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Maternal caesarean section infection (MACSI) in Sierra Leone: a case–control study

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Abstract

Sierra Leone is the country with highest maternal mortality and infections are the underlying cause in 11% of maternal deaths, but the real burden remains unknown. This study aims to determine the incidence and risk factors of surgical site infection (SSI) post-caesarean section (CS) in women admitted to Princess Christian Maternity Hospital (PCMH) in Freetown, Sierra Leone. A prospective case–control (1:3 ratio) study was implemented from 1 May 2018 to 30 April 2019 and 11 women presenting with suspected or confirmed infection post-CS were screened for inclusion as a case. For each case, three patients undergoing CS on the same day and admitted to the same ward, but not presenting with SSI, were selected as controls. The post-CS infection rate was 10.9%. Two hundred and fifty-four clinically confirmed cases were enrolled and matched with 762 control patients. By multivariable analysis, the risk factors for SSI were: being single (odds ratio (OR) 1.48, 95% confidence interval (CI) 1.36–1.66), low education level (OR 1.68, 95% CI 1.55–1.84), previous CS (OR 1.27, 95% CI 1.10–1.52), presenting with premature membranes rupture (OR 1.49, 95% CI 1.18–1.88), a long decision–incision time (OR 2.08, 95% CI 1.74–2.24) and a high missing post-CS antibiotic doses rate (OR 2.52, 95% CI 2.10–2.85).

Introduction

Two-thirds of the global maternal deaths in 2017 occurred in sub-Saharan Africa (SSA), and Sierra Leone was one of the countries with the highest maternal mortality ratios (MMRs) with 1360 deaths per 100 000 live-births in 2015 [1, 2]. The country also ranks 184th out of 189 countries on the human development index and has the third lowest life expectancy in the world [3, 4]. These maternal and neonatal mortality indices are lagging behind the United Nations Sustainable Development Goals for 2030 of an MMR of less than 70 deaths per 100 000 live-births and a neonatal mortality rate of less than 12 deaths per 1000 live-births [5].

Infections are the underlying causes in 11% of maternal, and one-fourth of newborn deaths, but the true burden of maternal infections and related complications remains unknown [6, 7]. Among maternal infections, surgical site infections (SSIs) play a dominant role. Caesarean section (CS) delivery is one of the most common operative procedures performed in SSA, and accounts for as much as 80% of the surgical workload with accompanying high morbidity and mortality rates [8, 9]. Notably, CS is the most important risk factor for infections in the immediate postpartum period, with a 5- to 20-fold increased risk compared to vaginal birth [10, 11]. Up to one in five women in Africa who deliver their baby by CS develop a wound infection, but reliable data are lacking from low resource settings, and in particular from Sierra Leone, where the incidence and risk factors for CS SSIs are still unexplored [6].

Although largely preventable, SSIs represent a considerable burden for health-care systems, particularly in low- and middle-income countries [12, 13]. In order to reduce the burden of maternal and neonatal infections, there is a need to improve our understanding of clinical, epidemiological and contextual factors impacting CS-related SSIs. Therefore, the aim of this 12-month prospective case–control study was to determine the incidence, risk factors and predictors of negative outcome of such infections in women admitted to a high-volume urban referral centre in Freetown, Sierra Leone.

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Table 1. Baseline characteristics of the 1016 enrolled patients

