4-1-2017

A prospective study of maternal, fetal and neonatal outcomes in the setting of cesarean section in low- and middle-income countries.

Margo S. Harrison
Columbia University

Omrana Pasha
Aga Khan University

Sarah Saleem
Aga Khan University

Sumera Ali
Aga Khan University

Elwyn Chomba
University of Zambia

See next page for additional authors

Authors
Margo S. Harrison, Omrana Pasha, Sarah Saleem, Sumera Ali, Elwyn Chomba, Waldemar A. Carlo, Ana L. Garces, Nancy F. Krebs, K. Michael Hambidge, Shivaprasad S. Goudar, Bhala Kodkany, Sangappa Dhaded, Richard J. Derman, Archana Patel, Patricia L. Hibberd, Fabian Esamai, Edward A. Liechty, Janet L. Moore, Dennis Wallace, Elizabeth M. Mcclure, Menachem Miodovnik, Marion Koso-Thomas, Jose Belizan, Antoinette K. Tshefu, Melissa Bauserman, and Robert L. Goldenberg

AOGS
Acta Obstetricia et Gynecologica Scandinavica

AOGS ORIGINAL RESEARCH ARTICLE

A prospective study of maternal, fetal and neonatal outcomes in the setting of cesarean section in low- and middle-income countries

MARGO S. HARRISON[1], OMRANA PASHA[2], SARAH SALEEM[2], SUMERA ALI[2], ELWYN CHOMBA[3], WALDEMAR A. CARLO[4], ANA L. GARCES[5], NANCY F. KREBS[6], K. MICHAEL HAMBIDGE[6], SHIVAPRASAD S. GOUDAR[7], BHALA KODKANY[7], SANGAPPA DHADED[7], RICHARD J. DERMAN[8], ARCHANA PATEL[9], PATRICIA L. HIBBERD[10], FABIAN ESAMAI[11], EDWARD A. LIECHTY[12], JANET L. MOORE[13], DENNIS WALLACE[13], ELIZABETH M. MCCLURE[13], MENACHEM MIODOVNIK[14], MARION KOSO-THOMAS[14], JOSE BELIZAN[15], ANTOINETTE K. TSHEFU[16], MELISSA BAUSERMAN[17] & ROBERT L. GOLDENBERG[1]

[1]Department of Obstetrics and Gynecology, Columbia University, New York, NY, USA, [2]Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan, [3]University Teaching Hospital, University of Zambia, Lusaka, Zambia, [4]Division of Neonatology, University of Alabama, Birmingham, AL, USA, [5]Planning Unit, Institute of Nutrition of Central America and Panama (INCAP), Guatemala City, Guatemala, [6]School of Medicine, University of Colorado, Denver, CO, USA, [7]Jawaharlal Nehru Medical College, KLE University, Belgaum, India, [8]Department of Obstetrics and Gynecology, Thomas Jefferson University, Philadelphia, PA, USA, [9]Lata Medical Research Foundation, Nagpur, India, [10]School of Public Health, Boston University, Boston, MA, USA, [11]School of Medicine, Moi University, Eldoret, Kenya, [12]School of Medicine, Indiana University, Indianapolis, IN, USA, [13]RTI International, Durham, NC, USA, [14]Pregnancy and Perinatology Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, USA, [15]Institute for Clinical Effectiveness and Health Policy, Buenos Aires, Argentina, [16]Kinshasa School of Public Health, Kinshasa, Democratic Republic of the Congo, and [17]Department of Pediatrics, Division of Neonatal-Perinatal Medicine, University of North Carolina School of Medicine, Chapel Hill, NC, USA

Key words
Cesarean section, low- and middle-income countries, maternal morbidity, maternal mortality, neonatal morbidity, neonatal mortality

Correspondence
Margo S. Harrison, Department of Obstetrics/Gynecology, Columbia University Medical Center, 622 W 168th Street, PH16, New York, NY 10032, USA.
E-mail: msh2154@cumc.columbia.edu

Conflict of Interest
Data and presentation of information has not been influenced by the personal or financial relationship of the authors with other people or organizations. The authors have no competing interests to disclose, financial or otherwise.

Please cite this article as: Harrison MS, Pasha O, Saleem S, Ali S, Chomba E, Carlo WA, et al. A prospective study of maternal, fetal and neonatal outcomes in the setting of cesarean section in low- and middle-income countries. Acta Obstet Gynecol Scand 2017; 96:410–420.

