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Effect of maternal chronic disease on obstetric complications in twin pregnancies in a U.S. cohort

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Abstract

Objective—To evaluate the effect of maternal chronic disease on obstetric complications among twin pregnancies.

Design—Multicenter retrospective observational study.

Setting—The 12 Consortium on Safe Labor (CSL) clinical centers (19 hospitals).

Patient(s)—Twin pregnancies (n=4,821) delivered 23 weeks of gestation and classified by maternal chronic disease (either none or any of the following: asthma, depression, hypertension, diabetes, and heart, thyroid, gastrointestinal or renal disease).

Intervention(s)—None.

Main Outcome Measure(s)—Gestational age at delivery, gestational hypertension, preeclampsia, gestational diabetes, placental abruption, placenta previa, hemorrhage, chorioamnionitis, maternal postpartum fever, premature rupture of membranes, labor onset (spontaneous versus nonspontaneous), route of delivery, and maternal admission to intensive care unit.

Result(s)—Women with chronic disease delivered earlier (mean gestational length, 34.1 vs. 34.6 weeks, $p < 0.0001$) and were less likely to have term birth (risk ratio (RR): 0.80; 95% confidence interval (95% CI): 0.70-0.90). Cesarean delivery after spontaneous labor (RR: 1.20; 95% CI: 1.05-1.37) was also increased with chronic disease. No statistically significant effects were observed for other complications studied. Women who used ART were more likely to hemorrhage, independent of chronic disease, but other findings were generally similar to the non-ART sample.

Conclusion(s)—Chronic disease was associated with additional risk of earlier delivery and cesarean section after spontaneous labor in a nationwide sample of US twin pregnancies.

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Capsule—Among twin pregnancies, maternal chronic disease was associated with additional risk of earlier delivery and cesarean section after spontaneous labor, but not with other obstetric complications.

Keywords

twins; obstetric complications; assisted reproductive technology (ART)

Introduction

In recent years, the prevalence of obesity, diabetes, and hypertension have increased significantly among fertile-aged United States (U.S.) women^{1,2}. These changes, along with a concurrent demographic shift to later childbearing, have resulted in a larger proportion of pregnancies complicated by chronic diseases. Recent U.S. estimates of the prevalence of chronic disease in pregnancy report 8% of pregnancies with asthma, 5% with chronic hypertension, 2% with pre-gestational diabetes, and 1% with heart disease¹⁻⁶. Maternal chronic diseases are known to complicate singleton gestations, including increased risks for cesarean delivery, preeclampsia, preterm delivery, placental abruption, and impaired fetal growth with associated maternal and perinatal morbidity^{1,2,7}.

Another consequence of delayed childbearing has been an increase in multiple gestations, especially twins^{8,9}. The U.S. twin birth rate rose from 18.9 to 33.3 per 1,000 births between 1980 and 2009, with about one third of this trend directly attributed to older maternal age^{9,10}. The use of fertility treatments and assisted reproductive technology (ART) has also contributed to the rise in twinning. From 1997–2000, the proportion of twins attributable to ART increased from 9.1% to 11.8%, while the proportion conceived using non-ART fertility treatments increased from 17.7% to 20.9%¹¹. Twin pregnancies are in general at increased risk for adverse pregnancy outcomes, including preterm birth, low birth weight infants, preeclampsia, and cesarean delivery¹⁰.

Based on our review of the literature, using search terms twin pregnancy, maternal chronic disease and obstetric complications, the extent to which maternal chronic disease further increases the risk of obstetric complications in twins is unknown. Given the increasing prevalence of this combination of risk factors, we investigated the effects of chronic disease during pregnancy on maternal obstetric outcomes among twin pregnancies in a large, nationwide U.S. cohort.