	Total (no. 1016; 100.0%)	SSI (no. 254; 25.0%)	Controls (no. 762; 75.0%)	*P*-value
Age (mean; S.D.)	25.5 (0.5)	26.4 (0.7)	25.9 (0.4)	0.53
BMI *n* (%)				
Low (<18)	90 (8.8)	57 (22.6)	33 (4.4)	**<0.0001**
Normal (18–25)	798 (78.5)	137 (53.8)	661 (86.8)	
High (>25)	128 (12.7)	60 (23.6)	68 (9.0)	
Status, *n* (%)				
Married	799 (78.6)	178 (70.3)	621 (81.5)	**<0.0001**
Single	247 (21.4)	76 (29.7)	141 (19.5)	
Occupation, *n* (%)				
Employed	224 (78)	41 (16.0)	183 (24.0)	**0.04**
Unemployed	792 (22)	213 (84.0)	579 (74.0)	
Education, *n* (%)				
Illiterate	87 (8.5)	61 (23.7)	26 (3.4)	**<0.0001**
Primary education level (<8 years)	829 (81.5)	170 (67.1)	659 (86.5)	
High education level (>8 years)	100 (10)	23 (9.2)	77 (10.1)	
Gravidity, *n* (%)				
Gravida 1	316 (31.1)	73 (28.9)	243 (31.9)	**<0.0001**
Gravida 2–4	632 (62.2)	141 (55.3)	491 (64.6)	
Gravida >4	67 (6.7)	40 (15.8)	27 (3.5)	
Comorbidity, *n* (%)	240 (23.6)	134 (52.7)	106 (13.9)	**<0.0001**
Referred from other health facilities *n* (%)	575 (56.6)	73 (28.9)	502 (65.9)	**<0.0001**
Presence of premature rupture of membranes, *n* (%)	330 (32.5)	174 (68.4)	156 (20.5)	**<0.0001**
Previous CS, *n* (%)	678 (66.7)	183 (72)	495 (65)	**0.03**
Time decision–incision, median (IRQ) (min)	80 (55 −120)	101 (90–160)	68 (55–94)	**<0.0001**
Duration of CS, mean (S.D.) (min)	32 (1.0)	36 (0.8)	28 (0.3)	0.10
Type of incision, *n* (%)				
Transverse	839 (82.5)	191 (75.0)	648 (85.1)	**0.04**
Midline	177 (17.5)	63 (25.0)	114 (14.9)	
Suture used for skin closure, *n* (%)				
Absorbable	896 (88.2)	214 (84.2)	682 (89.5)	**0.02**
Non-absorbable	120 (11.8)	40 (15.8)	80 (10.5)	
% Missing post-CS Antibiotic doses (not given/prescribed), *n* (%)				
Day of CS				
0–50%	87 (8.6)	75 (29.3)	12 (1.6)	**<0.0001**
51–100%	929 (91.4)	179 (70.7)	750 (98.4)	
Day 1 post-CS				
0–50%	101 (10)	74 (29.3)	27 (3.5)	**<0.0001**
51–100%	915 (90)	180 (70.7)	735 (96.5)	
Day 2 post-CS				
0–50%	101 (10)	89 (34.9)	12 (1.6)	**<0.0001**
51–100%	915 (90)	165 (65.1)	750 (98.4)	
Maternal death, *n* (%)	14 (13.8)	13 (5.3)	1 (0.1)	**<0.0001**

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Methods

Study design

This was a prospective matched case–control (1:3 ratio) study carried out from 1 May 2018 to 30 April 2019 at Princes Christian Maternity Hospital (PCMH) in Freetown, Sierra Leone. It is the largest urban maternity referral hospital in the country, serving a population of 1.5 million inhabitants. It has approximately 9000 admissions and 6000 deliveries per year of which around 30% are CSs [14]. The study protocol is registered on Clinicaltrials.gov with the reference number NCT03929991. Ethical approval of the protocol was obtained from the Ministry of Health of Sierra Leone Ethical Committee.

Study population

All pregnant women undergoing a CS in the hospital during the study period were enrolled, and all those admitted or already hospitalised with suspected or confirmed infection after CS were screened for inclusion as potential cases. Case confirmation was established by a daily detailed physical examination of all hospitalised women by an infectious disease specialist. All the post-caesarean surgical incision as well as the body temperature and other available clinical parameters were evaluated. Complex clinical cases were discussed in a multidisciplinary teamwork and diagnosis of SSIs was made according to current guidelines [15]. For each case, three patients undergoing a CS on the same day and admitted to the same ward, but not presenting with SSI from the day of enrolment until the end of hospital stay, were selected as controls.

Data collection

Clinical data, such as body mass index (BMI), gravidity, comorbidity, presence of premature rupture of membranes and breastfeeding, were recorded at the onset of SSI, and whether infections occurred post-CS or within the hospital stay for cases, and on the day of examination for controls. Socio-demographic data (age, occupation, level of education and referral from other health facilities) and information about the CS (i.e. previous, clinical indication, elective or emergency, antibiotic prophylaxis, time 'decision to incision', duration of operation, type of incision, type of anaesthesia, suture used for skin closure and closure style) was also recorded at the same time point. Time 'decision to incision' was calculated as the time elapsed between the gynaecologist's indication for urgent CS and the time of the incision. Both were recorded according to the study protocol.

