Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study

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Summary

Background Maternal and neonatal mortality is high in Africa, but few large, prospective studies have been done to investigate the risk factors associated with these poor maternal and neonatal outcomes.

Methods A 7-day, international, prospective, observational cohort study was done in patients having caesarean delivery in 183 hospitals across 22 countries in Africa. The inclusion criteria were all consecutive patients (aged ≥18 years) admitted to participating centres having elective and non-elective caesarean delivery during the 7-day study cohort period. To ensure a representative sample, each hospital had to provide data for 90% of the eligible patients during the recruitment week. The primary outcome was in-hospital maternal mortality and complications, which were assessed by local investigators. The study was registered on the South African National Health Research Database, number KZ_2015RP7_22, and on ClinicalTrials.gov, number NCT03044899.

Findings Between February, 2016, and May, 2016, 3792 patients were recruited from hospitals across Africa. 3685 were included in the postoperative complications analysis (107 missing data) and 3684 were included in the maternal mortality analysis (108 missing data). These hospitals had a combined number of specialist surgeons, obstetricians, and anaesthetists totalling 0·7 per 100 000 population (IQR 0·2–2·0). Maternal mortality was 20 (0·5%) of 3684 patients (95% CI 0·3–0·8). Complications occurred in 633 (17·4%) of 3636 mothers (16·2–18·6), which were predominantly severe intraoperative and postoperative bleeding (136 [3·8%] of 3612 mothers). Maternal mortality was independently associated with a preoperative presentation of placenta praevia, placental abruption, ruptured uterus, antepartum haemorrhage (odds ratio 4·47 [95% CI 1·46–13·65]), and perioperative severe obstetric haemorrhage (5·87 [1·99–17·34]) or anaesthesia complications (11·47 (1·20–109·20]). Neonatal mortality was 153 (4·4%) of 3506 infants (95% CI 3·7–5·0).

Interpretation Maternal mortality after caesarean delivery in Africa is 50 times higher than that of high-income countries and is driven by peripartum haemorrhage and anaesthesia complications. Neonatal mortality is double the global average. Early identification and appropriate management of mothers at risk of peripartum haemorrhage might improve maternal and neonatal outcomes in Africa.

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Introduction

Africa's population has the highest growth rate in the world and is estimated to exceed 1·7 billion people by 2030.[1] Mothers and their children continue to die at an unacceptable rate in Africa. Two-thirds of the global maternal deaths in 2015 occurred in sub-Saharan Africa,[2] and the maternal mortality rate is estimated to be more than double the global average of 546 maternal deaths per 100 000 livebirths.[2] The neonatal mortality rate is also highest in sub-Saharan Africa (28 per 1000 livebirths) compared with the global average of 19 per 1000 livebirths.[3] These maternal and neonatal figures are far removed from the Sustainable Development Goals for 2030 of a maternal mortality rate of less than 70 deaths per 1000 livebirths and neonatal mortality rate less than 12 deaths per 1000 livebirths.[3,4]

Caesarean delivery is one of the Bellwether procedures of the *Lancet* Commission on Global Surgery,[5] yet in Africa both the safety of this procedure and access to caesarean deliveries are poor. Although some middle-income countries are seeking to lower their caesarean delivery rates, countries with a caesarean delivery rate of less than 19 per 100 livebirths (which is characteristic of most African countries) are associated with a significantly increased maternal and neonatal mortality.[6] Poor access to caesarean delivery,[7] peripartum haemorrhage,[8] and provision of anaesthesia by anaesthesia

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Research in context

Evidence before this study

African maternal and neonatal mortality rates are unacceptably high. The maternal mortality rate in sub-Saharan Africa is estimated to be more than double the global average at 546 maternal deaths per 100 000 livebirths. Sub-Saharan Africa also has the highest neonatal mortality rate in the world at 28 deaths per 1000 livebirths. These outcomes are compounded by a lack of global focus on surgical care, something that has been largely ignored until the publication of the *Lancet* Commission on Global Surgery in 2015. Caesarean delivery is a Bellwether procedure of the *Lancet* Commission, yet few people have access to caesarean deliveries in Africa. Maternal and neonatal mortality increases significantly in countries where the caesarean delivery rate is less than 19 per 100 livebirths, which is the case for almost every country in Africa. Additionally, existing data are derived from complex modelling analyses of predominantly small or retrospectively collected datasets and do not describe the effect of baseline maternal comorbidities and perioperative complications on poor maternal and neonatal outcomes after caesarean delivery in Africa. The Sustainable Development Goal (SDG)'s target 3.1 is to reduce the global maternal mortality rate to less than 70 per 1000 livebirths by the year 2030, with no country exceeding 140. This goal currently appears unachievable in most African countries. To work towards the SDG for maternal mortality rate in Africa, more robust data are needed that describe the association between maternal risk factors and perioperative complications and subsequent maternal and neonatal outcomes.

Added value of this study

This obstetric substudy of the African Surgical Outcomes Study provides caesarean delivery data from 22 African countries. As a result of poor access to health care, mothers present for caesarean delivery with a high baseline preoperative risk; one in eight mothers have pre-eclampsia or eclampsia and one in 17 have a major risk of perioperative bleeding. A quarter of all anaesthetics are administered by non-physician anaesthesia providers. One in eight women will develop a perioperative complication, most frequently post-partum haemorrhage. One in four maternal deaths happen after severe obstetric haemorrhage and one in ten happen after anaesthesia complications. The result is that mothers in Africa are 50 times more likely to die after caesarean delivery than mothers in high-income countries. The neonatal mortality rate after caesarean delivery is also high at 44 per 1000 livebirths. The prognosis for neonates who survive is also poor. It is estimated that the incidence of subsequent cerebral palsy and epilepsy is 2–11 times higher than Sweden.

