The clinical presentation, utilization, and outcome of individuals with sickle cell anaemia presenting to urban emergency department of a tertiary hospital in Tanzania

Hendry R. Sawe1,2*, Teri A. Reynolds1,3, Juma A. Mfinanga1,2, Michael S. Runyon1,4, Brittany L. Murray1,5, Lee A. Wallis6 and Julie Makani7,8

Abstract

Background: Sickle cell anaemia (SCA) is prevalent in sub-Saharan Africa, with high risk of complications requiring emergency care. There is limited information about presentation of patients with SCA to hospitals for emergency care. We describe the clinical presentation, resource utilization, and outcomes of SCA patients presenting to the emergency department (ED) at Muhimbili National Hospital (MNH) in Dar es Salaam, Tanzania.

Methods: This was a prospective cohort study of consecutive patients with SCA presenting to ED between December 2014 and July 2015. Informed consent was obtained from all patients or patients’ proxies prior to being enrolled in the study. A standardized case report form was used to record study information, including demographics, relevant clinical characteristics and overall patients outcomes. Categorical variables were compared with chi-square test or Fisher’s exact test; continuous variables were compared with two-sample t-test or Mann-Whitney U-test.

Results: We enrolled 752 (2.7%) people with SCA from 28,322 patients who presented to the MNH-ED. The median age was 14 years (Interquartile range [IQR]: 6–23 years), and 395 (52.8%) were female. Pain 614 (81.6%), fever 289 (38.4%) were the most frequent presenting complaint. Patients with fever, hypoxia, altered mental status and bradycardia had statistically significant relative risk of mortality of 10.4, 153, 50 and 12.1 (p < 0.0001) respectively, compared to patients with normal vitals. Overall, 656 (87.2%) patients received Complete Blood Cell counts test, of these 342 (52.1%) had severe anaemia (haemoglobin < 7 g/dl), and a 30.3 (p = 0.02) relative risk of relative risk of mortality compare to patients with higher haemoglobin. Patients who had malaria, elevated renal function test and hypoglycemia, had relative risk of mortality of 22.9, 10.4 and 45.2 (p < 0.0001) respectively, compared to patient with normal values. Most 534 (71.0%) patients were hospitalized for in patients care, and the overall mortality rate was 16 (2.1%).

Conclusions: We described the clinical presentation, management, and outcomes of patients with SCA presenting to the largest public ED in Tanzania, as well as information on resource utilization. This information can inform development of treatment guidelines, clinical staff education, and clinical research aimed at optimizing care for SCA patients.

Keywords: Sickle cell anaemia, Emergency department, Anaemia, Sub-Saharan Africa

* Correspondence: hendry_sawe@yahoo.com

1Emergency Medicine Department, Muhimbili University of Health and Allied Sciences, P.O. Box 54235, Dar es salaam, Tanzania

2Emergency Medicine Department, Muhimbili National Hospital, Dar es salaam, Tanzania

Full list of author information is available at the end of the article

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Background
Sickle cell disease (SCD) is one of the most common genetic diseases in the world, with the highest prevalence in sub-Saharan Africa, the Caribbean, the Middle East and India [1]. The morbidity and mortality from Sickle Cell Anaemia (SCA) in developed countries has improved significantly over the last five decades, with studies showing median survival rates beyond the fifth decade of life [2]. In developing countries, however, SCA still causes significant morbidity and mortality with the greatest burden of the disease in sub-Saharan Africa. The World Health Organization (WHO) estimates over half of children born with SCA in sub-Saharan Africa will die before they reach adulthood [3]. Infectious diseases, such as malaria and pneumococcal disease (meningitis, pneumonia, and septicaemia) are thought to be the major cause of morbidity and mortality [4, 5].

