Pregnancy Outcomes in Women of Advanced Maternal Age

Mehrnaz Valadan; M.D., Fatemeh Davari Tanha; M.D., Azam Sepahi, M.D.

Department of obstetrics and gynecology, Mirza Koochak Khan Hospital, Tehran University of Medical Sciences, Tehran, Iran

Received March 2011; Revised and accepted May 2011

Abstract
Objective: The aim of this study was to investigate prenatal and obstetrical outcome in mothers aged 40 years or older.

Materials and methods: A prospective comparative study was conducted for the women aged 40 years and over who delivered at 20 week’s gestation or beyond from January 2004 to December 2005 at four Hospitals of Tehran University of Medical Sciences. For comparison, a control group of patients who were 20-29 years of age was considered.

Results: There were statistically significant increases in the rates of gestational diabetes, preeclampsia, caesarean section, breech presentation and stillbirth in women 40 years of age or older.

Conclusion: There is a need to offer older women special counseling both before and after conception so that they become informed of the increased risks involved.

Key words: Pregnancy, Outcomes, Advanced maternal age

Introduction
Advanced maternal age, defined as maternal age of 40 years or greater at the time of delivery, has important consequences for both mother and baby (1).

These women frequently request specific information regarding the likely outcome of their pregnancy. Given the trend towards delayed child bearing and the increasing availability of assisted reproductive techniques, women aged 40 and over may increasingly seek advice about the risks of embarking on a pregnancy.

Increasing maternal age is known to be associated with increased rates of cardiovascular disease, diabetes, obesity, uterine leiomyomata, multiparity and previous caesarean section, during pregnancy, there is an increased risk of hypertensive disorders of pregnancy, gestational diabetes, caesarean delivery and maternal mortality (2, 3).

There is an increased risk of chromosomal abnormalities in the fetus. The perinatal mortality rate is increased, although this can be partly explained by age related confounders (4).

We believed it was important to document the outcomes for women of advanced maternal age in our care, so as to be able to provide better advice to women in this situation. The aim of this study was to assess the outcome for women aged 40 years and over who delivered beyond 20 week’s gestation in four hospitals of Tehran University of medical sciences.

Methods & Materials
A prospective comparative study was conducted for the women aged 40 years and over who delivered at 20 week’s gestation or beyond from January 2004 to December 2005 in four teaching hospitals (Mirza...
Koochak Khan, Emam, Shariatii and Arash Hospitals) these obstetric services are staffed by residents, and faculty of the department of obstetrics and Gynecology of Tehran university of medical sciences.

The study was approved by the Ethics committee, Faculty of Medicine, university of Tehran. After written informed consent was obtained, patients were enrolled into this study.

Information was collected prospectively by the staff responsible for the care of the patients and includes demographic data, reproductive history, and complications during pregnancy, delivery, and neonatal period.

A control group of patients was obtained by retrieving records of all delivery patients who were 20-29 years of age on the day of delivery. Each group was divided into nulliparous and multiparous subgroups. We matched the two groups by mode of delivery, mean birth weight, and gestational age. We ascertained the incidence of several birth outcomes as well as maternal complications. We compared 100 women aged 40 years or over with 300 women who were 20-29 years of age on the day of delivery.

We considered the following covariates: maternal age, education, smoking and drinking alcohol during pregnancy. Parity refers to the total number of live deliveries of the mother and was classified into nullipara (<1), multipara (>1).

Complication during pregnancy was defined as history of gestational diabetes, pregnancy-induced hypertension, or preeclampsia. Pregnancy outcome such as stillbirth, birth weight, gestational age of delivery, and infant gender, were recorded in the delivery or pediatric records. Gestational age was calculated by using information from date of birth and estimated date of delivery as determined in early pregnancy. This is usually based on a first or second trimester ultrasound scan performed at no later than 18 completed weeks of gestation.