Abstract

Introduction. Cesarean section (CS) rates are increasing globally with an unclear effect on pregnancy outcomes. The study objective was to quantify maternal and perinatal morbidity and mortality associated with CS compared with vaginal delivery (VD) both within and across sites in low- and middle-income countries. *Material and methods.* A prospective population-based study including home and facility births in 337 153 women with a VD and 47 308 women with a CS from 2010 to 2015 was performed in Guatemala, India, Kenya, Pakistan, Zambia and Democratic Republic of Congo. Women were enrolled during pregnancy; delivery and 6-week follow-up data were collected. *Results.* Across all sites, CS rates increased from 8.6% to 15.2%, but remained low in African sites. Younger, nulliparous women were more likely to have a CS, as were women with higher education and those delivering an infant weighing 1500–2499 g. Across all sites, maternal and neonatal mortality was higher, and stillbirths were lower, in pregnancies delivered by CS. Antepartum and postpartum complications as well as obstetric interventions and treatments were more common among women who underwent CS. In stratified analyses, all outcomes were worse in women with a CS compared with VD in African compared to non-African sites. *Conclusions.* CS rates increased across all sites during the study period, but at more pronounced rates in the non-African sites. CS was associated with reduced postpartum hemorrhage and lower rates of stillbirths in the non-African sites. In the African sites, CS was associated with an increase in all adverse outcomes. Further studies are necessary to better understand the increase in adverse outcomes with CS in the African sites.

Received: 5 September 2016
Accepted: 9 January 2017

DOI: 10.1111/aogs.13098

Abbreviations: CS, cesarean section; GN, Global Network for Women's and Children's Health Research; LMIC, low and middle-income countries; MNHR, Maternal and Newborn Health Registry; NICHD, Eunice Kennedy Shriver National Institute of Child Health and Human Development; PPH, postpartum hemorrhage; VD, vaginal delivery; WHO, World Health Organization.

Introduction

The World Health Organization (WHO) has asserted that improving availability, accessibility, quality, and use of healthcare services is essential to reducing maternal mortality during pregnancy, labor, and delivery (1). This requires universal access to comprehensive emergency obstetrical care, defined as a health service organization's capability to provide antibiotics, uterotonics, magnesium sulfate, and blood transfusion, and to employ skilled providers who can perform manual placental extraction, remove retained products of conception, and perform operative vaginal delivery, neonatal resuscitation, and cesarean section (CS) (1). Per WHO, CS, at a rate of around 5–15%, is considered essential treatment for antepartum hemorrhage, dysfunctional labor, hypertensive disease, and fetal distress in order to prevent maternal, neonatal, and fetal morbidity and mortality (1).

Rates of CS are increasing globally. The average global CS rate has increased by 150% over the past 25 years, and is currently at 18.6% with an average rate of increase of 4.4% per year (2). Understanding how pregnancy outcomes are affected by delivery method in low- and middle-income countries (LMIC) is important to ensure that the intervention is, on balance, beneficial (3). Research has shown that the relative risks of maternal mortality, neonatal respiratory morbidity, hysterectomy, ureter and bladder injury, fetal death, placental previa, and uterine rupture in a future pregnancy are increased with CS compared with vaginal delivery (VD) (4). It has been suggested that research on health outcomes related to CS and testing of interventions to reduce unnecessary CS are essential (5). Hence, the objective of this study was to quantify maternal and perinatal morbidity and mortality in LMIC associated with CS compared with VD, both within and across study sites.

Material and methods

This analysis was conducted using data from a prospective study conducted in communities at seven sites in six low-income countries on births from 1 January 2010 through to December 2015 (Chimaltenango, Guatemala; Nagpur District and Karnataka District, India; western Kenya; Thatta District, Pakistan; Lusaka, Zambia; and Equateur, the Democratic Republic of the Congo) (the Democratic Republic of the Congo site initiated enrollment in 2014). These seven sites are in the Global Network for Women's and Children's Health Research (GN), a network of institutions which conducts research aimed at improving maternal and newborn outcomes. The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) in the USA funds the GN.

The GN's prospective registry, the Maternal and Newborn Health Registry (MNHR), includes outcomes from rural or semi-urban geographical areas. Each site includes between six and 24 distinct communities. The methods of the MNHR have been published (6). In general, each community represents the catchment area of a primary healthcare center, and about 300–500 births take place annually in each locale. Beginning in 2008, the study investigators at each site initiated an ongoing, prospective maternal and newborn health registry of pregnant women for each community. The objective is to enroll pregnant women by 20 weeks of gestation and to obtain data on pregnancy outcomes for all deliveries of registered women, regardless of birth location (i.e. home, health clinic or hospital). Each community employs a registry administrator who identifies and tracks pregnancies and their outcomes in coordination with community elders, birth attendants, and other healthcare workers.

The primary purpose of the MNHR is to quantify and analyze trends in pregnancy outcomes in defined low-resource geographic areas over time to provide population-based statistics on pregnancy outcomes, including stillbirths, neonatal and maternal mortality and

Key Message

Cesarean section was associated with reduced postpartum hemorrhage and stillbirth in Latin American and South Asian sites, whereas adverse pregnancy outcomes were worse after cesarean section in African sites.

morbidity. The analysis presented here uses the MNHR to determine maternal and fetal outcomes in the setting of CS and to compare these outcomes to a reference population, also from the registry, that underwent VD, both within and across study sites. VD includes both spontaneous and assisted vaginal deliveries. The rates of the latter remained stable at <1% of all deliveries during the course of the study.

