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The Burden of Sickle Cell Disease at a Tertiary Hospital in Malawi

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Abstract

Globally, there are 300,000 births per year of children with Sickle Cell Disease (SCD) and over 90% in Africa. There is paucity of data on its burden in Malawi which is critical in the development of disease specific interventions.

A retrospective review of clinical files of children with SCD was conducted. Data were analysed using Stata, version 13.0. Chi Square (or Fisher's exact) test was used to look for significant associations between variables. A binomial logistic regression was used to quantify the association between predictor and outcome variables.

From July 2016 to June 2019, a total of 16,333 admissions were made, of which, 512 were SCD patients representing 3.1%. About 13.2% were diagnosed in infancy. Anaemia (94.1%), septicaemia (79.5%) and painful crisis (54.3%) were the common complications. Patients with painful crisis, splenic and hepatic sequestration were 1.7, 2.1 and 2.4 times respectively more likely to be admitted for more than 5 days than those without these complications.

Our study has shown that SCD contributes a significant burden in Malawi with anaemia, septicaemia and painful crisis being the common complications, highlighting the need to invest more effort in disease management and control.

Keywords: Sickle cell disease; Burden; Children; Malawi; Neonatal screening

Abbreviations

SCD: Sickle Cell Disease; MCH: Mzuzu Central Hospital; SSA: Sub Saharan Africa; NCD: Non-Communicable Diseases; WHO: World Health Organization; RBC: Red Blood Cell; Hb: Haemoglobin; MCV: Mean Corpuscular Volume; MCHC: Mean Corpuscular Haemoglobin Concentration; WBC: White Blood Cell

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Introduction

Africa bears the highest burden of sickle cell disease (SCD) where up to 90% of the 300,000 global births of SCD per year occur and childhood mortality of about 50-90% take place [1,2]. Despite being one of the major killers of infants and children, similar to other diseases like malaria and HIV/AIDS, it remains a condition of low priority consideration in many countries [2]. In efforts to scale up its management and control, SCD is recognised as a significant cause of childhood mortality and has been identified by the World Health Organization (WHO) as an area requiring specific attention in order to meet the sustainable development goals [3].

In Malawi, SCD is equally a significant cause of childhood morbidity and consequently an important policy issue for the ministry of health [4]. However, there is scarcity of data to explain the magnitude of the disease burden. Lack of awareness and recognition about SCD by local health ministries' has largely made the disease an invisible health issue [5] and yet these patients will continue to suffer from complications of the disease and require lifelong care.

Mzuzu Central Hospital (MCH) which is located in the northern region of Malawi is one of the central hospitals in the country. The hospital attends to a large volume of patients and in patient data from paediatric department reveals that, at least five to six children with SCD are admitted weekly with various complications of the disease yet, the extent to which it contributes to paediatric hospital admissions is not known. This makes it hard to come up with a credible estimate of the total number of individuals currently affected by the disease and therefore compromise the evidence base of its burden. This information would be useful for the development of SCD national control programs in Malawi. This study sought to describe the burden of SCD, establish its common clinical features, the haematological profile, case fatality and the association between clinical features and hospital admission outcomes in children admitted to a tertiary hospital in Malawi.

Methods

Study design and setting

This was a retrospective cross-sectional study of children admitted to MCH paediatric ward between July, 2016 and June, 2019. MCH which is a teaching and regional referral hospital with a bed capacity of 410 serves a population of over 2,289,780 million people [6] including six district hospitals. The department of paediatrics has a capacity of 60 inpatient beds, which may increase to more than 150% mainly in the rainy season. The department attends to children from seven weeks to thirteen years old with various childhood conditions including SCD.

Study population and procedures

Data were collected from clinical files of children admitted to the ward due to SCD. All files of patients below 13 years of age admitted to the ward during the study period for one day or more and regardless of their gender or nationality were included in the study. Firstly, clinical files of all patients admitted to the ward were screened by trained data collectors in order to identify cases of SCD. The retrieved SCD cases underwent a detailed review to extract relevant data such as age, gender, clinical features, laboratory investigations done, outcome and length of hospital stay using a predesigned data extraction tool.