Small for gestational age (SGA) was defined as a birth weight below 2 standard deviations from the mean weight corrected for gestational age and gender (5). Large for gestational age (LGA) was defined as a birth weight more than 2 standard deviations from the mean weight corrected for gestational age and gender (5).

Perinatal mortality was defined as stillbirth or death during days 0-6. Neonatal death was defined as born alive and death during days 0-28. Data were analysed with SPSS using chi square & Fisher exact test for statistical tests. Results are presented in tables.

Results
During the study period four hospitals of Tehran University of medical sciences there was a total of 10275 Deliveries beyond 20 week’s gestation. One hundred pregnancies were recorded in women aged 40 or over during this time. This represents an incidence of 9.7 per 1000 births. A total of 300 patients as a control group were obtained by retrieving records of all delivering patients who were 20-29 years of age on the day of delivery. Table 1 demonstrates the obstetric complications by maternal age. Because some complications of pregnancy are affected by parity, each group was divided into a nulliparous and a multiparous subgroup; in case group 80 women were multiparous compared with 168 women in the 20-29 year age group. There were statistically significant increases in the rate of most complications of pregnancy in both the nulliparous and multiparous women in the case group versus the controls.

Data regarding parity is shown in table 2. The overall caesarean section rate in the nulliparous case group was 60%, as opposed to 18.9% in the nulliparous 20-29 year age group (P<0.05), but there wasn’t any significant difference in the caesarean section in multiparous groups. Gestational diabet occurred in 5 nulliparous ≥40 year age group (25%), compared to 4.5% in the nulliparous 20-29 year age group (P= 0.001).

There was a significant increase in gestational diabetes in multiparous old age women compared with the young age group (P Value= 0.01). The risk of developing preeclampsia increased with increasing maternal age in multiparous and nulliparous groups. (P Value= 0.002 and 0.01 respectively).

The risk of third trimester hemorrhage, PROM, P PROM, twin pregnancy and macrosomy were not increased in multiparous and nulliparous case group compared with the 20-29 year age group. Breach presentation and stillbirth were increased in the multiparous ≥40 year age group (P Value= 0.02).

Considering the frequency of preterm deliveries we found a significant increase in the multiparous old age group p< 0.04. Intra uterine growth retardation was increased in the nulliparous old age group compared with the 20-29 year age group. But there wasn’t any difference in multiparous group.

Discussion
The impact the decision to delay childbearing has on maternal and a perinatal outcome becomes increasingly relevant as more and more women postpone having children until they are over the age of 35 (6).
Advanced maternal age and pregnancy

Table 1: Obstetrical complications by maternal age.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Gestational Diabetes</th>
<th>Preeclampsia</th>
<th>Third trimester hemorrhage</th>
<th>Cesarean Section</th>
<th>PROM</th>
<th>Twin pregnancy</th>
<th>Breech presentation</th>
<th>Macrosomia</th>
<th>Stillbirth</th>
<th>Preterm labor</th>
<th>IUGR</th>
<th>Neonatal admission in NICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>17(5.6%)</td>
<td>20(6.6%)</td>
<td>8(2.6%)</td>
<td>96(32%)</td>
<td>10(3.3%)</td>
<td>4(1.3%)</td>
<td>8(2.6%)</td>
<td>6(2%)</td>
<td>8(2.6%)</td>
<td>34(11.3%)</td>
<td>6(2%)</td>
<td>12(4%)</td>
</tr>
<tr>
<td>≥40 Y</td>
<td>18(18%)</td>
<td>20(20%)</td>
<td>6(6%)</td>
<td>47(47%)</td>
<td>3(3%)</td>
<td>1(1%)</td>
<td>10(10%)</td>
<td>5(5%)</td>
<td>8(8%)</td>
<td>17(17%)</td>
<td>10(10%)</td>
<td>7(7%)</td>
</tr>
<tr>
<td></td>
<td>P Value &lt;0.001</td>
<td>&lt;0.001</td>
<td>0.11</td>
<td>0.007</td>
<td>0.87</td>
<td>1.14</td>
<td>&lt;0.05</td>
<td>0.11</td>
<td>0.05</td>
<td>1.14</td>
<td>0.25</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>Odds ratio 3.65</td>
<td>6.50</td>
<td>2.3</td>
<td>1.88</td>
<td>0.89</td>
<td>0.22</td>
<td>4.05</td>
<td>0.11</td>
<td>0.05</td>
<td>0.14</td>
<td>0.27</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>Confidence interval</td>
<td>1.80-7.41</td>
<td>0.78-6.88</td>
<td>1.18-2.99</td>
<td>0.24-3.32</td>
<td>0.23-1.42</td>
<td>1.55-10.58</td>
<td>0.77-8.64</td>
<td>0.72</td>
<td>0.88-3.01</td>
<td>0.70</td>
<td>0.69-4.72</td>
</tr>
<tr>
<td></td>
<td>Result S†</td>
<td>S</td>
<td>NS††</td>
<td>NS</td>
<td>S</td>
<td>NS</td>
<td>S</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