Implications of all the available evidence

Previous studies have provided only a small amount of data on risk factors and associated maternal and neonatal outcomes after caesarean delivery in Africa. Our findings suggest that the maternal and neonatal mortality in Africa is substantially higher than previously estimated. Obstetric haemorrhage and anaesthesia complications are associated with maternal death. The outcome of mothers and neonates in Africa might be improved by early identification of mothers at risk of obstetric haemorrhage, ensuring an appropriate level of care for high-risk obstetric patients and early and appropriate management of peripartum haemorrhage. Improvement of surgical outcomes could have a substantial effect on both maternal and neonatal mortality and could have an effect on stillbirth rates, with key global health gains. Our findings will potentially enable targeted, context-sensitive interventions aimed at reducing these negative outcomes.

care providers of lower levels[9] (ie, who are non-physicians) might all contribute to maternal and neonatal mortality in low-income and middle-income countries. To improve caesarean delivery safety in Africa, and to simultaneously improve maternal and neonatal outcomes, robust patient and outcomes data are required. Furthermore, to design effective interventional strategies to reduce morbidity associated with caesarean delivery, an understanding of the risk factors associated with maternal and neonatal mortality is necessary.[6,10,11] Unfortunately, it is impossible to achieve these objectives with the current data, which is modelled on predominantly retrospective or small datasets and mostly addresses mortality alone.

To address these limitations, we did a preplanned, prospective, observational substudy of adult patients having caesarean delivery within the African Surgical Outcomes Study (ASOS).[12] We hypothesised that obstetric outcomes are worse in Africa than in high-income countries.

Methods

Study design and participants

This obstetric substudy was a planned study of ASOS, a 7-day African, national, multicentre, prospective, observational cohort study of all patients (≥18 years) having in-patient surgery. Patients were recruited from 183 hospitals across 22 countries in Africa. These included 12 low-income countries (Benin [n=9], Burundi [n=6], Republic of the Congo [n=1], Democratic Republic of the Congo [n=16], Ethiopia [n=2], The Gambia [n=5], Madagascar [n=6], Mali [n=9], Niger [n=1], Tanzania [n=3], Uganda [n=8], Zimbabwe [n=19]) and ten middle-income countries (Algeria [n=2], Cameroon [n=5], Ghana [n=2], Kenya [n=5], Libya [n=6], Mauritius [n=6], Namibia [n=15], Nigeria [n=10], South Africa [n=44], Zambia [n=3]).

ASOS was done by a collaborative research network of over 1000 research clinicians from across Africa.[12] We sought to recruit as many centres as possible from each participating country through convenience sampling. To ensure a representative sample from each

hospital, we required each hospital's lead investigator to submit the total number of eligible patients during the recruitment week and required that each participating hospital provide complete data for at least 90% of the eligible surgical patients during the recruitment week.

At the discretion of the ASOS national leader, each country selected a single recruitment week for the study between February, 2016, and May, 2016. The inclusion criteria were all consecutive patients (aged ≥18 years) admitted to participating centres having elective and non-elective caesarean delivery during the 7-day study cohort period. Preoperative recruitment and follow-up until discharge was performed by local investigators. The study was censored at 30 days postoperatively for patients who were still in hospital. Hospital-specific data were also collected: number of hospital beds, number of operating rooms, number of critical-care beds, and numbers of anaesthesiologists and obstetricians working in the hospital.

Regulatory approval varied between countries, with some requiring ethics approval and others requiring only data regulatory approval. The primary ethics approval was from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (BE306/15). All sites approved a waiver of consent, with the exception of the University of the Witwatersrand, South Africa, which required informed consent from all patients, with the option of deferred consent for patients unable to give consent before surgery.

Procedures

We adopted the International Surgical Outcomes Study (ISOS) definitions, with minor changes, to provide data on surgical outcomes that are internationally consistent with the ISOS publication.[13,14] The definition and grading of complications were according to the European Perioperative Clinical Outcome definitions.[13] We collected the same potential risk factors as ISOS for in-hospital mortality and postoperative complications. An obstetric-specific case report form was added to the ASOS dataset for the obstetric substudy (appendix p 19), which included substudy specific data: history of pre-eclampsia, eclampsia, cardiac disease, placenta praevia, placental abruption, ruptured uterus, sepsis and antepartum haemorrhage; gravidity and parity, gestational age, fetal distress, and neonatal outcomes (1 and 5 min Apgar scores, need for cardiopulmonary resuscitation after delivery, and neonatal in-hospital mortality censored at 30 days). To ensure consistency in data definitions and interpretation, the data definition file used for ISOS was adopted for ASOS.[13] The corresponding author (BMB) made country visits where possible to meet with local study investigators. A website provided educational support and the webpage with frequently asked questions was updated regularly. The protocol and case report forms for the study were available in English and French on the study website.

Data were collected on paper case report forms and were pseudoanonymised—ie, unique numerical codes were generated during transcription of data onto an internet-based electronic case report form. Soft limits were set for data entry, prompting investigators when data were entered outside these limits. Each patient could only be identified on the electronic case report forms by their numerical code and thus the coordinating study team could not trace data back to an individual patient without contact with the gate-keeper investigator at the site. Access to the data entry system was user name and password protected. All electronic data transfers between participating hospitals and the coordinating centre were encrypted with the use of a secure protocol. This study is reported according to the STROBE statement.[15] The national leaders confirmed the face validity of the unadjusted outcome data for their countries.

