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Outcomes of multiple gestations with advanced maternal age

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Abstract

Objective. To investigate outcomes of twin gestations with advanced maternal age (AMA).

Study design. Historical cohort of twin gestations cared for by a maternal–fetal medicine faculty practice. Outcomes of patients with AMA (70) and non-AMA (75) were compared. AMA was defined as age ≥35. Analysis including mode of delivery, gestational age at delivery and overall complications was performed. Significance was determined using the chi-square test or the Student’s t-test.

Results. The Cesarean rate for AMA was significantly greater compared to non-AMA (80.0% vs. 54.7%; p = 0.001). The main reason for the increased rate was uterine dysfunction. The mean gestational age at delivery for AMA was significantly greater than for non-AMA (36.7 weeks vs. 35.4 weeks; p = 0.02). There were no differences in rates of other adverse outcomes including gestational hypertension, pre-eclampsia, gestational diabetes, suspected fetal growth restriction, preterm birth, low birth weight or low birth weight percentiles. This remained true when we compared the 32 women ages ≥40 years to 118 women ages <40 years.

Conclusion. Among twin pregnancies, AMA women are not at an increased risk of adverse pregnancy outcomes, aside from an increased rate of cesarean delivery.

Keywords: Multiple gestation, advanced maternal age, pregnancy

Introduction

Advanced maternal age (AMA) is associated with an increased risk perinatal morbidity and mortality in singleton pregnancies [1–5]. It has been presumed that pregnancy complications would be increased in AMA twin gestation versus non-AMA twin gestations as has been shown in singleton gestations. However, literature on multifetal pregnancy in older women is limited, and the published data seems to indicate that AMA does not increase the risk of adverse perinatal outcomes in twin pregnancies. One study from Greece that compared 57 women with twin pregnancies age 35 or older to 181 women with twin pregnancies younger than 35 found that adverse pregnancy outcomes were not increased in the AMA women, aside from an increased frequency of very low birthweight (VLBW) infants (28% vs. 17.5%; p = 0.01) [6]. Another study from Japan that compared 60 nulliparous women with twin pregnancies age 35 or older to 71 nulliparous women with twin pregnancies aged 20–29 did not find any increased risk of adverse perinatal outcomes in the AMA women [7]. A large retrospective study based on a national database developed by the National Center for Health Statistics found an increased risk of adverse perinatal outcomes in AMA women compared to younger women only in singleton pregnancies; AMA did not increase the risk of adverse perinatal outcome in twin pregnancies overall [8]. Our goal was to evaluate whether in our patient population there were
increased pregnancy risks associated with AMA in twin gestation.

**Material and methods**

This study included all twin gestations cared for by a Maternal–Fetal Medicine faculty practice over a 40-month period from December 1998 to March 2002. The plans for antenatal and intrapartum care of these patients were realised according to protocols of the faculty practice, which reflect the contemporary standard of care. This included fetal growth scans every 3–4 weeks starting at 24 weeks gestation. All pregnancies that presented at time of delivery with Twin A in vertex presentation were anticipated vaginal deliveries, unless contraindicated. Contraindications included prior uterine surgery, suspected discordancy (Twin B’s estimated fetal weight ≥20% more than Twin A) or patient’s desire for repeat Cesarean delivery.

Data were collected through a directed chart review by research staff. The data collection focussed on characteristics of the patients, their antenatal and intrapartum course, as well as the fetuses and on complications. Information gathered included the age of the patients at their first prenatal visit, their obstetrical history, the mode of delivery, and the use of assisted reproductive technology (ART) to conceive the pregnancy. AMA was defined as ≥35 years old at the time of delivery. The diagnosis of gestational hypertension or pre-eclampsia prior to the onset of labour was made using standard criteria [9]. We used published tables to determine birth-weight percentile [10]. Monoamniotic twin pregnancies were excluded. The accuracy of the data collection was assured by a second independent review of 46 randomly selected charts. The study was performed under the auspices of the Institutional Review Board.

Continuous variables were analysed using Student’s *t*-test and categorical variables were analysed using the chi square test (SPSS 12.0 for Windows copyright 1989–2003, Chicago). All *p*-values are two-sided with statistical significance evaluated at the 0.05 *α* level.

**Results**

There were 145 twin pregnancies included: 70 AMA and 75 non-AMA. There was a higher proportion of assisted reproduction in the AMA group (94.3% vs. 84%; *p* = 0.05), as well as IVF or ICSI in particular (91.4% vs. 64%; *p* < 0.001). The proportion of nulliparous patients was similar between the groups (77.1% vs. 74.7%; *p* = 0.73), as was the proportion of monochorionic pregnancies (0% vs. 4%; *p* = 0.09).

