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Research Article

Hospitalization Events among Children with Sickle Cell Disease in Ho, Ghana

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Abstract

Background: Sickle cell disease (SCD) is common in Ghana and is associated with high morbidity and mortality, especially in the paediatric population. In Volta Region, one of Ghana's ten provinces, the major drivers of harm in children with SCD has not previously been systematically explored. We sought to characterize hospitalization events among paediatric patients with SCD in a regional hospital in order to inform local quality improvement efforts.

Methods: Medical records were retrospectively investigated for all children aged 6 months to 12 years with SCD that were admitted to the Volta Regional Hospital (Ho, Ghana) from January to December 2016. Descriptive analyses were conducted for patient demographics, hospitalization events, and clinical outcomes. Multiple admission diagnoses were allowable. Bivariate analyses using Cross-tabulation and Chi-Square were employed to evaluate associations among study variables.

Results: Sixty-five admissions were recorded for 51 children with SCD, which accounted for 5% of all paediatric hospitalizations during the study period. The mean age at which patients had been diagnosed with SCD was 4.2 ± 3.4 years (range: 3 months-16 years), and the mean age at admission was 6 ± 2.6 years. There was a slight predominance of males (53% males vs. 47% females) and the haemoglobin phenotypes were Hb SS (n = 44; 86%) and Hb SC (n = 7; 14%). The most common causes for admission were vaso-occlusive crisis (81.3%) and infection (70.3%). *Plasmodium falciparum* malaria was the etiologic agent in one-third of patients admitted with infection (n = 14; 31%). All children received intravenous fluids during admission and 17 children (28%) received blood transfusions. The mean length of stay was 4.9 ± 3 days. There was no mortality.

Conclusion: Sickle cell disease is a substantial cause of paediatric hospital admissions in the study setting. The variable age at which individuals are diagnosed with SCD highlights a fundamental health systems gap in newborn screening and clinical management in early childhood. The commonest reasons for admission (vaso-occlusive crisis and infection) may be preventable in some patients. Future work will involve incorporation of directed anticipatory guidance into outpatient visits for children with SCD with the hopes that improved education for families about the disease may help to reduce severe complications that require hospitalization.

Keywords: *Children; Sickle Cell Disease (SCD); Ghana*

Introduction

Sickle cell disease (SCD) is an autosomal recessive disorder characterized by a point mutation in the beta chain of the haemoglobin [1]. The resultant is the production of abnormal haemoglobin that explains the clinical manifestations of lifelong pain, multiple hospital

admissions, disability and early death [2]. SCD is a major problem in Ghana since 2% of babies are born with the disease each year whiles a third of Ghanaians are carriers of the mutation [3]. However, patients with SCD are yet to benefit from comprehensive care throughout Ghana. In the Volta Region, the first sickle cell clinic started in 2013 at Volta Regional Hospital. The clinic, which used to enrolled both paediatric and adults patients, eventually published the first research on SCD in the region [4] which involved only adult patients. The paediatric sickle cell clinic was established much later and is dedicated to children with the disease. Bacterial infections have been estimated to responsible of 20% - 50% of deaths in SCD patients [5]. In Africa, an SCD patient is 19 times more likely to have invasive bacterial infections than the general population [6]. This and other conditions are responsible for relatively frequent hospitalizations in SCD patients compared to non-SCD patients. Reports from Ghana show that the most common bacteria responsible for invasive infections in children, which includes SCD patients are Non-typhi and Typhi *Salmonella* spp, *Staphylococcus aureus* and *Streptococcus pneumoniae*. Susceptibility of the *Salmonella* spp to ciprofloxacin, meropenem and ceftriaxone range from 93% - 100%, *Staphylococcus aureus* exhibited 76.6% and 67.7% susceptibility to cloxacillin and ciprofloxacin and *S. pneumoniae* exhibited 42.3% resistance to ciprofloxacin [7-9]. A retrospective analysis of all paediatric admissions for SCD in 2016 was undertaken to identify the most common complains and possible reasons for hospitalizations as well as antibiotic treatments given. It was expected that such analysis will drive new hypothesis and research questions that will help understand the disease and design interventions in children with SCD in the Volta Region and beyond.

