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INTERNATIONAL JOURNAL of  
MATERNAL and CHILD HEALTH and AIDS  
ISSN 2161-864X (Online)  
ISSN 2161-8674 (Print)  
DOI: 10.21106/ijma.346

## SHORT RESEARCH COMMUNICATION

# Stillbirths among Advanced Maternal Age Women in the United States: 2003-2017

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## ABSTRACT

The aim of the study was to evaluate the association between fetal stillbirth and advanced maternal age in the United States (US). This was a population-based study using the Natality and Fetal Death datasets for the years 2003-2017. We built Cox proportional regression models to examine the likelihood of stillbirth among women aged  $\geq 40$  years. Out of a total of 57,273,305 births, stillbirth was observed in 302,522, yielding a stillbirth rate of 5 per 1000. After adjusting for confounders, women of advanced age ( $\geq 40$  years) had a 40-50% greater risk of stillbirth compared to women 20-29 years of age.

**Keywords:** • Advanced maternal age • Stillbirth • Cox proportional regression • United States

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## 1. Introduction

With an increasing number of women getting educated and entering the workforce, there is an upshift in the average age at which couples have their first child. In the United States (U.S.), the average age of first time mothers has increased from 21 years in 1972 to 26.3 years in 2016, and for fathers the age has increased from 27 years to 31 years.<sup>1</sup> A similar trend has been observed in other developed countries such as Switzerland, Japan, Spain, Italy, and South Korea, where the average maternal age at first birth is 31 years.<sup>1</sup> Studies have shown that older women are more likely to have a range of pregnancy complications including gestational hypertensive disorders, gestational diabetes, postpartum hemorrhage, cesarean delivery,

iatrogenic and spontaneous preterm delivery.<sup>2</sup> The chances of conceiving for women go down drastically after the age of 35. The rates of infertility treatments and assisted reproductive technology (ART) come to the rescue in such cases, but the treatments increase the chances of multiple pregnancies, which could further complicate feto-infant birth outcomes, including premature birth, low birth weight, congenital defects, genetic disorders, neurodevelopmental disorders, etc. There is a dearth of literature in recent years regarding stillbirth among women of advanced maternal age in the U.S. Accordingly, the purpose of this study was to provide updated information on the association between stillbirth and maternal age.

## 2. Methods

We conducted a population-based retrospective cohort study using Birth Data and Fetal Death Data obtained from the Centers for Disease Control and Prevention (CDC) and made available through the National Vital Statistics System (NVSS). The Birth dataset abstracts information from the birth certificates registered in each of the states and contains information on all births occurring within the U.S. The Fetal Death dataset contains information regarding all intrauterine deaths including stillbirth. Information on socio-demographic and health characteristics associated with each live or stillbirth is available in the datasets. The information on maternal age segregation of 50+ years at delivery was available in Birth dataset from the year 1997, while the Fetal Death dataset dates back 2003. In this study, we included all singleton live births and stillbirths within the gestational age from 20 to 42 weeks, for the years 2003 through 2017.

The exposure or independent variable for the study was the age of the mother at the time of the delivery. The outcome variable was whether the pregnancy resulted in a live or stillbirth. Various demographic characteristics such as maternal age, race, birthweight of the fetus, sex and maternal comorbidities were considered. Records with missing information on the exposure, outcome and the covariates were excluded from the analyses. Descriptive statistics and the prevalence of stillbirth stratified by each of the demographic and maternal comorbid factors were calculated. Next, we conducted Cox proportional hazards regression to calculate the adjusted hazard ratios that quantified the association between maternal age and stillbirth. Lastly, we conducted sensitivity analysis by adjusting for factors like maternal age, race, sex of the fetus, plurality in the first model and all the demographic characteristics and maternal comorbidities like hypertension, eclampsia, diabetes, chronic and gestational hypertension, and maternal weight gain in the second model.

## 3. Results

Our study sample contained a total of 57,273,305 births that occurred in the U.S. from 2003 through

2017, out of which 302,522 or 0.5% resulted in stillbirth. A total of 1,587,202 (2.8%) women were in the age group of 40 to 49 years and 5,444 women were over the age of 50 years at the time of the delivery. The prevalence of stillbirth across various maternal ages was 0.6% among teenage mothers; 0.5% in mothers between 20 and 39 years; 0.9% among mothers 40 and 49 years; and 1.0% among 50 years and over.