Materials & Methods

The Consortium on Safe Labor (CSL) was a multicenter retrospective observational study conducted by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, which collected information on contemporary labor and delivery practice in the U.S. The CSL included 12 clinical centers (19 hospitals) across nine American College of Obstetricians and Gynecologists U.S. districts from 2002-2008, with 87% of births occurring between 2005 and 2007. A thorough description of the study is provided elsewhere¹². Detailed information was extracted from electronic medical records including maternal demographic characteristics, medical, reproductive and prenatal history, labor and delivery summary, and postpartum information. A validation study on several key variables indicated that the electronic medical records were an accurate representation of the medical charts¹². This project was approved by the Institutional Review Boards of all participating institutions.

Of the 228,562 total CSL deliveries, 5,050 were multiple gestation pregnancies, including 4,846 twins, 204 higher order multiples, and 25 repeat multifetal pregnancies for the same woman. Our analysis was restricted to the first twin pregnancy of women during the study to reduce unmeasured confounding and avoid statistical dependence within participants, resulting in an analytic sample of 4,821 twin pregnancies. Information for chronic diseases and pregnancy outcomes was obtained from electronic medical records and supplemented with International Classification of Diseases, 9th revision (ICD-9) codes in the discharge summary. Women were defined as having chronic disease if they had any of the following: asthma, depression, hypertension, diabetes, thyroid disorder, heart disease, gastrointestinal disorder, and renal disease (see Supplemental Table 1 for definitions and ICD-9 codes for each chronic disease). Preliminary analyses were conducted for each individual chronic disease, and then compared to the results for the aggregated group comprising any chronic disease. Because of sample size limitations and general similarity between findings for the individual diseases and the overall chronic disease group, we chose to only present findings for the overall chronic disease group. Outcomes included gestational age at delivery, hypertensive disorders of pregnancy (gestational hypertension, preeclampsia, eclampsia), gestational diabetes, placental abruption, placenta previa, hemorrhage (bleeding in the third trimester or postpartum or receiving blood transfusion postpartum), chorioamnionitis, maternal postpartum fever, premature rupture of membranes (PROM), preterm PROM (before 37 weeks), type of labor onset (pre-labor cesarean section, induction, spontaneous labor), route of delivery (cesarean section, vaginal, or combination (e.g. vaginal delivery of first twin and cesarean delivery of second twin)), and maternal admission to an intensive care unit (ICU). Mothers with chronic hypertension were excluded from the analyses for gestational hypertension/preeclampsia and mothers with diabetes were excluded from the analysis for gestational diabetes since the presence of the chronic condition precludes diagnosis of the gestational disorders.

We conducted bivariate analyses using the χ^2 test for categorical variables and t-tests for continuous variables. Multivariable regression estimated crude (adjusted for site) and fully adjusted risk ratios from models that include site, maternal age (continuous), race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander, and multiracial/other), pre-pregnancy body mass index (BMI), insurance type (private or public), and smoking during pregnancy (yes or no/unknown). Effect measures for labor admission status and route of delivery outcomes were also adjusted for prior uterine scar (yes or no). We present fully adjusted risk ratios only. Gestational age at delivery was analyzed as a binary outcome (preterm, defined as birth before 37 weeks, or term) using logistic regression, and as a continuous outcome using Kaplan–Meier survival analysis and the log-rank test.

We performed separate sensitivity analyses to determine if the effects of maternal chronic disease varied based on gestational age at delivery, sex of the twins, and use of ART. We also restricted the sample to women with normal pre-pregnancy BMI to assess whether chronic disease would have a similar impact on obstetric complications in the absence of obesity. Due to the increased risk of preterm birth among twins, and high prevalence of preterm birth (68%) in our study sample, we used stratified analyses to estimate distinct effect measures for preterm (n=3,255) and term (n=1,566) births^{13, 14}. Owing to the fact that information on twin chorionicity was not available, we used Weinberg's differential rule to estimate expected frequencies of monozygous, monochorionic, and dizygous twins^{15, 16}. We used discordant sex pairs (n=1,842) as a proxy for dizygous twin pairs and conducted an additional analysis among these pregnancies only. Of the 12 CSL sites, seven reported information on use of ART. We performed a separate analysis on these sites only (n=2,532 pregnancies), stratified by ART use. Low prevalence for maternal admission to the intensive care unit and combined delivery (vaginal/cesarean) prevented model convergence for these

outcomes in some analyses. We report frequencies, but no effect measures, for these associations. All analyses were performed using SAS 9.3 (SAS Institute, Cary, NC).