Other covariates were defined in accordance with the WHO definitions, described elsewhere (7). Gestational age at delivery was classified as term (≥37 weeks' gestation) or preterm (<37 weeks) for all deliveries, based on gestational age from last menstrual period and estimated due date. Infants originally classified as term or preterm with implausible birthweights for that classification were reclassified. Birthweight was the weight of the live birth or stillbirth taken at delivery or as soon as possible after delivery. Within the registry, stillbirth is defined as the death of a fetus at 20 weeks' gestational age or later, with the fetus showing no signs of life at birth, such as gasping, breathing, heartbeat, or movement. Postpartum hemorrhage (PPH) is defined as blood loss of ≥ 1000 mL from the genital tract after delivery through to 6 weeks postpartum.

Data were collected and entered into research computers at each study site and transmitted through secure methods to a central data-coordinating center (RTI International). All analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC, USA). Analyses included descriptive statistics. Relative risks were computed using log binomial generalized linear models with generalized estimating equations accounting for study clusters. In addition, because the results suggested that CS rates were different by birthweight, Cochran–Mantel–Haenszel tests stratified by site were performed to control for birthweight, as average birthweights vary by country within the registry.

The appropriate institutional review boards/ethics research committees of the participating institutions and the ministries of health of the respective countries approved the MNHR. Before initiation of the study, approval was sought from the participating communities. Individual informed consent for study participation was requested and obtained from each study participant. A Data Monitoring Committee, appointed by the NICHD, oversees and reviews the study semi-annually.

Results

In all, 384 461 women were screened and enrolled, 47 308 who had a CS and 337 153 who had a VD. Figure 1 illustrates CS rates over time within the GN. Whereas in the Central American and south Asian sites, the CS rates approximately doubled over the 5 years of data collection, there was little or no change in CS rates in Zambia, and in Kenya the CS rate increased from <1% to 2%. There are only 2 years of data (2014–2015) for the Democratic Republic of Congo.

Table 1 shows the maternal characteristics of women experiencing CS vs. VD within the GN. All characteristics were significantly different at $p < 0.05$. Women more likely to undergo CS were younger, nulliparous and more educated.

Table 2 presents infant characteristics including gestational age and birthweight by delivery method. The tests of differences are adjusted for GN site, to account for the fact that birthweights in African countries tend to be higher than those in south Asia. Babies in the birthweight

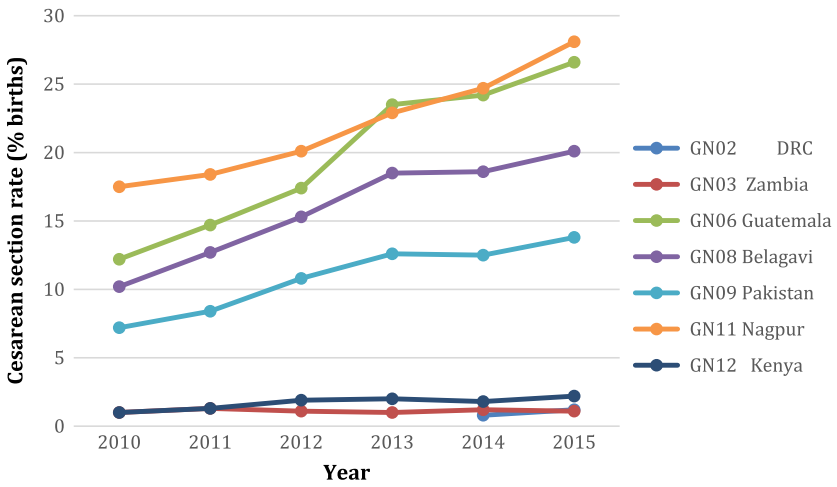

Figure 1. Cesarean section rates at Global Network sites, 2010–2015. [Color figure can be viewed at wileyonlinelibrary.com].

Table 1. Characteristics of women experiencing cesarean vs. vaginal delivery, 2010–2015.

Characteristic	Cesarean delivery	Vaginal delivery
Deliveries, *n*	47 308	337 153
Maternal age, *n* (%)	47 277	336 707
<20 years	4193 (8.9)	41533 (12.3)
20–35 years	41559 (87.9)	280743 (83.4)
>35 years	1525 (3.2)	14431 (4.3)
Parity, *n* (%)	46780	335036
0	22435 (48.0)	101462 (30.3)
1–2	19497 (41.7)	141587 (42.3)
≥3	4848 (10.4)	91987 (27.5)
Education, *n* (%)	47203	336100
No formal education	7021 (14.9)	91082 (27.1)
Primary	11775 (24.9)	114557 (34.1)
Secondary	20780 (44.0)	111899 (33.3)
University+	7627 (16.2)	18562 (5.5)

Table 2. Birth outcomes of women experiencing cesarean vs. vaginal delivery, 2010–2015.

Characteristic	Cesarean	Vaginal	*p*-value[a]
Births, *n*	48 219	339 980	
Gestational age, *n* (%)	46 978	325 720	0.9308
Preterm	5613 (11.9)	42284 (13.0)	
Term	41365 (88.1)	283436 (87.0)	
Birthweight, *n* (%)	48 166	339 334	<0.0001
<1000 g	101 (0.2)	1823 (0.5)	
1000–1499 g	494 (1.0)	3736 (1.1)	
1500–2499 g	7670 (15.9)	40445 (11.9)	
≥2500 g	39901 (82.8)	293330 (86.4)	

[a]Cochran–Mantel–Haenszel test adjusting for site.

range of 1500–2499 g were more likely to be delivered by CS, whereas babies who weighed ≥2500 g were more likely to have been delivered vaginally.

