


BMJ Open Time trends, sociodemographic and health factors associated with discharge and length of stay of hospitalised patients with sickle cell disease in Ghana: a retrospective analysis of national routine health database

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ABSTRACT

Objective Patients with sickle cell disease (SCD) are prone to multiple episodes resulting in frequent hospital visits. We determined the time trends, sociodemographic and health factors associated with length of stay (LoS) for patients with SCD in Ghana.

Design, participants, setting We retrospectively analysed SCD hospitalisation records of 22 680 patients from a nationwide database of the Ghana Health Service from 2012 to 2017.

Outcome measures Factors associated with LoS were estimated using Cox regression, while the cumulative incidence of being discharged alive was estimated with in-hospital death as a competing risk.

Results Patients admitted for SCD over 6 years constituted 22 680 (0.8%) of nearly 3 million admissions. The median age and LoS for the patients were 16 years (IQR=8–24) and 3 days (IQR=2–4), representing 14 202 (62.6%) of the patients discharged alive by the third day. Patients with sickle cell anaemia (6139, 52.6%) with a crisis were more frequent than those without a crisis. Increasing age was associated with shorter LoS when comparing age groups 10–14 years (HR=1.08, 95% CI 1.01 to 1.14) and 25–29 years (HR=1.27, 95% CI 1.17 to 1.37) to patients aged 0–4 years. Patients with comorbidities had a longer LoS compared with those without (HR=0.88, 95% CI 0.86 to 0.90).

Conclusion This is the largest study to date documenting factors associated with LoS for patients admitted for SCD. The association of younger age with increased LoS supports recent calls for early SCD screening, especially newborns. The emerging trends and factors accounting for SCD admission require a multisector approach as these patients already experience frequent episodes of pain and hospital visits.

INTRODUCTION

Global estimates of sickle cell disease (SCD) since 1992 show that it is an important public-health concern in sub-Saharan Africa

Strengths and limitations of this study

- The novelty of this study lies in its large sample size based on a nationwide routine health administrative health records on hospitalised individuals.
- The main strength of this study is it being the first to determine the sociodemographic and health factors associated with length of stay duration hospitalisation of patients with sickle cell disease in all 10 regions of Ghana.
- Although two teaching hospitals and some private hospitals were not included in this analysis, the participating hospitals in this study were representative.
- Multiple records (visits) per person could not be analysed due to the unavailability of unique patient IDs.

(SSA).^{1 2} SCD is known to have a genetic predisposition,^{1 3–6} and affects mainly young people^{4 7–9} with an estimated 50%–90% excess mortality among children in SSA.^{10 11} There is increasing evidence on the prevalence and complications of SCD in Africa, especially Ghana.^{4 12 13} In tropical African countries, the prevalence of the genetic predisposition was 25%–30%.¹ Specifically, the sickle cell trait prevalence in Ghana is reported to be 25% with an SCD prevalence of 2%.¹⁴ A recent study in the Volta Region of Ghana reported SCD prevalence as 16%.¹⁵

Despite increasing knowledge about SCD in Ghana, little is known about the resulting hospital admissions and associated lengths of stay (LoS). Patients diagnosed with SCD often require frequent health facility visits and hospitalisations.¹⁶ These result from episodes of severe pain, which can reoccur throughout life.^{5 16 17} Patients with SCD suffer a lot more complications from both communicable



and non-communicable comorbidities.^{2 13 18} It is estimated that patients with SCD in the USA made about 2.1 health facility visits per year on average, especially to the emergency department.¹⁹ Health facilities in low-income and middle-income countries (LMICs) are inadequately resourced,²⁰ which means frequent hospital visits and admissions would harm patients and the hospitals needing to admit them.

An extensive report²¹ indicated a mean LoS during SCD hospital admission of 5 days in the USA. SCD admissions and their direct cost to hospitals have been widely studied in high-income countries where the patient and medical cost records are readily available.^{21 22} In LMICs such as Ghana, there is usually no such national database on patients with SCD care, leading to a lack of empirical evidence. Although the SickInAfrica consortium has established an SCD registry,²³ the data contributed is not representative.