Table I describes twin pregnancy complications in patients with AMA and non-AMA. There were no differences in the rates of gestational hypertension, pre-eclampsia, gestational diabetes mellitus, suspected intrauterine growth restriction (IUGR), preterm birth <37 weeks and preterm birth <32 weeks. There were fewer preterm births <35 weeks in the AMA group, and the AMA group delivered on average a week later. The AMA group had a significantly higher rate of cesarean delivery (80% vs. 54.7%; *p* = 0.001). We re-analysed our data defining AMA as ≥40 years old. Comparing the 32 women ≥40 years old to the 113 women <40, there were no statistically significant differences in any of the above adverse outcomes.

Birth weight data were available for 287/290 (99%) of the newborns and is described in Table II. AMA women delivered larger children and were less likely to have birth weights <2500 g (Low Birth Weight, LBW). There was no difference in the proportion of newborns with a birthweight <1500 g (VLBW). There were no differences in the proportion of babies

Table I. Pregnancy outcomes in women with twin gestation, based on maternal age ≥35 or <35 years.

<table>
<thead>
<tr>
<th>Age ≥ 35 (n = 70)</th>
<th>Age &lt; 35 (n = 75)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational hypertension (%)</td>
<td>14.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Pre-eclampsia (%)</td>
<td>12.9</td>
<td>10.7</td>
</tr>
<tr>
<td>Gestational hypertension or pre-eclampsia (%)</td>
<td>24.3</td>
<td>14.7</td>
</tr>
<tr>
<td>Gestational diabetes (%)</td>
<td>10.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Suspected intrauterine growth restriction</td>
<td>4.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Preterm birth &lt;37 weeks (%)</td>
<td>44.3</td>
<td>58.7</td>
</tr>
<tr>
<td>Preterm birth &lt;35 weeks (%)</td>
<td>15.7</td>
<td>33.3</td>
</tr>
<tr>
<td>Preterm birth &lt;32 weeks (%)</td>
<td>7.1</td>
<td>16</td>
</tr>
<tr>
<td>Gestational age at delivery, weeks (mean ± SD)</td>
<td>36.7 ± 2.8</td>
<td>35.4 ± 3.4</td>
</tr>
<tr>
<td>Cesarean delivery (%)</td>
<td>80.0</td>
<td>54.7</td>
</tr>
</tbody>
</table>

Means compared with two independent sample *t*-test, proportions compared with chi square test.

Table II. Newborn birth weights and percentiles in women with twin gestation, based on maternal age ≥35 or <35 years.

<table>
<thead>
<tr>
<th>Age ≥ 35 (n = 139)</th>
<th>Age &lt; 35 (n = 148)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g) (mean ± SD)</td>
<td>2502 ± 619</td>
<td>2321 ± 645</td>
</tr>
<tr>
<td>Birth weight &lt;1500 g (%)</td>
<td>7.9</td>
<td>12.8</td>
</tr>
<tr>
<td>Birth weight &lt;2500 g (%)</td>
<td>41.7</td>
<td>55.4</td>
</tr>
<tr>
<td>Birth weight &lt;5th percentile (%)</td>
<td>21.6</td>
<td>18.2</td>
</tr>
<tr>
<td>Birth weight &lt;10th percentile (%)</td>
<td>36</td>
<td>34</td>
</tr>
</tbody>
</table>

Means compared with two independent sample *t*-test, proportions compared with chi square test.
with birth weights less than the 5th or 10th percentile for gestational age at delivery. This was also true when we used an age of 40 years as the cut-off for AMA.

Table III presents the indications for cesarean section for AMA vs. non-AMA twin gestations. The rates for arrest disorders and failed induction were both significantly increased in AMA women. There were no significant differences in the other indications for Cesarean section.

Nulliparity, prior vaginal delivery, IVF or ICSI, any use of ART, chorionicity, birth weight of twin A, birth weight of twin B, and gestational age at delivery were all not associated with cesarean delivery. Maternal age was the only characteristic significantly associated with cesarean delivery. The mean age of women who had a cesarean delivery was significantly higher than women with a vaginal delivery ($35.9 \pm 6.2$ vs. $32.6 \pm 6.2$; $p = 0.003$). The rate of cesarean delivery in the youngest one-third of women (aged 20–32), middle one-third (aged 33–37), and oldest one-third (aged 38–52) were 52%, 70% and 81%, respectively ($p = 0.008$).

Comment

Birth rates for women aged 35–39 and aged 40–45 in 2006 continued to increase in the United States to their highest level in at least 30 years: 47.3 and 9.4 births per 1000 women, respectively [11]. The number and rate of twin births continues to rise as well; in the United States in 2005, 3.2% of all births were twin births [11]. The increase in twin births is related to both the increased age at childbearing, as well as the increased use of assisted reproductive technologies.