Table 3 presents the relation to delivery method of antepartum complications, including obstructed labor/prolonged labor/failure to progress, antepartum hemorrhage, hypertensive disease, and malpresentation. Additionally, there was a comparison of women with no recorded antepartum complications who underwent CS vs. VD. Each of the antepartum complications evaluated was more likely to be present in pregnancies delivered by CS than those delivered vaginally. Women without one of these antepartum complications were more likely to deliver vaginally. Because Table 3 suggested that antepartum complications in the setting of CS were more common in African sites than in the other sites within the GN, African and non-African sites are compared in Table 4. Each of the antepartum complications evaluated had a higher relative risk of a CS in the African sites compared with the other sites studied.

Table 3. Antepartum complications in women experiencing cesarean section or vaginal delivery by country, 2010–2015.

	DRC		Zambia		Kenya		Guatemala		Belgaum		Nagpur		Pakistan		Total	
Characteristic	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD
Deliveries, *n*	128	13 321	460	40 858	852	50 094	10 643	40 113	15 181	85 182	12 699	45 298	7345	62 287	47 308	337 153
OL/PL/FTP, %	85.8	1.2	56.0	3.0	73.8	7.6	17.8	3.5	53.6	2.0	39.1	2.0	53.0	12.1	42.0	5.0
Antepartum hemorrhage, %	9.4	0.6	5.7	1.0	12.4	1.8	2.1	0.9	1.5	0.5	0.8	0.3	6.6	3.6	2.5	1.4
Hypertensive disease, %	2.4	0.1	9.5	0.8	7.6	1.3	11.1	2.3	8.2	1.5	5.7	1.2	10.4	5.1	8.5	2.0
Malpresentation, %	25.0	0.6	18.9	0.7	25.6	1.1	13.0	0.6	7.8	0.3	10.0	0.4	13.9	2.4	11.0	0.9
No specified complications, %	9.5	98.2	26.5	95.7	15.0	90.4	60.5	93.2	34.4	96.0	48.1	96.4	31.9	80.5	43.1	92.1

CS, cesarean section; DRC, Democratic Republic of Congo; OL/PL/FTP, obstructed labor/prolonged labor/failure to progress; VD, vaginal delivery.

Table 4. Antepartum complications in women experiencing cesarean section or vaginal delivery in African vs. non-African sites, 2010–2015.

	African sites			Other sites		
Characteristic	CS	VD	RR (95% CI)	CS	VD	RR (95% CI)
Deliveries, *n*	1440	104 273		45 868	232 880	
OL/PL/FRP, %	69.2	5.0	40.1 (28.9–55.7)	41.2	5.0	6.0 (5.2–7.1)
Antepartum hemorrhage, %	10.0	1.3	7.5 (5.5–10.3)	2.2	1.4	1.7 (1.6–1.8)
Hypertensive disease, %	7.7	0.9	8.0 (6.2–10.4)	8.5	2.6	2.7 (2.4–3.0)
Malpresentation, %	23.4	0.9	26.2 (20.1–34.1)	10.6	0.9	4.6 (4.2–5.1)
No specified complications, %	18.2	93.4	0.02 (0.01–0.02)	43.9	91.5	0.14 (0.12–0.17)

CS, cesarean section; OL/PL/FTP, obstructed labor/prolonged labor/failure to progress; RR, relative risk; VD, vaginal delivery.

Table 5 shows how postpartum complications and procedures were related to delivery method. Postpartum infection, maternal death, the use of dilatation and curettage, hysterectomy, and unplanned hospitalization, were all more common after CS than VD, although PPH was not. When the outcome of PPH related to CS was evaluated on a regional basis (Table 6), hemorrhage associated with CS was more common in the African sites, whereas PPH was less common in the non-African sites. In the African sites, all adverse maternal outcomes were more common in the setting of CS than in other sites. Adverse outcomes were up to 15 times more common after CS than VD in the African sites, but in the other settings they were about twice as likely to occur.

Table 7 shows an assessment of interventions commonly performed during and after delivery, and how prevalent those obstetric treatments were in the setting of CS vs. VD. These interventions include prophylactic antibiotics, preterm corticosteroid administration, uterotonic utilization, blood transfusion, and magnesium sulfate administration. With the exception of uterotonics, all interventions were used at least twice as often in the setting of CS compared with VD. In the setting of CS, the African sites were found to use all interventions at higher rates than sites in other regions (Table 8).