PPROM* Premature preterm rupture of membrane
PROM** Premature rupture of membrane
S† Significant
NS†† Non Significant

Being pregnant and giving birth at the age of forty or more years relatively common until the middle of the 20th century (5).

The major difference during the last 3 decades is that women are more often using the latter part of their reproductive period to have all their children and this trend of postponing childbearing has not yet shown any tendency to decrease (7-10).

The definition of advanced maternal age varies from study to study, with most of the earlier reports fixing the cutoff point at 35 years (3, 11-14) and the more recent ones around 40 years (7-9, 14-18). This is probably a reflection of improvement in birth outcomes over the years as a result of enhanced understanding of the risks associated with these pregnancies (1). There are numerous reports in the literature assessing the effect of advancing maternal age on pregnancy outcomes, but results are varied (6).

This study has demonstrated an increase in gestational diabet, preeclampsia, caesarean section, breech presentation, stillbirth in women 40 years of age or older. The increased incidence of diabetes is evidently related to the aging process in the mother (1). Preeclampsia is reported to be more common at the extremes of reproductive age and may actually be related to underlying chronic hypertension (1).

Table 2: Frequency of neonatal and maternal complications regarding parity in different age groups

<table>
<thead>
<tr>
<th>Nulliparous</th>
<th>≥ 40 years (n=20)</th>
<th>20-29 years (n=132)</th>
<th>P Value</th>
<th>Multiparous</th>
<th>≥ 40 years (n=80)</th>
<th>20-29 years (n=168)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational diabetes</td>
<td>(5)25%</td>
<td>4.5%(6)</td>
<td>0.001</td>
<td>16.2%(13)</td>
<td>6.5%(11)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>(5)25%</td>
<td>7.5%(10)</td>
<td>0.01</td>
<td>18.7%(15)</td>
<td>5.9%(10)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>3rd trimester hemorrhage</td>
<td>(1) 5%</td>
<td>3%(4)</td>
<td>&gt;0.05</td>
<td>6.3%(5)</td>
<td>2.3%(4)</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>Cesarean</td>
<td>(12) 60%</td>
<td>18.9%(25)</td>
<td>&lt;0.05</td>
<td>35%(28)</td>
<td>42.2%(71)</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>PROM</td>
<td>0</td>
<td>3.7%(5)</td>
<td>1</td>
<td>3.7%(3)</td>
<td>2.9%(5)</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Twin pregnancy</td>
<td>(2) 10%</td>
<td>6.3%(9)</td>
<td>0.6</td>
<td>5%(4)</td>
<td>12%(21)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Breech presentation</td>
<td>(2) 10%</td>
<td>2.2%(3)</td>
<td>0.13</td>
<td>7.5%(6)</td>
<td>0</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Macrosomia</td>
<td>(2) 10%</td>
<td>3%(4)</td>
<td>0.1</td>
<td>3.7%(3)</td>
<td>1.1%(2)</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Stillbirth</td>
<td>(1) 5%</td>
<td>3%(4)</td>
<td>0.5</td>
<td>8.7%(7)</td>
<td>2.3%(4)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Preterm labor</td>
<td>(2) 10%</td>
<td>13.6%(18)</td>
<td>0.65</td>
<td>18.7%(15)</td>
<td>9.5%(16)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>IUGR</td>
<td>(4) 20%</td>
<td>3.7%(5)</td>
<td>0.04</td>
<td>7%(6)</td>
<td>8.9%(15)</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>NICU admission</td>
<td>(2) 10%</td>
<td>4.5%(6)</td>
<td>0.33</td>
<td>6.2%(5)</td>
<td>3.5%(6)</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>