So far, the aetiological epidemiological data on admissions and the LoS of patients with SCD in the general population in Ghana has been scarce, not permitting non-biased studies to be carried out. This study analysed new nationwide data which will help to address these research gaps by determining the time trends, sociodemographic and health factors associated with discharge from hospital and LoS for patients admitted for SCD in Ghana. The new data have been provided by the District Health Information Management System II (DHIMS-II) database of the Ghana Health Service (GHS), which enables a nationally representative study. We expected to confirm findings with respect to age structure and risk factors for longer LoS for patients with SCD in Ghana as published in systematic reviews and cross-sectional studies by Grosse *et al* and Asare *et al*.^{10 16}

METHODS

Study setting/design/data sources

This study was carried out in the Republic of Ghana with a population of about 29 million, according to the 2010 Population and Housing Census. At the time of this study, Ghana has 10 administrative regions and 216 districts.²⁴ This study used individual visit-level records from the DHIMS-II of the GHS and population data from the Ghana Statistical Service. These records cover all government and some private hospitals in Ghana. To an extent, some tertiary hospitals migrated from regional hospitals to a teaching hospital also contribute data to the DHIMS-II. Currently there are 6 teaching hospitals, 3 university hospitals, 10 regional hospitals, 408 general hospitals, 130 district hospitals, 4 psychiatric hospitals and over 8500 smaller health facilities. Hospitals involved in this study although were self-selected as contributors to the DHIMS-II, they can be considered as representative of each region and district. The DHIMS-II data set included patients with at least one hospitalisation record diagnosed as SCD.²⁵ Patient records were anonymised per admission such that multiple admissions from the same

patient could not be linked. Following the Strengthening the Reporting of Observational Studies in Epidemiology and REporting of studies Conducted using Observational Routinely-collected Data (RECORD) guidelines^{26 27} for using secondary data from the DHIMS-II database, we analysed 22 680 records of hospital admissions due to SCD.

Patient and public involvement

Not applicable. Patients were not directly involved in this study, except for the use of their previously collected health data on SCD.

Measures

The hospitalisation data provided by the DHIMS-II mimic the admissions and discharge registers used in the hospitals and contains 14 variables, of which 12 were extracted. These included calendar-year as a continuous covariate while region, sex, age group, occupation, education, health insurance status, surgical procedure and comorbidity were categorical covariates. Of these variables, patient diagnoses are captured as principal and additional diagnoses. Other variables included socio-demographic characteristics, health-related facility factors and the vital status at the end of hospitalisation. Although the DHIMS-II captures other patient-related health data such as health history, diagnostic tests and results and treatment, these were not linked to the hospitalisation data and are not available for this analysis.

Data management

We assessed data completeness of all extracted variables. Records with missing values for age, sex or date of admission were excluded from the analysis. Duplicate records were identified and dropped based on the complete repetition of the values. In modelling the LoS, we excluded patients with a missing date of discharge as there was no information on LoS after admission since no plausible censoring date could be established.

Both principal and additional diagnoses were identified, coded and categorised according to the WHO International Classification of Diseases, 10th revision, (ICD-10).²⁸ For this study, we refer to principal diagnoses as SCD (which is coded as D57.0 for sickle cell anaemia with crisis and D57.1 for sickle cell anaemia without crisis). In the absence of an ICD-10 code in the DHIMS-II database, self-written Stata regular expressions were used in identifying the SCDs for coding and categorisation. We minimised bias by running plausibility and consistency checks for age and sex specific diagnoses and analysis of patterns of missing data. Data management and analysis were performed using Stata V.14.0 (StataCorp).

Statistical analysis

Descriptive statistics summarised categorical variables using absolute and relative frequencies. For the number of hospitalisations by year, region and age group, we estimated the crude rates based on the projected population of the Ghana Statistical Service.²⁴ The primary outcome