Table 9 focuses on perinatal outcomes in the setting of CS vs. VD. Overall, stillbirth was less common in the setting of CS, but neonatal mortality was more common. Table 10, which separates outcomes by region, shows that this was not the trend in sub-Saharan Africa. In the African sites, stillbirth was five times more common in women undergoing CS than VD [relative risk (RR) 5.6, 95% CI 4.3–7.1] and neonatal mortality was three times more common (RR 3.2, 95% CI 2.4–4.2) more likely (Table 10). In comparison, at non-African sites, the RR for stillbirth in women with CS vs. VD was less (RR 0.6, 95% CI 0.5–0.6), with little difference in the neonatal mortality.

Discussion

The study objective was to quantify maternal and perinatal morbidity and mortality in LMIC associated with CS compared with VD, both within and across sites. In summary, we found that younger, nulliparous women were more likely to have a CS, as were women with higher education and those delivering an infant weighing 1500–2499 g. Across all sites, maternal and neonatal mortality was higher, and stillbirths were lower, in pregnancies delivered by CS. Antepartum and postpartum complications as well as obstetric interventions and treatments were more common among women who underwent CS. In stratified analyses, all outcomes were worse in women with a CS compared with VD in African compared with non-African sites. PPH was lower among women undergoing CS in non-African sites.

Our analysis found that young, nulliparous, and more educated women were most likely to undergo CS. These findings are also consistent with previous publications that demonstrate that young, nulliparous patients are at increased risk of CS, which may be attributable to cephalopelvic disproportion and obstructed labor (8). The concern is that some women may become pregnant before their pelvises are fully developed, putting them at increased risk of dysfunctional labor that requires cesarean delivery (9). An analysis of nearly 80 000 adolescents supported this assertion as it showed that extremely young adolescents (<15 years old), were more likely than older women (20–24 years old) to undergo CS when the indication for CS was cephalopelvic disproportion (10). The finding that less-educated women have lower rates of CS suggests that, if education is used as a proxy for socio-economic status, that poorer, less-educated women may have less access to facility delivery and CS, or that care differs in the facilities to which poor women have access compared with richer women. For example, studies performed in Latin America found differences in CS rates in public vs. private hospitals and attributed the

Table 5. Postpartum morbidity and mortality in women experiencing cesarean section or vaginal delivery by country, 2010–2015.

	DRC		Zambia		Kenya		Guatemala		Belgaum		Nagpur		Pakistan		Total	
Characteristic	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD
Deliveries, *n*	128	13 321	460	40 858	852	50 094	10 643	40 113	15 181	85 182	12 699	45 298	7345	62 287	47 308	337 153
Postpartum hemorrhage, %	7.1	1.3	2.2	0.9	8.1	5.1	2.3	2.3	0.5	0.7	0.2	0.3	3.1	5.2	1.4	2.4
Postpartum infection, %	3.3	0.2	0.2	0.0	5.9	0.7	0.8	0.4	0.6	0.2	0.1	0.1	4.0	1.9	1.1	0.6
Dilation and curettage, %	0.0	0.1	2.9	0.2	16.6	7.5	0.1	1.0	5.8	5.0	21.4	14.5	1.7	1.0	8.5	5.2
Hysterectomy, %	5.6	0.0	0.8	0.1	0.4	0.2	0.4	0.1	0.1	0.0	0.0	0.1	0.3	0.0	0.3	0.1
Unplanned hospitalization, %	15.2	0.8	8.9	0.6	7.6	0.7	24.9	7.5	11.5	5.3	3.9	1.3	2.9	1.1	12.5	2.7
Maternal mortality <42 days, rate/100 000 deliveries	6299	196	1319	82	825	74	114	83	145	76	103	44	563	177	232	96

CS, cesarean section; DRC, Democratic Republic of Congo; VD, vaginal delivery.

differences to provider behavior instead of access to care (11,12).

The finding that CS is more common in infants weighing in 1500–2499 g may be explained by the fact that smaller fetuses might be more likely to have a malpresentation, to be growth restricted, to be delivered in the context of hypertensive disorders that require preterm delivery, or have another condition requiring CS, such as placental abruption. All antepartum complications were more common in pregnancies delivered by CS compared with those delivered vaginally. Vaginal delivery was significantly more common in pregnancies where no major antepartum complication was present (>90% of deliveries in all sites except Pakistan), suggesting that the majority of CS in the GN were performed for clinical indications. These antepartum complications may have contributed to the decision to perform CS. If the complications in the African sites are used as a proxy measure for indication, they are comparable to other major studies on indication for CS in the region (13).

Across all sites, maternal and neonatal mortality was higher in pregnancies delivered by CS, which is supported by the experience of other LMIC (14). However, stillbirth rates and PPH were lower among women undergoing CS in non-African sites. It was a surprising finding that PPH was reduced in the setting of CS in non-African sites, but there is some plausibility to this finding. A recent *Lancet* publication noted that the rate of CS performed before the onset of labor is increasing (15). Data from the USA have shown that potential short-term maternal benefits of planned cesarean delivery compared with a planned VD included a decreased risk of PPH and transfusion (16). Regarding stillbirth, 98% of stillbirths occur in LMIC, occurring at a rate of over 2.5 million per year, making stillbirth one of the most common adverse perinatal outcomes (17). If CS is associated with fewer stillbirths in the non-African sites, this suggests that CS may offer benefit for this outcome as well.

