Pregnancy at or beyond age 40 years is associated with an increased risk of fetal death and other adverse outcomes

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OBJECTIVE: The objective of the study was to determine the frequency of fetal death in women 40 years of age or older (AMA).

STUDY DESIGN: Retrospective study of all singleton pregnancies delivered at our institution between the years 1989 and 2004 was performed. The primary outcome measure was the risk of fetal death at various gestational ages. We also investigated the frequency of maternal comorbidities, preterm delivery (PTD), and low and very low birth weights (LBW, VLBW).

RESULTS: Data were available for 126,402 singleton deliveries. AMA was an independent risk factor for fetal death at 28-31 weeks (adjusted odds ratio [AOR] 2.93, 95% confidence interval [CI] 1.76-4.92), 32-36 (AOR 1.73, 95% CI 1.05-2.83), 37-39 weeks (AOR 1.63, 95% CI 0.97-2.75), and 40-41 weeks (AOR 2.28, 95% CI 1.18-4.4). AMA was associated with increased rates of PTD, LBW, and VLBW.

CONCLUSION: AMA is associated with an increased rate of fetal death and other adverse obstetrical outcomes. Antepartum fetal surveillance may be warranted in these women.

Key words: advanced maternal age, antepartum fetal surveillance, fetal death

More women are choosing to delay child-bearing until their educations are complete or their professional careers are established. As a result, the live birth rate to women of advanced maternal age (AMA) has increased steadily over the past 15 years.[1] The number of women delaying child-bearing until their 5th decade of life has increased.[2] Recent studies have examined perinatal morbidity and mortality of women in AMA groups such as preterm delivery (PTD), low and very low birth weight (LBW, VLBW), and fetal death (FD).[3,4,5] The objective of our study was to determine the frequency of FD in AMA groups, defined as women 40 years of age or older.

MATERIALS AND METHODS

A retrospective study of all singleton pregnancies delivered at the University of Miami/Jackson Memorial Hospital between the years 1989 and 2004 was performed. A computerized database was used to determine maternal age, parity, gestational age at delivery, birthweights, and medical comorbidities. Pregnancies complicated by lethal anomalies were excluded.

Women were divided into age groups of younger than 35 years, 35-39 years, and 40 years old or older. The primary outcome measure was the rate of FD at gestational ages of less than 28, 28-31, 32-36, 37-39, and 40-41 completed weeks. Fetal death was defined as death of a fetus at or beyond 20 weeks' gestation. The rates of other adverse obstetrical outcomes, including chronic hypertension (CHTN), pregestational and gestational diabetes (GDM), LBW, VLBW, PTD, and very PTD were also examined among these age groups as secondary outcome measures.

Statistical data were analyzed using SPSS 12.0 (SPSS Inc, Chicago, IL). Descriptive statistics were obtained for all variables. A 2-sample t test was used for continuous variables and χ^2 analysis for dichotomous variables. Logistic regression analyses were used to analyze variables independently and to calculate adjusted odds ratios (AOR), adjusting for CHTN, pregestational diabetes, GDM, preeclampsia, and parity. When analyzing AORs for LBW and VLBW, we also adjusted for gestational age. A P value of .05 was considered significant.

RESULTS

Complete information was available for 126,402 singleton deliveries. Women aged 40 years old or older comprised 3953 of the subjects (3.3 %). Maternal and demographic characteristics as well as pregnancy outcomes are shown in Table 1. A higher percentage of maternal complications including CHTN, pregestational diabetes, GDM, FD, and preeclampsia were noted among the 2 advanced maternal age groups.

Multivariate analyses were performed to determine the odds of FD according to gestational age and maternal age in Table 2. The odds of FD were increased in both advanced age groups. Pregnancies to women 40 years old or older were more likely to result in an FD than those to women in the 35- to 39-year-old age group and those younger than 35 years old for all gestational age categories.

TABLE 1
Patient characteristics and demographics by maternal age group

	Total\nn = 126,402	< 35 years\nn = 108,547	35-39 years\nn = 13,902	≥ 40 years\nn = 3953
Maternal characteristics				
Age (yrs), mean + SD	26 ± 6.63	25 ± 5.19	36 ± 1.37*	41 ± 1.66†
Gravidity	2.87 ± 1.95	2.0 ± 1.74	4.0 ± 2.39*	4.0 ± 2.82†
CHTN	3.6%	3.0%	6.7%*	11.1%†
Pre-GDM	0.9%	0.7%	1.6%*	2.2%†
GDM	3.1%	2.4%	6.9%*	8.7%†
Preeclampsia	7.15%	6.9%	7.4%*	9.3%†
Race and ethnicity				
Hispanic	37.9%	37.6%	40%*	37.4%†
Black non-Hispanic	40.2%	40.3%	38.6%*	42.8%†
White non-Hispanic	19.2%	19.5%	17%*	16.1%†
Other	2.8%	2.6%	3.7%*	3.8%†
Pregnancy outcomes				
Gestational age at delivery (wks), mean ± SD	39 ± 3.4	39 ± 3.5	39 ± 3.7	39 ± 3.5
Birthweight (g)	3268 ± 734	3261 ± 720	3306 ± 810*	3270 ± 830
Intrauterine FD	1.9%	1.7%	2.4%*	3.0%†

* $P < .005$ comparing 35-39 years with younger than 35 years.

