RESEARCH REPORT

Clinical picture and correlates for sickle cell anaemia among Zambian children attending Arthur Davison Children's Hospital Sickle Cell Disease clinic in Zambia

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Sickle cell anaemia (SCA) leads to high rates of morbidity and eventually death in persons aged 20-29 years. The objective of the study was to establish the clinical picture and correlates for SCA among Zambian children attending Arthur Davison Children's Hospital Sickle Cell Disease clinic in Zambia. All 320 records were reviewed. The proportion of patients with SCA attending a sickle cell disease clinic was 43.4%. Difficulty in breathing (64.5%), sore throat (64.5%), fever (62.9%), swollen/painful limbs/joints (46.8%), dizziness (35.5%) and jaundice (35.5%) were the most common signs and symptoms for SCA. Only age was significantly associated with SCA. Children aged less than one year were less likely to have SCA compared to children aged 10 years or older. Sickle cell anaemia manifests later in life. There is need for implementation of programmes that will diagnose the condition much earlier in life so that interventions directed at the commonest causes of medical admission are started early.

Introduction

Sickle cell disease (SCD), an autosomal recessive disease, is one of the most common genetic disorders in the world. Diallo and Tchernia [1] suggested that approximately 200 000 children are born with SCD worldwide every year and that three quarters of these births occur in sub-Saharan Africa [1]. The disease is a chronic debilitating disorder affecting erythrocytes (red blood cells), which is most common among people from Africa, India, the Caribbean, the Middle East, and the Mediterranean [2].

Sickle cell disease (SCD) is a disease in which people inherit abnormal haemoglobin gene called haemoglobin S or sickle haemoglobin in their red blood cells from parents [3]. When the haemoglobin S gene is inherited from both parents, haemoglobin SS, the disease is called sickle cell anaemia. Haemoglobin SS is the most common and severe form of SCD. The other forms of the SCD are Haemoglobin SC, Haemoglobin Sβ0 thalassemia, Haemoglobin Sβ+ thalassemia, Haemoglobin SD,

Figure 1 Determination of haemoglobin solubility test results

haemoglobin SO and Haemoglobin SE. People who inherit a haemoglobin gene "S" from one parent and a normal gene "A" from the other parent are said to have sickle cell trait [4].

SCA results in high rates of morbidity and subsequently death mainly before the age of 20-30 years [5]. Although in its heterozygous form, the haemoglobin S gene provides substantial protection against malaria, malaria is probably the most important cause of morbidity and mortality in SCD in Africa [6]. Athale and Chintu [7] reported that the SCA patients accounted for 2.9% of the total admissions and the average case fatality was 6.6% of the total SCA admissions. The highest mortality rate was noted in the 1-5 years age group (54.8%). The common causes of death were infections (29.5%), vasoocclusive crises (22.7%) and splenic sequestration crises (20.5%). Leg ulcers, priapisms [8,9], stroke [10] and vaso-occlusive pain episodes [11] are also common in individuals with SCA. It is important that characteristics of persons with SCA are established to appropriately manage these patients. There is limited information on clinical data on SCA on Zambia. Hence,

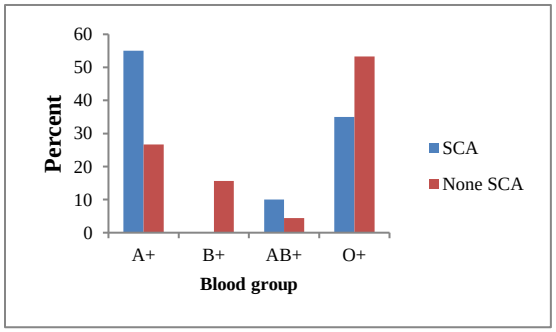

Figure 2 Distribution of blood groups

the objective of the study was to establish the clinical picture and correlates for SCA among Zambian children attending Arthur Davison Children's Hospital (ADCH) Sickle Cell Disease Clinic in Zambia.