Antepartum and postpartum complications, as well as obstetric interventions and treatments, were more common among women who underwent CS. This may be due to the fact that many of the vaginal deliveries in the GN occurred outside facilities, often in the home setting, where subsequent interventions would be less likely. Women with antepartum complications or complicated labors would likely be transferred to a facility where CS might possibly ensue. While some interventions such as prophylactic antibiotic administration are generally beneficial, other interventions such as dilatation and curettage and hysterectomy might have been performed in response to morbidities sustained by the performance of a poor quality CS. Blood transfusion and uterotonic use were also more common in women undergoing CS. With

Table 6. Postpartum morbidity and mortality in women experiencing cesarean section or vaginal delivery in African vs. non-African sites, 2010–2015.

	African sites			Other sites		
Characteristic	CS	VD	RR (95% CI)	CS	VD	RR (95% CI)
Deliveries, *n*	1440	104 273		45 868	232 880	
Postpartum hemorrhage, %	6.1	3.0	1.9 (0.9–4.0)	1.2	2.1	0.8 (0.7–0.9)
Postpartum infection, %	3.9	0.4	8.7 (4.4–17.2)	1.0	0.6	1.6 (1.4–1.8)
Dilatation and curettage, %	11.0	3.8	3.3 (2.2–4.9)	8.4	5.8	1.2 (1.0–1.6)
Hysterectomy, %	1.7	0.1	15.0 (6.6–33.9)	0.2	0.0	2.5 (1.9–3.2)
Unplanned hospitalization, %	9.8	0.7	13.3 (9.7–18.3)	12.6	3.9	2.3 (2.1–2.6)
Maternal mortality <42 days, rate/100 000 deliveries	1469	93	13.6 (9.3–19.9)	193	98	1.9 (1.6–2.2)

CS, cesarean section; RR, relative risk; VD, vaginal delivery.

respect to antibiotic administration, which we consider a sign of high-quality care, although rates >95% were observed with CS, the finding of antibiotic treatment in 45% of vaginal deliveries raises concern. It is not clear whether this represents prophylactic administration of medications or treatment of a postpartum infection; the latter would suggest very high rates of infection in our study sites. Many providers in LMIC administer prophylactic antibiotics after vaginal delivery, which probably accounts for this finding, but it does not represent standard of care per WHO recommendations (18). This is an area that warrants further research.

In stratified analyses, all outcomes were worse in women with a CS compared with VD in African compared with non-African sites. For example, when the African sites were compared with the other sites in the GN, maternal mortality appears to be 10 times more common in the setting of CS, suggesting that these women may be presenting for care in a significantly worse state, or that the quality of CS in the African sites, compared with the other sites, is far inferior. This finding potentially supports the WHO's assertion that quality of care is of primary importance to improving outcomes, not just increasing access and utilization of healthcare services (19). If women are presenting for care at more advanced stages of labor and in higher acuity situations, this raises the point that improved community and provider education regarding abnormal progress in labor may also be important to improve outcomes in these settings. Healthcare providers not knowing if the fetus was alive when the CS was performed may explain the higher rate of stillbirth in the African sites. If the providers knew the fetus was dead, there may have been obstetric or maternal indications such as obstructed labor or hemorrhage that required expedited delivery by CS to prevent further maternal morbidity and mortality.

Several other issues merit discussion. First, as CS rates of at least 2% are thought to be required to reduce maternal mortality and CS rates of 10–15% are required to have a significant impact on stillbirths, it is clear that there is a large unmet need for CS, especially in the African sites (20,21). Evidence from Uganda suggests that increasing access to CS is highly cost effective and additional evidence from across Africa suggests that increasing CS rates will reduce maternal and infant mortality (22). The low rates of assisted vaginal delivery across sites likely represent another unmet obstetrical need. Assisted vaginal delivery with vacuum or forceps may reduce the risk of delivery of an asphyxiated fetus, thereby preventing a stillbirth or neonatal death. Where neither CS nor assisted vaginal delivery is available, as often appears to be the case in the African sites, craniotomy and vaginal delivery, especially in the face of obstructed labor and stillbirth, may be life-saving for the mother. This procedure was not reported at any of our site hospitals during the study period. Furthermore, one limitation is that we did not collect data on uterine rupture, data that would contribute to our understanding of the unmet need for CS in many of our sites. Clearly, the issue of unmet obstetrical need is a crucial issue that bears further investigation.

This study has a number of limitations including the fact that many of the deliveries occurred at home with either a family member or a traditional birth attendant present. Additionally, for many deliveries occurring in a clinic or hospital, medical records were often incomplete. Although trained registry administrators interviewed the women and caregivers and reviewed the medical records within 48 h of delivery, determining the amount of blood loss or length of labor was often problematic. Recall bias may have occurred. Additionally, while our registry collects data on pregnancy complications, it did not specifically collect information on indication for CS, or timing of the CS with regards to onset of labor. It is generally unknown if stillbirths were diagnosed before the CS or were only diagnosed at delivery. Each of these issues

Table 7. Interventions and treatments received by women experiencing cesarean section or vaginal delivery by country, 2010–2015.

