

CLINICAL ARTICLE

Association of a single prior cesarean delivery with adverse birth outcomes at a tertiary referral hospital in southwestern Uganda: A secondary analysis of four observational studies

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Abstract

Background: Prior cesarean delivery (CD) is a leading indication for repeat CD and a key driver of rising cesarean rates in Sub-Saharan Africa. Evidence on associations between prior CD and adverse outcomes in low-resource settings remains limited.

Objective: We examined the association between one prior CD and adverse maternal and perinatal outcomes and examined current delivery mode as a mediator of this association among women delivering at Mbarara Regional Referral Hospital (MRRH), Uganda.

Methods: We conducted a secondary analysis of four prospective studies at MRRH (2014–2024). The exposure was having one prior CD, and outcomes included composite adverse maternal outcomes (postpartum hemorrhage, infection, blood transfusion, prolonged hospital stay, and others) and composite adverse perinatal outcomes (stillbirth, neonatal death, preterm birth, low birthweight, low Apgar score, and neonatal intensive care unit admission). We compared the odds of adverse outcomes for women with one prior CD to those with none using multivariable logistic regression. Causal mediation analysis was used to assess whether current CD mediated the effect of prior CD on adverse maternal outcomes.

Results: Of 2222 women with at least one prior delivery, 611 (27.5%) had one prior CD. Women with one prior CD more often delivered by cesarean (73.7% vs. 26.4%) and experienced more adverse maternal outcomes (24.5% vs. 15.4%, $P < 0.001$), including prolonged hospital stay (21.6% vs. 12.7%, $P < 0.001$). Prior CD was associated with increased odds of adverse maternal outcomes (adjusted odds ratio [aOR]: 1.99, 95% confidence interval [CI]: 1.54–2.57), with 88.9% of this effect mediated through current delivery mode (indirect odds ratio [OR]: 1.78, 95% CI: 1.41–2.25; direct OR: 1.09, 95% CI: 0.79–1.51, $P = 0.586$). Adverse perinatal outcomes (19.1%) did not differ by prior CD status ($P = 0.28$). HIV-positive serostatus (aOR: 1.29), referral (aOR:

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1.69), and low antenatal care (ANC) attendance (aOR: 1.66) independently predicted perinatal outcomes.

Conclusion: While prior CD was associated with higher odds of poor maternal outcomes due to repeat cesarean, HIV-positive serostatus, facility referral, and low ANC attendance (but not prior CD) independently predicted adverse perinatal outcomes. Individualized delivery planning and improving surgical safety for women with prior CD and strengthened antenatal surveillance are critical to reducing maternal and perinatal morbidity at referral facilities in low-resource settings.

KEYWORDS

child, delivery mode, maternal, perinatal, pregnancy, previous scar, Sub-Saharan Africa

1 | INTRODUCTION

Prior cesarean delivery (CD) is a one of the leading indications for repeat CD and a major contributor to the high CD rates in Sub-Saharan Africa, accounting for approximately 15%–20% of cesarean deliveries in regional cohorts.^{1,2} Although CD can be life-saving when medically indicated, rising CD rates in low-resource settings have not consistently led to improved maternal or perinatal outcomes.³ In many Sub-Saharan African contexts, CDs are frequently performed under emergency conditions with limited surgical safety, delayed decision-making, and inadequate facility readiness.^{4,5} This contributes to elevated risks of maternal complications, such as hemorrhage, infection, and anesthesia-related events.^{4,5} Further, maternal deaths following CD are disproportionately high in low-income countries, primarily caused by systemic delays in accessing surgery and gaps in perioperative care, including prolonged transfers between facilities, inadequate anesthesia services, limited blood transfusion capacity, and insufficient postoperative monitoring.^{5,6}

In high-income countries, having had a prior CD is associated with increased maternal and perinatal morbidity and mortality, regardless of whether the current pregnancy is managed through a trial of labor or repeat CD.^{7–13} The association between prior CD and subsequent maternal and perinatal outcomes remains insufficiently investigated in low-resource settings, including Uganda, where maternal and perinatal morbidity and mortality rates are substantially higher than in high-income countries.^{4,5} Recent studies from Uganda suggest that cesarean births are associated with elevated risks of adverse outcomes (including stillbirth, predischage neonatal death, and maternal mortality) compared to vaginal deliveries.⁵ Nonetheless, few studies have specifically assessed how a history of prior CD influences these risks in subsequent pregnancies, particularly in facilities

with limited emergency obstetric care. Moreover, mediation analysis has not been applied to assess whether current CD and/or antenatal care (ANC) attendance mediate these adverse outcomes. To address this gap in knowledge, we examined the association between one prior CD and adverse maternal and perinatal outcomes and examined current delivery mode as a mediator of this relationship, among women delivering at Mbarara Regional Referral Hospital (MRRH) in southwestern Uganda.

2 | METHODS

2.1 | Study design

We performed a secondary analysis of data collected from four studies conducted between 2014 and 2024 at MRRH in Uganda: three prospective longitudinal birth cohort studies (the Uganda Peripartum Infections and Mortality [UPIM] study, the Placental Inflammation (PI) study, and the Placentas, Antibodies, and Child Outcomes [PACO] study) and one cross-sectional study with data collection limited to the time of delivery and no postpartum follow-up (PV).

