

ABSTRACT

Background: Advanced maternal age (AMA) (≥ 35 yo) is considered to be a risk factor for fetal growth restriction (FGR), however research regarding this topic is conflicting. The increasing rates of chronic disease that disproportionately affect older women make it difficult to assess the independent effect of maternal age on incidence of FGR.

Objective: to determine the independent effect of maternal age on the rate of FGR.

Methods: This was a retrospective cohort study of women from the CDC National Vital Statistics System data from 2009 to 2013. All women aged 18-50 delivering a singleton with a gestational age of 24-42 weeks were included. Women with fetal anomalies or aneuploidy were excluded. Women were categorized into 3 age groups at the time of delivery: 1) 18yo-34yo 2) 35yo-39yo 3) ≥ 40 yo. The primary outcome of FGR at $< 5^{\text{th}}$ and $< 10^{\text{th}}$ percentile was compared between the three groups using a Chi square or one way ANOVA tests followed by Scheffe multiple comparisons. Multivariable logistic regression was done to determine whether maternal age group was associated with FGR.

Results: A total of 18,153,986 women were eligible for the analysis. Of these, 2,705,501 women were AMA. In univariate analysis, the rate of FGR both at the 5^{th} and at the 10^{th} percentiles was the lowest in the 35yo-39yo group (6.3% vs. 5.0% vs. 5.7%, $p < 0.001$ for FGR $< 5^{\text{th}}$ percentile and 11.6% vs. 9.21% vs. 10.1%, $p < 0.001$ for FGR $< 10^{\text{th}}$ percentile). In multivariable logistic regression, maternal age of 35yo-39yo continued to be associated with lower frequency of FGR both at the 5^{th} and at the 10^{th} percentiles. In contrast, maternal age of ≥ 40 yo was associated with an increased frequency of FGR at the 5^{th} and at the 10^{th} percentiles.

Conclusion: Advanced maternal age of ≥ 40 yo but not 35yo-39yo was associated with an increased risk of FGR. Our findings may have implications for routine sonographic growth surveillance in healthy women of advanced maternal age

BACKGROUND

- According to the CDC, the number of first time mothers age ≥ 35 increased from 7.4% to 9.1% between the years 2000 and 2016
- Advanced maternal age (AMA) is associated with certain adverse perinatal outcomes
- It remains uncertain whether AMA is associated with fetal growth restriction (FGR)

OBJECTIVE

To examine the association between AMA and FGR

METHODS

- Retrospective cohort from the CDC National Vital Statistics System
- 2009-2013
- Inclusion criteria:**
 - Pregnant women over 18 years of age
 - Gestational age 24-42 weeks
- Exclusion criteria:**
 - Multiple gestation
 - Chromosomal or congenital fetal abnormality
- Primary outcome: **FGR at $< 5^{\text{th}}$ or $< 10^{\text{th}}$ percentile**
- Analysis: Chi square, one way ANOVA tests followed by Scheffe multiple comparisons, multivariable logistic regressions