Tanzania ranks fifth in the world for number of SCD births with an estimated prevalence of 6 [interquartile range (IQR) 1–13] per 1000 births, equivalent to 11,000 SCD births per year [4, 6]. A study conducted at a university teaching hospital in Tanzania reported a SCA mortality rate of 1.9 per 100 person years of observation (PYO), with the highest incidence of death occurring in the first five years of life [7]. Overall median survival in this study was 33 years. Of note, life expectancy of Tanzanian residents is 52 years. Similar to other developing countries, morbidity and mortality due to SCA in Tanzania is highly influenced by comorbid conditions, such as infections (particularly malaria), anaemia, and poor nutrition [4].

Emergency department (ED) presentations of SCA complications are well characterized in developed countries, with the majority of these patients presenting with pain crisis [8–12]. Most of these patients are treated with aggressive pain management and fluid therapy and discharged home, with less than one-third admitted to the hospital. In 2010, Muhimbili National Hospital (MNH), which is the main University Teaching Hospital, opened the first full capacity, high-volume ED in Tanzania. This ED has provided an opportunity for early stabilization and resuscitation of acutely ill patients, including those with SCA. The study on mortality in SCA in Africa published in 2011 was conducted at the same hospital, at that time had no full capacity ED [7]. This is critical as little is known about the acute or emergent manifestations, management, and outcomes of SCA complications in Tanzania. The primary aim of this investigation is to describe the clinical presentation, ED management, and hospital outcomes of individuals known or suspected to have sickle cell disease and presenting to the MNH ED.

Methods
Study design and setting
This was a prospective observational study of consecutive patients presenting to the MNH ED in Dar es Salaam, Tanzania, from 1 December 2014 to 31 July 2015. MNH has a bed capacity of 1500 and serves as the top referral hospital in Tanzania. The ED was established in 2010 via a partnership between the Ministry of Health and Social Welfare, and Abbott Fund Tanzania. The ED is the first full capacity public ED in Tanzania, and the training site for the only emergency medicine (EM) residency program in the country. The department is staffed 24 h, seven days a week by locally trained specialist emergency physicians, who oversee the care of patients and training of interns, registrars, and EM residents. The ED sees an average of 45,000 patients annually, with an admission rate of around 65%. The top disease categories in all age groups are trauma, infectious disease, and mental health [13]. MNH is one of the largest SCD treatment and research centre in Tanzania. The diagnosis of SCA at MNH is normally confirmed by the haemoglobin electrophoresis, after initial sickling test or clinical suspicion at most of the referring hospitals. Patients confirmed to have SCA are enrolled into a Sickle Cell clinic, provided with dedicated medical record number and special follow up card. In this study, all patients with confirmed evidence of SCA presenting with acute illness at the ED were eligible for enrolment.

Study protocol
Screening and enrolment was completed by a research assistant and the study investigator (HS). A structured data sheet was used to record study information, including demographics, pre-referral information, chief complaints, initial vital signs, history and physical examination findings, laboratory results, treatment delivered, and final ED diagnoses and disposition. All diagnostic, treatment, and disposition decisions were made at the discretion of the treating physician. The research assistant followed up on all enrolled patients throughout the duration of their hospital study and recorded lengths of stay in hospital and intensive care unit (ICU) or high acuity ward, as well as final hospital diagnosis and clinical outcome (discharge or death) for each patient.

Data analysis
Information collected from the handwritten data sheets were transferred into an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA), verified, and checked for any errors and outliers. Data were subsequently imported into StatsDirect (version 3.0.167, StatsDirect Ltd., Cheshire, UK) for analysis. Categorical variables were summarized as frequencies and percentages, and continuous variables as means and standard deviations (SD) or
medians and interquartile ranges (IQR), depending on data distribution. Normality was assessed using the Shapiro-Wilk test. Ninety-five percent confidence intervals (CI) are presented where appropriate, and were calculated by the Clopper-Pearson (exact) method. Categorical variables were compared with chi-square test or Fisher’s exact test; continuous variables were compared with two-sample t-test or Mann-Whitney U-test. Two-tailed p-values of < 0.05 were considered statistically significant.

