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Health Facility Cost of Cesarean Delivery at a Rural District Hospital in Rwanda Using Time-Driven Activity-Based Costing

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Abstract

Objective To determine the health facility cost of cesarean section at a rural district hospital in Rwanda. *Methods* Using time-driven activity-based costing, this study calculated capacity cost rates (cost per minute) for personnel, infrastructure and hospital indirect costs, and estimated the costs of medical consumables and medicines based on purchase prices, all for the pre-, intra- and post-operative periods. We estimated copay (10% of total cost) for women with community-based health insurance and conducted sensitivity analysis to estimate total cost range. *Results* The total cost of a cesarean delivery was US$339 including US$118 (35%) for intra-operative costs and US$221 (65%) for pre- and post-operative costs. Costs per category included US$46 (14%) for personnel, US$37 (11%) for infrastructure, US$109 (32%) for medicines, US$122 (36%) for medical consumables, and US$25 (7%) for hospital indirect costs. The estimated copay for women with community-based health insurance was US$34 and the total cost ranged from US$320 to US$380. Duration of hospital stay was the main marginal cost variable increasing overall cost by US$27 (8%). *Conclusions for Practice* The cost of cesarean delivery and the cost drivers (medicines and medical consumables) in our setting were similar to previous estimates in sub-Saharan Africa but higher than earlier average estimate in Rwanda. The estimated copay is potentially catastrophic for poor rural women. Investigation on the impact of true out of pocket costs on women's health outcomes, and strategies for reducing duration of hospital stay while maintaining high quality care are recommended.

Keywords Obstetrics · Cost of surgery · Africa · TDABC · Out of pocket pay · Hospital stay

Significance

Rwanda, like many sub-Saharan African countries, routinely provides cesarean section at district hospitals, where 60% of all major surgeries are cesarean delivery. However, the estimates of the hospital cost of cesarean delivery are limited. Our study estimated a total hospital cost that is higher than a previous Rwandan estimate but similar to regional estimates. Importantly, we highlighted the potential cost burden for women, and believe these results can better inform resource allocation and hospital cost reimbursement guidelines.

Introduction

Globally, 99% of neonatal and maternal mortality occurs in low- and middle- income countries (LMICs) (WB, WHO and UNICEF 2015). A quarter of neonatal deaths are due to

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complications during labor or delivery (Wardlaw et al. 2014). The common causes of maternal mortality include complications such as hemorrhage, obstructed or prolonged labor, and pre-eclampsia/eclampsia (Berhan and Berhan 2014; Khan et al. 2006; Muchemi et al. 2016), which require cesarean delivery for remediation (Harrison and Goldenberg 2016; Thomas et al. 2016). In countries that have cesarean delivery rates below 10%, 63–90% of maternal mortality and morbidity can be reduced by increasing cesarean section rates (Alkire et al. 2012; Thomas et al. 2016; Weiser et al. 2015). The Lancet Commission on Global Surgery categorized cesarean section as one of the three essential Bellwether procedures to be provided at every district hospital, given its necessity to improve maternal and child health outcomes (Meara et al. 2016; Thomas et al. 2016; Ruhumuriza et al. 2018).

Investing in cesarean section is both feasible and highly cost effective in the majority of the LMICs (Alkire et al. 2012). Although cesarean delivery is the most common major surgery, accounting for up to 50% of all surgical procedures performed at district hospitals in sub-Saharan Africa (Galukande et al. 2010; Löfgren et al. 2015; Mock et al. 2015), cesarean delivery rates are still low among rural poor women in these settings (< 7%) (Harrison and Goldenberg 2016). Availability of trained staff, standard infrastructure, and sufficient supply of medicines and equipment at the health facility affect the availability of safe cesarean delivery (Ang et al. 2015; Arsenault et al. 2013; Harrison and Goldenberg 2016; Pearson and Shoo 2005). In addition, a pregnant woman's ability to obtain a cesarean delivery depends on the cost of the procedure and of reaching the facility providing care that she must cover out of pocket (Harrison and Goldenberg 2016; Pearson and Shoo 2005).

