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The effectiveness of antepartum surveillance in reducing the risk of stillbirth in patients with advanced maternal age

Nathan S. Fox [a,b,c,*], Andrei Rebarber [a,b,c], Michael Silverstein [a,b], Ashley S. Roman [c], Chad K. Klauser [a,b,c], Daniel H. Saltzman [a,b,c]

[a] Department of Obstetrics, Gynecology, and Reproductive Science, Mount Sinai School of Medicine, USA
[b] Maternal Fetal Medicine Associates, PLLC, Carnegie Imaging for Women, PLLC, USA
[c] Department of Obstetrics and Gynecology, New York University School of Medicine, New York, NY, USA

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ABSTRACT

Objective: To estimate the effectiveness of antepartum surveillance and delivery at 41 weeks in reducing the risk of stillbirth in advanced maternal age (AMA) patients.
Study design: Retrospective cohort study of all patients managed in one maternal–fetal medicine practice from June 2005 to May 2012. We included all singleton pregnancies delivered at ≥20 weeks of gestation. All AMA patients (age ≥35 years at their estimated delivery date) underwent weekly biophysical profile testing beginning at 36 weeks, as well as planned delivery at 41 weeks, or sooner if indicated. We compared the rate of fetal death at ≥20 weeks and fetal death at ≥36 weeks in AMA vs. non-AMA patients. Fetal deaths due to lethal and chromosomal abnormalities were excluded.
Results: 4469 patients met the inclusion criteria: 1541 (34.5%) were AMA and 2928 (65.5%) were non-AMA. Using our AMA protocol for surveillance and timing of delivery, the incidence of stillbirth was similar to the non-AMA population (stillbirth ≥20 weeks: 3.9 per 1000 vs. 3.4 per 1000, $p = 0.799$; stillbirth ≥36 weeks: 1.4 per 1000 vs. 1.1 per 1000, $p = 0.773$). When looking at women age <35, age 35–39, and age ≥40, the incidence of stillbirth ≥20 weeks and ≥36 weeks did not increase across the three groups. Our findings were similar when we excluded all patients with other indications for antepartum surveillance.
Conclusions: In AMA patients, antepartum surveillance and delivery at 41 weeks appears to reduce the risk of stillbirth to that of the non-AMA population. Routine antepartum surveillance should be considered in all AMA patients.

1. Introduction

In the United States, the average age of women giving birth is increasing. From 1980 to 2009, the mean maternal age rose from 25.0 to 27.5 years [1]. In 2009, women of advanced maternal age (AMA; 35 years and older) represented 14.2% of all live births in the United States, and women aged 40 years and older represented 2.8% of all live births [1]. It is well known that AMA women are at increased risk of various pregnancy complications, including stillbirth [2–7]. The risk of stillbirth, defined as fetal death at 20 weeks or more, has been quoted as 11–14 per 1000 in women age 35–39 and 11–29 per 1000 in women age 40 and over, compared to 6.4 per 1000 in the general population and 4.0–5.5 per 1000 in low-risk pregnancies [8,9]. Recent data from the United States show an overall decrease in stillbirth compared to prior data, but a continued increased prevalence among older women, with rates of 6.9 per 1000 in women age 35–39, 9.8 per 1000 in women age 40–44, and 13 per 1000 in women age 45 and older [10]. A recent meta-analysis of 96 population-based studies noted that AMA was a major risk factor for stillbirth, yielding a 7–11% population attributable risk value [11]. The same data indicate that AMA is associated with a 65% increase in the odds of stillbirth and could be responsible for almost 4226 stillbirths in high-income countries each year [11,12].

For women at increased risk of stillbirth due to other causes, such as hypertension and diabetes, antepartum surveillance has been widely integrated into clinical practice, despite a dearth of evidence from randomized controlled trials [13]. The American College of Obstetricians and Gynecologists (ACOG) does not specifically list AMA as an indication for antepartum fetal surveillance. They state, however, that since antepartum fetal surveillance has not been studied rigorously for any indications, all indications for testing should be considered relative, but in general,

* Corresponding author at: Maternal Fetal Medicine Associates, PLLC, 70 East 90th Street, New York, NY 10128, USA. Tel.: +1 212 722 7409; fax: +1 212 722 7185.
E-mail addresses: nfox@mfmnyc.com, nathan.fox@mssm.edu (N.S. Fox).

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antepartum fetal surveillance has been employed in pregnancies in which the risk of fetal demise is increased [13].

For comparison, the increased risk of stillbirth in AMA patients (OR 1.8–3.3) is similar to patients with chronic hypertension (OR 1.5–2.7), pregnancy-induced hypertension (OR 1.2–4.0), prior stillbirth (OR 1.4–3.2), and multiple gestation (OR 1.0–2.8), all of which are listed by ACOG as indications for antepartum surveillance [13]. Like other established and potential indications for antepartum surveillance, however, it is currently unknown for AMA patients whether antepartum surveillance actually reduces the risk of stillbirth. A recent publication from the Society for Maternal–Fetal Medicine reviews the increased of stillbirth in AMA patients, but also states that "there is insufficient evidence to confirm that antenatal testing for the sole indication of AMA reduces stillbirth or improves perinatal outcomes" [14].