Results

Maternal chronic disease complicated 25% of twin pregnancies (n= 1,186). The majority of women (84%; n=1,000) had only one chronic disease, with asthma being the most common (9%), followed by thyroid disease (5%) and depression (5%) (supplemental Table 2). Women with chronic disease (Table 1) tended to be slightly older (30.2 vs. 29.6 years), more likely to be non-Hispanic black and less likely to be Hispanic, and more likely to smoke during pregnancy (10 vs. 5%) than women without chronic disease. The chronic disease group had a higher proportion of overweight (BMI ≥ 25 kg/m²) and obese women (BMI ≥ 30 kg/m²) and was less likely to have missing insurance status compared to women without chronic disease.

Women with twin pregnancies and chronic disease delivered earlier than women with twin pregnancies without chronic disease (34.1 vs. 34.6 weeks, $p < 0.0001$). The distribution of deliveries by gestational age for women with and without chronic disease is shown in Figure 1. The curves begin to diverge after 27 weeks of gestation and 50% of women with chronic disease delivered by 35 weeks', compared to 36 weeks' for women without chronic disease. Figure 1 also shows proportions of deliveries by gestational age among women who reported ART use, stratified by chronic disease status. In this subgroup, the difference in mean gestational length between women with chronic disease (34.3 weeks) and women without chronic disease (34.4 weeks) was not significant.

Women with chronic disease were more likely to have a cesarean delivery after spontaneous onset of labor (RR: 1.20; 95% CI: 1.05-1.37), with no difference in pre-labor cesarean delivery (Table 2). While 68% of the twin cohort delivered preterm, twin pregnancies complicated by chronic disease were an additional 20% less likely to deliver at term (RR: 0.80; 95% CI: 0.70-0.90) compared to twin pregnancies without chronic disease. The other obstetric complications we studied did not differ significantly by chronic disease status. Rates of complications were 5% and 4% for gestational hypertension, 16% and 13% for preeclampsia, 9% and 7% for gestational diabetes, 4% and 3% for placental abruption, 12% and 12% for PROM, and 13% and 11% for intrapartum hemorrhage, among women with chronic disease and with no chronic disease, respectively.

In a sensitivity analysis restricted to the seven sites that collected information on use of fertility treatment (n=2,532, 53% of our analytic sample), 299 pregnancies (12%) reported ART use. The percentage of women with chronic disease and ART (n=84, 28%) was slightly higher than the proportion with chronic disease in the overall sample (n=1,186, 25%). Women who used ART were more likely to hemorrhage, independent of chronic disease status (with chronic disease, RR: 1.63; 95% CI: 1.07-2.48; without chronic disease, RR: 1.73; 95% CI: 1.24-2.41) (Table 3). Similar to the full study group, ART pregnancies complicated by chronic disease had a decreased risk of term delivery (RR: 0.72; 95% CI: 0.55-0.95), and increased risk of cesarean delivery after spontaneous labor (RR: 1.41; 95% CI: 1.00-2.00). Compared to women with no chronic disease and no ART, women with chronic disease and ART had reduced risk of placental abruption (RR: 0.32; 95% CI: 0.10-0.99) and women without chronic disease who used ART had an increased risk of preeclampsia (RR: 1.37; 95% CI: 1.01-1.86).

Sensitivity analyses of preterm deliveries, discordant sex twin pairs, and normal weight women generated estimated effect measures generally similar to those of the main analysis, though losses in statistical power due to reduced sample size limited precision. The analysis

on the proportions of discordant and concordant sex twin pairs estimated that approximately 18% (n=853) of the overall sample was monochorionic and the remaining 82% (n=3,968) were dichorionic¹⁷.

The similar results across several sensitivity analyses suggest our overall findings were robust.