The missing post-CS antibiotics dose rate was calculated as doses not given/doses prescribed, and recorded on day and then on the first and the second day post-CS. Information on the administration of antibiotic prophylaxis and operating procedures was recorded on the patient's file, and reviewed by an infectious disease specialist.

For cases only, the SSI was classified according to the CDC definition [15] as: superficial incision; deep incision and organ/space infection. Data were also collected on the interval; post-CS and onset of infection; the type of treatment and final outcomes.

Patients and newborns were assessed at hospital discharge, together with the length of hospital stay. The incidence of SSI post-CS was determined retrospectively from the operating theatre register for the total number of CS performed during the study period; data were cross checked with the labour ward register.

Table 2. SSI characteristics of the 254 enrolled cases

Classification, *n* (%)	
Superficial	90 (35.5)
Deep	98 (38.2)
Organ	66 (26.3)
Days from the CS to the onset, mean (S.D.)	4.4 (1.8)
Type of treatment, *n* (%)	
Antibiotics	81 (31.9)
Antibiotics + opening of the wound at the bedside	99 (39.0)
Antibiotics + minor surgery[a]	51 (20.1)
Hysterectomy	23 (9.0)
Final outcome, *n* (%)	
Complete resolution	241 (94.7)
Death	13 (5.3)

[a]Internal cleaning of uterus.

Statistical analysis

Data were reported as means and standard deviations (S.D.) for continuous variables. Absolute and relative frequencies (percentages) were used for categorical variables. Independent *t* test was used to compare groups for continuous variables, whilst a χ^2 test (with the Fisher's correction if less than five cases were present in a cell) was applied for categorical variables. A logistic regression model was implemented as follows. SSI was considered as a dependent variable and each one of the available factors at the baseline evaluation as independent variables (univariate analysis). In the multivariate analysis factors with a *P*-value <0.10 by univariate analysis were included. Multicollinearity among covariates was assessed through the variance inflation factor, taking a value of 2 as cut-off to exclude a covariate. However, no variable was excluded according to this pre-specified criterion. Odds ratios (ORs) as adjusted odds ratios (adj-ORs) with 95% confidence intervals (CIs) were used to measure the strength of the association between factors at the baseline (exposure) and treatment failure (outcome). The R^2 value to quantify the variability of the dependent variable was also determined. All statistical tests were two-tailed and statistical significance was assumed for a *P*-value <0.05. Analyses were performed using SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois).

Results

Overall, 254 clinically confirmed SSI post-CS were enrolled in the study as cases, these were matched with 762 control patients, accounting for a total of 1016 patients (mean age 25.5 years, S.D. 5.6). Baseline characteristics for cases and controls are presented in Table 1. HIV, HBV or HCV infections, diabetes, hypertension and other chronic diseases were recorded and considered comorbidities. Over the study period, 2323 CS interventions were registered at PCMH, giving an SSI incidence of 10.9%.

Table 2 shows that of the 254 cases of SSI, 90 (35.5%) were classified as superficial, 98 (38.2%) deep and 66 (26.3%) as organ/space. The onset of the infection was on average on the 4th day (1.8%). Treatment by antibiotic therapy alone was given for 81 (31.9%) patients, antibiotic plus opening of the wound at

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Table 3. Predictors of the SSI onset in the 1016 enrolled women undergoing to CS