**Results**

We enrolled 752 (2.7%) people with SCA from 28,322 patients who presented to the MNH ED from 1 December 2014 to 31 July 2015. The median age of enrolled patients was 14 years (Interquartile range (IQR) of 6–23 years), with 19.7% younger than age 5, and 52.9% were female. A total of 299 (40.2%) patients were referred from peripheral hospitals, the median length of admission at these peripheral facilities prior to referral was 2 days (IQR 1.3 days) Table 1.

**Patients’ baseline variables and presenting complaints**

Tachypnea 336 (44.7%) was the most frequent abnormal vital sign among enrolled patients, while bradycardia 14 (1.9%) was the least frequent abnormal sign. All the abnormality are based on age-appropriate vital signs [14]. Patients who presented fever 289 (17.4%), hypoxia 67 (8.9%), altered mental status 59 (7.8%) and bradycardia 14 (1.9%) had a statistically significant higher relative risk of death compared with those without bradycardia. Pain 614 (81.6%) and urinary symptoms 6 (0.8%) were most and least frequent presenting complaints respectively Table 2.

**Investigations ordered in the ED**

Nearly all patients 744 (99%) had at least one laboratory test done while receiving ED care. Complete blood cell counts were ordered for 656 (87.2%) patients. Of these 346 (52.7%) had elevated white blood counts (> 11 K/μL) and 342 (52.1%) had severe anaemia (Hb < 7 g/dL) of which 166 (25.3%) had (Hb < 5 g/dL). Of the 415 patients tested for malaria, 48 (11.6%) were positive. The relative risk of death among those with severe anaemia, malaria test positive, elevated renal function test and hypoglycaemia was 30.3, 22.9,10.4 and 45.2 respectively. X-ray of the chest was ordered in 85 (11.3%) of patients, and the relative risk of death among those with an abnormal chest x-ray was 4.0 (Table 3).

**Final ED diagnosis**

The top three ED diagnoses were painful crisis (n = 472; 62.8%), malaria (n = 176; 23.4%), and severe anaemia (n = 117; 15.6%) (Table 4).

**ED treatment and interventions**

In the ED, intravenous fluid bolus and intravenous dextrose were given to 370 (49.2%) and 129 (17.2%) of enrolled patients, respectively. A total of 489 patients (65.0%) received analgesics for pain, with 350 (71.6%) receiving opioid analgesics. Antimalarial were administered in the ED to 123 (16.4%) patients, while 220 (29.3%) received antibiotics, the majority of whom (89.2%) received intravenous ceftriaxone. Seventy-two patients (9.6%) received blood products (fresh whole blood, packed red cells, or fresh frozen plasma), with the majority (91.2%) receiving fresh whole blood.

**Patients’ disposition and hospital outcomes**

Of the 752 SCA patients seen in the ED, 534 (71%) were hospitalized for inpatient care, while five patients (0.7%) died in the ED. The median length of stay in hospital was 3 days (Interquartile range (IQR): 1–5) days. The overall mortality (ED plus inpatient) was 16 (2.1%). Overall, 8 (50%) of deaths’ occurred within 24 h of ED presentation (Table 5).

**Discussion**

The opening of a full capacity ED at MNH provided a unique opportunity for rapid assessment and early stabilization of acutely ill individuals, including those with SCA. Our study reports on the clinical profile and management of acutely ill individuals with SCA presenting to an urban ED in Tanzania. This information on ED access and resource utilization can be useful in developing local and countrywide strategies to improve access, treatment guidelines, and health outcomes among individuals with SCA.

In our study, the prevalence of SCA among acutely ill patients presenting ED was found to be 2.7%, and most of the patients were self-referral, highlighting the role of ED as a major mode of healthcare utilization in this patient population in Tanzania. Most of our patients were children below eighteen years, an observation.
consistent with previously published literature in the same settings [7].