Discussion

In this large, nation-wide U.S. cohort with 4,821 twin pregnancies, we expected to observe more obstetric complications among women with chronic disease compared to their healthier counterparts. Although chronic disease was common, affecting 25% of twin pregnancies, nearly all obstetric complications studied were similar regardless of maternal chronic disease, with the exception of 3.5 days earlier delivery and 20% increased risk of cesarean delivery after spontaneous onset of labor among women with chronic disease. Importantly, we found no associations for hypertensive disorders of pregnancy, gestational diabetes, placental abruption, placenta previa, hemorrhage, chorioamnionitis, maternal postpartum fever, PROM, preterm PROM, or maternal admission to ICU.

The fact that chronic disease was not an independent risk factor for nearly all obstetric complications we studied among twin pregnancies suggests that the already increased risks associated with twinning were more important than the marginal increase associated with chronic disease.

We did observe an impact of maternal chronic disease on the timing and mode of delivery. Women with chronic disease delivered 3.5 days earlier and cesarean deliveries were more common after spontaneous labor (but not overall). Our findings of increased cesarean delivery are generally consistent with previously published studies reporting increased cesarean delivery among singleton pregnancies with maternal chronic disease^{25, 26}.

Over the last 30 years, increasing trends in obesity among women of reproductive age have mirrored those of chronic disease increase in the U.S.^{1, 27}. Consistent with these population-level trends, women in our study with any chronic disease were more likely to be overweight or obese than women without chronic disease. Previous research implicates pre-pregnancy obesity as a strong risk factor for preterm birth in singletons and twins³³⁻³⁵. Though the complex relationship between chronic disease and obesity is difficult to characterize without longitudinal data, our sensitivity analysis indicated that women with a normal pre-pregnancy BMI experienced similar risks for obstetric complications as those of the overall sample, and adjustment for pre-pregnancy BMI in the overall sample did not change results. These findings suggest that obesity does not entirely explain our findings.

We recognize that monochorionic twins tend to have increased risk of spontaneous miscarriage and early or late fetal loss, fetal growth restriction of one or both twins, stillbirth, placental abnormalities, and twin-to-twin transfusion syndrome³⁹. While our study has a wealth of clinical data, information on chorionicity was not abstracted from the electronic medical records, which prevented us from evaluating effect modification. Since the CSL captured data on deliveries 23 weeks gestation or higher, our conclusions are only applicable to twin pregnancies that have reached viability. If monochorionicity was associated with early fetal loss in the source population, our estimated proportion of 18% monochorionic twins would be inflated and the sample would be even more representative of dichorionic twins. Previous research has estimated the prevalence of monochorionicity to be between 10-20% of twins⁴⁰⁻⁴². Similar to our overall findings, monochorionicity is associated with lower gestational age at birth, higher rates of preterm birth, and cesarean delivery^{42, 43}. We attempted to examine chorionicity using a sensitivity analysis restricted

to discordant sex twin pairs, a sub-sample of dichorionic twins. Associations among discordant sex twins were similar to overall findings, so it is unlikely that chorionicity was responsible for the associations we observed.

We did not observe independent effects of ART on the timing of delivery of twins, which is consistent with previous studies of twins^{44, 45, 45, 46, 46, 47}. We observed an increased risk for hemorrhage among ART users but this risk did not vary by chronic disease status. A retrospective cohort study found modest increases in risk of postpartum hemorrhage among singleton pregnancies conceived using in vitro fertilization and embryo transfer, though no such effect was found among pregnancies conceived using ovulation stimulation or intrauterine insemination⁴⁸. A prospective cohort of dichorionic twins found no differences for postpartum bleeding between pregnancies conceived by ART and spontaneously conceived pregnancies⁴⁴, though a retrospective study of twins found increased peripartum hemorrhage in twin pregnancies conceived using fertility treatment (versus spontaneously conceived twins)⁴⁹. A recent review of 47 studies indicates that ART pregnancies are at increased risk for preeclampsia and gestational hypertension, even after adjusting for confounding⁵⁰. In our study, preeclampsia was higher in women using ART who did not have chronic disease. We also observed a decrease in placental abruption among women using ART who had a chronic disease, but note that the numbers are very small and this may be due to chance. Another limitation of our study is that the electronic medical record data lacks detailed data on fertility treatment. We did not have information on ART use for all sites and where we did have information on ART, the type of fertility treatment used was not captured. We note that the American Society for Reproductive Medicine encourages offering elective single-embryo transfer to patients when their prognosis is good to lower the risks associated with twinning and higher order multiple deliveries⁵¹. These questions are increasingly important in the context of trends in fertility treatments and maternal age and warrant further study⁹.