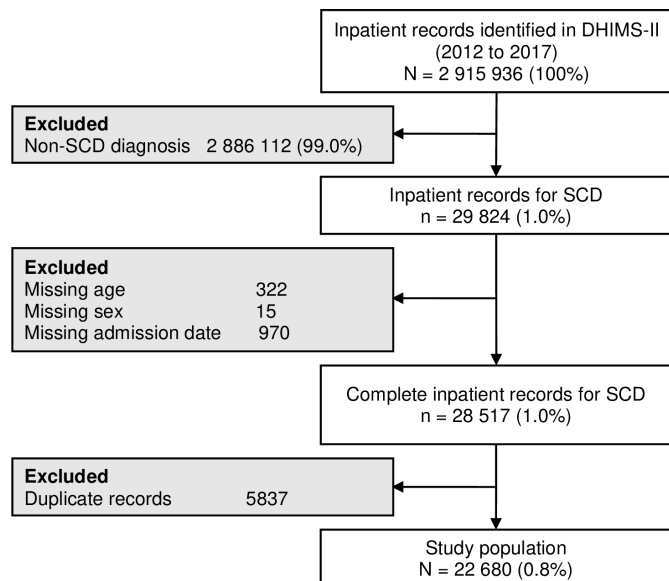


Figure 1 Flowchart of sickle cell disease (SCD) records (2012–2017) from the Ghana Health Service District Health Information Management System (DHIMS-II).

was LoS in the sense of ‘time from admission to being discharged alive’. The first analysis used Cox regression for the cause-specific hazard to determine causal influences on LoS.²⁹ For this analysis, patients who died in-hospital were censored on their date of death. In order to estimate the cumulative incidence of being discharged alive, we applied a Fine-Gray model with death as a competing risk.^{30–32} These two approaches have in recent years been advocated for an aetiological clinical study such as ours.^{29–33} Both models included calendar-year as a continuous variable and the remaining covariates as categorical variables. In addition, an age-by-sex interaction term allowed for sex-specific age effects. Both models were implemented in Stata *stcox*, *stcrreg* and *Stcurve*.³⁴ We report the HR, 95% CI and p values for all associations. HRs above 1 indicate a higher hazard for discharge and thus shorter LoS.

RESULTS

Data extraction, annual and regional distribution of SCDs

Patients with SCD accounted for 22 680 (0.8%) of all hospitalisation records from 2012 to 2017 (figure 1). There was no obvious temporal trend in the annual crude rates of SCD hospitalisations over the 6-year period, with 5327 admissions in 2016 representing the highest crude rate of (1.88/10 000), (table 1). Hospitalisation of patients with SCD varied between the 10 regions of Ghana with the Volta and Eastern regions recording the highest (3974 (crude rate=2.82/10 000) and 4695 (crude rate=2.71/10 000), respectively) and the Upper East and Northern regions recording the lowest (416 (crude rate=0.60/10 000) and 717 (crude rate=0.43/10 000), respectively) rates (table 1).

Patients and disease characteristics

Admissions of patients classified as having SCD with crisis (D57.0) were more frequent than those without crisis (D57.1), (11 675 vs 11 005). The gender distribution in patients with a crisis was nearly the same, while patients without crisis were predominately women (6139 (crude rate=1.40/10 000)) versus men (5536 (crude rate=1.37/10 000)) (table 1 and figure 2). Patients aged 15–19 years were the most frequent age group hospitalised for SCD (4106, 18.1% (crude rate=2.44/10 000)). Patients younger than 15 years represented 44% of all the SCD hospitalisations. Overall, 15 070 (66.5%) of patients with SCD had some form of formal education. Over one-third of the patients had comorbidities, and nearly 398 (2%) died during the hospital stay.

Factors associated with LoS in patients with SCD

Calendar-year was not associated with hospital length of stay. Patients with SCD hospitalised in the Eastern (HR=0.93, 95% CI 0.87 to 0.97, p value=0.001), Northern (HR=0.91, 95% CI 0.85 to 0.98, p value=0.017) and the Volta (HR=0.92, 95% CI 0.88 to 0.96, p value <0.001) regions had longer LoS, while patients in the Ashanti (HR=1.16, 95% CI 1.10 to 1.23, p value <0.001), Upper East (HR=1.14, 95% CI 1.03 to 1.28, p value <0.001), Upper West (HR=1.14, 95% CI 1.03 to 1.28, p value=0.016) and Western (HR=1.07, 95% CI 1.02 to 1.13, p value=0.007) regions had shorter LoS compared with the Greater Accra region. Increasing age was strongly associated with earlier discharge, especially in the age groups 10–14 years (HR=1.08, 95% CI 1.01 to 1.14, p value <0.001) and 25–30 years (HR=1.27, 95% CI 1.17 to 1.37, p value <0.001) compared with patients aged 0–4 years. Patients aged between 45 and 49 years were the earliest to be discharged (HR=1.36, 95% CI 1.15 to 1.62, p value <0.001). Gender was not associated with LoS. Patients with comorbidities versus those without (HR=0.88, 95% CI 0.86 to 0.90, p value <0.001) and patients who underwent a surgical procedure versus those who did not (HR=0.78, 95% CI 0.69 to 0.87, p value <0.001) during hospitalisation had later discharge (table 2).