In Rwanda, at least 95% of all deliveries occur at health facilities, and are assisted by skilled providers (Joharifard et al. 2012). Cesarean deliveries account for 13% of total deliveries (NISR, MoFEP and MoH 2015). The rates range between 8.5 and 9.9% among women with no education and with low wealth quintiles, and 11% in rural areas compared to 22% in urban settings. Although cesarean section is the most performed major surgery at district hospitals in Rwanda, accounting for 60% of surgeries at district hospitals (Petroze et al. 2012), information on the facility cost of cesarean section and the potential health facility cost burden for women is limited. This study estimated the cost of cesarean delivery in rural Rwanda to promote appropriate resource allocation and hospital cost reimbursement guidelines.

Methods

Study Setting

The study assessed the cost of cesarean delivery at Butaro District Hospital, a rural hospital in the Northern Province of Rwanda. Butaro District Hospital is managed by the Rwanda Ministry of Health (RMoH) and served a population of approximately 337,000 people in 2012 (GoR 2015). Partners In Health/Inshuti Mu Buzima (PIH/IMB), a health and social justice non-governmental organization has supported the RMoH since 2005 to improve health care delivery in selected districts through health worker training and resource mobilization. This support expanded to include Butaro District Hospital and corresponding catchment areas in 2007. Through this partnership, Butaro receives intermittent surgical specialist visits and in 2015, hired a general surgeon on staff. However, general practitioners perform cesarean delivery at Butaro District Hospital, consistent with standard practice in all public district hospitals in Rwanda.

In Rwanda, women in labor first present to health centers where nurses assess the progression of labor and provide skilled assistance for uncomplicated vaginal deliveries. Nurses transfer complicated cases to the district hospitals for appropriate care by a physician, which may include cesarean delivery. At district hospitals, pregnant women receive obstetrical exams, laboratory tests and ultrasound as appropriate, before being taken to the operating theater for cesarean delivery if indicated. After operation, midwives, nurses and doctors monitor women in the maternity wards and in the absence of complications, discharge the women. For women with community-based health insurance, the government covers 90% of hospital delivery costs and the women pay 10% out of pocket (NISR, MoFEP and MoH 2015). Women without insurance cover all care related costs through out of pocket expenditures.

Study Design, Population and Data Collection

In this retrospective costing study, we used time driven activity based costing (TDABC) (McBain et al. 2016) to estimate the cost of cesarean delivery at Butaro District Hospital. Baseline demographic data and details on the clinical care provided were collected as part of a larger study and available for 197 women who delivered by emergency cesarean section between January 1 and December 31, 2015 (Nyirahabimana et al. 2017). Of the 197 women, we performed additional extensive chart review on a smaller random sample of 30 women to collect detailed

information on medications, medical consumables, laboratory tests and imaging performed. Using a structured questionnaire, we interviewed the medical personnel involved in emergency cesarean delivery to develop a process map for patient clinical activities from admission to discharge. We interviewed 2–3 medical personnel per activity to obtain time estimates and reported average time for each activity in whole minutes, hours or days as appropriate. We gathered data on equipment and space size through observation. Through human resources records, financial expenditure report, purchase price list, and logistic records, we obtained data on staff salaries, staff annual clinical availability, hospital indirect costs, and unit costs of medicines, medical consumables and equipment.

Costing Analysis

Using a health facility perspective, we estimated the cost of the entire care cycle from admission to discharge, stratified by pre-operative, intra-operative and post-operative phases to understand the cost drivers for cesarean section. The following cost categories were included: personnel, infrastructure (included equipment, fuel, electricity, water and space), medicines, medical consumables and hospital indirect costs (included administration, operations, telecommunications, building renovation, repairs and maintenance, and cleaning and office consumables) (Table 1). For personnel, infrastructure and hospital indirect costs, we calculated capacity cost rate (CCR) defined as cost per minute for each specific variable. To obtain total costs, we multiplied the CCR by time spent by personnel or in a space. We extracted the unit costs in Rwandan Francs from relevant records then converted the costs to United States dollars (US$) using a yearly average conversion rate of 725.3 Rwandan Francs per US$ in 2015 (NBR 2018).