Outcomes

The primary outcome was in-hospital maternal mortality and complications. The secondary objectives were to describe preoperative maternal risk factors associated with maternal mortality, perioperative complications associated with maternal mortality, in-hospital neonatal mortality, and cardiopulmonary resuscitation and Apgar scores associated with neonatal mortality.

Statistical analysis

We described categorical variables as proportions and compared them using χ^2 tests and Fisher's exact tests as appropriate. We described continuous variables as mean (SD) or median (IQR) and compared using *t* tests or Mann-Whitney U tests as appropriate. We performed univariate analyses and binary logistic regression models to assess the risk factors for maternal and neonatal mortality. We assessed collinearity between potential risk predictors by identification of a variance inflation factor; we excluded risk predictors with a variance inflation factor of more than 2.

We wrote a statistical analysis plan for the ASOS obstetric substudy before data inspection and analysis. We expected a sample size of approximately 3000–4000 obstetric patients, with an expected maternal and neonatal mortality of between 0·5% and 1%. Therefore, to ensure that we fulfilled the criteria for a minimum of five to ten events per variable to construct acceptably reliable logistic regression models for maternal and neonatal mortality,[16] we planned models in which to enter risk factors: a preoperative maternal mortality risk model, a perioperative complications and maternal mortality model, and the neonatal mortality model. Based on the small number of risk factors to be entered into the models, we made an a-priori decision to assess risk factors based on clinical plausibility and our understanding of their potential association with maternal or neonatal mortality. For the maternal mortality models the preoperative risk factors included were pre-eclampsia or eclampsia,[17] major bleeding risk,[8] any chronic medical

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See **Online** for appendix

For the **study website** see www.asos.org.za

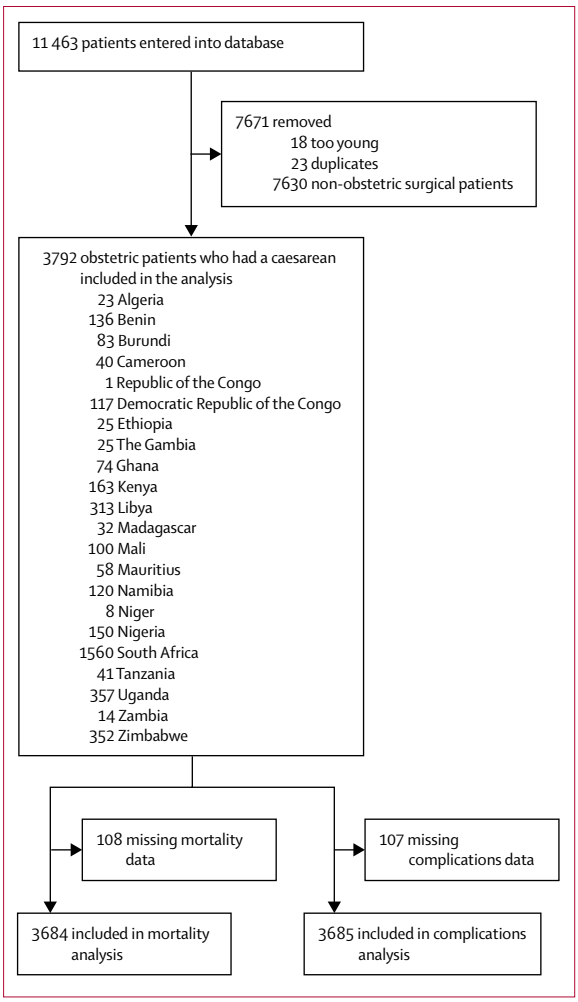

Figure 1: **Study population**

condition, and preoperative sepsis, and the perioperative complications included were severe infections,[12,17] severe cardiac complications,[7] severe obstetric haemorrhage,[11] and anaesthesia complications (appendix p 23).[9] For the neonatal mortality model, our a-priori decision was to include three neonatal risk factors based on the American Academy of Pediatrics Task Force on neonatal encephalopathy,[18] two Apgar scores (<7 at 1 min, and <5 at 5 min), and the need for cardiopulmonary resuscitation. We assessed two models on the basis of a gestational age of 35 weeks or less and more than 35 weeks. We calculated the average population attributable risk for the independent risk factors associated with maternal mortality.[19] We planned no prespecified subgroup analyses.

For all analyses, we performed a complete case analysis in which patients with missing data were excluded from an analysis. To control for potential bias with under-reporting of poor outcomes, we conducted sensitivity analyses for both maternal and neonatal mortality using data from hospitals that provided a representative sample, based on inclusion of least 90% of the eligible surgical patients during the recruitment week, and protocol compliant countries. We did further sensitivity analyses, which controlled for country and hospital clusters. To control for the effect of the level of hospital, and the level of the health-care provider on maternal and neonatal outcomes, we entered these risk factors into the logistic regressions. We did further sensitivity analyses to investigate the association between gestational age and the level of anaesthesia providers and surgical providers on maternal outcomes by forcing these variables into the logistic regression models. We report results as adjusted odds ratios (aOR) with 95% CI. $p<0·05$ was considered statistically significant. We did statistical analyses using the Statistical Package for the Social Sciences (SPSS), version 24 (SPSS, Chicago, IL, USA). We used RStudio statistical software package version 1.1.442 (R Foundation for Statistical Computing, Boston, USA) to compute the population attributable risks.

The study was registered on the South African National Health Research Database (KZ_2015RP7_22), and on ClinicalTrials.gov (Identifier: NCT03044899).

