Published in final edited form as:

Fertil Steril. 2007 August ; 88(2): 283–293.

Contemporary Risks of Maternal Morbidity and Adverse Outcomes With Increasing Maternal Age and Plurality

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Abstract

Objective: To evaluate the risks of pregnancy complications and adverse outcomes associated with increasing maternal age and higher plurality.

Design: Population-based, historical cohort study.

Setting: US birth certificates and infant death certificates.

Patients: Live births of ≥ 20 weeks gestation between 1995-2000: 22,991,306 singleton, 316,696 twin, and 12,193 triplet pregnancies.

Intervention: None

Main Outcome Measures: Pregnancy-associated hypertension, incompetent cervix, tocolysis, premature rupture of membranes, excessive bleeding at delivery, delivery < 29 weeks, and infant death.

Results: Compared to singletons, the risks for all adverse outcomes among multiple pregnancies were significantly elevated and were highest for tocolysis, delivery < 29 weeks, and infant mortality. Within pluralities, increasing maternal age was associated with significantly higher risks of pregnancy-associated hypertension, excessive bleeding, and incompetent cervix, but for twin and triplet pregnancies, significantly lower risks for tocolysis (ages ≥ 40 , singleton AOR 0.97, twin AOR 0.67, triplet AOR 0.72), delivery < 29 weeks (ages ≥ 40 , singleton AOR 1.55, twin AOR 0.72, triplet AOR 0.52), and infant mortality (ages ≥ 40 , singleton AOR 1.34, twin AOR 0.71, triplet AOR 0.42).

Conclusions: Older maternal age and higher plurality are each associated with increasing risks for many pregnancy complications, but with significantly lower risks of tocolysis, early preterm birth, and infant mortality.

Keywords

Maternal age; multiple pregnancy; pregnancy complications; early preterm birth; infant mortality

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Presented at the 26th Annual meeting of the Society for Maternal-Fetal Medicine, January 29-February 2, 2006, Miami, Florida

Introduction

In 2003 there were 136,328 infants born from multiple pregnancies in the United States, the highest number ever recorded (1). The incidence of multiple births has risen dramatically since 1980, with an 88% increase in twins and a 573% increase in triplet and higher-order births (quadruplets and quintuplets). During this same time period the percent of births among women ≥ 40 has increased more than threefold for singletons, sixfold for twins, and nearly twelve fold for triplet and higher-order multiples (1). Factors for this rapid rise include the widespread use and availability of infertility treatments, in combination with the trend of childbearing at older ages. Compared to singletons, infants of multiple pregnancies are much more likely to be born early preterm and very low birthweight, important well-documented factors that contribute to their excess morbidity and mortality (2-4). In contrast, far less is known about how multiple pregnancy affects the health of the mother. The contemporary population conceiving multiples includes a disproportionate number of older nulliparous women who, by virtue of their age and parity, are at higher risk for developing hypertension, preeclampsia, and gestational diabetes. These risks are magnified with a multiple pregnancy. Women pregnant with multiples are nearly six times more likely to be hospitalized during pregnancy, more than twice as likely to be admitted to intensive care compared to women pregnant with singletons (5-8). These hospital-based studies, though, are limited by their small sample size, lack of socioeconomic and racial diversity, and frequent failure to control for such potentially confounding factors as age and parity. The purpose of this study was to develop nationally-representative, population-based estimates of the increased risk of maternal morbidity associated with multiple pregnancy. We hypothesized that, compared to women pregnant with singletons, women pregnant with multiples experience excess morbidity that further increases with each additional fetus, and is greatest at the extremes of maternal age.

Materials and Methods

The data sets for this study include the Birth Cohort Linked Birth/Infant Death Data Set (1995-2000) and the Matched Multiple Birth Data Set (1995-2000) from the National Center for Health Statistics. For the Linked Birth/Infant Death Data Set, the birth certificates are linked to the infant death certificates, if the death occurred before one year of age. The Matched Multiple Birth Data Set reconstructs sibling sets in multiple pregnancies, also linking birth certificates to death certificates for infant deaths. For both of these datasets the most recent data available are from 1995-2000. Since the Birth Cohort Linked Birth/Infant Death Data Set includes a record for each live birth, the data were limited to only singleton births. In the Matched Multiple Birth Data Set infant death of one or more infants were identified, then the data was limited to the first birth within the dataset to avoid duplication of maternal characteristics. Both data sets were then combined, resulting in maternal and pregnancy-specific data on all singleton, twin, and triplet live births 20 weeks gestation or greater from 1995 to 2000. Analyses were conducted with and without women with diabetes or chronic hypertension. The characteristics of this dataset are given in Table 1. Institutional Review Board (IRB) approval was not sought for this study because we used a public-use, de-identified dataset, which is exempt research.