	DRC		Zambia		Kenya		Guatemala		Belgaum		Nagpur		Pakistan		Total	
Characteristic	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD
Deliveries, *n*	128	13 321	460	40 858	852	50 094	10 643	40 113	15 181	85 182	12 699	45 298	7345	62 287	47 308	337 153
Antibiotics, %	89.8	6.8	55.8	1.5	72.2	8.7	92.8	12.9	98.4	88.0	97.8	86.1	95.0	50.5	95.6	46.4
Corticosteroids, %	23.2	0.5	6.0	2.5	6.2	0.8	5.6	2.0	4.9	4.3	7.2	2.9	6.8	5.9	6.0	3.1
Blood transfusion, %	17.3	0.3	4.6	0.2	9.6	0.6	1.2	0.4	2.4	1.0	3.0	0.7	43.6	3.8	8.5	1.2
Uterotonics, %	79.2	42.0	61.2	62.7	73.7	50.1	69.2	37.6	65.0	82.3	71.6	77.6	80.4	68.1	70.2	64.2
Magnesium sulfate, %	0.0	0.0	2.9	0.1	13.7	0.8	8.4	1.5	7.3	0.5	3.4	0.7	2.0	0.7	5.7	0.7

CS, cesarean section; DRC, Democratic Republic of Congo; VD, vaginal delivery.

Table 8. Interventions and treatments received by women experiencing cesarean section or vaginal delivery in African vs. non-African sites, 2010–2015.

	African sites			Other sites		
Characteristic	CS	VD	RR (95% CI)	CS	VD	RR (95% CI)
Deliveries, *n*	1440	104 273		45 868	232 880	
Antibiotics, %	68.9	6.0	32.6 (21.7–49.1)	96.4	64.3	21.0 (9.8–44.6)
Corticosteroids, %	8.3	1.3	6.6 (3.3–13.3)	6.0	4.0	1.5 (1.2–1.9)
Blood transfusion, %	8.8	0.4	18.1 (14.0–23.3)	8.5	1.5	3.3 (2.9–3.8)
Uterotonics, %	70.5	52.7	2.2 (1.3–3.6)	70.2	69.2	1.0 (0.8–1.3)
Magnesium sulfate, %	9.2	0.4	17.6 (13.7–22.5)	5.6	0.8	3.1 (2.6–3.7)

CS, cesarean section; RR, relative risk; VD, vaginal delivery.

Table 9. Perinatal mortality in women experiencing cesarean section or vaginal delivery by country, 2010–2015.

	DRC		Zambia		Kenya		Guatemala		Belgaum		Nagpur		Pakistan		Total	
Characteristic	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD	CS	VD
Deliveries, *n*	128	13 321	460	40 858	852	50 094	10 643	40 113	15 181	85 182	12 699	45 298	7345	62 287	47 308	337 153
Stillbirths, rate/1000	345.3	33.7	55.0	18.2	100.2	19.9	12.5	20.8	10.4	27.2	10.3	26.4	34.9	48.3	17.8	28.3
Neonatal mortality, rate/1000	87.9	24.2	58.8	15.8	37.3	13.8	33.9	21.1	22.8	23.9	19.1	22.5	54.3	48.7	29.8	25.4

CS, cesarean section; DRC, Democratic Republic of Congo; VD, vaginal delivery.

Table 10. Perinatal mortality in women experiencing cesarean section or vaginal delivery in African vs. non-African sites, 2010–2015.

	African sites			Other sites		
Characteristic	CS	VD	RR (95% CI)	CS	VD	RR (95% CI)
Deliveries, *n*	1440	104 273		45 868	232 880	
Stillbirths, rate/1000	107.8	21.0	5.6 (4.3–7.1)	14.8	31.6	0.6 (0.5–0.6)
Neonatal mortality rate/1000	47.8	15.9	3.2 (2.4–4.2)	29.3	29.7	1.1 (1.0–1.2)

CS, cesarean section; RR, relative risk; VD, vaginal delivery.

indicates the importance of collecting more detailed information on the events leading up to and during CS so that audits can be performed to determine if CS are performed for appropriate indications and how associated pregnancy outcomes are affected. Each hospital should consider performing CS audits to evaluate appropriateness and safety of the procedures.

The strengths of this study include its large sample size, varied sites on three continents, data collected prospectively, and pre-specified outcomes that were defined similarly at all sites. In summary, CS is rapidly becoming an increasingly common surgery around the globe, and rates are increasing within the GN as well (23). This analysis shows that in LMIC, CS is an essential but complex healthcare service. The data suggest that in some locations, CS is not only associated with reduced stillbirth and PPH, but is also associated with adverse postpartum outcomes including severe morbidity and death and additional treatments and interventions. The WHO has asserted that women should deliver in facilities with skilled birth attendants to improve outcomes, but acknowledges that those outcomes may not improve unless high-quality care is provided. As the global health community supports the medicalization of childbirth, it must provide resources and guidelines to promote safe CS so that the most benefit and least harm will occur from increasing use of this procedure.