Role of the funding source

The study was funded by a self-initiated research grant from the Medical Research Council of South Africa awarded to BMB. The study website and data repository were maintained by Safe Surgery South Africa and the South African Society of Anaesthesiologists, who had no role in the study design, data acquisition, data analysis, or writing of the paper. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

183 hospitals from 22 African countries participated in the ASOS obstetric substudy. Eleven of the countries (Democratic Republic of Congo, The Gambia, Madagascar, Mali, Mauritius, Namibia, Niger, Nigeria, South Africa, Uganda, and Zimbabwe) provided data on more than 90% of the surgeries, in keeping with the study definition.

Hospital-specific data for the obstetric substudy were submitted for 173 (95%) of 183 hospitals, of which 139 (80%) were government-funded hospitals, 22 (13%) were privately funded, and 12 (7%) were jointly funded hospitals. 77 (46%) of 169 hospitals were university-affiliated. 39 (23%) of 173 were district hospitals, 58 (34%) were regional hospitals, 34 (20%) were central hospitals, and 42 (24%) were specialised hospitals. These hospitals (n=154) served a median population of 860 000 (IQR 265 317–2 000 000) people. Participating hospitals had a median of 339 beds (154–540), six operating rooms (2–7), and four critical care beds (1–7), allowing invasive ventilation. The median ratio of critical care beds allowing invasive ventilation to hospital beds was 2·3% (0·2–4·6). The hospitals were staffed by a median of three specialist surgeons (1–9),

	All patients	In-hospital mortality	Alive	Odds ratio (95% CI)	p value
Age, years	28·6 (6·3)	29·7 (5·7)	28·7 (6·3)	1·03 (0·96–1·10)	0·454
Parity	1 (0–2)	2 (1–3)	1 (0–2)	1·23 (0·98–1·55)	0·080
Gestational age, weeks	38 (37–39)	37 (36–39)	38 (37–39)	0·91 (0·84–0·99)	0·026
ASA category					
1	2010/3672 (54·7%)	8/20 (40%)	2002/3651 (54·8%)	1 (ref)	
2	1472/3672 (40·1%)	6/20 (30%)	1466/3651 (40·2%)	1·02 (0·36–2·96)	0·965
3	169/3672 (4·6%)	3/20 (15%)	165/3651 (4·5%)	4·55 (1·20–17·31)	0·026
4	21 (0·6%)	3/20 (15%)	18/3651 (0·5%)	41·71 (10·23–170·10)	<0·001
Urgency of surgery					
Elective	801/3668 (21·8%)	5/20 (25%)	796/3647 (21·8%)	1 (ref)	
Emergency	2867/3668 (78·2%)	15/20 (75%)	2851/3647 (78·2%)	0·84 (0·30–2·31)	0·732
Surgical checklist					
Yes	1824/3660 (49·8%)	8/20 (40%)	1816/3639 (49·9%)	1 (ref)	
No	1836/3660 (50·2%)	12/20 (60%)	1823/3639 (50·1%)	1·49 (0·61–3·66)	0·380
Known preoperative comorbidities					
Diabetes	67/3685 (1·8%)	1/20 (5%)	66/3664 (1·8%)	2·87 (0·38–2·87)	0·308
Hypertension	338/3685 (9·2%)	4/20 (20%)	334/3664 (9·1%)	2·49 (0·83–7·50)	0·104
HIV	579/3685 (15·7%)	1/20 (5%)	578/3664 (15·8%)	0·28 (0·04–2·10)	0·216
Maternal					
Pre-eclampsia or eclampsia	450/3685 (12·2%)	5/20 (25%)	445/3664 (12·1%)	2·41 (0·87–6·67)	0·090
Major bleeding risk*	216/3685 (5·9%)	4/20 (20%)	211/3664 (5·8%)	4·09 (1·36–12·35)	0·012
Preoperative sepsis	20/3685 (0·5%)	0/20	20/3664 (0·5%)		1·0
Fetal condition					
No fetal distress	2376/3493 (68·0%)	8/19 (42%)	2368/3473 (68·2%)	1 (ref)	
Fetal distress	1116/3492 (32·0%)	11/19 (58%)	1105/3473 (31·8%)	2·95 (1·18–7·35)	0·020
Anaesthesia provider					
Specialist	823/3665 (22·5%)	3/20 (15%)	820/3644 (22·5%)	1 (ref)	
Physician non-specialist	1985/3665 (54·2%)	8/20 (40%)	1976/3644 (54·2%)	1·11 (0·29–4·18)	0·881
Non-physician	850/3665 (23·2%)	9/20 (45%)	841/3644 (23·1%)	2·30 (0·79–10·84)	0·108
None	7/3665 (0·2%)	0/20	7/3644 (0·2%)		1·0
Surgical provider					
Specialist	953/3647 (26·1%)	5/20 (25%)	948/3626 (26·1%)	1 (ref)	
Physician non-specialist	2670/3647 (73·2%)	15/20 (75%)	2654/3626 (73·2%)	1·07 (0·39–2·96)	0·894
Non-physician	24/3647 (0·7%)	0/20	24/3626 (0·7%)		1·0
Anaesthesia technique					
Spinal	2941/3685 (79·8%)	9/20 (45%)	2932/3664 (80·0%)	1 (ref)	<0·001
Epidural	17/3685 (0·5%)	0/20	17/3664 (0·5%)		1·0
General anaesthesia	735/3685 (19·9%)	11/20 (55%)	723/3664 (19·7%)	4·89 (2·02–11·84)	<0·001
Local anaesthesia and sedation	44/3685 (1·2%)	0/20	44/3664 (1·2%)		1·0

Data are mean (SD) or n (%). Odds ratios were constructed for severe maternal outcomes with univariate binary logistic regression analysis. Denominators vary with the completeness of the data. ASA=American Society of Anesthesiologists. Ref=reference. *Major bleeding risk is defined as a composite of placenta praevia, placenta abruption, ruptured uterus, and antepartum haemorrhage.