Study site

This study was conducted at the Volta Regional Hospital (VRH), located in the Volta Region, of Ghana. The VRH has 330-bed capacity and is the major referral centre in Volta Region of Ghana. There is a once-weekly scheduled sickle cell clinic for children up to 12 years of age, with an estimated annual attendance of 300 patients (40% new). All children with SCD who required admission were either referred from other facilities or self-referred to the hospital. In the year 2016, 144 news cases of SCD were diagnosed out of 1026 Hb electrophoresis performed in both children and adults at the Hospital. Among the 144 new diagnosis, there were 92 (63.9%) and 52 (36.1%) cases of HbSS and HbSC respectively.

Patients and Methods

Data on children 6 months to 12 years of age admitted at the paediatric Ward of the Volta Regional Hospital between January 2016 and December 2016 were included in the analysis. Permission to access and use patient data in this analysis was sought from the hospital administration. Physicians routinely complete a standardized data collection form for all SCD patients as part of clinical assessments. Most data used for the current analysis was extracted from the forms. Where data collection forms were incomplete, the patient electronic health record was used to complete the data. Both paper and electronic health records were compared to ensure completeness. The Data collected included sex, age at presentation, haemoglobin type and date of diagnostic, number of admissions and blood transfusions in the previous year, presenting complaints, clinical findings, and results of complementary tests, treatment and outcome.

Statistical analysis

The data collected in this study was entered into MS Excel and analysed in SPSS statistics version 23.0. Descriptive analysis was performed on the study variables, and prevalence rates were reported as percentages with 95% confidence intervals. Bivariate analysis was used to evaluate significant associations among the study variables, and *p*-values of 0.05 were considered statistically significant. All data were anonymised.

Results

During the study period 300 children with SCD were seen at the paediatric sickle cell clinic. Of these, 73 admissions were recorded. Eight (8) admission records were excluded from analysis due to unavailable haemoglobin electrophoresis result. The admissions were recorded from 51 patients, some of whom had multiple admissions. Sixty-five complete admission records of 51 patients (36 old and 15

newly diagnosed) were included in the final analysis. The flowchart on the retrieval of data for analysis is provided in figure 1. The 51 patients included 27 (52.9%) males and 24 (47.1%) females with a mean age of 6 ± 2.6 years. There were 44 (86.3%) patients with Hb SS and 7 (13.7%) with Hb SC. The age at diagnosis was not recorded for 4 out of the 51 patients. The mean age at diagnosis was 4.2 ± 3.4 years [range: 3 months - 16 years]. Fifteen (41.7%) out of the 36 previously diagnosed patients had a history of blood transfusion.

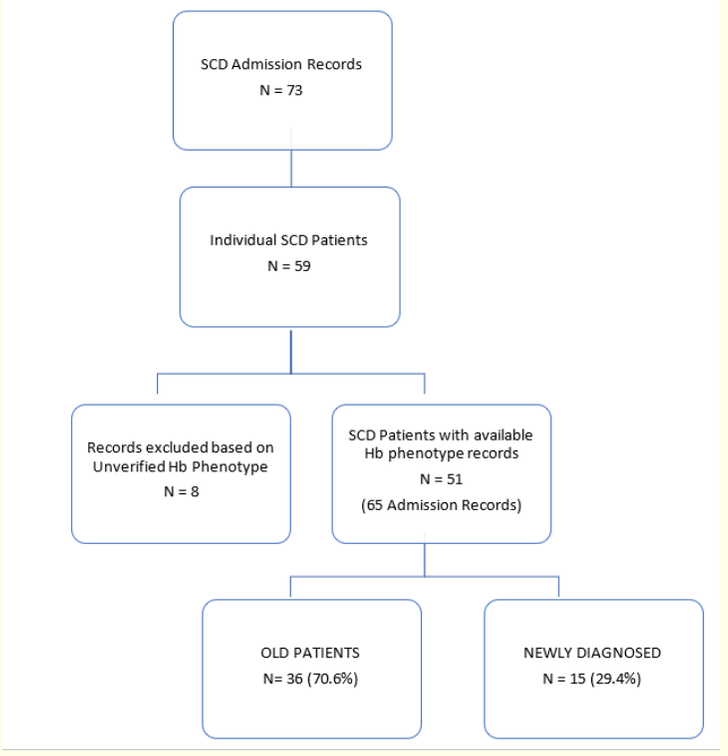

Figure 1: *Flowchart on retrieval of data.*

The 10 most common presenting complaints are shown in table 1. Pain (80%) and Fever (60%) were the most common complaints. The locations of the painful events were limbs (46.2%), abdomen (36.9%), chest (9.2%) and back (3.1%).