We estimated the cumulative incidence function (CIF) of being discharged alive. Due to the age-by-sex interaction term, the CIF can only be displayed for a specific patient group. Figure 3 shows the CIF for the sex and the age group with the highest number of records, considering the competing risk of death. For both men and women aged 15–19 years, the cumulative incidence of discharge was nearly 75% by day 5 and 95% by day 10. In both scenarios, women had a higher cumulative incidence of being discharged alive than men.

DISCUSSION

The GHS is one of the health institutions in the LMICs that invested in improving its routine health data management over the past few decades.³⁵ This investment has resulted in high quality data generated from the routine

Table 1 Socio-demographic characteristics of patients hospitalised in Ghana stratified by sickle cell disease type, 2012–2017

Variable	Sickle cell disease type		
	D57.0*, n=11 675	D57.1†, n=11 005	Total, N=22 680
Median (IQR)			
Age (years)	17 (9–24)	16 (8–24)	16 (8–24)
Length of stay (LoS) (days)	3 (2–4)	3 (2–4)	3 (2–4)
n (crude rate per 10 000 population)			
Calendar-year			
2012	1655 (0.64)	5 (<0.01)	1660 (0.64)
2013	2782 (1.05)	40 (0.02)	2822 (1.07)
2014	2591 (0.96)	1573 (0.58)	4164 (1.54)
2015	1429 (0.52)	2827 (1.02)	4256 (1.54)
2016	1854 (0.66)	3473 (1.23)	5327 (1.88)
2017	1364 (0.47)	3087 (1.07)	4451 (1.54)
Region			
Ashanti	1301 (0.42)	770 (0.25)	2071 (0.66)
Brong Ahafo	1536 (1.00)	1943 (1.26)	3479 (2.26)
Central	691 (0.48)	695 (0.49)	1386 (0.97)
Eastern	2549 (1.47)	2146 (1.24)	4695 (2.71)
Greater Accra	1869 (0.70)	1239 (0.46)	3108 (1.16)
Northern	294 (0.18)	423 (0.26)	717 (0.43)
Upper East	322 (0.47)	94 (0.14)	416 (0.60)
Upper West	161 (0.35)	161 (0.35)	322 (0.70)
Volta	1928 (1.37)	2046 (1.45)	3974 (2.82)
Western	1024 (0.61)	1488 (0.89)	2512 (1.50)
Age group (years)			
0–4	1485 (0.65)	1631 (0.71)	3116 (1.36)
5–9	1752 (0.87)	1720 (0.86)	3472 (1.73)
10–14	1690 (0.92)	1622 (0.88)	3312 (1.79)
15–19	2128 (1.26)	1978 (1.17)	4106 (2.44)
20–24	1717 (1.13)	1581 (1.04)	3298 (2.18)
25–29	1119 (0.83)	987 (0.74)	2106 (1.57)
30–34	658 (0.56)	490 (0.42)	1148 (0.98)
35–39	366 (0.37)	324 (0.33)	690 (0.70)
40–44	242 (0.29)	211 (0.25)	453 (0.55)
45–49	153 (0.22)	148 (0.22)	301 (0.44)
50–100	365 (0.18)	313 (0.15)	678 (0.33)
Sex			
Male	5536 (0.69)	5453 (0.68)	10 989 (1.37)
Female	6139 (0.73)	5552 (0.66)	11 691 (1.40)
n (column %)			
Education level			
No formal education	4087 (35.0)	3521 (32.0)	7608 (33.5)
Formal education	7587 (65.0)	7483 (68.0)	15 070 (66.5)
Missing	1 (<0.01)	1 (<0.01)	2 (<0.01)
Occupation			
Unemployed	8385 (71.8)	8202 (74.5)	16 587 (73.1)
Employed	2267 (19.4)	1914 (17.4)	4181 (18.4)

