

Outcomes of Twin Pregnancies in Women 45 Years of Age or Older

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OBJECTIVE: To investigate outcomes of twin gestations in women 45 years or older at the time of delivery.

METHODS: This was a retrospective cohort study of 139 women with twin gestations who were at least 45 years old when they delivered. They were cared for at two referral centers between 2005 and 2016. Analysis included baseline characteristics and pregnancy outcomes including mode of delivery, gestational age at delivery, hypertensive disease in pregnancy, gestational diabetes, and fetal growth restriction. Univariate analysis of the association between patient characteristics and outcomes was performed.

RESULTS: The mean maternal age at delivery was 47.3 ± 1.9 years with 99.3% undergoing in vitro fertilization and 95% using donor eggs. Patients had low baseline rates of hypertension (7.2%), obesity (9.5%), and pregestational diabetes (1.4%). The average gestational age of delivery was 35.4 weeks; 22.3% delivered before 34 weeks of gestation. There were high rates of cesarean delivery (93.5%, 95% confidence interval [CI] 87.7–96.8%), preeclampsia (44.6%, 95% CI 36.3–53.3%), and gestational diabetes (19%, 95% CI 13.0–26.8%). Preeclampsia developed in 50.5% of nulliparous women compared with 30.5% of women with a prior birth ($P=.028$). Preterm birth at less than 34 weeks of gestation occurred in 18.1% of women of white race compared with 30.3% of women of non-white race ($P=.036$).

CONCLUSION: Twin pregnancy in a predominantly healthy cohort of women who were at least 45 years old when they delivered was associated with high rates of cesarean delivery, preeclampsia, and gestational diabetes, but overall favorable outcomes.

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Pregnancies in the fifth and sixth decades of life have been increasing with the advancement of assisted reproductive technology and the use of donor oocytes.¹ The association of advanced maternal age with maternal and neonatal outcomes has traditionally been evaluated in women 35 years or older at the time of delivery. Advanced maternal age is associated with increased risk of perinatal morbidity and mortality in singleton pregnancies.^{2–5} However, prior studies included few women older than 45 years. One study looking at mostly singleton pregnancies in women 45 years old or older compared with younger women found an increase in gestational diabetes, hypertensive complications, and preterm delivery.⁶ In addition, multiple studies have found an increase in cesarean delivery in this age group.^{6,7}

The number and rates of twin births continue to rise and now account for 3.4% of all births in the United States.⁸ It is known that adverse maternal and perinatal outcomes are increased in twin gestation compared with singletons.⁹ It is generally believed that older gravidas with twin gestation are at increased risk compared with their younger counterparts in a similar or additive way as in singleton pregnancies. There is limited information, however, on how advanced maternal age contributes to these outcomes. One study found a higher cesarean delivery rate and a greater mean gestational age of delivery in women of advanced maternal age (35 years or older) compared with younger women with twins but otherwise no significant difference in adverse outcomes.¹⁰ This study, however, included few women who were at least 45 years old.

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Table 1. Baseline Characteristics of the Cohort

Characteristic	Value
No. of patients	139
Age at delivery (y)	47.3±1.9
Age (y)	45.0–53.2
White race	105 (75.5, 67.8–81.9)
Nulliparous	99 (71.2, 63.2–78.1)
Prepregnancy BMI (kg/m ²)	24.3±4.3
Prepregnancy obesity (BMI 30 or greater)	13 (9.5, 5.6–15.3)
In vitro fertilization	138 (99.3, 96.0–99.9)
Egg donor	132 (95.0, 90.0–97.5)
Multifetal pregnancy reduction	3 (2.2, 0.7–6.2)
Chorionicity	
Dichorionic–diamniotic	132 (95.0, 90.0–97.5)
Monochorionic–diamniotic	7 (5.0, 2.5–10.0)
Chronic hypertension	10 (7.2, 4.0–12.7)
Pregestational diabetes	2 (1.4, 0.4–5.1)
Anticoagulation in pregnancy	9 (6.5, 3.2–12.3)
Low-dose aspirin in pregnancy	60 (43.2, 34.9–51.8)

BMI, body mass index.

Data are n (%; 95% confidence interval) or mean±standard deviation.

The purpose of our study is to describe outcomes for women with twin pregnancies who were at least 45 years old at the time of delivery and to examine whether, in this cohort, there are risk factors associated with adverse outcomes.

MATERIALS AND METHODS

This was a retrospective cohort study of all twin deliveries at 24 weeks of gestation or greater at two large referral centers for twin pregnancies in New York City from June 2005 to June 2016. We identified all women 45 years or older at delivery and reviewed their electronic medical records for baseline characteristics and pregnancy outcomes. Institutional review board approval for this retrospective study was obtained at each center.