Women of AMA with singleton gestations are at increased risk of fetal death [3–5], preterm birth and small for gestational age infants [2,4,5], as well as complications because of diabetes and hypertensive disorders of pregnancy [4,5]. Maternal age in singleton gestations is also an independent risk factor for cesarean delivery [12–14]. Twin gestation is also associated with an increased risk of perinatal morbidity and mortality [15]. Rates for both gestational hypertension and pre-eclampsia are significantly higher in twins as well [15,16].

It is generally believed that older grvidas with twin gestations are at increased risk compared to their younger counterparts in a similar or additive way to singleton gestations. However, there is a paucity of objective data to advice patients of AMA of their risks associated with twin gestations [6–8]. On the basis of these prior studies, AMA appears only to increase the risk of VLBW infants among twin pregnancies; otherwise, AMA was not associated with an increased incidence of adverse perinatal outcomes, including cesarean delivery.

It has been previously shown that women who attend an infertility clinic expressed the desire to conceive a twin pregnancy, although they could not accurately estimate the probability of risks associated with this type of pregnancy. After being confronted with the actual probabilities of specified perinatal complications associated with twin pregnancy, women were less desirous of having a twin pregnancy than they had originally expressed [17].

The purpose of our study was to obtain objective data which would aid physicians in both pre-conception counselling of patients who are older and undergoing assisted reproductive technologies that increase their risk of multiple gestation, as well as for AMA patients with twins presenting for prenatal care to better understand their true overall pregnancy risks. We anticipate that the incidence of AMA twin pregnancies will continue to increase and these types of consultations will become more frequent.

We did not find an increased rate of most pregnancy complications including gestational hypertension, pre-eclampsia, gestational diabetes mellitus, suspected IUGR, preterm birth, LBW, VLBW or low birth weight percentiles. These findings differ from AMA singleton gestations where there has been a reported increased rate of both preterm delivery and fetal growth restriction [2,4,5]. It is important to note that there was no difference in the incidence of preterm birth or fetal growth restriction between the two groups, the major causes of morbidity and mortality in twin gestation. Although probably not clinically significant, in fact AMA twins delivered at a statistically significantly later gestational age than non-AMA twins.

There was a significantly greater incidence of Cesarean section for the AMA when compared with the non-AMA group (80% vs. 54.7%; $p = 0.001$), and appears to be due an increase in failed
inductions and arrest disorders. An advantage of our study was that care was uniform and provided by a
small group of maternal–fetal medicine physicians who agreed to minimal criteria that would contra-
indicate attempted vaginal birth.

The finding of an increased risk of cesarean delivery with advancing maternal age is well described
[12–14]. Older women are more likely to undergo cesarean delivery regardless of whether labour is
spontaneous or induced [13]. The main reasons for this increase was a higher rate of uterine dysfunction as
evidenced in our study by a significantly increased incidence of both arrest disorders and failed induc-
tion. Main et al. [14] found more cesarean deliveries for failure to progress with advancing maternal age.
Importantly, they noted that there was not a sudden increase in these outcomes at the age of 35 but rather
a steady change beginning at age 25, a pattern suggesting a gradual decrease in myometrial function
with increasing age. In contrast to singleton AMA gestations, which has been shown to have an
increased rate of cesarean sections for fetal distress [13,14], we did not find a difference in the rate for
this indication in our AMA twin gestations.

A limitation to our study is the small sample size. Despite this small sample size, we were able to
demonstrate a significantly higher rate of cesarean delivery in AMA twin pregnancies. Regarding the
other adverse outcomes where we did not see any differences, it is possible that if we had more twin
pregnancies, our results for other outcomes would have been different. A post-hoc power analysis reveals
that in order to have 80% power to demonstrate a difference in the rates of gestational hypertension or
pre-eclampsia from 24.3% to 14.7% (as seen in this study) with an z error of 5%, we would have needed
266 patients in each group. For gestational diabetes and growth restriction, because those were less
common than hypertension in our patients, we would have needed even more patients to have adequate power.

In conclusion, we found only the rate of Cesarean deliveries for AMA twin pregnancies to be signifi-
cantly higher than non-AMA. Otherwise, AMA was not associated with increased adverse outcomes.
This is important in counselling patients with AMA both during preconception who are undergoing
infertility treatments and at the initial prenatal visit for a new twin pregnancy so that women can better
understand their true pregnancy risks. Our findings are encouraging to patients and obstetricians that
AMA is not a significant contributor to adverse outcomes in twin pregnancies, aside from an
increased cesarean delivery rate.

Declaration of interest: The authors report no conflicts of interest. The authors alone are respon-
sible for the content and writing of the article.

References
6. Prapas N, Kalogiannidis I, Prapas I, Xiromeritis P, Karagiannidis A, Makedos G. Twin gestation in older women: antepartum, intrapartum complications, and perinatal out-