In our practice, we have been routinely performing antepartum fetal surveillance for AMA patients. This involves weekly assessment using the ultrasound portion of the biophysical profile (BPP) [15] testing beginning at 36 weeks of gestation, as well as planned delivery at 41 weeks of gestation, or earlier if indicated. The objective of this study was to estimate the effectiveness of this surveillance strategy in reducing the risk of stillbirth in AMA patients.

2. Materials and methods

After Biomedical Research Alliance of New York Institutional Review Boards approval was obtained, we queried the computer delivery database of our maternal–fetal medicine practice for all deliveries of singleton pregnancies ≥20 weeks over a 7-year period from June 2005 to May 2012. During the study period, our protocol for all patients aged ≥35 at their estimated date of delivery was to initiate weekly BPP testing at 36 weeks of gestation and planned delivery (induction of labor or cesarean delivery, as indicated) at 41 weeks of gestation, or earlier, as indicated. BPP testing did not include a non-stress test (i.e. the highest score was 8/8) [15]. All BPP testing was done at our affiliate imaging center, Carnegie Imaging for Women, PLLC, by RDMS-certified sonographers under the supervision of maternal–fetal medicine specialists. Abnormal testing was managed by either non-stress testing, prolonged fetal heart rate monitoring, repeat BPP testing, or delivery, as clinical circumstances dictated. Patients with oligohydramnios (amniotic fluid index <5 cm) were recommended delivery.

From the computerized database we extracted pregnancy and delivery outcomes for all patients, including maternal age, estimated delivery date (EDD), induction of labor, gestational age at delivery, stillbirth, parity, pre-gestational and gestational diabetes, chronic or gestational hypertension, systemic lupus erythematosis (SLE), and prior stillbirth ≥20 weeks. Data on stillbirth outcomes for patients who leave our practice after 20 weeks are maintained in our database and were included in this analysis. For women who left our practice and did not have a stillbirth, we did not have access to additional details regarding their pregnancies. All cases of stillbirth ≥20 weeks were reviewed. Any stillbirths due to known lethal fetal anomalies or chromosomal abnormalities were excluded. The maternal age was defined as the age at the estimated delivery date. Gestational age was determined by last menstrual period and confirmed by ultrasound in all patients. The expected date of delivery was revised if the discrepancy was >5 days between the calculation from the last menstrual period and ultrasound up to 13 6/7 weeks of gestation, >7 days if the dating ultrasound was performed between 14 and 20 weeks of gestation, or >14 days after 20 weeks (all patients had first or second trimester ultrasounds). If the pregnancy was the result of in vitro fertilization (IVF), gestational age was determined from the date of embryo transfer.

We compared stillbirth rates between AMA and non-AMA patients, as well as across three groups: women aged <35, 35–39, and ≥40. We used two definitions for stillbirth: ≥20 weeks, which is the standard definition [3], and stillbirth ≥36 weeks, which is when we initiate antepartum surveillance in AMA patients. For stillbirth ≥36 weeks, the denominator used was total deliveries after 36 weeks (i.e. excluding all deliveries prior to 36 weeks). We repeated our analysis excluding patients with any other indications for antepartum surveillance.

Chi square testing and Student's *t*-test were used for analysis using SPSS for Windows 16.0 (Chicago 2007). A *p*-value of ≤0.05 was considered significant. Since we did not have a group of untested AMA patients, we chose non-AMA patients as the control group. Our reasoning was that the increased risk of stillbirth in AMA patients has been established; therefore, if we were able to demonstrate with adequate power no difference in stillbirth rates between our AMA and non-AMA patients, who are all managed similarly in our practice aside from routine antepartum surveillance, it would suggest that our surveillance protocol ameliorates the increased risk of stillbirth in AMA patients. We did not perform a power analysis before the study as we planned to review all charts in our database, which was created in 2005. A power analysis was performed post hoc, however, in order to determine power for our results.

3. Results

Over the study period, we cared for 4469 patients with singleton pregnancies ≥20 weeks. 1541 (34.5%) were AMA and

Table 1
Description of the patients with stillbirths over the course of the study period.

Patient number	Maternal age	Gestational age	Details
1	38.2	39 1/7	Nuchal cord x3
2	41.7	38 4/7	Six days after successful external cephalic version. Elevated KB suggestive of feto-maternal hemorrhage
3	21.8	37 1/7	Nuchal cord x1, cord around body x2
4	30.1	36 5/7	Rh sensitized, but normal testing throughout pregnancy. Nuchal cord x1. No evidence of fetal anemia
5	34.7	36 3/7	X-linked icthyosis
6	32.9	34 5/7	Knot in cord and nuchal cord x1
7	27.3	34 3/7	Mild ventriculomegaly, normal karyotype
8	41.1	34 3/7	Unexplained. Normal karyotype
9	23.3	34 1/7	Unexplained
10	35.9	29 2/7	Unilateral clubbed foot, normal karyotype
11	35.8	28 6/7	Unexplained. Delivered at outside hospital
12	37.4	27 0/7	Nuchal cord x4
13	25.5	25 3/7	Originally a triplet pregnancy with spontaneous 3–1 reduction at 10 weeks. Normal karyotype
14	24.5	22 4/7	Suspected CMV from placental pathology
15	30.6	21 4/7	Unexplained
16	20.7	21 2/7	Suspected listeria from placental culture