Complaints (n = 55)*	Frequency	Percentage (%)
Pain	44	80.0
Fever	33	60.0
Cough	16	29.1
Dark urine	13	23.6
Vomiting	11	20.0
Yellow eyes	6	10.9
Weakness	6	10.9
Constipation	5	9.1
Diarrhoea	2	3.6
Headache	1	1.8

Table 1*: Ten most common presenting complaints.*

**: A single patient may have more than one complaint.*

On admission, there was fever in 41/56 (73.2%) cases and poor hydration in 10/44 (22.7%) cases. Concerning haematological parameters, the mean haemoglobin level, white blood cells and platelets counts were 7.1 ± 2.6 g/dL [range 2.3 - 10.7], 25.0 ± 17.4 x 10^3 cells per μL and 337 ± 189 x 10^3 cells per μL respectively. Out of 52 admission records, there were 27 (51.9%) and 17 (32.7%) cases of MCV values below -2SD and both MCV and MCH values below - 2SD respectively. Among those with low MCV values on admission, 66.7% of them had never received blood transfusion against 33.3% who were previously transfused.

Acute painful crisis (52/64; 81.2%) and infection (45/64; 70.3%) were the common reasons for admission (Figure 2). The details of infections are shown in figure 3. *Plasmodium falciparum* malaria was confirmed in 14/64 (21.8%) of admissions via blood smear and/or rapid diagnostic test. Blood culture and urine culture were performed in only 5 and 3 cases respectively and only one urine culture grew a pathogen (*Escherichia coli*).

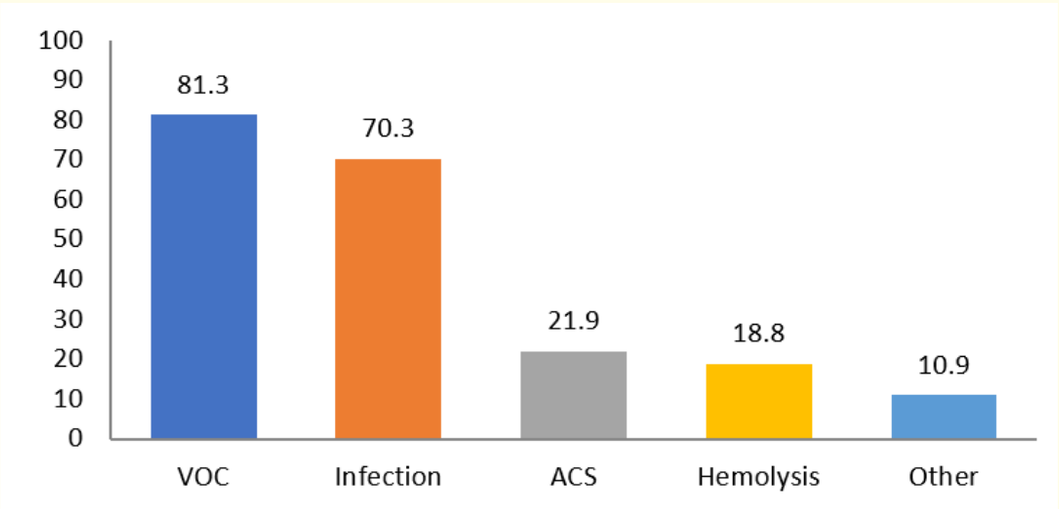

Figure 2: *Common diagnosis in hospitalized children with SCD (VOC = Vaso Occlusive Crisis; ACS = Acute Chest Syndrome).*