Funding

The study was funded by grants (U01 HD040477, U01 HD043475, U01 HD043464, U01 HD040657, U01 HD042372, U01 HD040607, U01HD040636, U01 HD040574, U01 HD40636) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

References

1. Monitoring Emergency Obstetric Care. A Handbook. Geneva: World Health Organization, 2009.
2. Betran AP, Ye J, Moller AB, Zhang J, Gumezoglu AM, Torloni MR. The increasing trend in cesarean section rates: global, regional, and national estimates: 1990–2014. PLoS ONE. 2016;11:e0148343.
3. Berghella V. Cesarean delivery: Technique. UptoDate. Available online at www.uptodate.com (accessed: April 18, 2015).
4. Belizán JM, Cafferata ML, Althabe F, Buekens P. Risks of patient choice cesarean. Birth. 2006;33:167–9.
5. Belizán JM, Althabe F, Cafferata ML. Health consequences of the increasing caesarean section rates. Epidemiology. 2007;18:485–6.
6. Goudar SS, Carlo WA, McClure EM, Pasha O, Patel A, Esamai F, et al. The Maternal and Newborn Health Registry Study of the Global Network for Women's and Children's Health Research. Int J Gynaecol Obstet. 2012;118:190–3.
7. Abera M, Gebremariam A, Belachew T. Predictors of safe delivery service utilization in Arsi Zone, South-East Ethiopia. Ethiop J Health Sci. 2011;21:95–106.
8. Chu K, Cortier H, Maldonado F, Mashant T, Ford N, Trelles M. Cesarean section rates and indications in sub-Saharan Africa: a multi-country study from Medecins sans Frontiers. PLoS ONE. 2012;7:e44484.
9. Wall LL, Arrowsmith SD, Briggs ND, Browning A, Lassey A. The obstetric vesicovaginal fistula in the developing world. Obstet Gynecol Surv. 2005;60:S3–51.
10. Conde-Agudelo A, Belizán JM, Lammers C. Maternal–perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: cross-sectional study. Am J Obstet Gynecol. 2005;192:342–9.
11. Althabe F, Sosa C, Belizán JM, Gibbons L, Jacquerioz F, Bergel E. Cesarean section rates and maternal and neonatal mortality in low-, medium-, and high-income countries: an ecological study. Birth. 2006;33:270–7.
12. Althabe F, Belizán JM. Caesarean section: the paradox. Lancet. 2006;368:1472–3.
13. Irani M, Deering S. Challenges affecting access to cesarean delivery and strategies to overcome them in low-income countries. Int J Gynaecol Obstet. 2015;131:30–4.
14. Gebhart GS, Fawcus S, Moodley J, Farina Z. Maternal death and cesarean section in South Africa: results from the 2011–2013 Saving the Mothers report of the National Committee for Confidential Enquiries into Maternal Deaths. S Afr Med J. 2015;105:287–91.
15. Vogel JP, Betran AP, Vindevoghel N, Souza JP, Torloni MR, Zhang J, et al. Use of the Robson classification to assess caesarean section trends in 21 countries: a secondary analysis of two WHO multicountry surveys. Lancet Glob Health. 2015;3:e260–70.
16. NIH State-of-the-Science Conference Statement on cesarean delivery on maternal request. NIH Consens State Sci Statements 2006;23:1–29. Available online at: http://consensus.nih.gov/2006/cesareanstatement.pdf (accessed December 1, 2016).
17. Cousens S, Blencowe H, Stanton C, Chou D, Ahmed S, Steinhardt L, et al. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. Lancet. 2011;377:1319–30.
18. WHO recommendations for prevention and treatment of maternal peripartum infections, 2015. Geneva, Switzerland. Available online at: http://apps.who.int/iris/bitstream/10665/186171/1/9789241549363_eng.pdf?ua=1 (accessed October 31, 2016).
19. Bohren MA, Hunter EC, Munthe-Kaas HM, Souza JP, Vogel JP, Gulmezogly AM. Facilitators and barriers to facility-based deliveries in low- and middle-income

countries: a qualitative evidence synthesis. Reprod Health. 2014;11:71.
20. Dubourg D, De Brouwere V, Leberghe WV, Richard F, Litt V, Derveeuw M. Th Unmet Obstetric Needs Network. Available online at: http://www.uonn.org/docs/pdf/Final%20UON%20report%20definitif.pdf (accessed December 21, 2016).
21. WHO Statement on Cesarean Section Rates. World Health Organization, 2015. Geneva, Switzerland. Available online at: http://apps.who.int/iris/bitstream/10665/161442/1/WHO_RHR_15.02_eng.pdf (accessed July 5, 2016).
22. Roberts G, Roberts C, Jamieson A, Grimes C, Conn G, Bleichrodt R. Surgery and obstetric care are highly cost-effective interventions in a sub-Saharan African District Hospital: a three-month single-institution study of surgical costs and outcomes. World J Surg. 2016;40:14–20.
23. Say L, Chou D, Gemmill A, Tuncalp O, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2:e323–3.