2.2 | Study population

All women enrolled in the parent studies who delivered at MRRH were eligible for this analysis. Women in all four studies were enrolled during pregnancy, with >95% enrolled during labor. The Uganda Peripartum Infections and Mortality (UPIM) study (2014–2015) aimed to determine the epidemiology, microbiology, and outcomes of postpartum infections at MRRH. The PI

study (2017–2018) investigated associations between maternal HIV infection and placental abnormalities. The PACO study (2019–2023) aimed to define the impact of maternal HIV infection and antiretroviral therapy on the placenta and early child health outcomes. The PV study (2024) was designed to develop a computer vision tool for assessing placenta features and lesions at birth using digital photographs.¹⁴ Notably, PI and PACO specifically enrolled women with and without HIV infection, resulting in a higher proportion of HIV-positive participants than would be expected in a general obstetric population; findings should be interpreted in this context. The key characteristics of each parent study, including study period, design, recruitment strategy, follow-up, and population, are summarized in Table 1. For this secondary analysis, we included all women enrolled in the parent cohort studies with at least one prior delivery. Regardless of parity, we compared outcomes for the most recent birth, corresponding to the index pregnancy for which they were enrolled in the respective parent study. We excluded women without information on prior mode of delivery, those with more than one prior CS (≥ 2) and nulliparous women (primigravidas).

2.3 | Study procedures

In each parent study, trained research assistants (nurse midwives) collected information through structured interviews with participants at admission (all studies) and in follow-up visits during the postpartum period (all studies except PV). Research assistants also abstracted clinical data (including obstetric history, delivery details, and maternal and neonatal outcomes) from patient charts using standardized data extraction forms. Data was collected using REDCap.¹⁵

2.4 | Variables

2.4.1 | Exposure

The primary exposure was having one prior CD, ascertained from obstetric history abstracted from patient charts by trained research assistants using standardized data extraction forms. Prior CD was defined as any documented previous cesarean delivery regardless of whether it was the most recent preceding delivery; women with an intervening vaginal birth between the prior CD and the index pregnancy were, therefore, included in the prior CD group.

2.4.2 | Outcomes

Outcome variables included individual and composite adverse maternal and perinatal (neonatal) outcomes, abstracted from patient charts. Adverse maternal outcomes included postpartum hemorrhage, puerperal endometritis, surgical site infection, blood transfusion, antepartum hemorrhage (previa and abruption), retained placenta, ruptured uterus, hysterectomy, re-operation (secondary closure or laparotomy), intensive care unit admission, maternal death, and prolonged hospital stay (>1 day for vaginal births or >3 days for cesarean). Adverse perinatal outcomes included stillbirth, neonatal death, preterm birth <37 weeks' gestational age, low birth weight <2.5 kg, low Apgar score (<7 at 5 min), and admission to the neonatal intensive care unit (NICU). Unlike the three longitudinal cohort studies, PV did not include postpartum follow-up; consequently, postpartum maternal outcomes (puerperal endometritis, wound infection, re-operation, maternal death, and prolonged hospital stay) and

TABLE 1 Characteristics of the four parent studies included in the secondary analysis, Mbarara Regional Referral Hospital, Uganda from 2014 to 2024.

Characteristic	UPIM	PI	PACO	PV
Study period	2014–2015	2017–2018	2019–2023	2024
Design	Prospective longitudinal cohort	Prospective longitudinal cohort	Prospective longitudinal cohort	Cross-sectional
Primary focus	Epidemiology, microbiology, and outcomes of postpartum infections	Maternal HIV and placental inflammation	Impact of maternal HIV and ART on placenta and child health outcomes	Computer vision tool for placenta assessment at birth
Recruitment	$>95\%$ enrolled in active labor at MRRH	$>95\%$ enrolled in active labor at MRRH	$>95\%$ enrolled in active labor at MRRH	$>95\%$ enrolled in active labor at MRRH
Follow-up	Postpartum	Postpartum	Postpartum	Delivery only (no postpartum follow-up)
Population	General obstetric	HIV-enriched (HIV+ and HIV- women)	HIV-enriched (HIV+ and HIV- women)	General obstetric
N enrolled	1921	354	881	1222

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus; MRRH, Mbarara Regional Referral Hospital; PACO, Placentas, Antibodies, and Child Outcomes study; PI, Placental Inflammation study; PV, PlacentaVision study; UPIM, Uganda Peripartum Infections and Mortality study.

perinatal outcomes (neonatal death and NICU admission) might be underrepresented in data contributed by PV.

2.4.3 | Covariates

Covariates included maternal age at delivery in years, marital status, maternal education level, parity, district of residence (Mbarara vs. non-Mbarara), referral status, maternal HIV serostatus, and ANC visit attendance (≥ 4 visits vs. < 4 visits).