For medicines and medical consumables, we used purchase price to determine allocated cost, weighted by the probability of women receiving that medicine or medical consumable. We included medicines and medical consumables used by at least 10% of the women in cost calculations, assuming that a less than 10% usage did not reflect a typical cost. We had details on the phase of surgery (pre-, intra- and post-operative phases) for medicine usage and thus assigned costs accordingly. For medical consumables, we had information on the overall use for the duration of hospital stay. Except for medical consumables specific for a particular surgical phase, we allocated usage to surgical

Table 1 Summary of costing categories and data sources

Cost category	Variables	Data sources
Personnel	Staff type and annual salary and benefits, activity involved in, availability time frame in a year, and duration of providing care for cesarean delivery	Human resources records, interview of medical staff
Infrastructure		
Equipment	All minor and major equipment in spaces used in service delivery, useful life years, purchase prices, availability time frame, and duration of usage	Equipment questionnaire filled through observation and logistics records, prices from logistics records, literature review on useful life years, interview of medical staff
Energy	Total cost of fuel, electricity and water per year, expect energy use per space based on space area, availability time frame and duration of usage	Expenditure report, interview of medical staff
Space	Area of spaces used in service delivery, construction cost per square meter, useful life years, availability time frame, and duration of usage	Space questionnaire filled through observation, interview of medical staff, prices from logistics records
Medicine	Antibiotics, anesthetics and muscle relaxants, infusions and symptomatic medications including painkillers, anti-pyretics, anti-acid (included unit dose, daily frequency of intake, duration and mode of intake)	Patient charts, interview of medical staff, prices from local pharmacy
Medical consumables	Sutures, oxygen, catheters (intravenous, foley), injection water, gloves (sterile and non-sterile), masks, urine bag, tubes (aspiration), scalpel, syringe and needle, disinfectants (include number used), wound dressing supplies	Patient charts, interview of medical staff, prices from local pharmacy
Hospital indirect costs	Administration, operations, telecommunications, building renovation, repairs and maintenance, and cleaning and office medical consumables costs, total outpatients, inpatients and hospital beds in 2015	Hospital expenditure report for 2015

phases based on duration of each phase. The total cost for cesarean delivery per patient was the sum of personnel, infrastructure, medicine, medical consumables and hospital indirect costs.

Summary of Assumptions

Online resource 1 highlights the assumptions for primary costing. Briefly, we used the median values for the duration of hospital stay, the time from admission to onset of surgery and the duration of surgery based on the full dataset including the 197 women. For infrastructure, we assumed each cost component was available for 24 h a day, 365 days in a year given inpatient admission of pregnant women. Given lack of room-specific energy consumption data at the hospital, we assumed energy distribution of 25% for laboratory based on the volume of electrical equipment in the laboratory and the projections by the hospital maintenance team. For non-laboratory spaces, we distributed the remaining 75% of energy consumption, allocating flat energy costs for each space based on its area in square meters, assuming the same amount of energy consumption per square meter. For hospital indirect costs, we assumed that the outpatient cost per minute was the same for inpatient.

Sensitivity Analysis

To report the total cost ranges, we conducted sensitivity analysis to obtain lower and upper bounds for the cost estimates by modifying assumptions. Lower bound estimates included 25th percentile data for duration of hospital stay and duration of surgery, and 75th percentile data for pre-operative time. Energy use distribution was adjusted to 15% for laboratory and 85% for non-laboratory spaces. For upper bound estimates, assumptions included 75th percentile data for duration of hospital stay and duration of surgery, and 25th percentile data for pre-operative time. We adjusted energy use distribution to 35% for laboratory and 65% for non-laboratory spaces, and assumed the hospital indirect cost per inpatient was twice per outpatient. All costs are rounded off to whole dollar values except for when costs are less than a dollar. Final total costs are rounded to the nearest US$1.

Ethics

Partners In Health/Rwanda Research Committee and the National Health Research Committee in Rwanda provided scientific review and approval. The Rwanda National Ethics Committee (IRB 00001497) and Harvard Medical School Institutional Review Board (IRB 15-3818) provided ethical review and approval. We also received approval from the Rwanda Ministry of Health and the leadership at the hospital for data collection. Since we used retrospective patient data from medical records, there was no informed consent. However, during data collection, we kept a separate paper file that linked patient identifiers to study identifiers and destroyed this file after data validation.