Table 1: **Characteristics of the African Surgical Outcomes Study obstetric substudy patient cohort**

two specialist anaesthesiologists (0–5), and three specialist obstetricians (1–6), with a median of 0·7 specialists per 100 000 population (0·2–2·0).

ASOS recruited 11 422 patients, 3792 (33·2%) of whom had caesarean delivery (figure 1). 13 (7%) of 183 hospitals did not provide data on more than 90% of the eligible patients for inclusion in the study during the recruitment week, equating to 255 [6·7%] of 3792 patients.

450 (12·2%) of 3685 mothers presented with pre-eclampsia or eclampsia, of whom one in five presented with eclampsia (table 1). 216 (5·9%) of 3685 mothers presented with a major preoperative bleeding risk, defined as placenta praevia (57 [26%]), placental abruption (79 [36%]), ruptured uterus (29 [13%]), and antepartum haemorrhage (77 [36%]). 26 women has more than one preoperative bleeding risk factor.

	Number of patients	Mild	Moderate	Severe	Mortality for all patients that developed complications
Infective complications					
Superficial surgical site	3627	84 (2·3%)	23 (0·6%)	8 (0·2%)	1/115 (1%)
Deep surgical site	3627	8 (0·2%)	7 (0·2%)	3 (0·1%)	0/18
Body cavity	3627	7 (0·2%)	3 (0·1%)	2 (0·1%)	0/12
Pneumonia	3627	10 (0·3%)	3 (0·1%)	2 (0·1%)	2/15 (13%)
Urinary tract	3627	17 (0·4%)	7 (0·2%)	4 (0·1%)	0/27
Bloodstream	3629	4 (0·1%)	3 (0·1%)	2 (0·1%)	1/9 (11%)
Total number of patients with infective complications	..	..	..	..	4/169 (2%)
Cardiovascular complications					
Arrhythmia	3627	1 (<0·1%)	2 (0·1%)	0	1/3 (33%)
Pulmonary oedema	3627	8 (0·2%)	3 (0·1%)	1 (<0·1%)	3/12 (25%)
Stroke	3613	0	0	1 (<0·1%)	1/1 (100%)
Cardiac arrest	3621	NA	NA	11 (0·3%)	9/11 (82%)
Total number of patients with cardiovascular complications	..	..	..	..	9/21 (43%)
Other complications					
Acute kidney injury	3626	8 (0·2%)	9 (0·2%)	2 (0·1%)	2/19 (11%)
Intraoperative bleed (>1000ml)	3747	NA	NA	133 (3·5%)	3/133 (2%)
Postoperative bleed	3629	26 (0·7%)	248 (6·8%)	18 (0·5%)	6/292 (2%)
ARDS	3626	1 (<0·1%)	1 (<0·1%)	3 (0·1%)	2/5 (40%)
All others	3616	43 (1·1%)	23 (0·6%)	13 (0·3%)	1/79 (1%)
Total number of patients with other complications	..	..	..	..	10/483 (2%)
Total number of patients with complications	..	..	..	..	14/626 (2%)

Data are n/N (%). Denominators vary with the completeness of the data. ARDS=acute respiratory distress syndrome. NA=not applicable.

Table 2: **Postoperative complications**

In-hospital mortality data was missing in 108 (2·8%) of 3792 patients. The caesarean delivery maternal mortality was 20 (0·5%) of 3684 patients (95% CI 0·3–0·8), with a maternal mortality rate of 543 per 100 000 operations (5·43 per 1000; appendix p 24). Mothers who died after caesarean delivery were of a higher parity and had a significantly higher preoperative comorbidity, reflected by higher American Society of Anesthesiologists (ASA) categories and a higher major bleeding risk. Mothers who died were more likely to have received general anaesthesia for delivery (table 1). Maternal mortality was similar between mothers of a gestation of 35 weeks or less or more than 35 weeks (3 [1%] of 346 *vs* 15 [0·5%] 3116; p=0·344).

Postoperative complications after caesarean delivery were reported in 633 (17·4%) of 3636 mothers (95% CI 16·2–18·6; table 2). The most common severe complications were intraoperative and postoperative bleeding, reported in 136 (3·8%) of 3612 mothers. 14 (2%) of 626 patients (1·1–3·4) had postoperative complications that were associated with in-hospital mortality. Cardiovascular complications had the highest associated mortality (nine [43%] of 21; [21·7–64·0]). The median length of stay in hospital was 3 (IQR 3–4) days.

The multivariable analyses of the a-priori associations between preoperative risk factors and maternal mortality are shown in table 3, and perioperative complications and maternal mortality are shown in table 4. A preoperative major bleeding risk was the only preoperative risk factor associated with maternal mortality (OR 4·47 [95% CI 1·47–13·65]). The perioperative complications independently associated with maternal mortality were severe obstetric haemorrhage (5·87 [1·99–17·35]) and anaesthesia complications (11·47 [1·20–109·20]). There was no collinearity with these associations. The sensitivity analyses for hospital compliant sites, country compliant sites, and hospital and country clusters were consistent with the main analyses (appendix pp 25–28). The independent associations with maternal mortality in the preoperative and intraoperative models remained unchanged when controlling for gestational age and the level of the anaesthesia or obstetric provider.