2.5 | Statistical analysis

We analyzed the data using Stata 19 (StataCorp, College Station, Texas, USA). We created a unique participant identifier for each of the four parent studies using study-specific numeric prefixes (UPIM: 1–4323; PI: 10001–10354; PACO: 100001–100881; PV: 1000001–1001399) and used this identifier to append and merge the datasets in Stata. We standardized variable definitions and coding across all four studies for key exposures and outcomes. Covariates included in the multivariable models were selected a priori based on clinical relevance and evidence from prior literature on risk factors for adverse maternal and perinatal outcomes in similar low-resource settings. We examined distributions of continuous variables and then summarized them as means and standard deviations or medians with interquartile ranges, if they were normally distributed or not. We summarized categorical variables as frequency with percentages. We compared participant characteristics by prior CD status using Student's *t*-test for continuous variables and χ^2 or Fisher's exact tests for categorical variables. We compared the proportion of participants who experienced adverse maternal and perinatal outcomes between those with and without a prior CD using χ^2 or Fisher's exact tests. We assessed the association of one prior CD with composite maternal and composite perinatal outcomes using univariable and multivariable logistic regression. We reported crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs). We adjusted the multivariable models for maternal age, marital status, ANC attendance, parity, HIV serostatus, and referral status. Missing data were handled using complete case analysis; participants with missing values on any covariate included in a given model were excluded from that analysis. We conducted a secondary analysis by including delivery mode in the current pregnancy as an additional covariate in the multivariable model for adverse maternal outcomes to estimate the direct association of prior CD independent of delivery mode. We performed formal causal mediation analysis based on the counterfactual framework to evaluate whether current delivery mode mediated the effect of prior CD on adverse maternal outcomes, decomposing the total effect into natural direct and indirect effects.¹⁶ Causal mediation analysis assumes no unmeasured confounding of the exposure–outcome, mediator–outcome, or exposure–mediator

relationships, and no exposure-induced mediator–outcome confounding. Given the observational nature of this secondary analysis, these assumptions cannot be verified, and mediation estimates should be interpreted with appropriate caution.

We conducted supplementary analyses to understand the unexpected association between ANC visits and adverse maternal outcomes. Logistic regression models were stratified by referral status, and ANC attendance (≥ 4 vs. < 4 visits) was compared between women with and without adverse maternal outcomes. Effect modification by prior CD was assessed by adding an interaction term to the adjusted model. Finally, causal mediation analysis was performed to test whether ANC attendance mediated the relationship between prior CD and adverse maternal outcomes, adjusting for current delivery mode in both mediator and outcome models. We set statistical significance at a *P*-value < 0.05 .

2.6 | Ethical approval and informed consent

We obtained ethical approval for the parent studies from the Mbarara University of Science and Technology (MUST) Research Ethics Committee, the Uganda National Council for Science and Technology, Partners (now Mass General Brigham) Healthcare, and The Pennsylvania State University under the following reference numbers: UPIM study (MUST 08/10-14, UNCST HS/1729, Partners 2014P002725), PI study (MUST 11/03-17, UNCST HS/2255, Partners 2017P001319), PACO study (MUST 10/06-19, UNCST HS/2697, Partners 2019P003248), and PV study (MUST 2023-859, UNCST HS3159ES, Penn State STUDY00020697). We obtained written informed consent from all participants before enrollment. All studies strictly adhered to the ethical standards in the 1964 Declaration of Helsinki and its later amendments.

3 | RESULTS

Of 4378 participants enrolled in the parent studies ($n=1921$ in UPIM, $n=354$ in PI, $n=881$ in PACO and $n=1222$ in PV), we included 2222 participants with at least one prior delivery in the analysis: 611 (27.5%) with one prior CD and 1611 (72.5%) with no prior CD. We excluded 2156 participants: 1584 (36.2%) primigravidae with no prior pregnancy, 299 (6.8%) participants with ≥ 2 prior CDs, 164 (3.7%) with missing data on parity, and 109 (2.4%) who lacked information on prior CD history.

3.1 | Participant characteristics

The mean age of included study participants was 28.2 (standard deviation 5.6) years. The majority were married (95.4%), resided

TABLE 2 Participant characteristics among 2222 women at Mbarara Regional Referral Hospital in Uganda from 2014 to 2024.

Characteristics at current pregnancy	Total N=2222 n (%)	1 prior CD		P-value	Missing n (%)
		Yes N=611 n (%)	No N=1611 n (%)		
Maternal age, years (mean ± SD)	28.2 (5.6)	26.9 (4.9)	28.7 (5.8)	<0.001*	6 (0.3)
Maternal age, years (n = 2216)				<0.001*	
<20	60 (2.7)	14 (2.3)	46 (2.9)		
20–34	1800 (81.2)	534 (88.0)	1266 (78.7)		
≥35	356 (16.1)	59 (9.7)	297 (18.5)		
Resides in Mbarara District (n = 2221)				0.50	1 (0.0)
No	845 (38.0)	239 (39.2)	606 (37.6)		
Yes	1376 (62.0)	371 (60.8)	1005 (62.4)		
Level of education completed (n = 1333) ^a				0.01	889 (40.0)
Primary or no school	774 (58.1)	183 (52.3)	591 (60.1)		
Secondary or higher school	559 (41.9)	167 (47.7)	392 (39.9)		
Marital status (n = 2219)				0.59	3 (0.1)
Not married	103 (4.6)	26 (4.3)	77 (4.8)		
Married	2116 (95.4)	585 (95.7)	1531 (95.2)		
Referred to MRRH from other facility (n = 2175)				0.49	47 (2.1)
No	1843 (84.7)	499 (83.9)	1344 (85.1)		
Yes	332 (15.3)	96 (16.1)	236 (14.9)		
Parity (n = 2222)				<0.001*	0 (0)
Multipara (2–4)	1800 (81.0)	541 (88.5)	1259 (78.2)		
Grand multipara (>5)	422 (19.0)	70 (11.5)	352 (21.8)		
Number of ANC visits (n = 2209)				0.02*	13 (0.6)
<4	591 (26.8)	141 (23.3)	450 (28.1)		
≥4	1618 (73.2)	465 (76.7)	1153 (71.9)		
HIV serostatus (n = 2194)				0.85	28 (1.3)
Negative	1608 (73.3)	429 (71.7)	1179 (73.9)		
Positive	586 (26.7)	169 (28.3)	417 (26.1)		
Median duration of labor in hours (IQR) (n = 2122)	12 (8–24)	13 (8–24)	12 (8–24)	0.99	100 (2.7)
Delivery mode (n = 2185)				<0.001*	37 (1.7)
Vaginal	1327 (60.7)	157 (26.3)	1170 (73.6)		
Cesarean	858 (39.3)	439 (73.7)	419 (26.4)		
Gestational age (weeks) (n = 2005)				0.59	217 (9.8)
≥37	1769 (88.2)	487 (88.9)	1282 (88.0)		
<37	236 (11.8)	61 (11.1)	175 (12.0)		
LOS (days), mean (SD) (n = 2197)	2.31 (3.23)	2.83 (2.11)	2.12 (3.54)	<0.001*	25 (1.1)