Statistical analysis

Data were entered in Microsoft excel 2016, validated and cleaned before importing into Stata, version 13.0 (Stata Corp. LP, College Station, TX, United States of America) for analysis. Descriptive analyses were performed to summarise patients' socio demographic and clinical characteristics. Chi Square (or Fisher's exact) test was used to look for significant associations between predictor and outcome variables with a p-value of less than 0.05 being statistically significant. A binomial logistic regression was used to quantify the association between predictor variables and outcome variables.

Results

Baseline characteristics

From July 2016 to June 2019, the paediatrics department had a total of 16,333 inpatient admissions, out of which 512 were SCD patients. This represents 3.1% of the total admissions.

Table 1 depicts the demographic characteristics of SCD patients admitted to paediatrics department within the study period. Overall, there were more males (58%) than females. The department admitted 25 (4.9%) children below twelve months during the study period. Slightly more than half of the patients (54.3%) were from outside Mzuzu city. Out of 512 patients, 68 (13.3%) received their SCD diagnosis during the study period, 9 (13.2%) of these were diagnosed in infancy (before twelve months of life). More than half (58.8%) were diagnosed between the ages of 12 to 59 months while 27.9% after their fifth birthday.

Common clinical features for SCD patients

The most common clinical features were anaemia (94.1%), sepsis (79.5%) and painful crisis (54.3%). Leg ulcers, priapism and dactylitis were the least common clinical features representing 0.6%, 1.0% and 0.6% respectively. No case of stroke was observed in this study. In addition to these clinical features, 68 (13.3%) patients had malaria by rapid diagnostic test (**Table 2**).

Haematological parameters of SCD children admitted at Mzuzu central hospital

Routine full blood counts showed that, haemoglobin ranged from 1.4-12 g/dl with a mean of 6.4 g/dl. Those with haemoglobin of less than 5 g/dL were 115 (25.8%). Red blood cells ranged from 0.6-6.3(×1012/L) with a mean of 2.4 (×1012/L) while white blood cells ranged from 2.7-145.4 (×109/L) with a mean of 26.4 (×109/L) and platelets ranged from 11-1424 with a mean of 358.8 (×109/L). These parameters were compared against the normal reference limits of the haematology analyzer (sysmex XP 300) which is not for the Malawian population (**Table 3**).

Table 1 Demographic characteristics of SCD patients.

Characteristic	Frequency	Percentage	Cumulative frequency
Sex			
Male	298	58.2	
Female	214	41.8	
Age(months)			
0-11	25	4.9	4.9
12-59	227	44.3	49.2
≥ 60	260	50.8	100.0
Location (n=254)			
Within Mzuzu city	116	45.7	
Outside Mzuzu city	138	54.3	
SCD History			
Known case	444	86.7	
Newly diagnosed cases	68	13.3	
Age (months) for newly diagnosed cases during study period (n=68)			
0-11	9	13.2	13.2
12-59	40	58.8	72.0
≥ 60	19	27.9	100.0

Mean age (range) = 67.8months (6-156); median age (IQR) = 60 months (30.5-108)

Case fatality and length of stay for SCD patients admitted at MCH

Death occurred in 7 (1.4%) children, with the under fives making a slightly high percentage (57.1%). The majority of the patients (84.8%) stayed in the hospital for 5 days or less (**Table 4**).

The association between clinical features and hospital admission outcomes among SCD patients admitted at MCH

Of the investigated clinical features, none were associated with case fatality. However, three of these features; painful crisis (p value=0.03), hepatic sequestration (p value=0.01) and splenic sequestration (p value=0.03) were significantly associated with length of hospital stay (**Table 5**).