As noted above, our analyses are limited to information in the medical record or discharge summary and no information is available on disease severity or management. We acknowledge that this unmeasured variability in chronic disease exposure could potentially modify the effects we observed, as milder chronic disease cases may not have been captured in the medical record and effective treatment may mitigate risks. However, the prevalence of chronic disease diagnoses captured is in the expected range which suggests we do not have significant underreporting in the medical records.

Our study has a population-based sample of twin pregnancies from across the U.S., a clear strength for generalizability. The sample size was large enough to include a broad range of chronic diseases, and sufficiently powered to estimate effects for multiple obstetric, labor, and delivery complications. To our knowledge, no prior studies have examined such risks associated with maternal chronic disease in twin pregnancies.

Among twin pregnancies, women with chronic disease were more likely to experience cesarean delivery after spontaneous labor, as well as deliver earlier, than healthier mothers. The finding that other obstetric complications were generally not increased in women with chronic disease can be reassuring for patients and for clinicians as they encounter increasing numbers of patients with twin pregnancies complicated by chronic disease. Future work is needed to confirm these findings and to clarify the effect of chorionicity and fertility treatments on obstetric complications in women with chronic disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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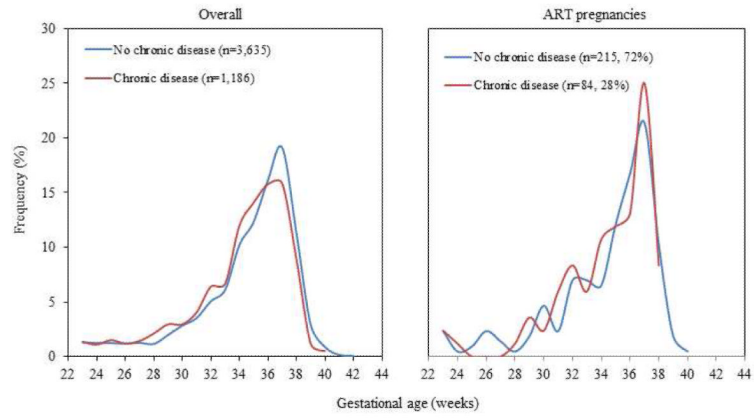


Figure 1. Distribution of gestational age at birth, stratified by chronic disease, for twin pregnancies in the Consortium on Safe Labor (n=4,821) and among twin pregnancies conceived using ART (n=299)

Table 1

Characteristics of women with twin pregnancies in the Consortium on Safe Labor (n=4,821)

	No chronic disease (n=3,635)	Any chronic disease (n=1,186)	<i>P</i>
Nulliparous	1,629 (45)	504 (43)	0.2
Maternal age (years)	29.6±6.5	30.2±6.4	0.004
Married ^a	2,362 (65)	729 (62)	0.4
Maternal race			
White, non-Hispanic	1,987 (55)	667 (56)	
African American, non-Hispanic	790 (22)	317 (27)	
Hispanic	528 (15)	114 (10)	
Asian/Pacific Islander	109 (3)	21 (2)	
Other/unknown	221 (6)	67 (6)	0.007
Pre-pregnancy BMI ^b			
<18.5	122 (3)	22 (2)	
18.5-<25	1,266 (35)	308 (26)	
25-<30	515 (14)	177 (15)	
30-<35	244 (7)	100 (8)	
35+	188 (5)	125 (11)	0.0002
Insurance			
Private	2,214 (61)	746 (63)	
Public	1,076 (30)	362 (31)	
Other/unknown	345 (10)	78 (7)	0.02
Use of ART ^c	215 (6)	84 (7)	0.2
Alcohol use during pregnancy	60 (2)	26 (2)	0.2
Smoking during pregnancy	192 (5)	117 (10)	<.0001