Pain was the most common presenting complaint among patients presenting to ED. Vaso-occlusive painful crisis phenomena is a well-documented reason for ED visit among sickle cell patients in different settings [7, 8], and it has been shown to be a potential marker of serious illness, which may be associated with increased morbidity and mortality [7, 15]. Respiratory compromise, denoted by tachypnea and hypoxia (oxygen saturation < 95%), was the most common physical examination finding at presentation. In this population, the most common reason for respiratory compromise was chest infection (pneumonia), followed by acute chest syndrome. Infection is the leading cause of preventable morbidity and mortality in patients with SCA, and

| Table 2 Patients’ baseline variables and presenting complaints |
|---------------------------------------------------------------|
| Clinical characteristics                                      | Overall | Died | Survived | Relative risk | P-value |
|---------------------------------------------------------------|---------|------|----------|---------------|---------|
| N (%)                                                         | n/N (%) | n/N (%) | n/N (%) | RR (95%CI) |        |
| Tachypnea [b]                                                 | 336 (44.7) | 10 (62.5) | 326 (44.3) | 2.1 (0.8–5.7) | 0.16    |
| Tachycardia[b]                                                | 186 (24.7) | 5 (31.3) | 181 (24.6) | 1.4 (0.5–3.9) | 0.5     |
| Fever                                                        | 614 (81.6) | 12 (75.0) | 602 (81.8) | 0.7 (0.2–2.1) | 0.5     |
| Abdominal Symptoms                                            | 159 (21.1) | 2 (12.5) | 157 (21.3) | 0.5 (0.1–2.3) | 0.4     |
| Respiratory Symptoms                                          | 156 (20.7) | 11 (68.8) | 145 (19.7) | 8.4 (3.0–23.8) | 0.0001  |
| Cardiovascular Symptoms                                       | 83 (11.0) | 2 (12.5) | 81 (11.0) | 1.2 (0.3–5.0) | 0.9     |
| Jaundice                                                     | 80 (10.6) | 1 (6.3) | 79 (10.7) | 0.6 (0.1–4.2) | 0.6     |
| Body Swelling                                                 | 54 (7.2) | 2 (12.5) | 52 (7.1) | 1.9 (0.4–7.9) | 0.4     |
| Neurological Symptoms                                         | 45 (6.0) | 6 (37.5) | 39 (5.3) | 9.4 (3.6–24.8) | < 0.0001  |
| Long Lasting Erection                                         | 20 (2.7) | 1 (6.3) | 19 (2.6) | 2.4 (0.3–17.6) | 0.4     |
| Urinary Symptoms                                              | 6 (0.8) | 1 (6.3) | 5 (0.7) | 8.3 (1.3–53.1) | 0.03    |

*a* SpO2 Saturation of oxygen in peripheral capillary *b* Age-adjusted variables *c* Measurements were all axillary

| Table 3 Investigations ordered in the ED |
|-----------------------------------------|
| Overall | Died | Survived | Relative risk | P-value |
|-----------------------------------------|
| n/N (%) | n/N (%) | n/N (%) | RR (95%CI) |        |
| Laboratory Tests                         |         |         |             |         |
| WBC [b] (> 11 K/μL)                      | 346/656 (52.7) | 11/16 (68.8) | 335/640 (52.3) | 2.0 (0.7–5.6) | 0.2 |
| Haemoglobin (< 7 g/dL)                   | 342/656 (52.1) | 16/16 (100) | 326/640 (50.9) | 30.3 (1.8–503) | 0.02 |
| Abnormal urine results [6]               | 11/63 (17.5) | 1/16 (6.3) | 10/47 (21.3) | 0.3 (0.04–2.11) | 0.2 |
| Malaria test positive [6]                | 48/415 (11.6) | 12/16 (75) | 36/399 (9.0) | 22.9 (7.7–68) | < 0.0001 |
| Elevated RFT [6]                         | 24/219 (11.0) | 9/16 (56.3) | 15/203 (7.4) | 10.4 (4.2–25.5) | < 0.0001 |
| Low RBG [η] (< 3 mmol/L)                 | 39/627 (6.2) | 12/16 (75) | 27/611 (4.4) | 45.2 (15.3–133.8) | < 0.0001 |
| Imaging Tests                            |         |         |             |         |
| Abnormal chest x-ray [a]                 | 30/85 (35.3) | 11/16 (68.8) | 19/69 (27.5) | 4.0 (1.5–10.5) | 0.004 |
| Abnormal brain CT scan [p]               | 7/26 (26.9) | 5/16 (31.3) | 2/10 (20) | 1.2 (0.67–2.2) | 0.5 |