In univariate logistic regression, painful crisis, splenic sequestration and hepatic sequestration were significantly associated with length of hospital stay. Sickle cell patients with painful crisis, splenic and hepatic sequestration were 1.7, 2.1 and 2.4 times respectively more likely to be admitted for more than 5 days than those without these complications. However,

Table 2 Common clinical features.

Clinical feature	0-11months n=25 Frequency (%)	12-59 months n=227 Frequency (%)	≥ 60months n=260 Frequency (%)	Total n= 512 Frequency (%)
Anaemia*	23 (92.0)	212 (93.4)	247 (95.0)	482 (94.1)
Sepsis	22 (88.0)	191 (84.1)	194 (74.6)	407 (79.5)
Painful crisis	12 (48.0)	89 (39.2)	177 (68.1)	278 (54.3)
Jaundice	11 (44.0)	62 (27.3)	106 (40.8)	179 (35.0)
Pneumonia	10 (40.0)	65 (28.6)	40 (15.4)	115 (22.5)
ACS	3 (12.0)	14 (6.2)	16 (6.2)	17 (6.6)
Arthritis	4 (16.0)	32 (14.1)	44 (16.9)	80 (15.6)
SS	3 (12.0)	30 (13.2)	27 (10.4)	60 (11.7)
Stroke	-	-	-	-
HS	3 (12.0)	18 (7.9)	21 (8.1)	42 (8.2)
Leg ulcers	-	1 (0.4)	2 (0.8)	3 (0.6)
Priapism †	-	1 (0.4)	2 (0.8)	3(1.0)
Dactylitis	3 (12.0)	-	-	3 (0.6)
Malaria	2 (8.0)	23 (10.1)	43 (16.5)	68(13.3)

† Out of 298 males; ACS=Acute chest syndrome; SS= Splenic sequestration; HS=Hepatic sequestration.
*Haemoglobin less than 10.9 g/dl, (normal reference limits 10.9-17.3 g/dl).

Table 3 Haematological parameters of SCD children admitted at MCH.

Parameter (unit)	n	Mean (SD)	Range	Normal reference limits
RBC (×1012/L)	322	2.4 (0.8)	0.6-6.3	4-6
Hb (g/dL)	445	6.4 (1.9)	1.4-12	10.9-17.3
MCV (fL)	310	82.8 (10.3)	43.1-121.6	71-95
MCHC (g/dL)	303	33.2 (2.7)	22.3-51.0	33-36
WBC (×109/L)	407	26.4 (14.8)	2.7-145.4	4-10
Platelets (×109/L)	380	358.8 (200.9)	11-1424	122-330

Those with Hb<5g/dl = 115 (25.8%); one child had WBC of 338.6 and was excluded from the WBC analysis because was considered as an extreme outlier. Other conditions might have been responsible for such an elevated white cell count.

Table 4 Admission outcome and length of hospital stay.

Admission outcome	Frequency	Percentage	Cumulative frequency
Survived	505	98.6	98.6
Died	7	1.4	100.0
Case fatality by age			
0-11	-	-	-
12-59	4	57.1	57.1
≥ 60	3	42.9	100.0
Length of hospital stay			
≤ 5 days	434	84.8	
>5 days	78	15.2	

Mean length of stay = 3.6 (range) 1-20days; median 3 days (IQR) 2-5 days. Note: 85% of the children were discharged by day five

Table 5 Association between clinical features and admission outcomes.