Data are n(%) or mean±standard deviation

^aMarried: missing for 228 participants^bBMI, body-mass index: missing for 1,754 participants^cART, assisted reproductive techniques: missing for 2,289 participants

Table 2

Adjusted risk and 95% confidence intervals for obstetric complications associated with chronic disease among women with twin pregnancies in the Consortium on Safe Labor (n=4,821)

	No chronic disease (n=3,635)	Any chronic disease (n=1,186)	Adjusted Risk Ratio
	n (%)	n (%)	RR (95% CI)
Gestational hypertension ^a	155 (4)	48 (5)	0.92 (0.66 - 1.28)
Preeclampsia ^a	486 (13)	160 (16)	1.04 (0.87 - 1.25)
Gestational diabetes ^b	262 (7)	94 (9)	1.07 (0.84 - 1.36)
Placental abruption	117 (3)	44 (4)	1.01 (0.71 - 1.44)
Placenta previa	40 (1)	17 (1)	1.23 (0.69 - 2.19)
Premature rupture of membranes (PROM)	451 (12)	143 (12)	0.92 (0.76 - 1.12)
Preterm PROM	395 (11)	132 (11)	0.96 (0.79 - 1.18)
Chorioamnionitis	177 (5)	49 (4)	0.81 (0.59 - 1.12)
Maternal fever	174 (5)	57 (5)	0.95 (0.70 - 1.29)
Hemorrhage	402 (11)	150 (13)	1.09 (0.90 - 1.31)
Exclusive vaginal delivery	1,146 (32)	316 (27)	0.89 (0.79 - 1.01)
Exclusive cesarean delivery	2,389 (66)	837 (71)	1.05 (0.97 - 1.14)
Pre-labor cesarean delivery	1,344 (37)	468 (39)	0.99 (0.89 - 1.10)
Spontaneous labors	1,651 (45)	546 (46)	1.08 (0.98 - 1.19)
Exclusive cesarean delivery	862 (24)	318 (27)	1.20 (1.05 - 1.37)
Combined vaginal/cesarean delivery	80 (2)	25 (2)	
Inductions	640 (18)	172 (15)	0.85 (0.72 - 1.01)
Exclusive cesarean delivery	179 (5)	48 (4)	0.87 (0.63 - 1.21)
Combined vaginal/cesarean delivery	24 (1)	11 (1)	
Term birth	1,252 (34)	314 (26)	0.80 (0.70 - 0.90)
Maternal admission to intensive care unit	13 (<1)	10 (1)	

All risk ratios (RR) adjusted for site, maternal age, race, pre-pregnancy BMI, insurance, and smoking during pregnancy; labor and delivery complications additionally adjusted for prior uterine scar.

^aExcludes participants with chronic hypertension.

^bExcludes participants with pre-existing diabetes.

PROM, premature rupture of membranes; ICU, intensive care unit.

Empty cells indicate that the model did not converge due to sparse data; risk ratios are not reported

Table 3

Adjusted risk and 95% confidence intervals for pregnancy complications associated with chronic disease among women with twin pregnancies in the Consortium on Safe Labor from sites reporting ART status (n=2,532)