† $P < .005$ comparing 40 years or older with younger than 35 years.

Table 3 shows the odds of preterm delivery, LBW, and VLBW. An association was noted between the above outcomes and increased maternal age. The strongest association was found in the analysis of VLBW among maternal age groups.

COMMENT

This study demonstrates an increase in the risk of FD and maternal complications in older women of our ethnically diverse population. In addition, the odds of PTD, LBW, and VLBW increase with maternal age. We found that age is an independent risk factor for FD.

It is unclear why AMA is associated with increased odds of FD in otherwise healthy women. Miller investigated uteroplacental insufficiency as a possible etiology of FD in older women.[6] However, no statistically significant difference in uteroplacental insufficiency between older women and those of younger age groups was found. Muhieddne et al[7] reported that 47% of

FDs in women 40 years old or older had no identifiable risk factor.

The use of antepartum fetal surveillance in older women continues to be debated. Fretts and Usher[8] reported that the rates of FD with conditions such as maternal diabetes and hypertension are lower than those of FD rates in AMA groups. Yet women with these conditions are aggressively managed in antenatal testing units. Based on our findings, antepartum fetal surveillance in women of advanced mater-

TABLE 2
Odds of FD to women aged 35-39 and ≥ 40 years old and older, compared with referent group

	< 35 years\nn = 108,547	35-39 years\nn = 13,902	≥ 40 years\nn = 3,953
FD at < 28wks AOR (95% CI), n = 3347	Referent	1.14 (0.92-1.41)	1.10 (0.76-1.59)
FD at 28-31 wks, n = 3019	Referent	1.06 (0.69-1.66)	2.93 (1.75-4.92)
FD at 32-36 wks, n = 15,064	Referent	2.03 (1.54-2.69)	1.73 (1.05-2.83)
FD at 37-39 weeks, n = 55,728	Referent	1.20 (0.85-1.70)	1.63 (0.97-2.75)
FD at 40-41 wks, n = 41,735	Referent	0.80 (0.44-1.45)	2.28 (1.82-4.40)

Adjusted for race/ethnic group, age, parity, CHTN, preeclampsia, pre-GDM, and GDM.
CI, confidence interval.

TABLE 3

Odds of PTD, LBW, and VLBW at ages 35-39 and 40 years or older, compared with referent group

	< 35 yrs	35-39 yrs	40-45 yrs
< 28 wks, AOR (95% CI)	Referent	1.24 (1.11 − 1.37)	1.27 (1.06 − 1.53)
< 32 wks	Referent	1.14 (1.06 − 1.24)	1.22 (1.06 − 1.39)
< 37 wks	Referent	1.07 (1.02 − 1.13)	1.11 (1.03 − 1.21)
LBW (< 2500 g)	Referent	1.19 (1.10 − 1.28)	1.40 (1.24 − 1.58)
VLBW (< 1500 g)	Referent	1.45 (1.25 − 1.69)	1.50 (1.17 − 1.93)

Adjusted for race/ethnic group, age, parity, CHTN, preeclampsia, pre-GDM, and GDM.
LBW and VLBW were also adjusted for gestational age at delivery.
CI, confidence interval.

nal age groups is a worthwhile addition to routine prenatal care, particularly after 37 weeks.

In conclusion, FD occurs more frequently with increasing age, as does the incidence of PTD, LBW, VLBW, and pregnancy complications such as CHTN, diabetes mellitus, GDM, and preeclampsia. Our findings suggest that antepartum testing is a reasonable consideration for women of AMA groups. A larger randomized trial would be useful to elucidate an answer. ■

REFERENCES

1. Salihu HM, Shumpert MN, Slay M, Kirby RS, Alexander GR. Childbearing beyond maternal age 50 and fetal outcomes in the United States. Obstet Gynecol 2003;102:1006-14.
2. Heffner LJ. Advanced maternal age—how old is too old? N Engl J Med 2004;351:1927-9.
3. Berkowitz GS, Skovron ML, Lapinski RH, Berkowitz RL. Delayed childbearing and the outcome of pregnancy. N Engl J Med 1990;322:659-64.
4. Lee KS, Feguson RM, Corpuz M, Gartner LM. Maternal age and incidence of low birth weight at term: a population study. Am J Obstet Gynecol 1988;158:84-9.
5. Jacobsson B, Ladfors L, Milsom I. Advanced maternal age and adverse perinatal outcome. Am J Obstet Gynecol 2004;104:727-33.
6. Miller DA. Is advanced maternal age an independent risk factor for uteroplacental insufficiency? Am J Obstet Gynecol 2005;192:1974-82.
7. Muhieddine AF, Nassar AH, Ihab MU, Melhem Z, Kazma A, Khalil AM. Impact of advanced maternal age on pregnancy outcome. Am J Perinatol 2002;19:1-7.
8. Fretts RC, Usher RH. Causes of fetal death in women of advanced maternal age. Obstet Gynecol 1997;89:40-5.