Definitions of Maternal Risks

The maternal risks evaluated in this study, as reported on the birth certificate (1), included: **Medical risk factors:** *diabetes*: metabolic disorder characterized by excessive discharge of urine and persistent thirst, includes juvenile onset, adult onset, and gestational diabetes during pregnancy; *chronic hypertension*: blood pressure persistently greater than 140/90 diagnosed prior to onset of pregnancy or before the 20th week of gestation; *pregnancy-associated hypertension*: an increase in blood pressure of at least 30 mm Hg systolic or 15 mm diastolic

on two measurements taken 6 hours apart after the 20th week of gestation; *incompetent cervix*: characterized by painless dilation of the cervix in the second trimester or early in the third trimester of pregnancy, with premature expulsion of membranes through the cervix and ballooning of the membranes into the vagina, followed by rupture of the membranes and subsequent expulsion of the fetus. **Complications of labor and delivery:** *tocolysis*: use of medications to inhibit preterm uterine contractions to extend the length of pregnancy and, therefore, avoid a preterm birth. *premature rupture of membranes* (more than 12 hours): rupture of the membranes at any time during pregnancy and more than 12 hours before the onset of labor. *All excessive bleeding in labor and delivery*: this risk was calculated as including the risk factors of abruptio placenta, placenta previa, and other excessive bleeding during labor and delivery.

The nine risks (diabetes, chronic hypertension, pregnancy-associated hypertension, incompetent cervix, tocolysis, premature rupture of membranes, excessive bleeding in labor and delivery, delivery <29 weeks, and infant death of one or more babies) were calculated as percents of plurality-specific births. Mantel-Haenszel odds ratios and 95% confidence intervals (9) were computed for each of these factors, adjusting for maternal age (in years, <20, 20-24, 25-29, 30-34, 35-39, and ≥ 40), race (white, black, and others), parity (0, 1-3, ≥ 4), and smoking status (smokers, nonsmokers, and unknown). Controlling for maternal education, trimester of prenatal care, and marital status did not significantly change the results (data not shown), and therefore the reported results are based on adjusting for the original four factors. The risks did not differ significantly with or without the women with diabetes or chronic hypertension, although both sets of analyses are shown for comparison. The reference group was singletons. These data are presented in Table 2.

Maternal Age-Specific Risks

Maternal morbidity, including the risks for complications of pregnancy and labor and delivery, delivery <29 weeks gestation, and infant death of one or more babies, was then evaluated by maternal age categories within each plurality, with age 25-29 years as the reference group. The results are given in Tables 3 and 4. The adjusted odds ratios were computed as described above except that age was not included in the adjustment.

Results

The study population included 22,991,306 singleton, 316,696 twin, and 12,193 triplet pregnancies. As shown in Table 1, all maternal characteristics differed significantly across pluralities, with mothers of multiples more likely to be older, white, of lower parity, higher education, nonsmokers, and married. Compared to singletons, mean gestation was 3.5 weeks shorter for twins and 7.0 weeks shorter for triplets. Delivery <29 weeks occurred in 0.7 percent of singletons births compared to 5.6 percent of twin births and 17.1 percent of triplet births.

The comparison of risk factors by plurality is given in Table 2. The highest increased risks for multiples compared to singletons (AORs greater than 3.0 for both twins and triplets) were for incompetent cervix, tocolysis, delivery <29 weeks of gestation, and infant mortality. Risk factors by maternal age within each plurality are given in Tables 3 and 4. Factors that generally increased with maternal age within each plurality included pregnancy-associated hypertension, and excessive bleeding in labor and delivery, while tocolysis decreased with maternal age within each plurality. The major differences by maternal age within pluralities were for PROM (increasing with maternal age for singleton pregnancies, but not significantly different across maternal age categories for twins and triplets), and delivery <29 weeks and infant mortality (u-shaped relationship for singletons, but decreasing significantly with maternal age for twins and triplets).

Discussion

This is the first population-based report to our knowledge of the contemporary risks for maternal morbidity with increasing maternal age and plurality in the United States. Our results quantify the magnification of risk with twins and triplets, including the eight-fold and 34-fold increased risk for delivery <29 weeks, and the fourfold and 13-fold increased risk for infant mortality, respectively. Within pluralities, these risks are highest among the youngest mothers of all pluralities and, surprisingly, lowest among the oldest mothers of twins and triplets.