Continued

Table 1 Continued

Variable	Sickle cell disease type		
	D57.0*, n=11 675	D57.1†, n=11 005	Total, N=22 680
Unspecified	1021 (8.8)	889 (8.1)	1910 (8.4)
Missing	2 (<0.01)	0 (<0.01)	2 (<0.01)
Insurance status			
No	1500 (12.8)	1516 (13.8)	3016 (13.3)
Yes	10 058 (86.2)	9469 (86.0)	19 527 (86.1)
Missing	117 (1.0)	20 (0.2)	137 (0.6)
Surgical procedure			
No	10 778 (92.4)	10 865 (98.7)	21 643 (95.4)
Yes	192 (1.6)	82 (0.8)	274 (1.2)
Missing	705 (6.0)	58 (0.5)	763 (3.4)
Comorbidity			
No	6925 (59.3)	6458 (58.7)	13 383 (59.0)
Yes	4750 (40.7)	4547 (41.3)	9297 (41.0)
Outcome of admission			
Alive	11 458 (98.1)	10 800 (98.1)	22 258 (98.1)
Died	202 (1.7)	196 (1.8)	398 (1.8)
Missing	15 (0.1)	9 (0.1)	24 (0.1)
LoS			
0–3 days	7457 (63.9)	6745 (61.3)	14 202 (62.6)
4–7 days	3022 (25.9)	2938 (26.7)	5960 (26.3)
>1 week	797 (6.8)	886 (8.1)	1683 (7.4)
Missing	399 (3.4)	436 (3.9)	835 (3.7)

*Sickle cell anaemia with crisis.

†Sickle cell anaemia without crisis.

health service provision which is available for administrative and research purposes. Our goal was to determine possible time trends, sociodemographic and health factors associated with hospital LoS for patients admitted for SCD in Ghana.

Based on the WHO ICD-10 broad categories, we categorised SCD into with and without crisis.²⁸ In the 6 years analysed, we did not see any obvious time trend in the annual crude rates of hospitalisation. However, the difference between the annual crude rate in 2012 and 2016 was about threefold. The differences in these rates were quite

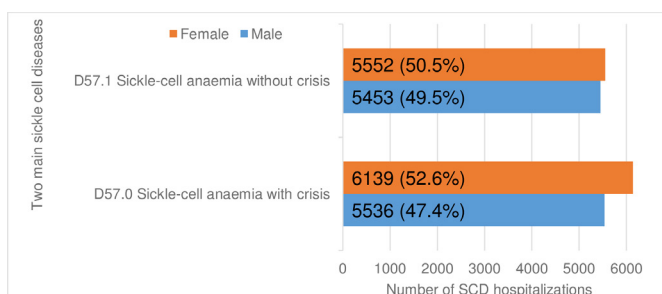


Figure 2 Types of sickle cell disease (SCD) from 2012 to 2017 according to the International Classification of Diseases, 10th revision classification.

similar for both hospitalised patients with SCD with or without a crisis. The regional crude rates of hospitalisations varied considerably among the 10 regions of Ghana. The Volta and Eastern regions with moderate projected populations have the highest crude rates of admission, and also had longer LoS compared with the Greater Accra region (reference region). Awaitey *et al* reported a 17% prevalence of SCD in the Volta region.¹⁵ Unsurprisingly, the Upper East and Upper West regions were among the regions with patients that stayed longer during hospitalisation. This is because of the inequity in the distribution of health facilities and resources in Ghana. However, patients in the Ashanti region with more resourced health facilities comparable to the Greater Accra region had the longest hospital stay for patients with SCD. The Ashanti region has contributed to a lot of SCD literature in Ghana for both children and adults.