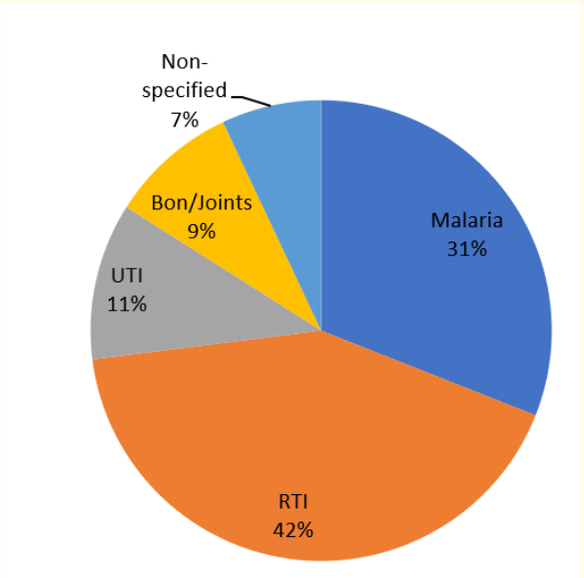

Figure 3: *Details of infections.*

Details of the treatment received during admission were shown in table 2. Antibiotics and antimalarial were administered in 53/60 (88.3%) and 23/60 (38.3%) admissions respectively. Seven (30.4%) out of the 23 who received antimalarials tested negative for *Plasmodium*, while testing was not done in 3/23 (13.0%) admitted patients. Eleven (78.6%) of the 14 confirmed malaria cases also received antibiotics. All children received intravenous fluids during admission and blood was transfused in 17 (28.3%) cases. The outcome was good for all but one admitted patient who was referred out for haemodialysis. The mean length of stay was 4.9 ± 3.0 days.

N = 60 admissions*	Frequency	Percentage (%)
Intravenous fluids	60	100.0
Blood transfusion	17	28.3
Antibiotics		
Ceftriaxone	28	46.7
Ciprofloxacin	21	35.0
Azithromycin	10	16.7
Clindamycin	9	15.0
Flucloxacillin	5	8.3
Crystapenicillin	5	8.3
Amoxicillin	4	6.7
Gentamicin	3	5.0
Cefpodoxime	3	5.0
Metronidazole	2	3.3
Cefotaxime	1	1.7
Antimalarial		
Oral Artemether and Lumefantrine	20	33.3
IV Artesunate	18	30.0
IM Quinine	1	1.7
Analgesics		
Paracetamol	48	80.0
Ibuprofen	42	70.0
Morphine	23	38.3
Micronutrients		
Multivitamins	28	46.7
Iron	17	28.3

***Table 2**: Treatment received.*

**: A single patient may have received more than one form of treatment.*

Discussion

Our data shows an important proportion of children diagnosed with SCD during acute illness at a relatively older age. This is because there is no newborn screening (NBS) programme in the Volta Region and the one started in the Ashanti is yet to become nationwide. Moreover, sickling and Hb electrophoresis testing are not systematically done in all ill children in the hospital. Therefore, the proportion

of SCD admission reported is likely underestimated. The proportion of hospitalised children with HbSC (13.7%) was lower as compared to that of those with HbSS since HbSC is associated with a milder disease course than HbSS. There was high proportion of previous blood transfusion. SCD is characterised by chronic anaemia, which can be severe when the diagnosis of SCD is not made and comprehensive management started earlier. Severe anaemia is also an independent factor of mortality among children with SCD [10].

Most of our patients complained of pain and fever. SCD is characterized by lifelong pain usually triggered by infection, trauma, stress, and dehydration among others. Infection is found to be the most common trigger is developing countries like Ghana. We reported respiratory tract infection and malaria as the main causes of infection in our cohort. Unfortunately, apart from *Plasmodium falciparum*, other organisms causing infections in our patients could not be identified, except for one case of *E. coli*. This was because septic screen was not done systematically, usually for financial reasons. Also, there was no previous work done on the causes of infections in SCD in the Hospital to inform the choices of antibiotics in this population. Most SCD patients presenting with fever are treated empirically with antibiotics to prevent the devastating outcome of prolonged hospitalisation and increased deaths [11]. While this practice is justified in this vulnerable population in our low resourced setting, it can also lead to antibiotic resistance and increased costs of hospitalization for parents. There is therefore an urgent need to characterise the organisms causing infections in children with SCD. This will add to existing guidelines on the management of SCD in Ghana [12]. The short stay of our patients and the absence of mortality may imply an improvement of the care given to hospitalised children with SCD. Microcytosis was present in 51.7% of our patients and this may be due to iron deficiency. Other causes of microcytosis are anaemia of chronic disease, thalassemia, led poisoning and sideroblastic anaemia, which is very rare. Studies conducted in sub-Saharan Africa (SSA), comparing MCV values in patients with SCD to controls revealed that SCD patients have higher MCV than controls when they where systematically supplemented with iron [13-15]. Moreover, iron deficiency is very common in children in SSA and is known to be associated with increased morbidity and mortality [16]. While MCV levels alone is not enough to diagnose iron deficiency in patients with SCD, determination of iron status must be considered in the work-up of children with SCD in Africa. Currently, children with SCD are not systematically evaluated for the presence of other chronic complications such as vascular complications and psychosocial impact of the disease on the patients and family at our hospital. A more comprehensive approach is needed to improve the quality of life and the survival of children with SCD.