Infertility affects an estimated 15 percent of women of reproductive age (10). The use of fertility-enhancing therapies, including assisted reproductive technologies (ART), has risen steadily in the United States due to several factors, including older maternal ages and increasing insurance coverage (11,12). The use of ART carries a 30-50% risk of resulting in a multifetal pregnancy, depending on the medications and techniques used. Older maternal age requires more aggressive therapies to achieve a pregnancy, including transferring more embryos. The twin and triplet and higher-order multiple rates for pregnancies conceived by assisted reproductive technology is estimated to be 14-fold and 54-fold higher, respectively, than for the US as a whole (13). A growing body of literature suggests an excess of adverse outcomes in pregnancies after infertility treatment, particularly among singleton pregnancies (14-16). An important underlying mechanism may be a genetic predisposition to factors associated with infertility, including allelic variants in cytokine genes known to stimulate inflammation or those known to down-regulate the anti-inflammatory response. Recent investigations have evaluated the association between HLA DQ alleles and interleukin-10 (IL-10) polymorphism associated with Chlamydia trachomatis-related tubal factor infertility (17,18), interleukin-6 (IL-6) in women with infertility from endometriosis (19), cytokine gene polymorphism and implantation (20), and matrix metalloproteinase-9 (MMP-9) and preterm premature rupture of membranes (21). In a recent review, Ness (22) suggests that although women with a robust inflammatory response may be more likely to survive to reproduce, their reproductive experiences may be less successful than women who are less responsive. In women with assisted conceptions, the genetic factors that may have lead to their infertility may also contribute to inflammation during pregnancy and result in fetal growth restriction and preterm birth.

Older maternal age, although a well-established risk factor in singleton pregnancies, may have a different implication for multiple pregnancies resulting from ART (23,24). In spontaneous conceptions, there is a concern that older maternal age may be associated with an increase in obstetric complications secondary to a higher incidence of underlying medical disease, decreased cardiovascular reserve, and diminished ability to adapt to physical stress that may accompany aging. The increased incidences of diabetes, chronic hypertension, and pregnancy-induced hypertension in our study confirms prior reports (25,26), and most likely reflects these age-related changes. In ART pregnancies, the proportion of women who use donor eggs increases exponentially after age 40 (<5% of cycles among women <35 years of age to 77% of cycles among women >45 years of age) (27). The use of donor eggs may decrease the fetal genetic contribution to both inflammation and prematurity and helps explain the surprising findings in this study that there is no significant increase in PROM and significantly less tocolysis and early preterm delivery among older mothers of twins and triplets (28,29).

The only other population-based maternal morbidity risk estimates for multiple pregnancy are from the Latin America Center for Perinatology and Human Development in Montevideo, Uruguay (8). These analyses are based on more than 885,000 live births and stillbirths of at least 20 weeks gestation, including more than 15,000 multiple pregnancies delivered between 1985-97. All multiple births were grouped together, and included 15,407 sets of twins, 71 sets of triplets, five sets of quadruplets, and one set of quintuplets. Adjusting for potentially

confounding factors (including maternal age and parity), women pregnant with multiples vs singletons had significantly higher risks for preeclampsia (AOR 2.2, 95% CI, 1.9-2.5), preterm labor (AOR 3.8, 95% CI, 3.6-4.0), anemia (AOR 1.8, 95% CI 1.6-2.1), postpartum hemorrhage (AOR 2.0, 95% CI, 1.9-2.0), and puerperal endometritis (AOR 1.8, 95% CI 1.7-1.9). Although these risks are generally in agreement with our results, they are not completely comparable. By grouping all multiple pregnancies together, these researchers have masked the higher risks with increasing plurality. In addition, these results are hospital-based and from 18 developing countries, where both patient characteristics and healthcare (including the availability and use of ART) differ substantially from that of the US.

Extremes of maternal age are well-established risk factors for adverse pregnancy outcomes, but with different etiologies. For the woman less than 20 years of age, there may be competition with the growing fetus or fetuses for nutrients, as the woman may still be growing herself. The adolescent mother is also more likely to have unfavorable social and economic circumstances. In their analysis of over 850,000 Latin American women younger than age 25 who gave birth to singletons between 1985-2003, Conde-Agudelo et al (30) also reported lower rates of bleeding and higher risks for early preterm birth, which were comparable to our findings. Although growth restriction and prematurity account for a substantial proportion of infant mortality, particularly for multiples, even normal infants have a higher mortality rate when born to adolescent mothers (31). In their study of singleton first births, Phipps et al (31) reported that healthy full-term infants born to the youngest mothers (≤ 15 years of age) had a threefold higher risk of postneonatal death compared to those born to mothers ages 23-29. Although the risk decreased with advancing age and was highest among the youngest mothers, it was still significantly higher for women ages 20-22 (AOR 1.5, 95% CI, 1.4-1.7). Following a similar pattern, the risk of postneonatal mortality due to possible neglect or abuse was highest among the youngest age group (AOR 5.1, 95% CI 4.0-6.5), but was still significantly elevated for infants born to women ages 20-22 (AOR 2.1, 95% CI 1.8-2.5) compared to those born to women ages 23-29.