Complication	No ART use (n=2,233)				ART use (n=299)			
	n	Risk	No chronic disease (n=1,675) n (%)	Any chronic disease ^a (n=558) RR (95% CI)	n (%)	No chronic disease ^a (n=215) RR (95% CI)	Any chronic disease ^a (n=84) RR (95% CI)	n (%)
Gestational hypertension ^b	41	0.02	17 (3)	1.21 (0.72 - 2.04)	11 (5)	1.52 (0.78 - 2.97)	3 (4)	1.85 (0.80 - 4.27)
Preeclampsia ^b	232	0.14	62 (13)	0.85 (0.65 - 1.09)	45 (21)	1.37 (1.01 - 1.86)	15 (19)	1.16 (0.78 - 1.72)
Gestational diabetes ^c	113	0.07	42 (8)	1.19 (0.86 - 1.64)	19 (9)	1.14 (0.74 - 1.76)	11 (14)	1.35 (0.80 - 2.30)
Placental abruption	70	0.04	21 (4)	0.85 (0.53 - 1.37)	2 (1)	0.37 (0.13 - 1.05)	2 (2)	0.32 (0.10 - 0.99)
Placenta previa	18	0.01	9 (2)	1.13 (0.52 - 2.48)	5 (2)	0.59 (0.20 - 1.71)	0 (0)	0.66 (0.18 - 2.40)
PROM	222	0.13	70 (13)	0.87 (0.67 - 1.13)	31 (14)	1.04 (0.73 - 1.47)	10 (12)	0.90 (0.59 - 1.39)
Preterm PROM	185	0.11	61 (11)	0.90 (0.69 - 1.19)	27 (13)	1.07 (0.73 - 1.56)	9 (11)	0.97 (0.61 - 1.53)
Chorioamnionitis	123	0.07	32 (6)	0.72 (0.49 - 1.06)	8 (4)	0.89 (0.46 - 1.70)	3 (4)	0.64 (0.30 - 1.37)
Maternal fever	113	0.07	33 (6)	0.92 (0.64 - 1.36)	10 (5)	0.80 (0.46 - 1.42)	4 (5)	0.75 (0.39 - 1.46)
Hemorrhage	182	0.11	66 (12)	0.94 (0.73 - 1.23)	39 (18)	1.73 (1.24 - 2.41)	13 (15)	1.63 (1.07 - 2.48)
Exclusive vaginal deliveries	576	0.34	161 (29)	0.84 (0.71 - 1.00)	69 (32)	1.01 (0.79 - 1.28)	18 (21)	0.85 (0.63 - 1.13)
Prelabor cesarean delivery	648	0.39	239 (43)	1.06 (0.92 - 1.22)	77 (36)	1.02 (0.83 - 1.26)	38 (45)	1.08 (0.84 - 1.38)
Spontaneous labors	696	0.42	237 (42)	1.08 (0.94 - 1.24)	94 (44)	1.00 (0.82 - 1.23)	35 (42)	1.08 (0.85 - 1.38)
Exclusive cesarean delivery	291	0.17	112 (20)	1.25 (1.02 - 1.53)	49 (23)	1.13 (0.85 - 1.51)	21 (25)	1.41 (1.00 - 2.00)
Combined vaginal/cesarean delivery	54	0.03	17 (3)	0.84 (0.50 - 1.43)	8 (4)	0.69 (0.33 - 1.42)	2 (2)	0.58 (0.24 - 1.40)
Inductions	331	0.20	82 (15)	0.73 (0.58 - 0.92)	44 (20)	1.03 (0.76 - 1.41)	11 (13)	0.75 (0.51 - 1.11)
Exclusive cesarean delivery	91	0.05	21 (4)	0.76 (0.49 - 1.17)	12 (6)	1.01 (0.58 - 1.77)	5 (6)	0.77 (0.38 - 1.55)
Combined vaginal/cesarean delivery	15	0.01	8 (1)	1.41 (0.59 - 3.40)	0 (0)		0 (0)	
Term birth	607	0.36	155 (28)	0.80 (0.68 - 0.94)	73 (34)	0.90 (0.72 - 1.13)	28 (33)	0.72 (0.55 - 0.95)
Maternal admission to ICU	3	<0.01	0 (0)		1 (<1)		1 (1)	

All risk ratios (RR) adjusted for site, maternal age, race, pre-pregnancy BMI, insurance, and smoking during pregnancy; labor and delivery complications additionally adjusted for prior uterine scar.

^aReference group: no ART, no chronic disease.

^bExcludes participants with chronic hypertension.

^cExcludes participants with pre-existing diabetes.

PROM, premature rupture of membranes; ICU, intensive care unit.

Empty cells indicate that the model did not converge due to sparse data; risk ratios are not reported.