SCD is generally known to affect very young persons as most of these patients are predisposed genetically. Hence, it was not surprising that we found patients with SCD less than age 15 years to have increasing crude rates of admission which then drop with age. Similarly, increasing age was associated with shorter LoS, with a growing effect until age 30 years and no clear pattern for older age groups. The

Table 2 The HR and 95% CI from the Cox regression model of risk factors for hospitalised sickle cell disease records, 2012–2017

Variables	HR	95% CI	P value
Calendar-year (years)	0.99	0.99 to 1.00	0.151
Age group (years)			
0–4	ref		
5–9	0.99	0.94 to 1.05	0.830
10–14	1.08	1.01 to 1.14	0.018
15–19	1.17	1.10 to 1.24	<0.001
20–24	1.18	1.11 to 1.26	<0.001
25–29	1.27	1.17 to 1.37	<0.001
30–34	1.21	1.09 to 1.34	<0.001
35–39	1.08	0.93 to 1.24	0.301
40–44	1.20	1.01 to 1.41	0.036
45–49	1.36	1.15 to 1.62	<0.001
50–100	1.11	0.98 to 1.26	0.107
Sex			
Male	ref		
Female	1.03	0.98 to 1.10	0.259
Region			
Greater Accra	ref		
Ashanti	1.16	1.10 to 1.23	<0.001
Brong Ahafo	0.96	0.92 to 1.01	0.099
Central	0.99	0.94 to 1.05	0.797
Eastern	0.93	0.89 to 0.97	0.001
Northern	0.91	0.85 to 0.98	0.017
Upper East	1.14	1.03 to 1.26	0.009
Upper West	1.14	1.03 to 1.28	0.016
Volta	0.92	0.88 to 0.96	<0.001
Western	1.07	1.02 to 1.13	0.007
Employment status			
Unemployed	ref		
Employed	1.01	0.96 to 1.05	0.759
Unspecified	0.97	0.93 to 1.02	0.271
Education level			
No formal education	ref		
Formal education	1.01	0.98 to 1.04	0.523
Health insurance ownership			
No	ref		
Yes	0.98	0.95 to 1.02	0.366
Surgical procedure on admission			
No	ref		
Yes	0.78	0.69 to 0.87	<0.001
Comorbidity			
No	ref		
Yes	0.88	0.86 to 0.90	<0.001

Continued

Table 2 Continued

Variables	HR	95% CI	P value
Age and sex interaction			
0–4 years#Female	ref		
5–9 years#Female	1.02	0.94 to 1.11	0.568
10–14 years#Female	0.99	0.91 to 1.08	0.894
15–19 years#Female	1.03	0.95 to 1.12	0.406
20–24 years#Female	0.96	0.88 to 1.05	0.396
25–29 years#Female	0.88	0.80 to 0.98	0.017
30–34 years#Female	0.90	0.79 to 1.03	0.116
35–39 years#Female	0.96	0.81 to 1.14	0.653
40–44 years#Female	0.93	0.76 to 1.14	0.489
45–49 years#Female	0.88	0.70 to 1.10	0.251
50–100 years#Female	0.89	0.76 to 1.04	0.148

large cohort of young patients with SCD being hospitalised could be explained by the dominance of this age group among patients with SCD which is reflected in several SCD cross-sectional studies reviewed by Grosse *et al*,¹⁰ a systematic review and cross-sectional studies by Owusu *et al*,^{36,37} and another cross-sectional study in Uganda by Ndeezi *et al*.³⁸ Hospitalisation and LoS were dominated by women, which is consistent with smaller studies conducted in Ghana and elsewhere,^{16,39–41} although some studies reported more men.^{42,43}

Patients in over two-thirds of the hospitalisation records analysed had some kind of formal education. Although education was not associated with LoS, we believe that considering the median age of these patients, hospitalisations due to SCD would be a major disruption in their schooling calendar. This phenomenon could further be explained by the fact that the median age of our study population was 16 years, the age at which most of the Ghanaian population is in Senior High or a Vocational