Note: Percentages are based on non-missing data; missing values are shown separately.

Abbreviations: ANC, antenatal care; CD, cesarean delivery; IQR, interquartile range; LOS, length of hospital stay; SD, standard deviation.

^aEducation data were not collected in the Uganda Peripartum Infections and Mortality (UPIM) study (n = 1921), accounting for the majority of missing values.

*P < 0.05.

in Mbarara District (62.0%), and had four or more ANC visits (73.2%). Women who had a prior CD were significantly more likely to be younger (26.9 vs. 28.7 years), to have completed secondary education or higher (47.7% vs. 39.9%), and to deliver via cesarean for the current pregnancy (73.7% vs. 26.4%). Additionally, participants who had a prior CD had significantly longer hospital stays (2.83 vs. 2.12 days) for the current delivery (Table 2).

3.2 | Comparison of adverse maternal and perinatal adverse outcomes among women with or without one prior cesarean delivery

3.2.1 | Adverse maternal outcomes (unadjusted)

Among the 2222 participants, 17.9% experienced one or more adverse maternal outcomes, with a significantly higher proportion

among women with one prior CD (24.5% vs. 15.4%, $P < 0.001$). Prolonged hospital stay (>1 day for vaginal births or >3 days for cesarean) was also significantly more common in the prior CD group (21.6% vs. 12.7%, $P < 0.001$). No statistically significant differences were observed between groups for other maternal outcomes (Table 3).

3.2.2 | Adverse perinatal outcomes (unadjusted)

Among the 2222 births analyzed, 19.1% experienced one or more adverse perinatal (neonatal) outcomes, with no statistically

significant difference between women with one prior CD and those without (17.6% vs. 19.6%, $P = 0.28$). Similarly, none of the individual perinatal outcomes (including preterm birth, low birthweight, stillbirth, low Apgar score at 5 min, neonatal death, or NICU admission) differed significantly between the two groups (Table 4).

3.2.3 | Multivariable analysis of one prior cesarean delivery and adverse maternal outcomes

In the multivariable logistic regression model, having one prior cesarean was significantly associated with nearly twice the

TABLE 3 Comparison of maternal outcomes among 2222 women with or without one prior cesarean delivery at Mbarara Regional Referral Hospital in Uganda from 2014 to 2024.

Outcomes	Total N = 2222 n (%)	One prior CD		P-value
		Yes n = 611 n (%)	No n = 1611 n (%)	
Adverse maternal outcomes (≥ 1) ^a	398 (17.9)	150 (24.5)	248 (15.4)	$<0.001^*$
Ruptured uterus (n = 1316)	9 (0.7)	4 (1.2)	5 (0.5)	0.21
Antepartum hemorrhage (n = 1622)	9 (0.6)	3 (0.7)	6 (0.5)	0.68
Hysterectomy (n = 1622)	5 (0.2)	0 (0.0)	5 (0.3)	0.17
Postpartum hemorrhage (n = 2222)	53 (2.4)	14 (2.3)	39 (2.4)	0.86
ICU admission (n = 1311)	1 (0.1)	0 (0.0)	1 (0.1)	0.55
Endometritis (n = 1445)	2 (0.1)	1 (0.3)	1 (0.1)	0.44
Wound infection (n = 635)	2 (0.3)	0 (0.0)	2 (0.4)	0.42
Re-operation (n = 1314)	5 (0.4)	1 (0.3)	4 (0.4)	0.75
Blood transfusion (n = 1319)	29 (2.2)	9 (2.6)	20 (2.1)	0.56
Maternal death (n = 2198)	3 (0.1)	1 (0.1)	2 (0.3)	0.13
Prolonged hospital stay (n = 2197)	332 (15.1)	130 (21.6)	202 (12.7)	$<0.001^*$

Abbreviation: ICU, intensive care unit.

^aIncludes all the variables below in this table.

* $p < 0.05$.

TABLE 4 Comparison of perinatal outcomes among 2222 women with or without one prior cesarean delivery at Mbarara Regional Referral Hospital in Uganda from 2014 to 2024.

Outcomes	Total N = 2222 n (%)	One prior CD		P-value
		Yes n = 611 n (%)	No n = 1611 n (%)	
Adverse perinatal outcomes (≥ 1) ^a	423 (19.1)	107 (17.6)	316 (19.6)	0.28
Preterm birth (<37 gestation weeks) (n = 2005)	236 (11.8)	61 (11.1)	175 (12.0)	0.59
Low birthweight (<2.5 kg) (n = 2199)	148 (6.7)	35 (5.8)	113 (7.1)	0.29
Stillborn (n = 2219)	56 (2.5)	13 (2.1)	43 (2.7)	0.47
Apgar score at 5 min (n = 2115)	26 (1.2)	9 (1.5)	17 (1.1)	0.64
Neonatal death (n = 2176)	14 (0.6)	6 (1.0)	8 (0.5)	0.20
NICU admission (n = 758)	92 (12.1)	24 (12.8)	68 (11.9)	0.76

Abbreviation: ICU, intensive care unit.

