Pregnancy Over 35→40

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Learning Objectives

- Review maternal and fetal morbidity associated with advanced maternal age pregnancy
- Review screening for fetal chromosomal abnormalities in advanced maternal age pregnancy
- Review risk and rates of fetal loss associated with advanced maternal age pregnancy
- Discuss age as a factor in considering non-medically indicated (elective) deliveries before 39 weeks
- Review recommendations for antenatal care of pregnant women over age 35
Disclosure

I have no financial relationship with a commercial entity producing health-care related products and/or services.
Case #1 - HB

HB is a 46 year-old African-American woman, gravida 2 para 1001, who presents to your office for a first prenatal visit. She had a previously uncomplicated natural pregnancy at age 41 and underwent an elective induction of labor at term. She has no medical conditions. A 9 weeks singleton gestation is confirmed on ultrasound. She is happy though anxious about this unexpected pregnancy and has many questions regarding her risk for pregnancy complications.
What is the age related risk for chromosomal abnormality in pregnant women over age 40?

<table>
<thead>
<tr>
<th>Maternal Age</th>
<th>Risk of Trisomy 21</th>
<th>Risk of All Chromosome Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>1/353</td>
<td>1/178</td>
</tr>
<tr>
<td>36</td>
<td>1/267</td>
<td>1/148</td>
</tr>
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<td>37</td>
<td>1/199</td>
<td>1/122</td>
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<td>1/148</td>
<td>1/104</td>
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<tr>
<td>39</td>
<td>1/111</td>
<td>1/80</td>
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<td>40</td>
<td>1/85</td>
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<td>41</td>
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<tr>
<td>50</td>
<td>1/25</td>
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</tr>
</tbody>
</table>

What is the age related risk for chromosomal abnormality in pregnant women over age 40?

**TABLE 1** Calculated risk at term for a chromosomal abnormality among infants of women aged 40 to 46 years

<table>
<thead>
<tr>
<th>Maternal age (yrs)</th>
<th>Singleton</th>
<th>Down syndrome</th>
<th>All chromosomal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>White twins</td>
<td>Black twins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One or both</td>
<td>Both affected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One or both</td>
<td>Both affected</td>
</tr>
<tr>
<td>40</td>
<td>1/106</td>
<td>1/56</td>
<td>1/973</td>
</tr>
<tr>
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<td>41</td>
<td>1/82</td>
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<td>1/27</td>
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</tr>
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<td>1/319</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>1/38</td>
<td>1/20</td>
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<td></td>
<td>1/381</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>1/30</td>
<td>1/16</td>
<td>1/269</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1/348</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>1/23</td>
<td>1/12</td>
<td>1/160</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1/284</td>
<td></td>
</tr>
</tbody>
</table>

Source: OBG Management November 2014 Vol. 26 No. 11
What are available options for genetic screening?

- Maternal serum cell free DNA screening (noninvasive prenatal testing (NIPT) for aneuploidy) for trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) or trisomy 13 (Patau syndrome)  *Recommended*

- First trimester maternal serum screening +/- ultrasound (10-14 weeks)

- Second trimester maternal serum screening +/- with ultrasound (15-20 weeks)

- 1\textsuperscript{st} and 2\textsuperscript{nd} trimester - Integrated, stepwise sequential or contingency screening

- Chorionic villus sampling (CVS) (10 – 13 weeks gestation)

- Amniocentesis (15 – 18 weeks gestation though can be done earlier)

Source: ACOG Practice Bulletin No. 77 Jan 2007 and ACOG Committee Opinion No. 545 December 2012
What are available options for genetic screening?

- Maternal serum cell free DNA sequencing (MaterniT21, verify, Harmony, Panorama)
  - Offered starting at 10 weeks (singleton and twins, not higher order multiples)
  - Detection rates for Down syndrome above 99% and false positive rates that are <1%
- Most appropriate for high risk women:
  - Maternal age of 35 years or older at delivery
  - Fetal ultrasound findings indicating an increased risk of aneuploidy
  - History of a prior pregnancy with a trisomy
  - Positive first- or second-trimester screening test results for aneuploidy
  - Parental balanced Robertsonian translocation with an increased risk of fetal trisomy 13 or trisomy 21
- Is a screening test and does not replace the precision of chorionic villus sampling (CVS) or amniocentesis

Source: ACOG Practice Bulletin No. 77 Jan 2007 and ACOG Committee Opinion No. 545 December 2012
What is the risk of miscarriage associated with advanced maternal age?

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate of loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 35</td>
<td>12-15%</td>
</tr>
<tr>
<td>35-40</td>
<td>16-22%</td>
</tr>
<tr>
<td>40-44</td>
<td>33-50%</td>
</tr>
<tr>
<td>44 and over</td>
<td>&gt;60%</td>
</tr>
</tbody>
</table>

Risk of spontaneous abortion in nulliparous and parous women according to maternal age at conception and number of spontaneous abortions in preceding 10 years.
Risk of fetal loss from spontaneous abortion, ectopic pregnancy, and stillbirth according to maternal age at conception.
MR is a 40 year-old Irish-American woman, gravida 3 para 1011, at 34 weeks gestation, who reports one day of decreased fetal movement. She has a medical history of infertility and chronic hypertension. At age 18, she underwent a first-trimester, medical termination. At age 31, she had a healthy, uncomplicated pregnancy followed by several years of infertility including four failed IVF cycles. She conceived this pregnancy spontaneously. A non-stress test performed is non-reactive. A biophysical profile performed is 8/10. She asks if she should have further testing and asks to schedule an induction of labor before her due date at 40 weeks gestation.
What are the risks of antepartum stillbirth, perinatal death and neonatal morbidity associated with advanced maternal age?