Neonatal outcomes data were missing for 410 (10·8%) of 3792 mothers. The neonatal mortality was 153 (4·4%) of 3506 infants (95% CI 3·7–5·0). Cardiopulmonary resuscitation was required in 313 (9·3%) of 3371 of neonates, of whom 55 (17·6%) died. The associations with neonatal outcomes are shown in table 5. The neonatal mortality was 140 (4·1%) of 3382 infants (3·5–4·8) for the first born, and 13 (11%) of 121 infants (5·2–16·3) for the second born neonate. Of the deliveries, 347 (9·9%) of 3497 were at 35 weeks or less gestation and 3150 (90·1%) were at more than 35 weeks gestation. The neonatal mortality was 75 (2·5%) of 3002 for more than 35 weeks gestation and 62 (18·0%) of 344 for 35 weeks or less gestation. 140 (3·9%)

	All patients	Patients who died	Patients who survived	β weight	Odds ratio (95% CI)	p value	PAR (95% CI)
Pre-eclampsia or eclampsia	450/3685 (12·2%)	5/20 (25%)	445/3664 (12·1%)	0·90	2·47 (0·87–7·10)	0·090	..
Major bleeding risk*	216/3685 (5·9%)	4/20 (20%)	211/3664 (5·8%)	1·50	4·47 (1·47–13·65)	0·009	34·39 (9·51–59·27)
Sepsis	20/3685 (0·5%)	0/20	20/3663 (0·5%)	–15·92	..	1·000	..
Any medical condition	1101/3685 (29·9%)	7/20 (35%)	1094/3664 (29·9%)	0·18	1·20 (0·46–3·10)	0·708	..
Constant	..	..	..	–5·60	0·004	<0·001	..

Data are n/N (%). Denominators vary with the completeness of the data. Odds ratios were constructed for severe maternal outcomes with univariate binary logistic regression analysis. PAR=population attributable risk. *Major bleeding risk is defined as a composite of placenta praevia, placenta abruption, ruptured uterus, and antepartum haemorrhage.

Table 3: **Multivariable analysis of preoperative risk factors and maternal mortality**

	All patients	Patients who died	Patients who survived	β weight	Odds ratio (95% CI)	p value	PAR (95% CI)
Severe infective complications*	37/3685 (1·0%)	1/20 (5%)	36/3664 (1·0%)	1·76	5·79 (0·73–45·80)	0·096	..
Severe cardiac complications†	2/3685 (0·1%)	2/20 (10%)	0/3664	26·13	..	1·000	..
Severe obstetric haemorrhage‡	201/3685 (5·5%)	5/20 (25%)	195/3664 (5·3%)	1·77	5·87 (1·99–17·35)	0·001	45·32 (22·39–68·25)
Anaesthesia complications§	12/3865 (0·3%)	2/20 (10%)	9/3664 (0·2%)	2·44	11·47 (1·20–109·20)	0·034	6·93 (5·22–8·63)
Constant	..	..	..	–5·65	0·004	<0·001	..

Data are n/N (%). Denominators vary with the completeness of the data. Odds ratios were constructed for severe maternal outcomes with univariate binary logistic regression analysis. PAR=population attributable risk. *A composite of all severe infection complications. †A composite of all severe cardiovascular complications including cardiac arrest, which was not reported as an anaesthetic complication. ‡A composite of antepartum haemorrhage, >1000 mL intraoperative bleeding, and severe postoperative bleeding. §A composite of failed intubation, aspiration, cardiac arrest, and hypoxia.

Table 4: **Multivariable analysis of perioperative complications and maternal mortality**

	All patients	Patients who died	Patients who survived	Odds ratio (95% CI)	p value
≤35 weeks gestation					
Apgar ≥7 at 1 min	214/342 (63%)	8/214 (4%)	206/214 (96%)	1 (ref)	
Apgar <7 at 1 min	128/342 (37%)	53/128 (41%)	75/128 (59%)	3·26 (1·17–9·05)	0·023
Apgar ≥5 at 5 min	294/342 (86%)	22/294 (8%)	272/294 (97%)	1 (ref)	
Apgar <5 at 5 min	48/342 (14%)	39/48 (81%)	9/48 (19%)	25·98 (9·51–70·99)	<0·001
Need for cardiopulmonary resuscitation	73/343 (21%)	30/73 (41%)	43/73 (59%)	3·08 (1·27–7·46)	0·013
>35 weeks gestation					
Apgar ≥7 at 1 min	2618/2992 (87·5%)	8/2618 (0·3%)	2610/2618 (99·7%)	1 (ref)	
Apgar <7 at 1 min	374/2992 (12·5%)	67/374 (17·9%)	307/374 (82·1%)	15·61 (6·25–39·00)	<0·001
Apgar ≥5 at 5 min	2918/2992 (97·5%)	20/2918 (0·7%)	2898/2918 (99·3%)	1 (ref)	
Apgar <5 at 5 min	74/2992 (2·5%)	55/74 (74·3%)	19/74 (25·7%)	76·18 (35·47–163·61)	<0·001
Need for cardiopulmonary resuscitation	236/2998 (7·9%)	25/236 (10·6%)	211/236 (89·4%)	0·91 (0·41–1·99)	0·806

Data are n/N (%). Denominators vary with the completeness of the data. Ref=reference.

Table 5: **Neonatal outcomes according to gestational age at delivery**

of 3630 neonates had an Apgar score of less than 5 at 5 min. Apgar scores of less than 7 at 1 min and less than 5 at 5 min were independently associated with neonatal mortality, regardless of the gestational age (table 5). The need for cardiopulmonary resuscitation was only independently associated with mortality in neonates of ≤35 weeks gestational age. These results are consistent with the sensitivity analysis of the protocol-compliant countries and hospital clusters (appendix p 29).