^aIncludes all the variables below in this table.

odds of an adverse maternal outcome (adjusted OR 1.99, 95% CI 1.54–2.57, $P < 0.001$). Preterm birth was similarly associated with significantly increased odds of adverse outcomes (adjusted OR 2.02, 95% CI 1.44–2.83, $P < 0.001$). Referral from another health facility was independently associated with higher odds of an adverse maternal outcome (adjusted OR 2.12, 95% CI 1.58–2.85, $P < 0.001$). In contrast, attending <4 ANC visits was paradoxically associated with reduced odds of adverse maternal outcomes (adjusted OR 0.57, 95% CI 0.42–0.78, $P < 0.001$); this finding is explored further in a supplementary analysis below. Maternal age, marital status, HIV serostatus, and grand multiparity were not

significantly associated with adverse maternal outcomes in the adjusted model (Table 5).

3.2.4 | Secondary analysis: Association between prior cesarean delivery and adverse maternal outcomes adjusted for current delivery mode

In a secondary analysis including current delivery mode as an additional covariate, having one prior CD was not significantly associated with experiencing one or more adverse maternal outcomes (adjusted

TABLE 5 Association of one prior CD and one or more adverse maternal outcomes, with adjusted estimates for covariates from logistic regression models, among 2222 women at Mbarara Regional Referral Hospital, Uganda, 2014–2024.

Variables	Adverse maternal outcome		Unadjusted analysis		Adjusted analysis	
	Yes (n=398) n (%)	No (n=1824) n (%)	Crude OR [95% CI]	P-value	Adjusted OR [95% CI]	P-value
<i>Primary exposure</i>						
Had one prior CD						
No	248 (62.3)	1363 (74.7)	1		1	
Yes	150 (37.7)	461 (25.3)	1.79 [1.42, 2.25]	$<0.001^*$	1.99 [1.54, 2.57]	$<0.001^*$
<i>Covariates</i>						
Maternal age (years)						
<20	12 (3.0)	48 (2.6)	1.18 [0.62, 2.25]	0.61	1.66 [0.82, 3.38]	0.16
20–34	314 (79.3)	1486 (81.6)	1		1	
≥ 35	70 (17.7)	286 (15.7)	1.16 [0.86, 1.55]	0.32	1.04 [0.72, 1.50]	0.83
Marital status						
Not married	24 (6.0)	79 (4.3)	1.42 [0.88, 2.26]	0.15	1.38 [0.81, 2.34]	0.24
Married	374 (94.0)	1742 (95.7)	1		1	
HIV serostatus						
Negative	284 (72.1)	1324 (73.6)	1		1	
Positive	110 (27.9)	476 (26.4)	1.08 [0.84, 1.37]	0.55	1.17 [0.89, 1.53]	0.26
Parity						
Multipara	309 (77.6)	1491 (81.7)	1		1	
Grand multipara	89 (22.4)	333 (18.3)	1.29 [0.99, 1.68]	0.06	1.36 [0.97, 1.91]	0.08
Gestational age (weeks)						
≥ 37	286 (81.2)	1483 (89.7)	1		1	
<37	66 (18.8)	170 (10.3)	2.01 [1.47, 2.75]	$<0.001^*$	2.02 [1.44, 2.83]	$<0.001^*$
Referred to MRRH from other facility						
No	295 (74.9)	1548 (86.9)	1		1	
Yes	99 (25.1)	233 (13.1)	2.23 [1.71, 2.91]	$<0.001^*$	2.12 [1.58, 2.85]	$<0.001^*$
ANC visits						
<4	84 (21.3)	507 (27.9)	0.70 [0.54, 0.91]	0.007*	0.57 [0.42, 0.78]	$<0.001^*$
≥ 4	310 (78.7)	1308 (72.1)	1		1	

Abbreviations: ANC, antenatal care; CD, cesarean delivery; CI, confidence interval; HIV, human immunodeficiency virus; MRRH, Mbarara Regional Referral Hospital; OR, odds ratio.

* $p < 0.05$.

OR 0.93, 95% CI 0.70–1.25, $P=0.649$; Table S1). In contrast, current CD was strongly and independently associated with increased odds of adverse maternal outcomes (adjusted OR 5.85, 95% CI 4.37–7.82, $P<0.001$). Preterm birth was also independently associated with increased odds of adverse outcomes (adjusted OR 2.38, 95% CI 1.66–3.41, $P<0.001$). Referral from another health facility remained significantly associated with adverse outcomes (adjusted OR 1.60, 95% CI 1.17–2.20, $P=0.003$). Attending <4 ANC visits was associated with reduced odds of adverse maternal outcomes (adjusted OR 0.58, 95% CI 0.42–0.80, $P=0.001$). Maternal age, marital status, HIV serostatus, and grand multiparity were not significantly associated with adverse outcomes in this model.