The steep increase in triplet and higher-order births that occurred in the late 1990s has abated, with rates stable since peaking in 1999 (1). This reflects efforts on the part of the American College of Obstetricians and Gynecologists and the American Society of Reproductive Medicine to prevent higher-order multiple pregnancies through their national recommendations (32,33), as well as refinements in ART procedures and other factors during recent years (34,35). As indicated by the findings in this study, multiple pregnancies are at greatly increased risk for adverse outcomes, for both the mother and her infants, risks that are often not appreciated by women seeking infertility treatment. A substantial proportion of these women want a multiple pregnancy, particularly if they have no prior children (36). Recent studies indicate that multiple births are associated with fivefold increased risk of severe parenting stress (37), as well as twice the risk of lower quality of life, social stigma, and maternal depression (38). Although the study by Phipps et al (31) on young maternal age and the risk of postneonatal death was based on singleton births, it is very likely that the risks are magnified even further with twins and triplets.

One of the limitations of this analysis is the inability to differentiate pregnancies which were the result of infertility treatment. With the 2003 revision of the birth certificate, this will be possible, including information on types of treatments (medications and ART). The revision will also include additional measures of maternal morbidity (maternal transfusion, ruptured uterus, unplanned hysterectomy and admission to intensive care). Known limitations of birth certificate data include the unreliability of selected items (such as maternal weight gain), the high rate of missing values for other items (such as age of father) (1). In addition, it is known that because of variation in the birth certificate from State to State, a percent of records in the national data file will have items that are not stated: 0.5% for obstetric procedures, 0.6% for

complications of labor and/or delivery, 0.5% for method of delivery, 1.0% for abnormal conditions of the newborn, and 0.9% for congenital anomalies of the newborn (1). A recent population-based validation study from Washington State (39) compared data on the birth certificate to hospital discharge data. These researchers found that medical conditions and complications were underreported on birth certificates by about 50 percent. This suggests that the magnitude of the risks may be even higher than reported in our study.

In summary, our study found that within each plurality (singletons, twins, and triplets), increasing maternal age was associated with significantly higher risks of pregnancy-associated hypertension, excessive bleeding, and incompetent cervix, but surprisingly for multiples, lower risks for tocolysis, delivery <29 weeks, and infant mortality. Compared to pregnancy outcomes for women ages 25-29 years, the risk for delivery <29 weeks increased for women <20 years of age by 42 percent, 52 percent, and 47 percent, respectively, with singletons, twins, and triplets. Likewise, compared to women ages 25-29 years, the risk of infant mortality of one or more babies for women <20 years of age increased by 63 percent, 89 percent, and more than 200 percent, respectively, with singletons, twins, and triplets. These findings highlight the need for specialized prenatal care to reduce complications and adverse outcomes in twin and triplet pregnancies (40), and the need for ongoing social and medical care beyond the prenatal and perinatal periods, particularly for younger mothers and mothers of multiples.

Acknowledgements

This study was supported by grants R03 HD048498 and R03 HD047627 from NIH/NICHD.

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Table 1

Live Births by Maternal Characteristics and Plurality, 1995-2000*

Study Population Characteristic (N)	All Women			P Value	Women Without Diabetes or Chronic Hypertension			P Value
	Singletons (22,991,306)	Twins (316,696)	Triples (12,193)		Singletons (21,982,911)	Twins (298,172)	Triples (11,075)	
Maternal Age (years)	26.96 (6.2)	28.87 (6.1)	31.75 (5.1)	<0.0001	26.9 (6.1)	28.8 (6.1)	31.7 (5.2)	<0.0001
Maternal Age Groups (%)								
<20	12.7	6.8	1.5		13.0	7.1	1.5	
20-24	24.8	19.0	6.4		25.1	19.3	6.7	
25-29	27.3	26.8	23.1	<0.0001	27.3	27.0	23.3	<0.0001
30-34	22.7	28.4	40.5		22.4	28.2	40.5	
35-39	10.4	15.6	23.1		10.1	15.2	22.6	
>40	2.1	3.4	5.5		1.9	3.2	5.4	
Maternal Race (%)								
White	83.7	81.8	90.6		79.1	79.0	89.4	
Black	15.0	16.7	7.7	<0.0001	15.5	17.2	7.9	<0.0001
Other	1.3	1.5	1.7		5.4	3.8	2.7	
Maternal Parity (%)								
0	41.0	35.9	53.3	<0.0001	41.2	35.9	53.3	<0.0001
1-3	54.9	58.5	43.5		54.8	58.5	43.6	
>4	4.1	5.6	3.2		4.0	5.6	3.1	
Maternal Education (yrs. %)								
≤12	54.4	46.1	26.0		54.5	46.3	26.2	
>12	55.8	47.5	27.7	<0.0001	44.1	52.3	72.2	<0.0001
Unknown/Not Stated	1.4	1.4	1.7		1.3	1.4	1.6	
Marital Status (%)								
Married	67.2	72.3	90.7		66.9	72.0	90.5	
Unmarried	32.8	27.5	8.7	<0.0001	33.1	27.8	9.0	<0.0001
Unknown/Not Stated	0.0	0.2	0.6		0.0	0.2	0.6	
Trimester Care Began (%)								
First or Second	93.9	94.3	94.2		94.0	94.4	94.2	
Third or No Care	3.8	2.6	1.1	<0.0001	3.8	2.5	1.2	<0.0001
Unknown/Not Stated	2.3	3.1	4.7		2.2	3.0	4.6	
Smoking during pregnancy (%)								
Smoker	9.7	8.6	2.8		9.8	8.7	3.0	
Nonsmoker	69.9	73.7	81.7	<0.0001	70.0	73.9	82.1	<0.0001
Unknown/Not stated	20.4	17.7	15.5		20.2	17.4	14.9	
Length of Gestation (weeks, SD)	38.9 (2.5)	35.5 (3.6)	32.0 (4.0)	<0.0001	39.0 (2.5)	35.5 (3.6)	32.0 (4.0)	<0.0001

