

TO THE EDITOR:

Sustainability of low maternal mortality in pregnant women with SCD in a low-resource setting

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Pregnant women with sickle cell disease (SCD) are at an increased risk for both pregnancy and SCD related morbidity and mortality in low, middle, and high-income countries.¹ The maternal death rate in pregnant women with SCD in sub-Saharan Africa is 7% to 12%.²⁻⁴

At the Korle-Bu Teaching Hospital (KBTH), a national referral center in Accra, Ghana, the maternal and perinatal mortality rates were 10 791 per 100 000 live births (case fatality rate: 9.5%) and 60.8 per 1000 total births, respectively, between January 2014 and April 2015.⁵ In May 2015, the multidisciplinary sickle cell disease (SCD) obstetrics team started the following interventions: a joint obstetrics and hematology outpatient visit, weekly case conference to discuss challenging cases with SCD, and simple protocols for inpatient management of acute chest syndrome (ACS) and acute pain episodes. Periodic training of nursing and medical staff on the management of pregnant women with SCD both on outpatient and in-patient basis was also provided. These interventions resulted in a dramatic reduction in maternal and perinatal mortality in this cohort by 89.1% and 62.2%, respectively, after just 13 months of intervention. The maternal and perinatal mortality rates after intervention were reduced to 1176 (1/85) per 100 000 live births (case fatality rate: 1.1%) and perinatal mortality rate of 23.0 per 1000 total births, respectively.⁵

Using our preestablished protocols for care of pregnant women with SCD,^{5,6} the multidisciplinary SCD obstetrics team at KBTH tested the hypothesis that the low maternal and perinatal mortality incidence rates at KBTH will be sustained over 3 years. We conducted a retrospective cohort postintervention quality assessment study of standard care (1 June 2016 to 31 December 2019 [43 months]: sustainability period) and compared the results to our previously documented postintervention period (1 May 2015 to 31 May 2016; 13 months) as a historical control.⁵ Institutional approval was obtained from the KBTH Institutional Review Board. The study was performed in accordance with the Declaration of Helsinki. Maternal and perinatal mortality were the principal variables assessed. Members of the team adjudicated all acute maternal events requiring hospitalization and all maternal deaths. As per our previously published case series, all deaths before arrival at the hospital, and those without documented evidence of hemoglobin phenotype were excluded.⁷ We also excluded all cases that were nonattendants at the multidisciplinary SCD obstetrics outpatient clinic. The maternal mortality records, patients' admission and discharge files, labor ward records, and autopsy reports of all SCD-related maternal deaths within the study period were retrieved and reviewed by the team. We defined maternal death as direct and indirect obstetric causes according to the World Health Organization International Classification of Diseases (ICD-10).⁸ Data were summarized as simple descriptive statistics. The Mann-Whitney *U*-test and Fisher exact test evaluated differences between pregnant women with Hemoglobin SS (HbSS) vs Hemoglobin SC (HbSC). *P* < .05 was considered statistically significant. SPSS version 24 (IBM Corporation) was used for analyses.

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Requests for data sharing may be submitted to Samuel A. Opong (saoppong@ug.edu.gh).

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Table 1. Baseline characteristics and pregnancy outcomes of women with sickle cell disease in the post intervention and sustainability periods