3.2.5 | Mediation analysis of current delivery mode on the relationship between prior cesarean delivery and adverse maternal outcomes

Women with a prior CD were significantly more likely to undergo repeat CD, and current delivery mode was a strong determinant of adverse maternal outcomes. Causal mediation analysis revealed that the effect of prior cesarean on adverse maternal outcomes operated almost entirely through its influence on current delivery mode. The natural direct effect—representing the effect of prior CD independent of current delivery mode—was small and statistically non-significant (OR 1.09, 95% CI 0.79–1.51, $P=0.586$). In contrast, the natural indirect effect, mediated through current CD, was substantial and highly significant (OR 1.78, 95% CI 1.41–2.25, $P<0.001$),

accounting for 88.9% of the total effect (95% CI 50.8–126.9%). The total effect of prior CD on adverse maternal outcomes was OR 1.95 (95% CI 1.52–2.49, $P<0.001$) (Figure 1).

3.2.6 | Antenatal care attendance and maternal outcomes

We further explored the counterintuitive finding from the adjusted logistic regression model, where attending <4 ANC visits was associated with reduced odds of adverse maternal outcomes (adjusted OR 0.57, 95% CI 0.42–0.78, $P<0.001$). Women with adverse maternal outcomes were more likely to have attended ≥ 4 ANC visits (78.7% vs. 72.1%, $P=0.007$), and ANC attendance did not differ significantly by referral status (16.5% vs. 14.9% with <4 visits, $P=0.36$). Women attending ≥ 4 ANC visits were also significantly more likely to deliver by cesarean (adjusted OR 1.30, 95% CI 1.02–1.65, $P=0.04$). Stratified analyses showed that the inverse association persisted among non-referred women (OR 0.59, 95% CI 0.43–0.80, $P=0.001$) but was absent among referred women (OR 0.96, 95% CI 0.57–1.61, $P=0.868$). The interaction between prior cesarean and ANC attendance was non-significant (OR 1.03, 95% CI 0.53–1.98, $P=0.94$). Mediation analysis showed no evidence that ANC attendance mediated the relationship between prior cesarean and adverse outcomes: prior cesarean did not predict ANC attendance (OR 1.06, 95% CI 0.81–1.38, $P=0.67$), and both the natural indirect and direct effects were non-significant (indirect OR 1.00, 95% CI 0.98–1.03; direct OR 0.94, 95% CI 0.73–1.22), as was the total effect (OR 0.95, 95% CI 0.73–1.23).

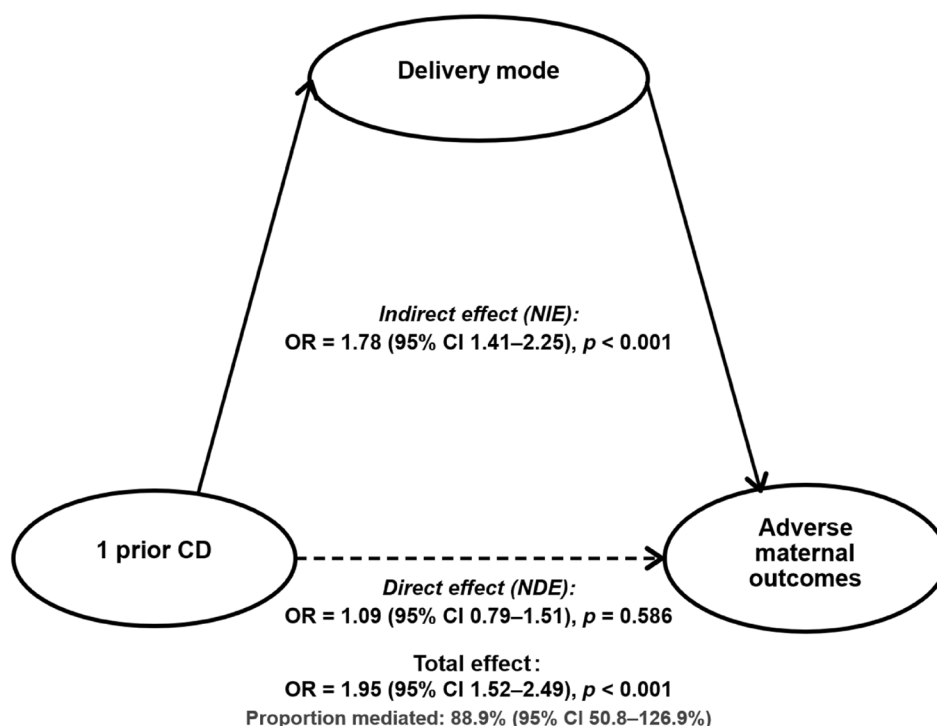


FIGURE 1 Directed acyclic graph of the mediation pathway between prior CD and maternal adverse outcomes via current delivery mode. CD, cesarean delivery; CI, confidence interval; NDE, natural direct effect; OR, odds ratio.

3.2.7 | Association of one prior cesarean delivery and adverse perinatal outcomes

After adjusting for covariates, having had one prior CD was not significantly associated with one or more adverse perinatal outcomes (adjusted OR 0.85, 95% CI 0.64–1.13, $P=0.257$). Maternal HIV-positive serostatus was independently associated with increased odds of an adverse perinatal outcome (adjusted OR 1.29, 95% CI 1.01–1.65, $P=0.045$). Referral from another health facility was also strongly associated with higher odds of an adverse perinatal outcome (adjusted OR 1.69, 95% CI 1.28–2.25, $P<0.001$). Similarly, attending <4 ANC visits was significantly associated with increased odds of an adverse perinatal outcome (adjusted OR 1.66, 95% CI 1.31–2.10, $P<0.001$) (Table 6).