	Unadjusted analysis of SSI risk		Adjusted analysis of SSI risk	
Characteristics	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age (years)	1.02 (0.98–1.04)	0.53	–	0.46
Single	1.32 (1.01–1.52)	**<0.0001**	1.48 (1.36–1.66)	**<0.0001**
Low BMI (<18)	1.80 (1.42–2.02)	**<0.0001**	1.42 (1.18–1.72)	**<0.0001**
High BMI (>25)	1.50 (1.28–1.74)	0.05	1.85 (1.02–2.68)	**<0.0001**
Referred from other health Facilities	1.34 (1.10–1.66)	**<0.0001**	2.35 (2.18–2.59)	**<0.0001**
Gravida >4	0.51 (0.43–0.70)	0.04	0.64 (0.59–0.83)	**0.19**
Unemployed	1.85 (1.35–2.45)	0.04	1.74 (1.24–2.21)	**<0.0001**
Low education	2.02 (1.27–2.53)	**<0.0001**	2.19 (1.71–2.33)	**<0.0001**
Presence of premature rupture of membranes	1.20 (0.84–1.85)	**<0.0001**	1.49 (1.18–1.88)	**<0.0001**
Time decision–incision, median (IRQ)	1.76 (1.45–2.25)	**<0.0001**	2.08 (1.74–2.24)	**<0.0001**
Suture used for skin closure absorbable	0.90 (0.65–1.15)	0.02	0.98 (0.88–1.19)	0.06
Missing post-CS Antibiotic doses (>51%)	1.80 (1.50–2.00)	**<0.0001**	2.52 (2.10–2.85)	**<0.0001**
Previous CS	1.34 (1.19–1.54)	0.03	1.27 (1.10–1.52)	0.02

*$P < 0.05$.

the bedside for 99 (39.0%), antibiotic plus re-operation for 51 (20.1%) and hysterectomy for 23 (9.0%) patients. Complete resolution of the SSI was observed in 241 (94.7%) patients, while 13 (5.3%) women died.

Cases more frequently had an abnormal BMI (low or high), were more often unemployed and with a lower educational level than the control group, and less frequently referred from other health facilities. Cases also presented with a higher incidence of premature rupture of membranes and comorbidities, as well as a higher rate of missing antibiotic doses over the first 3 days post-CS. Regarding factors related to surgical intervention, bivariate analysis showed that a midline CS incision and the use of non-absorbable sutures for skin closure were more frequently associated with infection ($P < 0.05$). There were no differences regarding the anaesthesia received, the type of suture and the closure style. All patients were administered prophylactic antibiotic therapy pre C/S section. (Complete information on cases and controls is shown in Supplementary Material.)

By multivariable analysis, several factors were found to be independently associated with an increased risk of SSI (Table 3). These were being single (OR 1.48, 95% CI 1.36–1.66), having an abnormal BMI (low (OR 1.42, 95% CI 1.18–1.72); high (OR 1.85, 95% CI 1.02–2.68)), admitted from home (OR 2.35, 95% CI 2.18–2.59), unemployed (OR 1.74, 95% CI 1.24–2.21), low education level (OR 1.68, 95% CI 1.55–1.84), presenting with premature rupture of membranes (OR 1.49, 95% CI 1.18–1.88), a long decision–incision time (OR 2.08, 95% CI 1.74–2.24), frequent missing post-CS antibiotic doses (OR 2.52, 95% CI 2.10–2.85) and previous CS (OR 1.27, 95% CI 1.10–1.52).

Discussion

The primary findings of this study were that (1) one in 10 women undergoing CS at PCMH developed an SSI that led to death in 5.3% of them; (2) the predictors of SSIs were social and demographic i.e. being single, being unemployed, with low education level, having an abnormal BMI, both low and high, health-system related (coming from home instead of being referred from a health facility), obstetric (previous CS, presenting with premature membranes rupture, a long decision–incision interval) and clinical (a high rate of missing post-CS antibiotic doses).

Many of these demographic variables reflect a common scenario for a large proportion of the Sierra Leone population. Similarly, low BMI, low socio-economic status or educational levels predispose patients to be less aware of their clinical condition. Likewise, they are less able to buy drugs for their comorbidities, or lack confidence in hospital care and thereby increasing their risk of acquiring SSIs. Hence, these variables serve as proxies of discomfort experienced by such populations in Sierra Leone which has undergone a prolonged civil war (1991–2002) followed by Ebola virus disease outbreak (2014–2016). These events have profoundly affected the already fragile healthcare system, leading to significant worsening of maternal health indicators [16, 17].