Patient characteristic	Postintervention period: 13 mo (n = 90)	Sustainability period: 43 mo (n = 342)	P*
Age, n (%), y			
<20	4 (4.4)	12 (3.5)	.477
20-34	73 (81.1)	262 (76.6)	
≥35	13 (14.4)	68 (19.9)	
Mean age (SD), y	28.8 (4.9)	29.6 (5.2)	.192
Phenotype, n (%)			
HbSS	35 (38.9)	139 (40.6)	.763
HbSC	55 (61.1)	203 (59.4)	
Parity, n (%)			
0-1	71 (78.9)	254 (74.3)	.366
2-5	19 (21.1)	88 (25.7)	
Gestational age at enrollment, n (%)			
First trimester (up to 13 wk)	17 (18.9)	41 (12.0)	.096
Second trimester (13 wk 1 d up to 26 wk)	37 (41.1)	126 (36.8)	
Third trimester (26 wk 1 d up to 40 wk)	36 (40.0)	175 (51.2)	
Mean gestational age at enrollment (SD), wk	23.9 (8.6)	25.2 (8.8)	.190
Gestational age at delivery (n = 430)			
Extreme preterm (<28 wk gestation)	3 (3.4)	14 (4.1)	.922
Very preterm (28 to 32 wk gestation)	2 (2.2)	5 (1.5)	
Moderate preterm (32 wk 1 d to 34 wk gestation)	5 (5.6)	20 (5.9)	
Late preterm (34 wk 1 d to 37 wk gestation)	12 (13.5)	56 (16.4)	
Term (37 wk 1 d to 42 wk gestation)	67 (75.3)	246 (72.1)	
Fetal outcome, n (%)			
Spontaneous abortion	3 (3.3)	10 (2.9)	.969
Intrauterine fetal death	2 (2.2)	8 (2.3)	
Stillbirth	0 (0.0)	1 (0.3)	
Died in utero with mother	0 (0.0)	2 (0.6)	
Alive	85 (94.5)	320 (93.6)	
Unknown	0 (0.0)	1 (0.3)	
Type of delivery, n (%) (n = 426)			
Caesarean	42 (46.7)	212 (63.1)	.012
Vaginal	45 (50.0)	112 (33.3)	
Not delivered†	3 (3.3)	12 (3.6)	
Perinatal outcome			
Perinatal deaths, n (%)	2 (2.2)	9 (2.7)	1.000
Perinatal deaths per 1000 total births	23.0	27.4	
Maternal outcome			
Maternal deaths, n (%)	1 (1.1)	9 (2.6)	.695
Maternal deaths per 100 000 live births	1,176	2,812	
Causes of maternal death			
Indirect obstetric (SCD-related) deaths			
Acute chest syndrome (ACS)	0	6	
Venous thromboembolism (VTE)	1	1	
Congestive cardiac failure (CCF)	0	1	
Direct obstetric deaths			
Obstetric hemorrhage	0	1	

* χ^2 or Fisher's exact test for categorical variables, and *t* test for continuous variables.

†Not delivered comprises spontaneous abortions, hysterectomies, and dying in utero with mother.

Table 2. Underlying causes of maternal death in women with SCD categorized by SCD phenotype, clinical events, and autopsy findings

				Groups of underlying causes of death using WHO-ICD 10 mm			Cause of death		
Number	Phenotype	Age, y	Parity	Duration of hospitalization before death	Estimated time of death	Type of maternal death	Group name	Clinical events	Autopsy findings
1	HbSC	27	1	5 d	Postpartum day 4	Indirect obstetric death	Nonobstetric complications	I. ACS	VTE (massive bilateral pulmonary embolism)
Sustainability period (June 2016 to December 2019)									
1	HbSC	34	3	6 d	Postpartum (< 1 wk)	Indirect obstetric death	Nonobstetric complications	I. ACS II. Severe anemia (hyperhemolytic crisis and acute splenic sequestration crisis) III. Pre-eclampsia	I. ACS II. Cerebral edema III. Acute splenic sequestration crisis
2	HbSC	21	0	8 d	Postpartum day 1	Indirect obstetric death	Nonobstetric complications	I. ACS II. VOC III. Pre-eclampsia	ACS
3	HbSS	30	0	3 d	23 wk 4 d gestation	Indirect obstetric death	Nonobstetric complications	I. ACS II. VOC III. Severe anemia (intravascular haemolysis and acute sequestration crisis)	I. ACS II. 1. Severe anemia 2. Acute sequestration crisis
4	HbSS	31	2	5 d	Postpartum day 0	Direct obstetric death	Obstetric complications	I. Haemorrhagic shock II. Haemoperitoneum post caesarean delivery III. VOC	Haemorrhagic shock with end organ failure
5	HbSC	30	1	6 d	Postpartum day 6	Indirect obstetric death	Nonobstetric complications	I. ACS (rapidly progressive) II. VOC IIIa. Severe anemia (acute splenic sequestration crisis and intravascular haemolysis) IIIb. Coagulopathy IIIc. Stroke	ACS
6	HbSS	33	2	5 d	Postpartum day 1	Indirect obstetric death	Nonobstetric complications	I. ACS II. VOC III. Pre-eclampsia	ACS
7	HbSC	27	1	8 d	Postpartum day 0	Indirect obstetric death	Nonobstetric complications	I. ACS II. VOC III. Gestational hypertension	VTE (massive bilateral venous thromboembolism from left popliteal vein thrombus)
8	HbSS	31	1	3 d	27 wk 6 d gestation	Indirect obstetric death	Nonobstetric complications	I. CCF II. Severe anemia (intravascular haemolysis) IIIa. VOC IIIb. Twin gestation	I. CCF II. Dilated cardiomyopathy III. SCD
9	HbSC	29	2	2 d	24 wk gestation	Indirect obstetric death	Nonobstetric complications	ACS (rapidly progressive)	Not done