* data presented as means (SD) or percentages

Table 2
Comparison of Pregnancy Complications and Adverse Outcomes for Twins and Triplets versus Singletons*

ALL WOMEN	SINGLETONS			TWINS			TRIPLET			
	Percent	AOR [§]	Percent	AOR [§]	95% CI	P Value	Percent	AOR [§]	95% CI	P Value
Diabetes	2.70	1.00	3.57	1.23	1.20-1.25	<0.0001	6.29	2.05	1.89-2.22	<0.0001
Chronic hypertension (<20 weeks)	0.75	1.00	1.07	1.28	1.23-1.33	<0.0001	1.34	1.46	1.23-1.73	<0.0001
Pregnancy-associated hypertension	3.75	1.00	8.13	2.33	2.30-2.36	<0.0001	11.17	2.79	2.62-2.96	<0.0001
Incompetent cervix	0.24	1.00	0.91	3.47	3.33-3.62	<0.0001	4.69	18.57	16.93-20.38	<0.0001
Tocolysis	2.06	1.00	8.55	4.54	4.47-4.60	<0.0001	21.10	13.27	12.65-13.92	<0.0001
Premature rupture of membranes (>12 hours)	2.68	1.00	6.17	2.39	2.35-2.43	<0.0001	9.61	3.36	3.15-3.59	<0.0001
All excessive bleeding in L&D ^{**}	1.38	1.00	2.68	1.91	1.86-1.95	<0.0001	3.95	2.82	2.55-3.11	<0.0001
Delivery <29 weeks gestation	0.76	1.00	5.59	8.00	7.86-8.15	<0.0001	16.90	32.59	30.91-34.35	<0.0001
Infant death of one or more babies	0.61	1.00	2.42	4.17	4.07-4.28	<0.0001	6.17	13.26	12.22-14.38	<0.0001
WOMEN WITHOUT DIABETES OR CHRONIC HYPERTENSION	SINGLETONS			TWINS			TRIPLET			
	Percent	AOR [§]	Percent	AOR [§]	95% CI	P Value	Percent	AOR [§]	95% CI	P Value
Pregnancy-associated hypertension	3.40	1.00	7.79	2.45	2.42-2.48	<0.0001	11.17	3.04	2.86-3.22	<0.0001
Incompetent cervix	0.22	1.00	0.85	3.45	3.32-3.60	<0.0001	4.66	19.81	18.12-21.66	<0.0001
Tocolysis	1.97	1.00	8.27	4.56	4.49-4.62	<0.0001	20.59	13.30	12.70-13.93	<0.0001
Premature rupture of membranes (>12 hours)	2.58	1.00	6.11	2.44	2.40-2.48	<0.0001	10.00	3.61	3.39-3.84	<0.0001
All excessive bleeding in L&D ^{**}	1.32	1.00	2.61	1.93	1.89-1.98	<0.0001	3.85	2.83	2.57-3.12	<0.0001
Delivery <29 weeks gestation	0.73	1.00	5.57	8.10	7.97-8.24	<0.0001	17.11	33.89	32.21-35.66	<0.0001
Infant death of one or more babies	0.59	1.00	2.42	4.21	4.11-4.31	<0.0001	6.24	13.58	12.56-14.69	<0.0001

* Models adjusted for maternal age, race, parity, and smoking status.