[a] WBC-White Blood Cell
[b] Presence of blood in urine, leukocytes, nitrites, albumin, or glucose
[c] Signs of infection or stroke
[d] RFT-Renal function test
[e] RBG-Random Blood Glucose
[f] Pneumonic changes
[g] Signs of stroke
were admitted

φ Includes only inpatients

ϖ Includes ED and inpatient deaths

Table 5 Patients’ disposition and hospital outcomes

| Disposition                          | N = 752 | % (95% CI) |
|--------------------------------------|---------|------------|
| Admitted                             | 534     | 71.0 (67.6–74.2) |
| Discharged from ED                   | 213     | 28.3 (25.1–31.7) |
| Died in ED                           | 5       | 0.7 (0.3–1.5)   |
| Death within 24-h of ED presentation | 8       | 1.1 (0.5–2.1)   |
| Inpatient mortality                  | 11      | 2.1 (1.2–3.7)   |
| Overall mortality                    | 16      | 2.1 (1.3–3.4)   |

Median length of hospital stay

| Disposition                          | Median | IQR |
|--------------------------------------|--------|-----|
| Admitted                             | 3 days | 1–5 days |
Limitations
The generalizability of our results may be limited due to the single-centre nature of our study. The ED at MNH is the entry point to the largest tertiary referral hospital in Tanzania, and receives acutely ill patients from all over the country. Therefore, the sample seen at the MNH ED might be different than that seen at the district hospitals and health centres. The exclusion of undiagnosed SCD in our study might have under-estimated the overall proportion of SCD in our study population. In addition, the assessment of factors associated with mortality was limited by the number of deaths in our study population.

Conclusions
We have provided a description of the clinical presentation, management, and outcomes of patients with SCA presenting to the largest public emergency department in a tertiary referral hospital in Tanzania. These data will inform development of strategies to provide education for clinical staff, treatment guidelines, and clinical research aimed at optimizing care of the SCA patient population.

Abbreviations
CBC: Complete Blood Count; CRF: Case Report Form; ED: Emergency Department; MNH: Muhimbili National Hospital; MUHAS: Muhimbili University of Health and Allied Sciences; WHO: World Health Organization

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Availability of data and materials
The dataset supporting the conclusions of this article is available from the authors on request.

Authors’ contributions
HS contributed to the conception and design of the study; acquired, analysed, and interpreted the data; and drafted and revised the manuscript. JAM contributed to the design of the study, data acquisition and entry, and also revised the manuscript. BLM each contributed to the conception and initial design of the study; assisted in initial design of the study; and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The institutional review board and the committee on research of the Muhimbili University of Health and Allied Sciences (MUHAS) approved the study protocol. MNH administration provided permission for in-hospital follow-up. Written informed consent was obtained from patients or patient proxies when a patient was a child or unable to provide their own consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no conflicts of interest.

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Author details
1Emergency Medicine Department, Muhimbili University of Health and Allied Sciences, P.O. Box 54235, Dar es salaam, Tanzania. 2Emergency Medicine Department, Muhimbili National Hospital, Dar es salaam, Tanzania. 3Department of Emergency Medicine, University of California San Francisco, San Francisco, CA, USA. 4Department of Emergency Medicine, Carolinas Medical Center, Charlotte, NC, USA. 5Division of Pediatric Emergency Medicine, Emory University School of Medicine/Children’s Hospital of Atlanta, Atlanta, GA, USA. 6Division of Emergency Medicine, University of Cape Town, Cape Town City, South Africa. 7Nuffield Department of Medicine, University of Oxford, Oxford, UK. 8Department of Haematology and blood transfusion, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania.

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