Case fatality		Length of hospital admission				
Variable	**Died**	**Discharged**	**p-value***	**≤ 5 days**	**>5 days**	**p-value‡**
Gender						
Male	4	294	0.62	248	50	0.25
Female	3	211		186	28	
Age						
0-11	0	25	0.79	23	2	0.58
12-59	4	223		191	36	
≥ 60	3	257		220	40	
Anaemia						
Yes	7	475	0.65	410	72	0.45
No	0	30		24	6	
Sepsis						
Yes	7	400	0.34	342	65	0.36
No	0	105		92	13	
Painful crisis						
Yes	5	273	0.47	227	51	0.03
No	2	232		207	27	
Hepatic Sequestration						
Yes	1	41	0.45	30	12	0.01
No	6	464		404	66	
Splenic Sequestration						
yes	1	59	0.58	45	15	0.03
No	6	446		389	63	
Acute Chest Syndrome						
Yes	2	32	0.07	25	9	0.06
No	5	473		409	69	
Pneumonia						
yes	1	114	1.00	96	19	0.66
No	6	391		338	59	
Arthritis						
Yes	1	79	1.00	64	16	0.20
No	6	426		370	62	
Leg ulcer						
Yes	0	3	1.00	3	0	1.00*
No	7	502		431	78	
Malaria						
Yes	0	68	0.59	57	11	0.95
No	6	339		291	55	

*statistical testing by Fisher's exact; ‡ statistical testing by Chi square

Table 6 Regression analysis for length of hospital stay and clinical features.

Length of hospital admission stay	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p Value
Painful crisis				
Yes	1.7 (1.04-2.85)	0.03	1.7 (1.02-2.86)	0.04
No (reference)	-	-	-	-
Splenic sequestration				
Yes	2.1 (1.08-3.91)	0.03	1.9 (0.92-3.73)	0.08
No (reference)	-	-	-	-
Hepatic sequestration				
Yes	2.4 (1.19-5.02)	0.02	1.9 (0.89-4.24)	0.09
No (reference)	-	-	-	-

in multivariate analysis, only painful crisis was significantly associated with length of hospital stay. Sicklers who suffered painful crisis were 1.7 times more likely to stay for more than five days than those who did not suffer from painful crisis (**Table 6**).

Discussion

Our study reports on the burden of sickle cell disease at a tertiary facility in Malawi including other critical aspects such as age at disease diagnosis, common clinical features, haematological parameters, case fatality and the association between clinical features and hospital admission outcomes among children with SCD admitted at the paediatric department between July, 2016 and June, 2019. This information can be useful as it will bring forth awareness about the burden of the disease which was lacking in Malawi.

Our study has revealed that, SCD constituted a significant proportion (3.1%) among the admitted children. These results are slightly higher compared to findings documented in Kuwait, Kenya, Sudan and Uganda by Akar and Adekile [7], Uyoga et al. [8], Elderdery et al. [9] and Ndeezi et al. [10] where SCD contributed to about 0.6%, 0.8%, 1.5% and 0.7% respectively. This highlights the need to improve and prioritize health needs of children with SCD which remains a largely neglected and under prioritised health problem in our setting.

It should however, be noted that, the results of our study may be an underestimate given that, it only focussed on admitted patients and therefore missed those at the outpatient department or those that visited other health facilities. Furthermore, retrospective hospital-based studies are likely to miss children with mild disease phenotype who are never diagnosed [11].

Our study revealed that more than half of the patients (54.3%) came from outside urban areas of Mzuzu, mainly from the peri urban, rural setting and surrounding districts, highlighting the pivotal role played by the hospital in managing SCD patients, but also the health care burden placed on the hospital by children with SCD. This trend is likely to continue considering that there is no public secondary facility within Mzuzu urban to attend to these patients and the hospital will continue to bear the health burden of SCD patients since it is a lifelong condition. These findings give an undeniable evidence of limited health facilities in our setting, subjecting patients to walk long distance to access care.

Lack of dedicated sickle cell centres and programmes was also observed in Nigeria [1,12] which is likely to make patients have a high burden of complications leading to increased morbidity and mortality rate. As noted by Mulumbu & Wilson [13], the high mortality rates in Sub-Saharan Africa are influenced by poor access to care and lack of comprehensive SCD management programs. These results stress the need to establish more comprehensive peripheral health facilities within and outside Mzuzu city to meet the health care needs of SCD patients.