** Includes abruptio placenta, placenta previa, and other excessive bleeding during labor and delivery.

Table 3
Complications of Pregnancy, Delivery, and Infant Mortality by Maternal Age and Plurality, All Women

Factor	Age	Singletons				Twins				Triplets			
		Percent	AOR [*]	95% CI	P Value	Percent	AOR [*]	95% CI	P Value	Percent	AOR [*]	95% CI	P Value
Diabetes	<20	0.87	0.30	0.30-0.30	<0.0001	1.02	0.31	0.26-0.36	<0.0001	3.36	0.60	0.25-1.43	0.26
	20-24	1.70	0.61	0.61-0.62	<0.0001	2.02	0.62	0.58-0.67	<0.0001	3.81	0.69	0.45-1.06	0.09
	25-29	2.68	1.00	---	---	3.23	1.00	---	---	5.56	1.00	---	---
	30-34	3.57	1.37	1.36-1.38	<0.0001	4.34	1.37	1.29-1.44	<0.0001	6.22	1.13	0.91-1.40	0.27
	35-39	4.87	1.89	1.87-1.91	<0.0001	5.19	1.64	1.54-1.75	<0.0001	7.81	1.42	1.13-1.80	0.003
Chronic Hypertension (<20 weeks)	≥40	6.69	2.64	2.60-2.68	<0.0001	7.03	2.24	2.03-2.46	<0.0001	7.28	1.32	0.91-1.92	0.14
	<20	0.26	0.33	0.32-0.34	<0.0001	0.48	0.46	0.36-0.59	<0.0001	2.65	2.16	0.69-6.82	0.21
Pregnancy-associated hypertension	20-24	0.45	0.63	0.62-0.64	<0.0001	0.72	0.76	0.67-0.87	<0.0001	0.30	0.24	0.06-0.97	0.045
	25-29	0.67	1.00	---	---	0.89	1.00	---	---	1.22	1.00	---	---
	30-34	0.94	1.46	1.44-1.48	<0.0001	1.16	1.39	1.25-1.54	<0.0001	1.17	0.96	0.61-1.51	0.85
	35-39	1.54	2.43	2.39-2.47	<0.0001	1.62	1.94	1.73-2.17	<0.0001	1.65	1.36	0.84-2.20	0.21
	≥40	2.71	4.27	4.17-4.37	<0.0001	2.67	3.24	2.77-3.80	<0.0001	3.36	2.73	1.24-6.00	0.01
Incompetent cervix	<20	0.11	0.44	0.42-0.46	<0.0001	0.59	0.54	0.44-0.67	<0.0001	1.34	0.24	0.06-0.97	0.04
	20-24	0.18	0.72	0.70-0.74	<0.0001	0.60	0.65	0.57-0.75	<0.0001	2.74	0.56	0.34-0.91	0.02
	25-29	0.24	1.00	---	---	0.89	1.00	---	---	5.44	1.00	---	---
	30-34	0.31	1.29	1.26-1.32	<0.0001	1.07	1.25	1.12-1.39	<0.0001	5.42	1.00	0.80-1.24	0.98
	35-39	0.39	1.64	1.59-1.68	<0.0001	1.11	1.32	1.16-1.50	<0.0001	3.73	0.69	0.52-0.91	0.007
Tocolysis	≥40	0.42	1.74	1.65-1.84	<0.0001	1.15	1.33	1.06-1.66	0.012	3.17	0.55	0.33-0.93	0.02
	<20	2.38	1.18	1.16-1.19	<0.0001	10.35	1.16	1.10-1.23	<0.0001	23.33	1.19	0.80-1.77	0.39
	20-24	2.19	1.08	1.07-1.09	<0.0001	9.13	1.03	0.99-1.07	0.167	21.31	1.01	0.82-1.25	0.91
	25-29	2.01	1.00	---	---	9.09	1.00	---	---	22.27	1.00	---	---
	30-34	1.88	0.94	0.93-0.95	<0.0001	8.12	0.88	0.84-0.91	<0.0001	22.19	0.98	0.87-1.10	0.72
PROM(>12 hours)	35-39	1.87	0.93	0.92-0.94	<0.0001	7.27	0.78	0.75-0.82	<0.0001	18.91	0.81	0.70-0.93	0.003
	≥40	1.99	0.99	0.97-1.02	0.628	6.37	0.67	0.61-0.73	<0.0001	16.11	0.66	0.51-0.84	0.001
	<20	2.78	0.79	0.78-0.80	<0.0001	6.85	0.94	0.88-1.01	0.100	12.00	1.17	0.68-2.00	0.58
	20-24	2.58	0.91	0.90-0.92	<0.0001	6.06	0.94	0.90-0.99	0.017	12.04	1.31	1.00-1.73	0.054
	25-29	2.58	1.00	---	---	6.13	1.00	---	---	9.68	1.00	---	---
All excessive bleeding in L&D ^{**}	30-34	2.68	1.16	1.15-1.17	<0.0001	6.15	1.04	1.00-1.09	0.076	9.53	0.99	0.84-1.18	0.95
	35-39	2.84	1.31	1.30-1.33	<0.0001	6.07	1.05	1.00-1.11	0.059	8.78	0.92	0.76-1.13	0.43
	≥40	3.21	1.50	1.47-1.53	<0.0001	6.36	1.07	0.98-1.18	0.149	9.83	1.03	0.75-1.41	0.85
	<20	1.13	0.87	0.86-0.89	<0.0001	2.28	0.95	0.84-1.06	0.340	3.97	1.08	0.46-2.52	0.87
	20-24	1.21	0.91	0.90-0.92	<0.0001	2.27	0.93	0.86-1.00	0.066	2.73	0.77	0.46-1.27	0.31
	25-29	1.30	1.00	---	---	2.45	1.00	---	---	3.97	1.00	---	---
	30-34	1.50	1.17	1.16-1.18	<0.0001	2.83	1.17	1.09-1.24	<0.0001	3.74	0.92	0.71-1.19	0.53
	35-39	1.86	1.45	1.43-1.47	<0.0001	3.19	1.33	1.23-1.43	<0.0001	4.43	1.10	0.83-1.46	0.50
	≥40	2.39	1.87	1.82-1.91	<0.0001	4.35	1.82	1.62-2.05	<0.0001	4.78	1.17	0.75-1.81	0.49