After adjusting for demographic and perinatal characteristics in model 1, we observed a statistically significant increased risk of stillbirth among women 30 – 39 years (HR: 1.16, 95% CI: 1.15-1.17), 40 – 49 years (HR: 1.57, 95% CI: 1.54-1.59) and ≥50 years (HR: 1.31; 95% CI: 1.02-1.69) as compared to women 20 – 29 years (Table 1). When we adjusted for all demographic, perinatal and maternal comorbid factors, we observed about 20%, 49% and 40% increased likelihood of stillbirth among mothers 30 – 39 years, 40 – 49 and 50+ years, respectively as compared to those in the 20 – 29 years age group (Table 1). We also observed an increased likelihood of experiencing stillbirth among Non-Hispanic Blacks when compared with Non-Hispanic Whites. As compared to fetuses of normal birthweight, fetuses of low birthweight had a much higher risk of stillbirth; and male fetuses were almost 28% more likely to die in utero. Also, women with gestational hypertension had elevated chances of experiencing fetal death. Compared to women who gained 21-30 pounds, women who gained only up to 20 pounds of weight during pregnancy had higher likelihood of experiencing stillbirth.

## 4. Discussion, Conclusion and Global Health Implications

Rates for all births, not just of the first child, to women over the age of 35, have been rising over the past 20 years.<sup>3</sup> There are many benefits of having a child at a later stage in life including, educational and professional advancement, emotional maturity, financial stability, etc.; there are also numerous global health implications. For example, from a demographic lens, delayed pregnancy and heightened stillbirth diminish population growth and, therefore, re-population. Since older mothers tend to have

**Table 1: Prevalence of stillbirths using the Cox proportional hazards regression model estimates**

	Stillbirth - N	Prevalence of stillbirth	Model 1- HR and 95% CI	Model 2- HR and 95% CI
<b>Mother's age</b>				
20-29 years	148751	0.5%	Reference	Reference
<= 19 years	31696	0.6%	0.99 (0.98-1.00)	0.96 (0.93-0.96)
30-39 years	107528	0.5%	1.16 (1.15-1.17)	1.20 (1.19-1.21)
40-49 years	14488	0.9%	1.57 (1.54-1.59)	1.49 (1.46-1.52)
50+ years	59	1.1%	1.31 (1.02-1.69)	1.40 (1.06-1.85)
<b>Race</b>				
Whites	196872	0.8%	Reference	Reference
Blacks	87804	1.7%	1.20 (1.19-1.21)	1.05 (1.04-1.05)
Others	17846	0.1%	0.15 (0.14-0.16)	0.14 (0.13-0.16)
<b>Birthweight</b>				
Normal	52585	0.1%	Reference	Reference
Low birthweight	244020	6.2%	5.36 (4.68-6.08)	4.16 (4.12-4.18)
Macrosomic	5917	0.1%	0.99 (0.96-1.01)	1.22 (1.19-1.25)
<b>Sex</b>				
Female	142180	0.8%	Reference	Reference
Male	160060	0.8%	1.28 (1.27-1.29)	1.28 (1.27-1.29)
<b>Hypertension Eclampsia</b>				
No	281002	0.6%	-	Reference
Yes	1881	1.5%	-	0.74 (0.70-0.77)
<b>Diabetes</b>				
No	266282	0.6%	-	Reference
Yes	16601	0.7%	-	0.65 (0.64-0.66)
<b>Chronic Hypertension</b>				
No	269645	0.5%	-	Reference
Yes	13238	2.1%	-	1.03 (1.01-1.04)
<b>Gestational Hypertension</b>				
No	267950	0.6%	-	Reference
Yes	14933	0.7%	-	1.39 (1.36-1.41)
<b>Weight gain</b>				
21-30 pounds	30331	0.2%	-	Reference
Up to 20 pounds	246272	1.8%	-	4.15 (4.12-4.18)
31-40 pounds	15373	0.1%	-	0.79 (0.78-0.81)
Over 40 pounds	10546	0.1%	-	0.82 (0.80-0.84)

HR = adjusted hazards ratio; Note: The column totals may differ because missing values have been removed

fewer children, population replacement is slowed considerably, a process that could negatively impact industrial workforce and productivity due to insufficient replacement of retirees with younger workers.<sup>3</sup> A limitation of this study was our inability to delineate the causes of the stillbirths identified in our

analysis. However, we speculate that the predominant cause was placental insufficiency since we observed a positive dose-response relationship between maternal age and reduced placental efficiency as well as altered placental function.<sup>5</sup> Further studies should explore this and other potential causes.

### Compliance With Ethical Standards

**Conflicts of Interest:** Authors declare that they have no conflict of interest. **Funding:** None.

**Ethics Approval:** Study was approved by the Baylor College of Medicine Ethical Review Board.

#### Key Messages

- Women aged 30 years and above were found to have increased likelihood of experiencing stillbirth as compared to younger mothers.
- After adjusting for confounders, women of advanced age ( $\geq 40$  years) had a 40-50% greater risk of stillbirth compared to women 20-29 years of age.

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