The sample size is small due to the short span of data collection. Despite this, data from this study will constitute a background for improvement of care and future research designs and interventions.

Conclusion

Sickle cell disease is a substantial cause of paediatric hospital admissions in the study setting. The variable age at which individuals are diagnosed with SCD highlights a fundamental health systems gap in newborn screening and clinical management in early childhood. The commonest reasons for admission that are vaso-occlusive crisis and infection are preventable or their impact can be minimised in children with SCD. The establishment of a more comprehensive service will contribute significantly to improve the quality of life of children with SCD at the Volta Regional Hospital.

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Bibliography

1. Bunn H. "Pathogenesis and treatment of sickle cell disease". *New England Journal of Medicine* 337.11 (1997): 762-769.

2. Piel FB., *et al*. "Sickle Cell Disease". *New England Journal of Medicine* 376.16 (2017): 1561-1573.

3. Ohene-Frempong K., *et al*. "Screening Newborns for Sickle Cell Disease in Ghana". *Pediatrics* 121 (2008).

4. Fisher AE., *et al*. "Presentations of sickle cell disease patients to hospital in Ghana: key findings from a preliminary study at Volta Regional Hospital". *British Journal of Haematology* (2016).

5. Booth C., *et al*. "Infection in sickle cell disease: A review". *International Journal of Infectious Diseases* 14.1 (2010): 2-12.

6. Ramakrishnan M., *et al*. "Increased risk of invasive bacterial infections in African people with sickle-cell disease: a systematic review and meta-analysis". *Lancet Infectious Diseases* 10.5 (2010): 329-337.

7. Nielsen MV., *et al*. "Incidence and Characteristics of Bacteremia among Children in Rural Ghana". *PLos One* 7.9 (2012): e0044063.

8. Sothmann P., *et al*. "Urbanicity and Paediatric Bacteraemia in Ghana - A Case-Control Study within a Rural- Urban Transition Zone". *PLos One* (2015): 1-11.

9. Nkrumah NO., *et al*. "Trends in paediatric and adult bloodstream infections at a Ghanaian referral hospital: a retrospective study". *Annals of Clinical Microbiology and Antimicrobials* (2016): 1-10.

10. Makani J., *et al*. "Mortality in Sickle Cell Anemia in Africa: A Prospective Cohort Study in Tanzania". *PLoS One* 6.2 (2011): e14699.

11. Ansong D., *et al*. "Sickle cell disease: Management options and challenges in developing countries". *Mediterranean Journal of Hematology and Infectious Diseases* 5.1 (2013): 1-6.

12. Ministry of Health. Standard Treatment Guidelines. Sixth edition. (Ghana National Drugs Programme, edition). Accra, Ghana (2010).

13. Sadarangani M., *et al*. "An observational study of children with sickle cell disease in Kilifi, Kenya". *British Journal of Haematology* 146.6 (2009): 675-682.

14. Akinbami A., *et al*. "Haematological values in homozygous sickle cell disease in steady state and haemoglobin phenotypes AA controls in Lagos, Nigeria". *BMC Research Notes* 5 (2012): 396.

15. Gomez S., *et al*. "Comparative analysis of iron homeostasis in sub-Saharan African children with sickle cell disease and their unaffected siblings". *Frontiers in Pediatrics* 4 (2016).

16. World Health Organization. Department of Nutrition for Health and Development. Iron Deficiency Anaemia: Assessment, Prevention and Control: A Guide for Programme Managers. (Geneva: World Health Organization, edition). Geneva, Switzerland (2001).

Volume 9 Issue 7 July 2020