- Maternal age of 40 years and older is an independent risk factor for stillbirth

- The risk of stillbirth rises with age (peak risk is 41 weeks gestation)
  - 1 in 382 for women 35-39 at 37 to 41 weeks
  - 1 in 267 for women age 40 and over at 37 to 41 weeks (higher in nulliparous women over 40)
  - Over the pregnancy, the rate is 11-14/1000 (age 35 and over)

- Fetal/Neonatal Morbidity
  - Fetal aneuploidy and fetal malformation
  - Perinatal death
  - Low birth weight
  - NICU Admission

Figure Hazard (risk) of stillbirth for singleton births without congenital anomalies by gestational age, 2001-2002.

Uma M. Reddy, Chia-Wen Ko, Marian Willinger

Maternal age and the risk of stillbirth throughout pregnancy in the United States

Do you offer further antenatal testing?

- Not for age alone

- Testing may increase cost, morbidity due to premature intervention for false positive results and an increase in late term delivery

- In Case #2, weekly antenatal testing would occur due to her comorbid condition of chronic hypertension

- Though women over 35 are at an increased risk for stillbirth, a National Institute of Child Health and Human Development workgroup found insufficient evidence to support antenatal fetal testing for the sole indication of advanced maternal age

- Options include
  - Maternal - Fetal movement assessment
  - Nonstress test (NPV 99.8%)
  - Fetal biophysical profile (NPV 99.9%)
  - Modified biophysical profile (NPV 99.9%)
  - Umbilical artery Doppler velocimetry (NPV 100%)

How do you manage this patient’s request for an early, elective delivery?

- Elective delivery prior to 39 weeks is not recommended

- Many maternity facilities have “hard stops” against elective induction without medical indications such as:
  - Hypertensive disorders (gestational HTN, chronic HTN, preeclampsia, eclampsia, HELLP)
  - Gestational diabetes with complications
  - Preterm premature rupture of membranes
  - Placenta previa or abruption
  - Maternal medical conditions, e.g., diabetes, renal disease, chronic pulmonary disease, antiphospholipid syndrome
  - Fetal compromise, e.g., severe Intrauterine Growth Restriction (IUGR), isoimmunization, oligohydramnios
  - Multiple gestation
  - Prior uterine surgery with compromise to myometrial strength/risk of rupture

Joint Commission National Quality Core Measures 2010a, Perinatal Care Core Measure Set 2009
How do you manage this patient’s request for an early, elective delivery?

- Reasons often cited and no longer accepted
  - History of fast labors
  - Advanced cervical dilation
  - Prodromal or impending labor
  - Previous maternal pelvic floor injury (e.g., 4th degree laceration)
  - Distance from home to delivery hospital
  - Provider convenience/schedule
- Psychosocial issues:
  - Partner leaving town such as military leave
  - Family in town
  - Maternal exhaustion or discomforts
  - Psychiatric issues (anxiety or depression)
  - Adoption

Source: March of Dimes Early Elective Delivery Toolkit
How do you manage this patient’s request for an early, elective delivery?

- Fetal benefits to delaying induction to 39 weeks
  - Decreased stillbirth rate by >50%, with greatest improvement in the 37-38 week groups
  - Decreased rates of postpartum anemia
  - Decreased rates of meconium aspiration
  - Decreased low Apgar scores

Case #3 - JL

JL is a 43 year-old, Latina woman, gravida 1 para, with a diamniotic/dichorionic twin gestation presents at 36 weeks with regular uterine activity. She is a successful lawyer who has delayed childbearing. She underwent in vitro fertilization using her own oocytes with two embryos transferred. No chromosomal abnormalities were detected on genetic screening. On examination, she has normal fetal growth, normal amniotic fluid volume and breech presentation of the presenting fetus. She is 5cm dilated and elects to undergo a cesarean delivery.
What are the risks of maternal morbidity associated with advanced maternal age?

- **Maternal**
  - Chronic hypertension, gestational hypertension and preeclampsia
  - Gestational diabetes
  - Premature labor and preterm premature rupture of membranes
  - Cholestasis of pregnancy
  - Preterm delivery (as a consequence of underlying complications)
  - Multiple gestation

- **Placental**
  - Abnormal placentation
  - Molar pregnancy

What are the risks for postpartum and postoperative complications associated with advanced maternal age?

- Sphincter rupture
- Cesarean delivery (54% in women 40 and over)
- Venous thromboembolism

Key Take Home Points for Caring for Women over 35>40

1. Women are delaying childbirth such that the mean age at first pregnancy is increasing
2. Risk for chromosomal abnormality and fetal loss, maternal morbidity, fetal morbidity and postpartum/postoperative complications increase with increased maternal age

3. Recommendations
   - First trimester: Genetic screening (e.g. maternal serum cfDNA) and Ultrasound for viability and count
   - Second trimester: Ultrasonographic fetal anatomy screening
   - Third trimester: Routine screening for IUGR (ie growth scan at 28 weeks)
   - Increased fetal surveillance for routine indications (such as HTN or diabetes) not age alone
   - If routine antenatal screening elected for age over 35, weekly testing stating at 37 weeks with amniotic fluid volume assessment is recommended
   - No recommendation for elective delivery prior to 39 weeks; though consider delivery by 40 weeks due to the risk of stillbirth (39 weeks with a favorable Bishop score)

4. Routine GYN care for women over 35 is an opportunity for pre/inter-conception counseling for health promotion, risk reduction and patient(couple)/provider shared decision making in birth planning
Thank you

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