was a significant difference in the rate of caesarean delivery between women of advanced maternal age and younger patients. This is consistent with other studies (2, 3, 15-18). Possible reasons for this include obstetrician and patient preference, the impact of aging on myometrium efficiency and elasticity of pelvic joints, and age related confounders including the increased risk of fetal distress due to underlying cardiovascular disease, non-vertex presentation due to leiomyoma and multiparity, increased rates of placenta previa with multiparity and the requirement for repeat caesarean sections with multiparity (4). In this study we found one of the highest cesarean delivery rates reported. This may be due to this point that the four hospitals in which we conducted the study are dependant to Tehran University of Medical Sciences which is a referral center for higher-risk patients. Conduction of labor by residents may be the other reason for this unusual high rate. In our study the cesarean delivery rate in nulliparous women in advanced age was significantly higher than the rate in multiparous women in advanced age. In the study by Herng-ching lin et al, one other cause contributing to the high cesarean section among older women was physician preference. A majority of obstetricians may believe that older women are more likely to be at risk for adverse pregnancy outcomes. Therefore, this perception on the part of physicians produces a greater tendency to perform caesarean section on nulliparous older women (19).

So in addition to medical factors, there has been much speculation about other factors contributing to this high C/S rate among older women. Factors such as socioeconomic status, parental anxiety, previous infertility and physician beliefs.

We compared maternal and neonatal complications in two groups with regard to parity. The multiparous women in our study who were aging 40 years or older had significant increases in rates of gestational diabetes, preeclampsia, breach presentation, stillbirth and preterm labor compared with multiparous younger controls.

In the Gilbert study, mean gestational age at delivery in the old women was statistically significantly lower than for the control population. Gestational age was lower even when parity was taken into account (7). Likewise in the study by Astolfi, the frequency of preterm deliveries was lowest in mothers aged between 20 and 30 years, but this increased sharply as maternal age increased (20). The causes are unknown but may relate to underlying maternal or fetal problems such as diabetes, chronic hypertension and fetal distress.

The nulliparous women in our study who were age 40 or older had significant increases in rates of gestational diabetes, preeclampsia, caesarean section, IUGR compared with nulliparous younger women.

Our study was confined to women with a pregnancy progressing beyond 20 weeks. Thus it does not provide data regarding the rates of termination of pregnancy for chromosomal abnormalities or spontaneous abortion in these groups of women.

Another possible factor that could have influenced our result is the effect of assisted reproduction technology. Although the absence of information on assisted reproduction technology in our data set limits our ability to investigate its role in fetal birth outcomes, it is still possible to reasonably discuss its likely impact in this study. Studies have found that pregnancies resulting from assisted reproduction technology have less favorable outcomes compared with naturally conceived among older mothers compared with 20-29 year olds (1). In conclusion, we found increased risks for some maternal and neonatal complications among women age forty or more.

Consequently, there is a need to offer older women special counseling both before and after conception so that they become informed of the increased risks involved.

Acknowledgement

There is no conflict of interest among the authors. Funding: no.

References

Advanced maternal age and pregnancy