Results

Of the 197 women, the majority were aged 25–34 years (56.5%, n = 109/193), married (96.3%, n = 181/188), farmers (92.3%, n = 180/195) and had community-based health insurance (92.7%, n = 179/193) (Table 2). Three women (1.5%) experienced intra-operative complications, two (66.7%) of which were hemorrhage and one (33.3%) was hypotension. Post-operative complications were observed in 14 women (7.1%), and these were mostly hemorrhage (35.7%, n = 5), wound disruption (28.6%, n = 4), surgical site infection (14.3%, n = 2), and abdominal conditions including abdominal pain, epigastric pain and urinary retention (14.3%, n = 2). The median pre-operative time was 10.3 h (inter-quartile range [IQR]: 1.8, 42.2), median length of surgery was 55.0 min (IQR: 41.0, 75.5), and the median duration of hospital stay was four days (IQR: 4.0, 6.0). Maternal outcomes included one death (0.5%) while neonatal outcomes included four deaths (2.2%) and 25 (12.2%) admissions to neonatal unit.

For the smaller sample of thirty women assessed for detailed clinical management, all women received HIV, blood type and cross matching and full blood count tests, and 76.6% (n = 24) had Rhesus factor test (Fig. 1). Only 26.7% (n = 8) had an ultrasound. All women received antibiotics ampicillin and gentamycin (100.0%, n = 30), and the common anesthetic drug was bupivacaine (100.0%, n = 30) (Table 3). For infusions, all women received glucose, normal saline, and Ringer's Lactate solution (100.0%, n = 30), and for symptomatic medications, all women received painkillers or antipyretics and cytotec or oxytocin (100.0%, n = 30), 50.0% received ephedrine (n = 15), and 33.3% (n = 10) received gastro-intestinal drugs.

The total cost for personnel was US$46: US$10 (21.7%) in the pre-operative period, US$17 (37.0%) in the intra-operative period and US$19 (41.3%) in the post-operative period (Table 4). The midwife spent most time and money providing care (486 min, 52.7%, US$24).

The total cost of a cesarean delivery was US$339 inclusive of intra-operative costs of US$118 (35%) and pre and post-operative costs of US$221 (65%) (Table 5). Infrastructure was the largest cost driver for pre-operative costs (US$16, 35%). Intra-operatively, medical consumables (US$54, 46%) and medicines (US$45, 38%) were the largest cost drivers. The same pattern existed for post-operative

Table 2 Demographic characteristics and clinical outcomes for women delivering through cesarean section (N = 197)

Variables	n	%
Age (years), N = 193		
< 25	56	29.0
25–34	109	56.5
35–46	28	14.5
Marital status, N = 188		
Single	5	2.7
Married	181	96.3
Divorced/widowed	2	1.0
Occupation, N = 195		
Unemployed	4	2.1
Student	2	1.0
Farmer	180	92.3
Self-employed	3	1.5
Employed	6	3.1
Insurance, N = 193		
None	3	1.6
Community-based health insurance	179	92.7
Other insurance	11	5.7
Maternal outcome, N = 197		
Intra-operative complications	3	1.5
Hemorrhage	2	66.7
Hypotension	1	33.3
Post-operative complications	14	7.1
Hemorrhage	5	35.7
Wound disruption	4	28.6
Surgical site infection	2	14.3
Abdominal conditions[a]	2	14.3
Unplanned re-operation	1	7.1
Discharged	191	97.0
Death	1	0.5
Unknown	5	2.5
Neonatal outcome, N = 208		
Discharged	170	83.3
Admitted to neonatal unit	25	12.2
Transferred to another hospital	5	2.5
Death	4	2.0
Unknown	4	2.0
	Median	(IQR)
Admission to surgery start (hours) (N = 179)	10.3	(2.8, 42.2)
Length of surgery (minutes) (N = 172)	55.0	(41.0, 75.5)
Duration of hospital stay (days) (N = 193)	4.0	(4.0, 6.0)