4 | DISCUSSION

This study examined associations between one prior CD and adverse maternal and perinatal outcomes among women delivering at a tertiary referral hospital in southwestern Uganda. Our findings revealed that women with a single prior CD were significantly more likely to experience adverse maternal outcomes compared to those without, such as prolonged hospital stay, consistent with findings from prior studies.^{17,18} However, this association was no longer significant after adjusting for delivery mode, suggesting that the current CD itself, rather than the history of prior CD, is the primary driver of maternal risk. Mediation analysis confirmed this interpretation: prior CD strongly predicted repeat CD, and delivery mode in turn was a

TABLE 6 Association of one prior CD and adverse perinatal outcomes as estimated from logistic regression models among 2222 women at Mbarara Regional Referral Hospital in Uganda from 2014 to 2024.

Variables	Adverse perinatal outcome		Unadjusted analysis		Multivariable analysis	
	Yes (N=423)	No (N=1794)	Crude OR	P-value	Adjusted OR	P-value
	n (%)	n (%)	[95% CI]		[95% CI]	
<i>Primary exposure</i>						
Had 1 prior CD						
No	316 (74.7)	1293 (72.1)	1		1	
Yes	107 (25.3)	501 (27.9)	0.87 [0.69, 1.11]	0.28	0.85 [0.64, 1.13]	0.26
<i>Covariates</i>						
Maternal age (years)						
<20	13 (3.1)	47 (2.6)	1.23 [0.66, 2.31]	0.51	1.33 [0.70, 2.52]	0.38
20–34	329 (78.1)	1468 (81.9)	1		1	
≥35	79 (18.8)	277 (15.5)	1.27 [0.96, 1.68]	0.09	1.11 [0.80, 1.55]	0.52
Marital status						
Not married	29 (6.9)	74 (4.1)	1.72 [1.10, 2.68]	0.02*	1.46 [0.92, 2.33]	0.11
Married	392 (93.1)	1720 (95.9)	1		1	
HIV status						
Negative	292 (69.7)	1314 (74.2)	1		1	
Positive	127 (30.3)	457 (25.8)	1.25 [0.99, 1.58]	0.06	1.29 [1.01, 1.65]	0.04*
Parity						
Multipara	326 (77.1)	1470 (81.9)	1		1	
Grand multipara	97 (22.9)	324 (18.1)	1.35 [1.04, 1.74]	0.02*	1.26 [0.92, 1.72]	0.15
Referred to MRRH from other facility						
No	324 (78.5)	1519 (86.2)	1		1	
Yes	89 (21.5)	243 (13.8)	1.72 [1.31, 2.25]	<0.001*	1.69 [1.28, 2.25]	<0.001*
Delivery mode						
Vaginal births	241 (57.5)	1086 (61.5)	1		1	
Cesarean	178 (42.5)	680 (38.5)	1.18 [0.95, 1.46]	0.13	1.24 [0.96, 1.58]	0.09
ANC attendance						
<4	151 (36.0)	439 (24.6)	1.72 [1.37, 2.16]	<0.001*	1.66 [1.31, 2.09]	<0.001*
≥4	269 (64.0)	1346 (75.4)	1		1	

Abbreviations: ANC, antenatal care; CD, cesarean delivery; CI, confidence interval; HIV, human immunodeficiency virus; MRRH, Mbarara Regional Referral Hospital; OR, odds ratio.

* $P<0.05$.

significant determinant of adverse maternal outcomes, while the direct effect of prior CD was not significant. The indirect effect of prior CD through delivery mode was large and highly significant, indicating that maternal risk operates almost entirely via the pathway of repeat CD. Notably, one previous CD increases the likelihood of undergoing a repeat cesarean, which subsequently heightens the risk of adverse outcomes such as extended hospital stay. These findings align with evidence from Uganda and other low- and middle-income countries, as well as studies conducted in high-resource settings, all of which highlight the cumulative risk associated with repeat CD.^{5,18-20}

The strong association between repeat CD and adverse maternal outcomes aligns with existing evidence from both high- and low-resource settings, where surgical delivery is linked to increased morbidity, particularly in contexts with limited emergency obstetric capacity.²¹ The elevated risk of uterine rupture among women with prior CD underscores the importance of timely intrapartum decision-making and skilled monitoring, especially for those undergoing trial of labor.^{20,22} These findings reinforce the need for facility readiness (including access to surgical expertise, blood transfusion services, and rapid response systems) to safely manage labor in women with prior cesarean scars.²² Strengthening these systems is essential to mitigate risk and improve outcomes for both mothers and newborns.

We also observed an unexpected association between ANC attendance and adverse maternal outcomes: <4 ANC visits appeared protective, while ≥ 4 ANC visits were associated with increased risk. Additional analyses clarified that this pattern did not reflect a causal effect of ANC attendance but rather appeared to reflect reverse causality: women who developed complications during pregnancy were more likely to attend more ANC visits due to increased clinical surveillance. This pattern is consistent with confounding by indication, whereby women perceived by clinicians to be at higher risk are scheduled for more frequent ANC contacts. These interpretations were supported by the higher proportion of women with adverse outcomes who had ≥ 4 visits and by the persistence of the inverse association only among non-referred women and the finding that women attending ≥ 4 ANC visits were significantly more likely to deliver by cesarean, and CD was itself strongly associated with adverse maternal outcomes. Neither effect modification nor mediation analyses supported a causal pathway involving ANC attendance; ANC did not mediate the relationship between prior cesarean and adverse maternal outcomes, and the interaction between ANC attendance and prior cesarean was non-significant. While confounding by indication and reverse causality represent the most plausible explanations, other mechanisms including residual confounding by unmeasured disease severity or differential clinical management of high-risk women cannot be fully excluded, and this finding should therefore be interpreted with caution. These findings align with multi-country evidence from Ethiopia, Kenya, South Africa, and India, highlighting that ANC quality and risk detection, rather than visit counts, drive improved outcomes.²³ While the World Health Organization recommends at least eight ANC visits emphasizing both number and quality,²⁴ variability in ANC quality and risk stratification across Sub-Saharan Africa means that women perceived to be at highest risk often attend more visits,

making ANC attendance a proxy for underlying clinical risk rather than an independent determinant of maternal outcomes.²⁵