Baseline characteristics examined were maternal age, race, parity, use of assisted reproduction, chorionicity, medical comorbidities including obesity (prepregnancy body mass index [calculated as weight (kg)/[height (m)]² 30), hypertension, diabetes, and the use of anticoagulation and low-dose aspirin. Pregnancy outcomes analyzed were gestational age at delivery, preterm birth and indicated preterm birth, birth weight, and birth weight percentiles.¹¹ Pregnancy complications included placental abruption, placenta previa, fetal demise, and fetal anomaly. Adverse maternal outcomes included gestational diabetes, preeclampsia, transfusion, hysterectomy, and cesarean delivery. Gestational age was determined

Table 2. Outcomes of the Cohort of Women at Least 45 Years Old When They Delivered Twins

Characteristic	Value
No. of patients	139
Gestational age at delivery (wk)	35.4±2.3
Any preterm birth (wk of gestation)	
Less than 28	1 (0.7, 0.0–4.5)
Less than 32	10 (7.2, 4.0–12.7)
Less than 34	30 (22.3, 15.2–29.5)
Less than 37	101 (72.7, 64.7–79.4)
Indicated preterm birth at less than 34 wk of gestation	19 (13.7, 8.6–20.8)
Cesarean delivery	
All	130 (93.5, 87.7–96.8)
After labor	11/19 (57.9, 34.0–78.9)
Placental abruption	1 (0.7, 0.0–4.5)
Placenta previa	4 (2.9, 0.9–7.7)
Preeclampsia	62 (44.6, 36.3–53.3)
Gestational diabetes	26/137 (19.0, 13.0–26.8)
Transfusion	7 (5.0, 2.2–10.5)
Hysterectomy	2 (1.4, 0.3–5.6)
Either twin Fetal demise	1 (0.7, 0.0–4.5)
Either twin 5-min Apgar score less than 7	3 (2.2, 0.6–6.7)
Birth weight (g)	
Larger twin	2,467±543
Smaller twin	2,140±502
Either twin birth weight less than 10%	66 (47.5, 39.0–56.1)
Either twin birth weight less than 5%	31 (22.3, 15.9–30.3)
Birth weight discordancy greater than 20%	30 (21.5, 15.2–29.5)
Major anomaly	2 (1.4, 0.3–5.6)

Data are n (%; 95% confidence interval), n/N (%; 95% confidence interval), or mean±standard deviation.

by reproductive technology timing or, in spontaneous pregnancies, by first-trimester ultrasonography.

We performed several analyses to examine risk factors for adverse outcomes. First, we compared outcomes between women 50 years and older and women 45–49 years old. Second, we compared baseline differences between women who did and did not develop preeclampsia. Finally, we compared baseline differences between women who did and did not deliver at less than 34 weeks of gestation. For statistical analysis, we used χ^2 and Student *t* test for parametric data and Fisher exact test and Mann Whitney *U* test for nonparametric data. Analyses were performed using SPSS 22.0.

RESULTS

A total of 139 twin pregnancies were included. The mean maternal age at delivery was 47.3±1.9 years



old. The majority of women were white and nulliparous (Table 1). Nearly all were a result of in vitro fertilization with egg donation. The average prepregnancy body mass index was 24.3 ± 4.3 ; 9.5% had prepregnancy obesity. The rates of comorbid conditions were low with chronic hypertension in 7.2%, pregestational diabetes in 1.4%, and anticoagulation use in 6.5%. Low-dose aspirin (81 mg daily) was taken by 43.2% of women.

The mean gestational age at delivery was 35.4 ± 2.3 weeks with 22.3% (95% confidence interval [CI] 15.2–29.5%) delivering before 34 weeks of gestation (Table 2). Only 13.7% (95% CI 8.6–20.8%) had an indicated preterm birth at less than 34 weeks of gestation. The cesarean delivery rate was 93.5% (95% CI 8.7–96.8%) in all women and 57.9% (95% CI 34.0–78.9%) among women who labored and attempted vaginal delivery. The rates of gestational diabetes and preeclampsia were 19% (95% CI 13.0–26.8%) and 44.6% (95% CI 36.6–53.3%), respectively. Birth weight less than 10% in at least one twin was seen in 47.5% (39.0–56.1%) of pregnancies and birth weight less than 5% in at least one twin was seen in 22.3% (95% CI 15.9–33.3%) of

pregnancies. The rates of severe adverse outcomes were generally low: fetal demise 0.7%, 5-minute Apgar score less than 72.2%, and major anomaly 1.4%, transfusion 5.0%, hysterectomy 1.4%, abruption 0.7%. Although there were no statistically significant differences in pregnancy outcomes between women 50 years or older and women 45–49 years old (Table 3), as a result of the small number of patients older than 50 years, the statistical power to discern differences was low.