Methods

A hospital case record review was conducted at Arthur Davison Children's Hospital Sickle Cell Disease Clinic between April and June 2015. All 320 records for SCD patients were reviewed. Patients were examined by attending doctors who recorded their findings in patient files. Haemoglobin (Hb) SS, AA

Table 1 Sample description

	Total	Male	Female	
Factor	n (%)	n (%)	n (%)	p value
Age (years)				
<1	48 (15.0)	31 (17.7)	17 (11.6)	0.349
1-4	104 (32.4)	58 (33.1)	46 (31.5)	
5-9	102 (31.8)	50 (28.6)	52 (35.6)	
10+	67 (20.9)	36 (20.6)	31 (21.2)	
Residence				
Low density	26 (8.1)	11 (6.3)	15 (10.3)	0.192
High density	295 (91.9)	164 (93.7)	131 (89.7)	
Blood group				
A^+	38 (27.0)	25 (29.1)	13 (23.6)	0.662
B^+	25 (17.7)	17 (19.8)	8 (14.5)	
AB^+	11 (7.8)	6 (7.0)	5 (9.1)	
O^+	67 (47.5)	38 (44.2)	29 (52.7)	
Malaria frequency				
1	106 (66.2)	63 (67.0)	43 (65.2)	0.806
2+	54 (33.8)	31 (33.0)	23 (34.8)	
Weight for age (Percentile)				
<2.5	163 (58.4)	92 (60.5)	71 (55.9)	0.435
2.5+	116 (41.6)	60 (39.5)	56 (44.1)	
Sickle Cell Anaemia				
Yes	62 (43.4)	28 (37.3)	34 (50.0)	0.127
No	81 (56.6)	47 (62.7)	34 (50.0)	

and AS were determined using a solubility test for detection of haemoglobins [12]. A red band of flocculate on the surface of a clear yellowish solution indicated Hb SS (sickle cell anaemia), while a clear pinkish solution indicated Hb AA, a test result resembling that of Hb AS indicated Hb SS +F and a sharply defined red band of flocculate on the surface of a pink coloured solution indicated Hb AS (Figure 1). Non-Hb SS was defined as none sickle cell anaemia. Giemsa staining was used to detect malaria parasites [13]. Parasite count for thin film of 5-10% in 1000 RBCs indicated that the infection was mild, 10-30% indicated that the infection was moderate and over 30% suggested that the infection was severe and the slide was negative if no parasites were seen.

A check list was used to abstract data from the records. The variables abstracted included age, sex, blood group, genome, residential address, signs and symptoms and associated conditions.

Data was computerised using Epi Data version 3.1 [14] and exported to SPSS version 16.0 [15] for data analysis. Associations between qualitative variables were established using the Chi-squared test at the 5% significance level. Independent factors associated with the outcome were determined using a multivariate logistic regression analysis. Odds ratio (OR) and 95% confidence interval (CI) are reported.

Results

A total of 320 records of patients attending a sickle cell disease clinic were reviewed of which 54.5% were males. Socio-demographic factors were not associated with sex (Table 1). Overall, most patients were of ages 1-4 years (32.4%) and 5-9 years (31.8%). The majority (91.9%) of the patients resided in high density suburbs.

Table 2 Correlates for Sickle cell anaemia

Factor	Total n (%)	With SCA n (%)	Without SCA n (%)	p value
Sex				
Male	75 (52.4)	28 (45.2)	47 (58.0)	0.127
Female	68 (47.6)	34 (54.8)	34 (42.0)	
Age (years)				
<1	30 (21.0)	6 (9.7)	24 (29.6)	<0.001
1-4	62 (43.4)	27 (43.5)	35 (43.2)	
5-9	38 (26.6)	26 (41.9)	12 (14.8)	
10+	13 (9.1)	3 (4.8)	10 (12.3)	
Residence				
Low density	7 (4.9)	2 (3.2)	5 (6.2)	0.418
High density	136 (95.1)	60 (96.8)	76 (93.8)	
Malaria frequency				
1	53 (73.6)	21 (77.8)	32 (71.1)	0.534
2+	19 (26.4)	6 (22.2)	13 (28.9)	
Weight for age (Percentile)				
<2.5	66 (53.2)	28 (50.0)	38 (55.9)	0.514
2.5+	58 (46.8)	28 (50.0)	30 (44.1)	

About a third (33.8%) of the patients had two or more episodes of malaria within 18 months. About 4 in 10 (41.6%) of the patients were in the 2.5 percentile or more weight for age category. The most common blood group was A+ among SCA patients (55.0%), while the most common blood group among none SCA patients was O+ (53.3%) as shown in Figure 2. The distribution of the genotypes was as follows: Hb AA (3 or 2.1%), Hb AS (78 or 54.5%) and Hb SS (62 or 43.4%), indicating that 43.4% of the patients had SCA. The most frequent signs and symptoms among the patients who had SCA were: difficulty in breathing (64.5%), sore throat (64.5) and fever (62.9%). About a third of the patients had dizziness (35.5%) and jaundice (35.5%) as shown in Table 3.