RESULTS

Clinical Variable	Maternal age group (years)			P value
	18-34 (N=15,448,485)	35-39 (N=2,182,543)	≥ 40 (N= 522,958)	
BMI group (kg/m ²)				<0.001
Underweight (<18.5)	495,875 (4.1%)	42,450 (2.5%)	8,759 (2.2%)	
Normal weight (18.5 - 24.9)	5,727,422 (47.4%)	790,975 (46.5%)	181,066 (44.5%)	
Overweight (25.0 - 29.9)	3,051,672 (25.2%)	53,502 (26.7%)	113,917 (28%)	
Obese I (30.0 – 34.9)	1,581,257 (13.1%)	233,941 (13.8%)	60,424 (14.9%)	
Obese II (35.0 – 39.9)	737,180 (6.1%)	106,037 (6.2%)	25,985 (6.4%)	
Obese III (≥ 40)	496,105 (4.1%)	72,863 (4.3%)	16,714 (4.1%)	
Maternal Race/ethnicity				<0.001
Non-Hispanic White	8,348,952 (54.4%)	1,218,958 (55.8%)	283,722 (54.3%)	
Non-Hispanic Black	2,313,483 (15.0%)	234,924 (10.8%)	64,069 (12.3%)	
Hispanic	3,660,739 (23.7%)	468,611 (21.4%)	112,722 (21.6%)	
Other	1,026,958 (6.7%)	239,964 (11.0%)	55,498 (10.6%)	
Missing	98,353 (0.6%)	20,086 (1.0%)	6,947 (1.2%)	
Paternal age (median, IQR)	29.5 (25,33)	37.9 (35,41)	41.8 (39,45)	<0.001
Paternal Race/ethnicity				<0.001
Non-Hispanic White	7,245,339 (46.9%)	1,187,303 (54.4%)	290,302 (52.5%)	
Non-Hispanic Black	1,761,127 (11.4%)	221,706 (9.7%)	59,166 (10.7%)	
Hispanic	3,228,733 (20.9%)	412,500 (18.9%)	97,587 (18.7%)	
Other	998,703 (6.4%)	205,159 (9.4%)	45,452 (8.7%)	
Missing	2,224,581 (14.4%)	165,873 (7.6%)	51,978 (9.4%)	
Nulliparity	5,406,969 (35%)	364,484 (16.7%)	76,874 (14.7%)	<0.001
Pre-gestational hypertension	177,657 (1.2%)	52,381 (2.4%)	19,349 (3.7%)	<.0001
Gestational hypertension/preeclampsia	648,837 (4.2%)	80,087 (4.5%)	23,563 (5.5%)	<.0001
Pre-gestational diabetes	92,690 (0.6%)	27,500 (1.3%)	9,256 (1.8%)	<.0001
Gestational diabetes	633,387 (4.1%)	178,968 (8.2%)	53,864 (10.3%)	<.0001
Tobacco use in pregnancy	1,489,233 (9.6%)	96,686 (4.4%)	22,800 (4.4%)	<0.001

RESULTS

Pregnancy outcomes	Maternal age group (years)			P value
	18-34 (N=15,448,485)	35-39 (N=2,182,543)	40-50 (N= 522,958)	
Fetal Growth Restriction				<.001
<5 th percentile	943,670 (6.1%)	105,960 (4.8%)	28,978 (5.5%)	
<10 th percentile	1,746,500 (11.3%)	196,705 (9.0%)	51,472 (9.8%)	<.001
Birth weight (g) (median, IQR)	3301 (3005,3635)	3347 (3040,3705)	3306 (3000,3685)	<.001
Gestational age at delivery (weeks) (median, IQR)	38.7 (38,40)	38.5 (38,40)	38.3 (38,39)	<.001
Induction of labor	3,678,077 (23.8%)	451,793 (20.7%)	110,266 (21.1%)	<.001
Mode of delivery				<.001
Spontaneous vaginal delivery	10,273,242 (66.5%)	1,241,866 (56.9%)	262,995 (50.3%)	
Operative vaginal delivery	571,594 (3.7%)	65,476 (3.0%)	15,218 (2.9%)	
Cesarean delivery	4,603,649 (29.8%)	876,727 (40.1%)	244,744 (46.8%)	
5 minute apgar <7	237,906 (1.5%)	32,519 (1.5%)	9,413 (1.8%)	<.001
NICU admission	963,985 (6.2%)	151,031 (6.9%)	44,451 (8.5%)	<.001
Neonatal demise	21,627 (0.1%)	2,837 (0.1%)	941 (0.2%)	<.001
Blood transfusion	33,986 (0.2%)	5,674 (0.3%)	1,934 (0.4%)	<.001

Multivariable Logistic regression for the association between maternal age and FGR

Multivariable logistic regression	FGR $< 5^{\text{th}}$ percentile Adjusted OR* (95% CI)	FGR $< 10^{\text{th}}$ percentile Adjusted OR* (95% CI)
Maternal age 18 – 34	1 (referent)	1 (referent)
Maternal age 35 – 39	1 (0.99 – 1.01)	0.98 (0.97 – 0.99)
Maternal age ≥ 40	1.17 (1.15 – 1.19)	1.10 (1.08 – 1.11)

Adjusted for BMI, maternal race/ethnicity, paternal age, paternal race/ethnicity, nulliparity, smoking, pre-gestational diabetes, gestational diabetes, pre-gestational hypertension, gestational hypertension/preeclampsia

Conclusion

- Advanced maternal age of 35-39yo was not associated with FGR
- Advanced maternal age of ≥ 40 yo was associated with increased risk of FGR
- These findings should help tailor sonographic surveillance among healthy women of advanced maternal age