IQR interquartile range

[a]Includes abdominal pain, epigastric pain and urinary retention

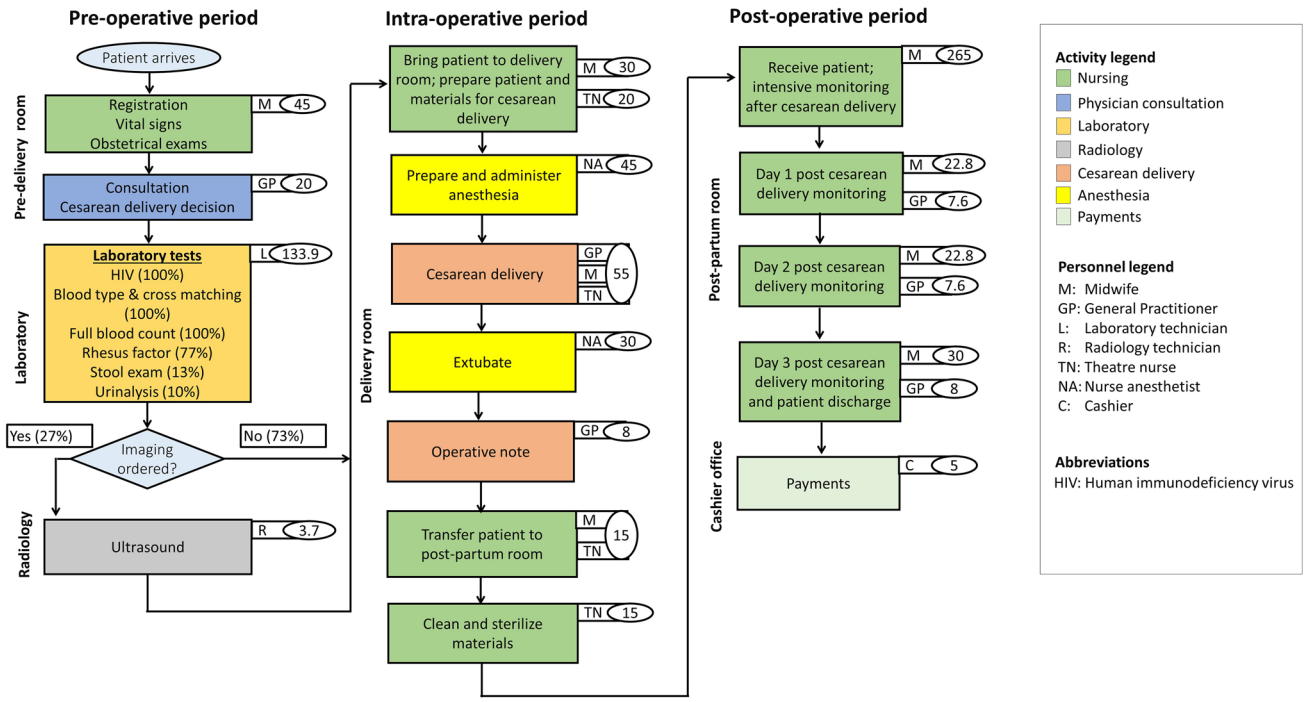

Fig. 1 Process map for cesarean section delivery. Large boxes show activities, arrows show the direction of events, small ovals show time in minutes that health provider spends in every activity, small boxes show the providers involved. Time displayed is the average of the times reported from interviews of 2–3 medical personnel who perform, assist or supervise that task

costs: medical consumables (US$60, 35%) and medicines (US$55, 32%). In primary costing, the overall costs per category in descending order included US$122 (36%) for medical consumables, US$109 (32%) for medicines, US$46 (14%) for personnel, US$37 (11%) for infrastructure, and US$25 (7%) for hospital indirect costs. The cost of cesarean delivery ranged between US$320 and US$380 in the lower and upper bound estimates. We estimated community-based health insurance copay at $34 (data not shown in tables). Duration of hospital stay was the main marginal cost variable, increasing overall cost by $27 (8%) in the upper bound estimates (Online resource 2).