Findings from our study observed that, only 25 (4.9%) infants with SCD below the age of twelve months were admitted at the facility in the past three years. This explains the role of fetal haemoglobin which inhibits sickling. It has previously been documented that, sickle haemoglobin is present at birth, but most infants do not show signs until they are six months old or shortly before, given that the predominant haemoglobin at that time is fetal haemoglobin [14,15]. And by the time an infant reaches the age of six months, the fetal haemoglobin is replaced by sickled haemoglobin and the cells begin to sickle [3].

Our study revealed that, only 13.2% of the patients were diagnosed with SCD during infancy and up to 58.8% were diagnosed between the ages of 12 to 59 months and more than a quarter (26.5%) got diagnosed after their fifth birthday. These findings highlight compelling evidence for delayed diagnosis of SCD in Malawi. This is not surprising, since routine newborn screening programs are nonexistent, diagnosis is often made late and follow up of suspected cases of SCD are rarely done [4,16,17]. There is no specific age for diagnosis of SCD in Malawi, a situation which is similar to other African countries [14,18].

Due to lack of systematic screening at our setting, patients may visit the health facility for several times without being screened for SCD despite showing critical signs of SCD. Lack of awareness about the burden of disease and inadequate knowledge on disease management by health workers [5,19] have all contributed to delayed diagnosis. Furthermore, since the disease mimic signs and symptoms of other conditions such as malaria, anaemia and pneumonia, along with the high burden of these conditions in the region, health workers tend to focus more on those diseases than investigating for SCD resulting in delayed diagnosis.

Delayed diagnosis of SCD is also documented in studies from Tanzania, Democratic Republic of China and Nigeria [14,20,21]. This highlights the need to invest more effort in newborn screening and diagnosis within the African region where more than 90% of children with SCD die early before diagnosis can be made [21]. It is recommended that early detection of SCD be done at birth and neonatal period or at the latest, between six and nine months [5,14,22]. As previously documented, early diagnosis allows for prompt treatment and prevention of complications, provides an opportunity to educate parents about the child's condition and ultimately improve survival [14,15,18].

In our study, anaemia was the most common clinical feature presented by patients with SCD, followed by sepsis and then painful crisis, representing 94.1%, 79.5% and 54.3% respectively. This is not surprising because patients with SCD only have chronic anaemia as a constant feature of the disease [23]. However, the incidence of anaemia and sepsis in our study are much higher given that, our local treatment guidelines recommend that all patients with SCD get a daily dose of folic acid and monthly injection of prophylactic penicillin to prevent them from these complications which are recorded to be the most leading causes of morbidity and mortality in patients with SCD [24].

It is of particular interest to note that, painful crisis was the third common clinical feature observed in our study contrary to previous studies where it was the top most complication for children with SCD [7,20,25]. The authors feel that, this could probably be due to positive efforts by the hospital in educating parents on the prevention of pain triggers at home. These educational sessions are conducted through a parents support group program at the facility.

In our study, pneumonia (22.5%) was the most common chest infection followed by acute chest syndrome (6.6%) which is consistent with other studies conducted in Africa [21,24]. The low frequency of acute chest syndrome was also observed in previous studies [4,21,22] and is thought to be due to its underestimation by health workers [24].

The frequency of leg ulcers (0.6%), priapism (1%) and dactylitis (0.6%) in our study was low which is consistent with previous studies [21,26,27]. The prevalence of leg ulcers is generally low in younger children while dactylitis is usually common for those aged one to two years [15,28] and therefore had a low frequency due to small sample for this age group in our study. On the other hand, the prevalence of priapism is usually low due to lack of awareness by physicians and underreporting by patients [29].

It is very interesting to note that; there was no case of stroke

recorded within the study period although it has been documented that, the risk of developing stroke among SCD patients is estimated to be 250 times higher than those without SCD due to the high prevalence of several risk factors including low haemoglobin, leukocytosis and the Bantu haplotype [30]. Our results are in contrast to other studies conducted locally and in other African countries where they found high frequencies of stroke ranging from 6.8% to 16.9% [4,20,21,31].