Factor	Age	Singletons [§]			Twins [§]			Triplets [§]		
		Percent	AOR [§]	95% CI	P Value	Percent	AOR [§]	95% CI	P Value	P Value
Delivery <29 weeks	<20	1.20	1.48	1.46-1.51	<0.0001	10.50	1.57	1.47-1.66	<0.0001	0.03
	20-24	0.79	1.09	1.08-1.11	<0.0001	6.93	1.16	1.11-1.22	<0.0001	0.009
	25-29	0.63	1.00	---	---	5.54	1.00	---	---	---
	30-34	0.62	1.07	1.05-1.08	<0.0001	4.49	0.85	0.81-0.89	<0.0001	<0.0001
	35-39	0.78	1.33	1.31-1.36	<0.0001	4.14	0.80	0.76-0.85	<0.0001	<0.0001
Infant death of one or more babies	≥40	0.97	1.62	1.56-1.68	<0.0001	3.82	0.72	0.64-0.81	<0.0001	<0.0001
	<20	0.91	1.67	1.64-1.70	<0.0001	4.91	1.89	1.73-2.07	<0.0001	0.25
	20-24	0.69	1.26	1.24-1.28	<0.0001	3.22	1.33	1.24-1.43	<0.0001	0.001
	25-29	0.51	1.00	---	---	2.50	1.00	---	---	---
	30-34	0.74	0.96	0.94-0.97	<0.0001	1.87	0.86	0.80-0.92	<0.0001	0.0003
	35-39	0.55	1.10	1.08-1.13	<0.0001	1.68	0.77	0.71-0.85	<0.0001	<0.0001
	≥40	0.74	1.44	1.38-1.50	<0.0001	1.51	0.69	0.57-0.83	<0.0001	<0.0001

Values in italics are based on small numbers (<20 in numerator or denominator) and should be interpreted with caution.

* Models adjusted for maternal race, parity, and smoking status.

** Includes abruptio placenta, placenta previa, and other excessive bleeding during labor and delivery.

Table 4
Complications of Pregnancy, Delivery, and Infant Mortality by Maternal Age and Plurality, Women Without Diabetes or Chronic Hypertension