Discussion

The total cost of cesarean delivery in our study ($339) fell within previous estimates in sub-Saharan Africa, which range between $24 and $361 (Alkire et al. 2012; Collins et al. 2011; Debas et al. 2015; Deboutte et al. 2013; Harrison and Goldenberg 2016; Witter et al. 2010). Cost variability has been seen for other general surgical procedures (Ogola and Shafi 2016) and could be due to cost specificity by country or inclusion of different cost items in analysis (Debas et al. 2015; Vonlanthen et al. 2011). While our costs were higher than a previous estimate from Rwanda in 2011 which ranged between $146 and $243, the original estimates in this national health costing analysis varied with indication for cesarean section ($161 for preterm labor and $285 for preeclampsia) and substantially increased with some types of postpartum complications (as high as $3000 for hemorrhage) (Collins et al. 2011). Similar to other studies, medicines and medical consumables accounted for the majority of costs (Arsenault et al. 2013; Debas et al. 2015) where supplies and drugs consumed 62% of total cesarean delivery costs (Schecter and Adhikar 2015).

Nearly all women in our study had community-based health insurance that covers 90% of all hospital care costs. While such insurance increases access to cesarean section (Harrison and Goldenberg 2016; Joharifard et al. 2012; Kitui et al. 2013), if women are charged at 10% of our estimate, the US$34 out of pocket to cover hospital care could be prohibitive or catastrophic. Further, our estimate excludes other expenditures such as transportation and food for both the woman who delivered and her caregiver(s). Studies in Mali and Morocco found that women spent between US$65 and US$163 on transportation and treatment despite a government policy of free emergency obstetric care (Arsenault et al. 2013; Boukhalfa et al. 2016; Ravit et al. 2015), with rural women spending significantly more (Ravit et al. 2015). The overall out of pocket expenditure for women in this setting and the effect of the out of pocket expenditures on the women's timely access to cesarean section, treatment outcomes and family welfare need further assessment.

Table 3 Detailed clinical management of a smaller sample of women delivering through cesarean section (N = 30)

Variables	n	%
Common medications		
Antibiotics		
Ampicillin	30	100.0
Gentamycin	30	100.0
Amoxicillin	7	23.3
Metronidazole	5	16.7
Anesthetics and muscle relaxants		
Bupivacaine	30	100.0
Lidocaine	5	16.7
Infusions		
Glucose	30	100.0
Normal saline	30	100.0
Ringer's Lactate	30	100.0
Symptomatic medications		
Painkillers or antipyretics[a]	30	100.0
Obstetric medications[b]	30	100.0
Vitamin K1	15	50.0
Ephedrine hydrochloride	15	50.0
Pomade	11	36.7
Gastro-intestinal/Anti-acid[c]	10	33.3

[a]Painkillers or antipyretics include diclofenac, ibuprofen, paracetamol, pethidine, pomade

[b]Includes cytotec or oxytocin

[c]Includes butylscopolamine, cimetidine, or ondansetron

Duration of hospital stay provided the largest marginal increase in overall cost. Previous studies have linked long duration of hospital stay with severity of illness (Khan et al. 2006; Ogola and Shafi 2016), severity of post-operative complications (Khan et al. 2006; Vonlanthen et al. 2011), inadequate hospital staffing (Dexter and Lubarsky 2004), challenges with patient mobility and continuity of care at home (Johnson et al. 2005), and pregnancy overweight (Mamun et al. 2011). The recommended duration of hospital stay for cesarean delivery is 4 days (NICE 2011), similar to the current study's median hospital stay. In addition to increased costs, long hospital stays can expose patients to new infections (Decoster and Kozyrskyj 2000) and can delay admission of new patients due to limited bed availability (Decoster and Kozyrskyj 2000; Nkurunziza et al. 2016; Smith et al. 2016). However, early discharge can make women more vulnerable to post-operative complications in the absence of proper care at home. Future studies should assess factors linked to longer duration of hospital stay and high cost of hospitalization for women who receive cesarean section in this setting in order to develop appropriate cost-containment policies and interventions that maintain high

Table 4 Capacity cost rates and total costs for personnel supporting cesarean delivery in rural district hospitals in Rwanda