Table 2 shows factors associated with SCA. Only age was significantly associated with SCA. SCA is less likely to be manifested in the <1 year age group (OR=0.42, 95% CI [0.19, 0.91]) and more likely to be manifested in 5-9 years group (OR=3.64, 95% CI [1.89, 7.03]) compared in persons aged 10 years or older (Table 4).

Discussion

The proportion of patients with SCA attending a sickle cell disease clinic in the

current study was 43.4%. Difficulty in breathing, sore throat, fever, swollen/painful limbs/joints, dizziness and jaundice were the most common signs and symptoms. Only age was significantly associated with SCA. Children aged less than one year were less likely to have SCA compared to children aged 10 years or older. A proportion of SCA of 43.4% observed in the current study is lower than the 62% that was observed by Gill et al [16] in the United States of America.

Table 3 Distribution of signs and symptoms for Sickle Cell disease patients by Hb SS genotype

	SCD Total=322	SCA Total=62	None SCA Total=81
Sign/symptom	n (%)	n (%)	n (%)
Fever	210 (65.2)	39 (62.9)	64 (79.0)
Headache	58 (18.0)	9 (14.5)	13 (16.0)
Vomiting/ Diarrhoea	75 (23.3)	14 (22.6)	23 (28.4)
Reduced appetite	69 (21.4)	9 (14.5)	32 (39.5)
Dizziness	112 (34.8)	22 (35.5)	34 (42.0)
Cough	8 (2.5)	1 (1.6)	3 (3.7)
Sore throat	205 (63.7)	40 (64.5)	60 (74.1)
Backache	48 (14.9)	12 (19.4)	14 (17.3)
Abdominal pain	42 (13.0)	9 (14.5)	7 (8.6)
Swollen/painful limbs/joints	114 (35.4)	29 (46.8)	24 (29.6)
Difficulty in breathing	193 (59.9)	40 (64.5)	50 (61.7)
Chest pain	61 (18.9)	13 (21.0)	23 (28.4)
Pallor	44 (13.7)	5 (8.1)	8 (9.9)
Jaundice	125 (38.8)	22 (35.5)	31 (38.3)
Sneezing	117 (36.3)	18 (29.0)	26 (32.1)
Runny nose	70 (21.7)	12 (19.4)	27 (33.3)
General body pain	29 (9.0)	9 (14.5)	9 (11.1)
General body weakness	37 (11.5)	8 (12.9)	8 (9.9)
Splenomegaly	39 (12.2)	5 (8.1)	16 (19.8)
Hepatosplenomegaly	4 (1.2)	3 (4.8)	3 (3.7)
Eye discharge	14 (4.3)	1 (1.6)	4 (4.9)
Ear discharge	7 (2.2)	1 (1.6)	0(0)

The common signs and symptoms for SCA in the current study were: difficulty in breathing, sore throat, fever, swollen/painful limbs/joints, dizziness and jaundice. Meanwhile, painful crises and acute chest syndrome were the most common sickle cell-related events in SCD patients in the United States of America [16]. Meanwhile, painful events, splenic sequestration, hemolytic crisis,

Table 4 Magnitude of association of age with Sickle Cell Anaemia

Age (year)	Odds ratio (95% Confidence Interval)
<1	0.42 (0.19, 0.91)
1-4	1.30 (0.73, 2.29)
5-9	3.64 (1.89, 7.03)
10+	1

foot-hand syndrome, infection and acute chest syndrome were the common clinical phenotypes reported by da Silva Filho et al [17] in under 6 year-old-children in Rio de Janeiro, Brazil.

Age was significantly associated with SCA in the current study. SCA is more likely to be manifested in age groups older than one year. SCA complications start in early life, but become more apparent with increasing age [2]. Foetal haemoglobin (Hb F) may be responsible for the lack of clinical symptoms in new-borns with SCD [18].

It is possible that some cases may have been misclassified as non-sickle cell anaemia because of having recently received transfusion of blood with Hb AS or normal blood. Our findings may have been biased to the extent of this misclassification. However, we believe that this bias may have been negligible because the cases attending the SCD clinic may have been tested for genotype more than once.

In conclusion, sickle cell anaemia manifests later in life. There is need for implementation of programmes that will diagnose the condition much earlier in life so that interventions directed at the commonest causes of medical admission are started early.

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