In terms of perinatal outcomes, one prior CD was not independently associated with increased risk after adjusting for potential confounders. This is similar to findings from prior studies.²⁶ Although stillbirth was more frequent among women with prior CD, the association did not persist in multivariable analysis. However, prior studies have associated one prior CD with antepartum stillbirth and neonatal death.^{7,27,28} In our cohort, maternal HIV-positive serostatus and low ANC attendance (<4 visits) emerged as significant predictors of adverse perinatal outcomes. These findings reinforce the critical role of integrated HIV care and proactive antenatal engagement in improving neonatal survival. Prior studies have similarly demonstrated that maternal HIV serostatus and ANC utilization each contribute distinctly to neonatal risk profiles.^{23,29-31}

Overall, this study contributes important evidence from a low-resource setting, where cesarean rates are rising but health system capacity remains constrained. The results suggest that while prior CD might signal elevated risk, it is the current mode of delivery and underlying clinical context that most strongly influence maternal and perinatal outcomes. Strengthening antenatal surveillance, optimizing delivery planning, and improving surgical safety protocols are essential strategies to mitigate risk among women with prior CD.

This study has several strengths. First, it draws on a large, combined cohort spanning a decade (2014–2024), allowing for temporal diversity and increased robustness of findings; sensitivity analyses showed no significant variation in adverse maternal outcomes across the four parent studies, further supporting the consistency of findings across the study period. Second, it utilizes data from a high-volume tertiary referral hospital, enhancing the generalizability of findings to similar low-resource settings. The inclusion of both maternal and perinatal outcomes provides a comprehensive assessment of clinical risk associated with prior cesarean delivery. Importantly, the use of formal causal mediation analysis allowed us to disentangle direct and indirect pathways, clarifying that delivery mode mediates the relationship between prior CD and adverse maternal outcomes. Finally, the study contributes locally grounded evidence to a global discourse on cesarean safety, informing context-specific clinical and policy decisions.

However, several limitations must be acknowledged. As a secondary analysis, the study was constrained by the scope and quality of existing data, with potential for unmeasured confounding, particularly around provider decision-making, labor management, and facility-level capacity. The exclusion of women with multiple prior CDs limits generalizability to populations with higher surgical histories. Reliance on chart review may also have introduced misclassification or missing data for some outcomes, potentially leading to underdiagnosis, and documentation practices may have differed systematically between provider types, particularly midwives and doctors. We could not confirm whether the prior CD was the most recent birth before the index pregnancy, since some women may have had an intervening vaginal birth; this could have introduced misclassification in the exposure definition. As PV was a cross-sectional study with data collection limited to the time of delivery,

postpartum maternal outcomes (puerperal endometritis, wound infection, re-operation, maternal death, and prolonged hospital stay) and perinatal outcomes (neonatal death and NICU admission) may be underrepresented in the pooled analysis. The 10-year study period enhanced sample size and temporal diversity, but changes in obstetric practice or referral patterns across this period cannot be entirely excluded as a potential source of heterogeneity. Finally, the observational design precludes causal inference; the assumptions required for causal mediation analysis, including no unmeasured mediator-outcome confounding, cannot be fully guaranteed, and findings on residual confounding should be interpreted with caution.

5 | CONCLUSION AND RECOMMENDATIONS

In conclusion, while a single prior CD was associated with adverse maternal outcomes, mediation analysis demonstrated that this risk operates almost entirely through repeat cesarean delivery, with no significant direct effect of prior CD independent of delivery mode. Prior CD was not independently associated with adverse perinatal outcomes. HIV-positive serostatus, facility referral, and low ANC attendance were independent predictors of adverse perinatal outcomes, highlighting the multifactorial nature of perinatal risk in this setting. These findings underscore the need to enhance ANC to prioritize early identification of high-risk pregnancies and individualized birth planning; establish clear clinical guidelines for trial of labor after cesarean supported by skilled monitoring and timely emergency access; invest in surgical safety through staff training, equipment readiness, and postoperative care protocols; and strengthen integrated HIV services and outreach to women with limited ANC attendance. These strategies are essential to improve maternal and perinatal outcomes in settings where cesarean rates are rising amid constrained health system capacity.

AUTHOR CONTRIBUTIONS

LT, JN, AAB, and LMB conceptualized and designed the study. LT conducted formal data analysis and drafted the manuscript. LMB, ADG, REW, JW, JAG oversaw study implementation and were responsible for data acquisition. KC, LMB, AAB, and LT designed the statistical analysis. All authors—LT, JN, KC, JW, JAG, REW, ADG, AAB, and LMB—critically reviewed and revised the manuscript for intellectual content. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The datasets used during this study are available from the corresponding author upon reasonable request.

CONSENT FOR PUBLICATION

Not applicable.

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