The post- CS SSI rate of 10.9% reported in our cohort is comparable with some reports from Ethiopia and Gambia [2, 18, 19], but was markedly lower than the 15.6% incidence found in SSA [20]. However, many context-related factors, such as urban *vs.* rural hospital settings, make direct comparison of infection rates in different countries difficult. Nevertheless, it is important to note that despite the relatively moderate infection rate found in this series, maternal deaths (5.3%) and hysterectomies (9%) represent an important disability especially in the African context.

Among all predictors of mortality, the role of antibiotics deserves special attention. According to hospital guidelines and local clinical practice, the antibiotic prophylactic schedule was: 2 g of ampicillin IV 15–60 min before the skin incision and continued for 48 h after the CS with empiric therapy [21]. Also, it is noteworthy that as antibiotic prophylaxis was a key factor for the prevention of surgical infections, this – together with a possible indirect study effect – could explain the universal pre-operative antibiotic coverage observed, which is generally uncommon in low-income contexts. Nevertheless, despite the high coverage rate of prophylactic antibiotics, the SSI cohort had a higher frequency of missing antibiotic doses over the first 2 days post-CS

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compared to the controls. It is known that prophylactic antibiotics work synergistically with the appropriate antiseptic measures before and during surgery [22, 23], so such factors might also have impacted the observed low SSI rate. Indeed, it is widely recognised that infection prevention requires the integration of a range of control procedures before, during and after surgery [24–27].

We found that the high rate of incomplete antibiotic dosing was an important predictor of infection, resulting in a two and half fold increase of infection risk for each missed dose. It is worth noting that the WHO no longer recommends a prolonged antibiotic prophylaxis strategy, especially in a context of low resources [28, 29]. Indeed, the lack of antibiotics is a serious concern in this setting, where despite being an irreplaceable weapon against infections, frequent misuse facilitates the development of multi-drug-resistant bacteria [30–32]. The data on the missing antibiotic doses prompted us to reflect on antibiotic prescribing practice. In low resource settings such as Sierra Leone where there is a significant lack of drugs, antimicrobials must be prescribed accurately and following the international guidelines. In this regard, the current protocol of prescribing an antibiotic for 48 h post-caesarean should be reviewed. We suggest that antibiotic prophylaxis should be limited to 24 h post-caesarean which in turn would lead to a better use of these drugs and also reduce the rate of missing doses with a resulting reduced infectious risk.

A second interesting study finding was the role of time and duration of the CS. It is recommended that CS should be performed in less than 30 min to reduce the risk of SSI [33], and long decision–incision time has been shown to double the risk of infection [34–38]. As suggested by the American College of Obstetrics and Gynecology (ACOG) guidelines, the CS defined as 'urgent' should activate a rapid protocol that takes the patient to the theatre as soon as possible, and within half an hour [39]. However, the achievement of this high-quality standard requires important and significant investment in terms of public health organisation, surgical team training and structural improvements, all of which require a coordinated approach. Moreover, patients with low socio-economic status remain the most vulnerable in terms of post-caesarean infections and will always need more medical attention and follow-up [40–42].

This study had several limitations. Since the study site was a tertiary referral hospital, it is possible that it served to centralise cases of the most complicated pregnancies at higher risk of infection, thereby limiting the applicability of our results to the district hospital setting. In this perspective, a comparison with primary or secondary level of care would be important to achieve. Likewise, the lack of microbiological confirmation of cases and scarcity of post-discharge patient information is an important limitation from an epidemiological viewpoint and which we hope to address in further investigations.

In conclusion, the key message from our findings is on the role of antibiotics in ensuring universal coverage. This requires appropriate administration and dosing and in selecting eligible patients for treatment, in order to avoid resource waste and the development of antibiotic-resistance. These aspects have a key role in national infection control and antibiotic stewardship programmes and should be prioritised in the national health strategy particularly in low resource countries, where the availability of antimicrobials is very limited and the emergence of multi-drug-resistant bacteria is a reality [42, 43]. Understanding the determinants and predictors of SSIs and their outcomes involves wider interventions that go beyond the patients themselves in order to reduce the burden of diseases in mothers and children. Our findings from Sierra Leone highlight the need to urgently tackle SSIs more stringently.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0950268820000370.

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