I, immediate cause of death; II, underlying cause of death; III, other maternal disease or morbid condition.

A total of 342 (HbSS: 139; HbSC: 203) pregnancies by women with SCD were evaluated during the sustainability period of 43 months. There was no difference in the demographic characteristics of the study participants in both the postintervention and sustainability groups (Table 1). During the postintervention and sustainability intervals, the maternal mortality rates were 1176 (1/85) per 100 000 live births (case fatality: 1.1% [95% confidence interval (CI), 0.0%-6.4%]) and 2800 (9/320) per 100 000 live births (case fatality: 2.8% [95% CI, 1.3%-5.3%]), respectively ($P = .69$). During the postintervention and sustainability periods, the perinatal mortality rates were comparable at 27.4 (2/90) per 1000 total births (case fatality: 2.2% [95% CI, 0.2%-7.8%]) and 23.0 (9/342) per 1000 total births (case fatality: 2.7% [95% CI, 1.2%-4.9%]), respectively ($P = 1.0$).

The single death during the postintervention period was a participant with clinical evidence of ACS, later confirmed by autopsy as a massive bilateral pulmonary embolism 4 days postpartum (Table 2). In comparison, the causes of death during the sustainability period included 6 cases of ACS, 1 case of autopsy-confirmed massive bilateral pulmonary embolism from a left popliteal vein thrombus, 1 case of congestive cardiac failure, and 1 case of obstetric hemorrhage (Table 2).

In a case series of deaths in pregnant women with SCD at KBTH from January of 2010 through December 2016, ACS was the cause of nearly 87% (33 of 38) of SCD-related maternal deaths.⁹ Approximately 80% of ACS cases occur during the third trimester and early postpartum period <2 weeks.⁹ Similarly, an ACS diagnosis was the most common cause of death in the current study; 2 pregnant women with HbSC phenotype had a clinical diagnosis of rapidly progressive ACS¹⁰ with multiorgan failure, requiring ventilatory support.¹⁰ Both women developed thrombocytopenia (<80 000/ μ L), multiorgan failure (hepatic dysfunction, coagulopathy), altered mental status, and stroke.

We provide further evidence that, as standard care, establishing a multidisciplinary SCD and obstetric team in a low-resource setting can reduce the maternal and perinatal mortality rates. Our next challenge is to determine whether our low-budget multidisciplinary strategy is expandable to other settings in Ghana and parts of Africa in hospitals without SCD expertise.

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Authorship: Contribution: S.A.O., M.R.D., A.K., and E.O. designed the study; A.S.-D., R.A.B., E.V.A., T.K.B., and S.A.O. collected the data; S.A.O., E.O., Y.D.-A., T.K.B., C.H.-B., A.S.-D., R.A.B., E.V.A., M.R.D. and A.K. adjudicated on the case files; A.S.-D., E.V.A., R.A.B., J.A.-N., M.R.D., and M.R. performed the analyses; and M.R.D., A.S.-D., R.A.B., E.V.A., and S.A.O. interpreted the results. All authors participated in writing the article and reviewed and approved the manuscript before submission. S.A.O. confirms that he had full access to all the data in this study and had final responsibility for the decision to submit for publication.

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