Our findings should therefore be interpreted with caution given that, several factors including poor history taking [20] and patient physical examination by health workers, inadequate knowledge about stroke burden among sickle cell patients, lack of well stipulated protocols and equipment for conducting stroke screening in patients may all contribute to these findings.

Although it has long been assumed that malarial infection is a major cause of morbidity and mortality among SCD patients [13,30,32], our study observed that, out of 414 (80.8%) patients who were tested for Malaria, only 68 (13.3%) were found positive. The low frequency of malaria cases in our study is similar to findings by other studies in Africa which reported malaria frequency of between 11.6% and 15.6% [24,33]. The reason for such a low frequency on our part could probably be due to the use of anti malarial prophylaxis (sulfadoxine-pyrimethamine) which according to our local treatment guidelines is given to all patients with SCD every month. In addition to that, it may also indicate the effectiveness of our health education measures on the use of insecticide-treated bed nets.

Among laboratory parameters, severe anaemia (hb <5 g.dL) was seen in 25.8% of the children which is slightly higher than previous studies which reported about 13.3% [34]. The reduced haemoglobin is as a result of chronic hemolysis in patients with SCD [35].

Mortality frequency in our study was low (1.4%), an observation which is similar to other studies conducted in Africa which reported a frequency of between 1.9% and 3.8% [16,23]. However, this is most likely an underestimate as many children are likely to have died while at home or in other secondary health facilities while others before diagnosis of SCD was made [11,22] as such, these results must be interpreted with caution.

The majority (84.8%) of patients in our study were hospitalized for at most five days, signifying that in our setting, the optimal length of hospital stay for SCD children is five days or less. Painful crisis, splenic and hepatic sequestrations are the complications that lead to longer (>5 days) hospital stay. Previous studies also observed longer hospital stay for painful crisis [36,37]. In our setting, this might be a result of inadequate use of clinical guidelines to manage these complications. Enforcing adherence to clinical guidelines may help in proper management of these complications and result in quick recovery.

Limitations and Recommendations

Our study had some limitations. Given that the data were collected from clinical files, we experienced problems of incomplete data on some relevant variables. Since our study focussed on admitted patients only and excluded those that visited the emergency department, this might likely underestimate study findings. In view of the fact that, this is a single centre study, the generalizability of the results is likely to be limited. Despite these limitations, our study has provided the evidence base of the burden of sickle cell disease in Malawi highlighting the need for high level commitment at national level.

The authors recommend on the great need to establishment SCD prevention and control programmes at national level as recommended by the World Health Organization. The programme should specifically focus on implementing appropriate interventions for systematic newborn screening and diagnosis for SCD. Comprehensive clinical care should focus on the most common debilitating complications of SCD such as anaemia, infection and painful crisis. Lastly, much effort should also be invested on stroke screening and prevention for all at risk children.

Although we have provided data that will inform policy regarding the burden of SCD in Malawi and other countries, the study has highlighted the areas for further research. We propose that priority should be given to a study which should quantify the economic burden on the health facility by patients with SCD in order to plan for their lifelong health needs.

Conclusion

Our study has shown that SCD contributes a significant burden in Malawi with anaemia, sepsis and painful crisis being the most common clinical features presented by the patients. The study has further revealed that the diagnosis of SCD is delayed in our setting and contrary to our expectation; our study has demonstrated a low case fatality of children with SCD. The study has brought forth useful information which was lacking in Malawi. This might eventually help the Ministry of Health plan future needs of these children but also consider establishing SCD prevention and management programmes.

Declarations

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Authors' contributions

All the authors contributed equally towards study conception, study design, data collection, analysis, interpretation and manuscript preparation. They all read and approved the manuscript.

Ethics approval

The National Health Sciences Research Committee and MCH Research and Publication committee approved the study protocol (Protocol ♯19/05/2320). MCH administration provided permission to use patients' clinical files to get study data.

Consent for publication

Not applicable

Disclosure

The authors report no conflict of interest in this work.

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Availability of data and materials

The dataset supporting the conclusions of this article is available from the authors on request.

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