Factor	Age	Singletons			Twins			Triplets		
		Percent	AOR*	95% CI	P Value	Percent	AOR*	95% CI	P Value	P Value
Pregnancy-Induced Hypertension	<20	4.07	0.88	0.88-0.89	<0.0001	9.18	1.01	0.95-1.07	0.76	0.24-1.00
	20-24	3.48	0.96	0.96-0.97	<0.0001	7.51	0.99	0.95-1.03	0.67	0.58-1.07
	25-29	3.31	1.00	-----	-----	7.57	1.00	-----	-----	-----
	30-34	3.01	0.99	0.99-1.00	<0.0001	7.51	1.01	0.97-1.04	0.73	0.99-1.35
	35-39	3.28	1.17	1.16-1.18	<0.0001	7.75	1.08	1.03-1.12	0.001	0.93-1.33
Incompetent Cervix	≥40	4.00	1.50	1.47-1.52	<0.0001	10.88	1.49	1.39-1.60	<0.0001	1.16-1.98
	<20	0.11	0.43	0.42-0.45	<0.0001	0.57	0.54	0.44-0.65	<0.0001	0.10-1.28
	20-24	0.17	0.71	0.69-0.73	<0.0001	0.58	0.66	0.58-0.76	<0.0001	0.22
	25-29	0.22	1.00	-----	-----	0.83	1.00	-----	-----	0.13-0.62
	30-34	0.28	1.28	1.25-1.32	<0.0001	0.99	1.26	1.13-1.39	<0.0001	0.69-1.26
Tocolysis	35-39	0.35	1.63	1.59-1.68	<0.0001	1.04	1.35	1.20-1.53	<0.0001	0.49-1.01
	≥40	0.37	1.76	1.67-1.85	<0.0001	0.99	1.28	1.03-1.59	0.028	0.37-1.25
	<20	2.27	1.19	1.17-1.20	<0.0001	9.93	1.14	1.08-1.21	<0.0001	0.71-1.75
	20-24	2.11	1.09	1.08-1.10	<0.0001	8.84	1.03	0.99-1.07	0.142	0.75-1.26
	25-29	1.93	1.00	-----	-----	8.75	1.00	-----	-----	0.842
PROM (>12 hours)	30-34	1.80	0.94	0.93-0.95	<0.0001	7.89	0.89	0.86-0.92	<0.0001	0.79-1.10
	35-39	1.77	0.93	0.92-0.94	<0.0001	7.07	0.80	0.76-0.83	<0.0001	0.73-1.05
	≥40	1.83	0.97	0.94-0.99	<0.0001	6.11	0.67	0.62-0.74	<0.0001	0.53-0.97
	<20	2.68	0.78	0.77-0.78	<0.0001	6.76	0.92	0.87-0.99	0.017	0.77-2.46
	20-24	2.48	0.89	0.88-0.89	<0.0001	6.00	0.94	0.90-0.98	0.007	1.38
All excessive bleeding in L&D	25-29	2.53	1.00	-----	-----	6.08	1.00	-----	-----	0.83-1.61
	30-34	2.59	1.13	1.13-1.14	<0.0001	6.06	1.04	0.99-1.08	0.093	1.16
	35-39	2.74	1.27	1.26-1.28	<0.0001	6.02	1.06	1.00-1.11	0.032	1.00
	≥40	3.03	1.42	1.40-1.45	<0.0001	6.28	1.07	0.98-1.17	0.155	0.94
	<20	1.09	0.91	0.89-0.92	<0.0001	2.26	0.97	0.87-1.08	0.527	0.70-1.15
Delivery <29 weeks	20-24	1.15	0.93	0.92-0.94	<0.0001	2.25	0.95	0.88-1.02	0.168	0.50-1.15
	25-29	1.25	1.00	-----	-----	2.38	1.00	-----	-----	0.96-4.74
	30-34	1.44	1.16	1.15-1.17	<0.0001	2.74	1.15	1.08-1.23	<0.0001	2.13
	35-39	1.77	1.42	1.40-1.42	<0.0001	3.11	1.32	1.23-1.41	<0.0001	0.67
	≥40	2.23	1.76	1.72-1.80	<0.0001	4.10	1.75	1.57-1.96	<0.0001	1.00
Infant death of one or more babies	<20	1.14	1.42	1.39-1.44	<0.0001	10.27	1.52	1.43-1.61	<0.0001	0.97-2.23
	20-24	0.75	1.06	1.05-1.08	<0.0001	6.84	1.16	1.11-1.21	<0.0001	1.47
	25-29	0.60	1.00	-----	-----	5.47	1.00	-----	-----	0.97-2.23
	30-34	0.59	1.08	1.06-1.09	<0.0001	4.55	0.88	0.84-0.92	<0.0001	0.87-1.43
	35-39	0.73	1.32	1.29-1.34	<0.0001	4.23	0.83	0.78-0.88	<0.0001	1.12
	≥40	0.90	1.55	1.50-1.60	<0.0001	3.80	0.72	0.65-0.81	<0.0001	1.00
	<20	0.88	1.63	1.60-1.66	<0.0001	4.89	1.89	1.74-2.05	<0.0001	0.69
	20-24	0.67	1.24	1.22-1.26	<0.0001	3.15	1.32	1.24-1.41	<0.0001	0.58-0.82
	25-29	0.50	1.00	-----	-----	2.27	1.00	-----	-----	0.47-0.71
	30-34	0.46	0.95	0.93-0.97	<0.0001	1.91	0.88	0.82-0.94	<0.0001	0.37-0.75
	35-39	0.53	1.07	1.05-1.09	<0.0001	1.74	0.81	0.74-0.88	<0.0001	1.23-3.46

Factor	Age	Singletons			Twins			Triplets		
		Percent	AOR [§]	95% CI	P Value	Percent	AOR [§]	95% CI	P Value	P Value

Values in italics are based on small numbers (<20 in numerator or denominator) and should be interpreted with caution.

* Models adjusted for maternal race, parity, and smoking status.

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