Maternal mortality was similar between primary (three [1%] of 422), secondary (five [0·4%] of 1217), and tertiary (12 [0·6%] of 1885) level hospitals (p=0·656). Neonatal mortality also did not differ across primary (17 [4%] of 401), secondary (46 [4·0%] of 1160), and tertiary (74 [4·2%] of 1700) level hospitals (p=0·878).

The addition of the hospital level to the logistic regression did not alter the overall associations with maternal and neonatal mortality.

Discussion

The principal findings of this prospective observational study were that maternal mortality after caesarean

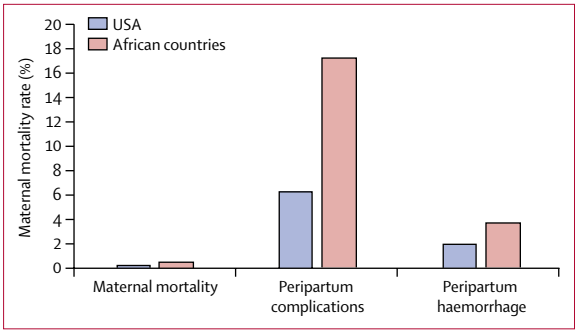

Figure 2: **In-hospital mortality and complications after caesarean section in the USA (2006–12) and African countries (2016)**
Data from United States National Surgical Quality Improvement Program.[20]

delivery in Africa was 5·43 per 1000 operations (95% CI 3·1–7·8), and neonatal mortality was 44 per 1000 births (37–51). Scarce specialist cover is available to provide perioperative care during caesarean delivery with a median of 0·7 specialists per 100 000 population (IQR 0·2–2·0). African mothers are at least 50 times more likely to die after caesarean delivery compared with mothers in high-income countries (appendix p 30).[20,21] Previous estimates based on modelling strategies have substantially underestimated the risk of mortality after caesarean delivery in sub-Saharan Africa.[10] The neonatal mortality rate is approximately double the global average, nearly one in 20 babies will die in the early neonatal period.[3] Gestational age and Apgar scores are independently associated with early neonatal mortality.

Low access to caesarean delivery in Africa[6] results in mothers presenting for surgery with a high perioperative risk (figure 2). High ASA status was independently associated with mortality, highlighting its importance in predicting outcomes. Perioperative complications are common, with approximately one in six women developing a perioperative complication after caesarean delivery—nearly 3 times that of women in the USA—although more than three quarters of caesarean deliveries in our study were performed as emergencies.[20]

The perioperative complications independently associated with maternal mortality in Africa are obstetric haemorrhage and anaesthesia complications. One in 17 patients presented with a major preoperative bleeding risk, which is an independent preoperative risk factor for in-hospital maternal mortality. It is possible that the morbidity associated with a major preoperative bleeding risk is increased in Africa due to low access to caesarean delivery. Haemorrhage accounts for nearly 70% of all complications, and 25% of all deaths occurred after severe obstetric haemorrhage.

A previous systematic review[9] suggested that anaesthesia contributes up to 2·8% of all maternal deaths after obstetric procedures in low-income and middle-income countries and 13·8% of deaths after caesarean delivery. Our prospectively collected data suggest that in Africa, the contribution of anaesthesia to maternal mortality is similar at 10%. Despite the high preoperative maternal risk profile, and the high prevalence of complications, nearly a quarter of all anaesthetics for caesarean delivery in our study are administered by non-physician anaesthesia providers. It is unclear, due to the small numbers and large CIs, whether the level of the anaesthesia provider contributes directly to maternal mortality in Africa, although the point estimate favours increased maternal mortality with non-physician anaesthetists. This finding is consistent with existing literature.[9] Identification of high-risk patients is possible in the preoperative period, especially mothers at risk of obstetric haemorrhage, and this identification should initiate processes for the provision of care by more senior surgical and anaesthesia staff.[9]

The neonatal mortality rate for our study was higher than expected but in an exclusively postsurgical population. The global average neonatal mortality rate for all deliveries in 2016, was 19 per 1000 deliveries, with sub-Saharan Africa at 28 per 1000 deliveries.[3] The higher rate in our study might be due to under-reporting in global studies or because we are studying a higher risk population (operative deliveries alone, as opposed to all deliveries). One in 11 neonates in Africa required cardiopulmonary resuscitation, and one in 23 neonates died after caesarean delivery. For those neonates that survive the early neonatal period, the prognosis is still markedly poorer than neonates born to mothers in high-income countries. Although we did not collect more detailed neonatal data associated with neonatal encephalopathy, such as neonatal acid base status, we observed that 3·9% of the neonates had an Apgar score of less than 5 at 5 min, which is a crude measure of the likelihood of developing neonatal encephalopathy.[18] Furthermore, low Apgar scores, particularly at 5 min, have been associated with an increased incidence of cerebral palsy and epilepsy.[22–25] In a Swedish study,[25] the incidence of Apgar scores from 0 to 6 was 1·8% and was 0·4% for scores less than 4 after caesarean delivery, suggesting that an Apgar score of less than 5 is between 2·2 and 10·7 times more frequent in Africa. Therefore, improvements in early neonatal care after caesarean delivery in Africa could decrease the long-term health-care burden of cerebral palsy and epilepsy.