Type of health worker	CCR (US$)	Pre-operative phase		Intra-operative phase		Post-operative phase		Total health worker costs		
		Mean time[a]	Costs (US$)	Mean time[a]	Costs (US$)	Mean Time[a]	Costs (US$)	Mean Time[a]	Costs (US$)	% of personnel cost
General practitioner	0.055	20	1	63	3	23	1	106	6	13
Midwife	0.050	45	2	100	5	341	17	486	24	53
Theatre nurse	0.043			105	5			105	5	10
Nurse anesthetist	0.054			75	4			75	4	9
Laboratory technician	0.054	134	7					134	7	15
Radiology technician	0.048	4	0.2					4	0.2	0
Cashier	0.036					5	0.2	5	0.2	0
Total			10		17		19		46	

CCR capacity cost rate (US$): cost of a personal on a specific activity per minute in United States dollars

[a]Probability weighted time (measured in minutes): total time allocated to a specific activity weighted by the probability that personnel type completed the activity; costs are rounded off to the nearest whole dollar value except for when costs are less than a dollar

Table 5 Total costs and cost drivers for cesarean delivery by operative stage including lower and upper bound estimates in rural district hospitals in Rwanda

	Primary analysis								Sensitivity analysis			
	Pre-operative costs		Intra-operative costs		Post-operative costs		Total primary costs		Lower bound estimates[c]		Upper bound estimates[d]	
	Costs (US$)[a]	% cost	Costs (US$)[a]	% cost	Costs (US$)[a]	% cost	Costs (US$)[a]	% cost	Costs (US$)[a]	% cost	Costs (US$)[a]	% cost
Personnel	11	23	17	14	19	11	46	14	43	13	52	14
Infrastructure[b]	16	35	1	1	20	11	37	11	27	8	53	14
Medicines	9	20	45	38	55	32	109	32	109	34	109	29
Medical consumables	7	16	54	46	60	35	122	36	116	36	124	33
Hospital indirect costs	3	6	1	1	21	12	25	7	25	8	42	11
Total	46		118		175		339		320		380	

[a]Allocated costs

[b]Includes the cost of equipment, fuel, electricity, water and space. Costs are rounded off to whole dollar values

[c]Assumptions include: the duration of hospital stay is 4 days, the duration of surgery is 41 min (these are the 25th percentile data), and duration from admission to surgery start is 42.2 h (75th percentile data). Energy use distribution is 15% for laboratory and 85% for non-laboratory spaces

[d]Assumptions include: the duration of hospital stay is 6 days, the duration of surgery is 75.5 min (these are the 75th percentile data), and the duration from admission to surgery start is 2.8 h (the 25th percentile data). Energy use distribution was 35% for laboratory and 65% for non-laboratory spaces and the total hospital indirect cost per inpatient was twice per outpatient

quality of care and health outcomes for women and their neonates.

Our study had the following limitations. The costs are health facility focused covering the time from patient admission to discharge in a rural district hospital. With an estimated 95% of deliveries in Rwanda occurring at a health facility, home deliveries are rare (Joharifard et al. 2012). Future studies should include the care costs at the health center prior to transfer to the district hospital, women's actual expenditures including transport and food, assess the effect of these expenditures on women's welfare, and compare the costs for women in rural and urban settings. This study also has limited generalizability given that it only included one rural district hospital supported by a non-governmental organization. However, cesarean section is a routine surgery in all district hospitals in Rwanda, and we believe that the type of care provided and resources used in the provision of care are similar across other rural district hospitals in Rwanda and the region. As much as possible, we minimized the use of assumptions, relying on retrospective data and conducting multiple interviews to reduce the effect of recall bias and sensitivity analyses to provide a cost range.

Conclusions

The overall cost of cesarean section in our study is similar to previous estimates in the region and is driven by the cost of medicines and medical consumables. Additional studies on what rural women spend out of pocket to receive cesarean section and the effect of such expenditures on women's health and welfare is needed. Policy makers and hospital managers can use this information to better cover costs for current cesarean deliveries and to plan improved availability of cesarean section in rural settings.

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Author Contributions JO and JR led study design and protocol development. JO, JR and YL led data collection. JO led analysis and manuscript development. BHG supervised the research process. BHG, TN, RR and YL contributed to study design. BHG, TN, RR, MS, YL, JMO, TM, GT, AL and CR supported protocol development. All authors critically reviewed the first drafts of the manuscript, supported results interpretations and approved the final manuscript for publication.

Compliance with Ethical Standards

Conflict of interest Authors declare that they have no conflict of interest.

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