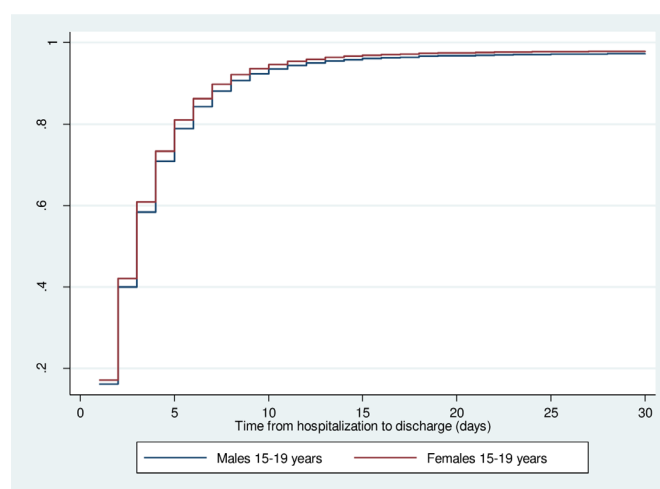


Figure 3 Cumulative incidence function of discharge among hospitalised patients with sickle cell disease, taking into account the competing risk of death.

Technical School.³⁹ Therefore, paying closer attention to outpatient management of patients with SCD could help reduce school absenteeism. Patients hospitalised for SCD with comorbidities and patients who had a surgical procedure during admission were more likely to be discharged later compared with those without comorbidity or did not undergo any surgical procedure. The plausible explanation for this finding could imply that the main reason for hospitalisation might not necessarily be SCD as patients with SCD are more vulnerable to other conditions such as infectious and non-infectious diseases. A considerable literature on these comorbidities has been published both locally and internationally.^{20 36–39 43 44} The strong association of comorbidities with SCD has two implications: first, patients should have the opportunity to take preventive measures against other diseases. Second, public health education and hospital management of patients with SCD should be tailored towards comorbidities within a particular region or area due to the regional effects on hospitalisation. Also, the fact that the admitted patients with SCD who underwent a surgical procedure were discharged later than those who did not undergo any surgical procedure could imply that the condition requiring surgery necessitated hospitalisation.

The interpretability and generalisability of the results in this study are subject to certain limitations. Two premier teaching hospitals in Ghana do not contribute data to the DHIMS-II database due to their autonomy. Also, the DHIMS-II does not cover all private hospitals. However, the number of persons treated in these teaching and private hospitals are small and do not affect very much the overall results. Our study did not include information on other risk factors such as patient health history, diagnostic tests and treatment. Other limitations in this study that could have affected the hospitalisation rates and LoS of patients with SCD include that each admission was treated as a unique record. Therefore, the extracted data could not be linked to individual patients to determine multiple visits. Finally, in order to minimise the bias that might be introduced in statistical models' due to multiple admissions of the same patient, we specified the sandwich estimator for the residual variance making the results robust to non-independence of observations. Furthermore, hospitalisation for a disease depends on several factors, implying that our hospitalisation estimates do not directly reflect disease incidence or prevalence. A survival related bias might have been introduced since our study only included patients with SCD who survived long enough to receive medical care in a hospital. In spite of its limitations, the study adds to our aetiological understanding of the patients with SCD requiring hospitalisation in Ghana.

CONCLUSION

Despite its exploratory nature, this nationwide study in Ghana offers insight into the factors associated with hospital LoS for patients admitted for SCD. There were no obvious temporal trends in crude hospitalisation rates, however, some unexplained spikes were noticed especially in 2016.

Hence, the provision of focused resources and education on significant factors such as comorbidities and surgery during admission will enhance the health of patients with SCD and reduce hospitalisations. In addition to the frequent episodes of pain and hospital visits experienced by patients with SCD. These factors are multifaceted, which require a multisector approach to secondary and tertiary preventions. The impact of these could not be overlooked, as they have dire consequences for individuals, families and the country. Ensuring appropriate health systems, services, support and public health education for patients with SCD should be a priority for stakeholders.

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Contributors CTN and MB conceptualised the idea for the study. CTN, MB and DW contributed to designing the study supervised by MB and DW. CTN, AO and JD contributed to data extraction and cleaning. CTN and DW performed the analyses and interpreted the data supervised by MB. CTN, JD, AO, MB and DW wrote and revised the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. Data used in this study would be published with the manuscript. Extra data is available by emailing the first author.

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