Our data has shown a high incidence of adverse outcomes across 22 countries in Africa, confirming previous work. While country-specific maternal mortality rates are often derived, some data from resource-poor settings are available. One prospective study[26] collected data from 314 623 women across four continents who delivered either vaginally or by caesarean delivery with the use of the maternal severity index and near-miss approach. Conversely, our paper specifically targets an African surgical population and showed a significantly higher rate of bleeding (3·8 *vs* 2·7%), hypertensive disease (12·2% *vs* 2·5%), and far worse neonatal outcomes (44 *vs* 26 per 1000 livebirths). These results might have been expected in an exclusively post-caesarean population but illustrate that with higher event

rates, interventions that target the surgical population might have a substantial affect.

African countries need to improve both access to caesarean delivery and the safety of this procedure. Paradoxically, while many countries are aiming to reduce the caesarean delivery rate, increasing the rate of caesarean delivery remains a priority in Africa. In sub-Saharan Africa, the caesarean delivery rate is static at 3·5%, despite an increasing pattern in rates globally.[27] Improving access to surgery might allow patients to present earlier and thus mitigate against adverse outcomes. This improvement must occur in parallel with programmes aimed at improving patient safety during caesarean delivery. Context-sensitive interventions aimed at addressing the adverse outcomes highlighted in our study need to follow. Areas that should be targeted include early risk identification (eg, ASA status, risk of bleeding) linked to a contextualised bundle of care, including checklists and a higher level of monitoring (eg, involving relatives, proximity of the bed to the nursing station); consideration of a lower threshold for the use of antifibrinolytic drugs (tranexamic acid) as prophylaxis against post-partum haemorrhage, especially where availability of blood is low; improvement of access to blood and blood products with long shelf lives, such as freeze-dried plasma and fibrinogen; and novel methods of training of non-physician anaesthetists, including online support and mobile-based applications.

Our study also had some limitations. The WHO has developed a near-miss tool for the monitoring of quality of health care, which has subsequently been developed into the WHO near-miss approach.[28] This system was designed for use in individual institutions and collects data in three distinct areas (clinical, laboratory-based, and management-based criteria). Although this tool is a useful method of assessing institutions, we did not include the large number of data fields suggested for the near-miss tool, for reasons of study pragmatism. Additionally, the WHO tool often requires local modification, which might have precluded its use in a multinational study.[29] Although near-miss data has been reported for several African countries, the process is often driven by international research teams involved in quality improvement initiatives or represents a single audit process at selected institutions and therefore might not result in broadly generalisable data.[29–33] Our study aimed to address this shortfall by collecting morbidity data in obstetrics and neonatology in a multinational African study, thereby generating more generalisable data for Africa.

Second, although we recruited almost 4000 patients, the data are limited to some degree through disproportionate recruitment. The data is predominantly from government hospitals (80%) in middle-income countries (66·3%). Only 22% of the patients received their operations at district level hospitals. Furthermore, in 26% of cases a specialist obstetrician was involved and in 22% of cases a specialist anaesthesiologist was involved in the management, which is unlikely to reflect the broader African context. The outcomes presented here might therefore be better than that expected across Africa. Reverse causality might also exist, in which the sickest and more complex patients are referred to a higher level with worse outcomes. However, data from the confidential enquiry process in South Africa suggests that mortality is higher in district hospitals, a group that is under-represented in our sample.[17]

Third, we were unable to collect data in several potentially useful areas. We did not collect the number of normal deliveries occurring at the institutional level, meaning we were unable to calculate and comment on the caesarean delivery rate or link this to maternal and neonatal outcomes. We were also unable to calculate the overall maternal mortality rate for the study period and did not assess the indication and timeliness of operative intervention. These data might have provided further insight into the service context at an institutional level. We did not collect related data, such as the adequacy of antenatal care or the availability of blood bank services, which might have provided insight into the contribution of available resources towards maternal outcomes. Our study included only adults: we are thus unable to comment on the outcomes in teenage pregnancy (a high-risk group).

Fourth, we advise caution in generalising the findings of this study to Africa. Eleven of the included countries did not provide per-protocol data samples for this study, which might compromise the generalisability to these countries. Our sensitivity analysis, however, showed little difference between per-protocol compliant hospitals and the entire cohort. Furthermore, although 22 African countries participated, this number is still fewer than half of the countries in Africa, of which several non-participating countries are low-income countries. We also pooled maternal deaths from all participating countries for the regression analysis; given the potentially different contexts within countries, which might further compromise generalisability. Controlling for hospital and country clusters however resulted in similar findings to the main analyses.

Finally, the data submitted were not validated, with the exception of the soft data limits at the time of data submission and the queries to investigators of data outliers during data cleaning.

The strength of our work is that we have done a large, prospective study across Africa. This study suggests that the incidence of both maternal and neonatal complications in Africa is substantially higher than previously appreciated. Furthermore, these data have enabled us to identify risk factors independently associated with maternal mortality, which include preoperative risk factors for obstetric haemorrhage and the perioperative complications of peripartum haemorrhage and anaesthesia complications. Attention should therefore be focused on these areas to improve maternal and neonatal outcomes in Africa.

Contributors

All authors were involved in the design and conduct of the study. ASOS local investigators collected and collated data. BMB analysed the data

analysis. DB and BMB wrote the first draft of the paper. BMB redrafted the paper after critical review by all authors.

Declaration of interests

RMP has received research grants from Edwards Lifesciences, Nestlé Health Sciences, and Intersurgical, has given lectures or performed consultancy work for Nestlé Health Sciences, Medtronic, Edwards Lifesciences, Braun, and GlaxoSmithKline, and is a member of the associate editorial board of the British Journal of Anaesthesia. All other authors declare no competing interests.

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