Because preeclampsia was a common adverse outcome in this population, with an incidence of 44.6%, we examined risk factors for preeclampsia. Nulliparity was the only baseline risk factor significantly associated with preeclampsia. Preeclampsia developed in 50.5% of nulliparous women compared with 30.5% of women with a prior birth ($P=.028$).

Race was the only risk factor associated with preterm birth at less than 34 weeks of gestation. Preterm birth at less than 34 weeks of gestation occurred in 18.1% of women of white race compared with 30.3% of women of nonwhite race ($P=.036$).

Table 3. Outcomes for Women 45–49 Years Old Compared With Those 50 Years or Older When They Delivered Twins

Outcome	Age (y)		P*
	45–49 (n=125)	50 or Older (n=14)	
Gestational age at delivery (wk)	35.9 (34.1–37.0)	35.7 (34.0–37.1)	.980
Any preterm birth (wk of gestation)			
Less than 28	1 (0.8)	0 (0.0)	.999
Less than 32	10 (8.0)	0 (0.0)	.598
Less than 34	28 (22.4)	3 (21.4)	.999
Indicated preterm birth at less than 34 wk of gestation	18 (14.4)	1 (7.1)	.692
Cesarean delivery			
All	116 (92.8)	14 (100.0)	.598
Labored	10/18 (55.6)	1/1 (100.0)	.999
Abruption	1 (0.8)	0 (0.0)	.999
Placenta previa	4 (3.2)	0 (0.0)	.999
Preeclampsia	59 (47.2)	3 (21.4)	.089
Gestational diabetes	24 (19.4)	2 (15.4)	.999
Transfusion	6 (4.8)	1 (7.1)	.533
Hysterectomy	2 (1.6)	0 (0.0)	.999
Either twin fetal demise	1 (0.8)	0 (0.0)	.999
Either twin 5-min Apgar score less than 7	3 (2.4)	0 (0.0)	.999
Birth weight (g)			
Larger twin	2,508 (2,128–2,836)	2,425 (2,298–2,985)	.492
Smaller twin	2,190 (1,769–2,523)	2,245 (1,815–2,493)	.649
Either twin birth weight less than 10%	60 (49.2)	5 (35.7)	.405
Either twin birth weight less than 5%	28 (23.0)	2 (14.3)	.734
Birth weight discordancy greater than 20%	25 (20.5)	4 (28.6)	.497
Major anomaly	2 (1.6)	0 (0.0)	.999

Data are median (interquartile range), n (%), or n/N (%) unless otherwise specified.

* Fisher exact test or Mann-Whitney U.



DISCUSSION

In this study, we found that twin pregnancy in women who were 45 years or older when they delivered was associated with high rates of cesarean delivery, preeclampsia, and gestational diabetes, but overall favorable outcomes. A previous study by Fox et al¹⁰ compared twin pregnancy outcomes in women of advanced maternal age (35 years or older) with those of younger women. Aside from an increased cesarean delivery rate, pregnancy outcomes between the two groups were comparable, including rates of preeclampsia: 12.9% and 10.7%, respectively.¹⁰ In the present study, the much higher rate of preeclampsia of 44.6% could be explained both by the higher age of the population as well as the high proportion of donor eggs that is a known risk factor for the development of preeclampsia.¹² The rates of birth weight less than the 10th percentile and less than the fifth percentile were also high in our study, but these are similar to rates in twin pregnancies overall.¹³

The U.S. Preventative Services Task Force recommends low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia.¹⁴ This is recommended for women with a greater than or equal to 8% risk for developing preeclampsia in pregnancy and includes all women with multifetal pregnancies. Our study did not show an association between preeclampsia and low-dose aspirin use, but we may have been underpowered to show a difference, and it is unclear from chart review why some women were recommended low-dose aspirin and others not.

The women in our study had low rates of baseline comorbidities that are typically seen with increased age. The rate of prepregnancy obesity was only 9.5% and chronic hypertension and pregestational diabetes were only present in 7.2% and 1.4%, respectively. This cohort therefore represents a relatively healthy patient population. Thus, the findings in this study may not be extrapolated to women with medical comorbidities known to worsen pregnancy outcomes.

Strengths of this study include the relatively large number of patients and the completeness and availability of their medical records. The main weakness of this study is that the homogenous and healthy nature of the studied women limits its generalizability.

In conclusion, in a well-selected population of healthy women who at the time of delivery were at least 45 years old, twin pregnancy is associated with a high rate of preeclampsia, gestational diabetes, and

cesarean delivery. However, other adverse outcomes are not markedly high, and the risk of severe outcomes such as stillbirth, hysterectomy, and major anomalies is low. In properly selected and counseled women with an expected age at delivery of 45 years or older, age alone should not be a contraindication to twin pregnancy.

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