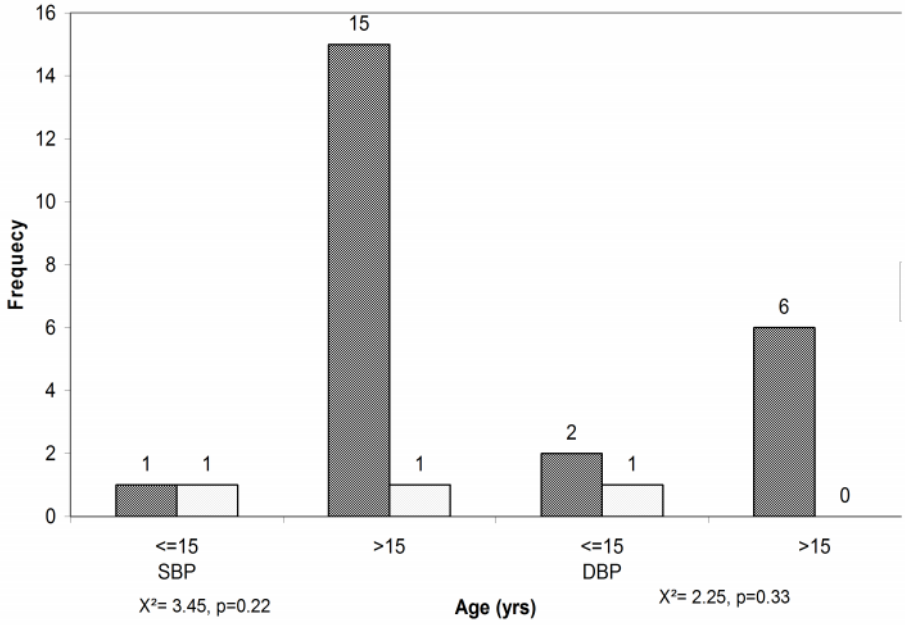

Fig. 1: Association of Age, Pre-hypertension and Hypertension of the Study Population

patients because they carry the Arabian/ Indian haplotype, they still found bone pain crisis constituting 60% of hospital admissions. In one of the American series by Orah *et al* [6] reported that SCA patients suffer mainly from acute episodes of pains, acute chest syndrome and stroke. Current review also highlight the fever were caused mainly by; malaria. Other causes were respiratory tract infections, septicaemia, osteomyelitis and urinary tract infections. The high frequency of vaso-oclusive crisis (VOC) observed in this review has been reported by other workers.[12,13] This may be because the precipitant of VOC are common such as infections, infestations, dehydration and extreme of weathers.

Bone pain crisis and hand-foot syndrome in younger children were due to vascular occlusion by sickled cells or aggregates of sickled cells. It may also explain most of the abdominal pain reported in this study. Our patients were not on any of the anti-sickling agents though several anti-sickling agents have been tried in the past with no proven efficacy.[14] Some of the newer anti-sickling agents may offer hope in the future. Current study has shown some factors capable of precipitating painful crisis. These include fever and respiratory tract infection. Some have reported over exposure to cold and exertion to precipitate painful crisis.[15]

In Africa, malaria and respiratory tract infection were the commonest precipitating factors of painful crisis.[9, 10] This was also observed in this present review. Malaria has been found to be very common in present review, even in the neighbouring Kebbi State, Yvonne[16] has reported that malaria was the commonest cause of admission generally in children. Contrary to our findings, Kaine[10] and Konotey-Ahulu[17] reported low incidence of malaria which they attributed to the use of antimalarial prophylaxis. Most of our patients were on antimalarial prophylaxis; however we can not come out categorically that we have Proguanil resistance malaria. There may be need to review the antimalarial prophylaxis being given to SCA children for better therapeutic effectiveness.

The several cases of other infections such as septic arthritis, pneumonia, osteomyelitis, UTI, typhoid fever observed in both sexes in current study highlight the need for care giver or mothers to recognize infections of such magnitude and the need for prompt treatment accordingly. There is also the need to introduce immunization such as pneumococcal and Haemophilus influenza vaccines, this may reduce the incidence of infections, this has been done in the developed world. There were 9 (2.7%) cases of pulmonary tuberculosis (PTB) seen in present review, similarly Santer,[7] has reported cases of pulmonary tuberculosis and extrapulmonary tuberculosis in sickle cell anaemia patients. This highlights the fact that SCA is not all about crisis but call for physicians to critically review all patients in case they might have tuberculosis. Anaemic crisis was one of the main causes of hospitalisation in this study and majority of the patients in this review presented with severe form of anaemia. This agrees with the finding of Kaine in her study of the morbidity of homozygous SCA,[10] which was reported as a result of rapid haemolysis, bone marrow aplasia and sequestration into the spleen or the liver. The jaundice observed in present study 82 (16.1%) suggested increased haemolysis may be responsible for high incidence of anaemic crisis seen in this review. This was in agreement with similar study done in Enugu-Nigeria.[10] These patients need to be treated promptly as severe anaemia has been found to be responsible for high mortality in sickle cell anaemia in East and Central Africa.[18]

This study has shown that the pattern of morbidity is the same in both males and females. The high morbidity among SCA in this review has also been reported in other part of Africa,[7, 19] this has been attributed to adverse environmental factors which favour infections and consequently sickle cell crises. The study has also shown objective signs of diseases such as septicaemia, septic arthritis, pneumonia, UTI, malaria and cellulites. This review showed that age influences morbidity in SCA patients. The incidence of infection and sickle cell crises among patients has shown progressive pattern of decline with increasing age, with a sharp decline after 10 years of age.

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