First trimester screening for preeclampsia and IUGR

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No disclosure
Pregnant women 12 weeks

<table>
<thead>
<tr>
<th>Age: 35 years</th>
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<tbody>
<tr>
<td>Blood test 11.2 wks: PAPP-A =1 MoM, bHCG =0.7 MoM</td>
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<td>US 11.5 wks: normal anatomy, NT 1.2 mm (0.8 MoM)</td>
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<tr>
<td>Risk for Down’s syndrome 1/1200</td>
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<table>
<thead>
<tr>
<th>¿Risk for preeclampsia?</th>
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<tbody>
<tr>
<td>early preeclampsia</td>
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</table>
PREECLAMPSIA
Disease of the vascular endothelium which requires

- baseline hyperstimulation state (gestation)
- + maternal predisposition
- +/- additional insult (anomalous placentation)
PREECLAMPSIA

- Hypertension
- Proteinuria
- Liver enzymes
- Hemolysis
- Low platelets
- Eclampsia

IUGR

- Placental insufficiency
- Growth restriction
- Fetal hypoxia
- Abruptio placentae

Clinical variability

Sibai'06, Levine'06, Crispi'06, Egbor'06, Zhang'03, Sibai'03
Age: 35 years
Blood test 11.2 wks: PAPP-A =1 MoM, bHCG =0.7 MoM
US 11.5 wks: normal anatomy, NT 1.2 mm (0.8 MoM)
Risk for Down’s syndrome 1/1200

Risk for preeclampsia?
previous history and BP…

<table>
<thead>
<tr>
<th>early preeclampsia</th>
<th>late preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3-2%</td>
<td>2-8%</td>
</tr>
</tbody>
</table>
Epidemiological risk

- Antiphospholipid s. or previous PE
- BMI $\geq 35$ kg/m$^2$ or diabetes mellitus
- Nulilipara, twins, familiar history
- Age $\geq 40$y, chronic hypertension, renal/autoimmune disease, pregnancy $>10$y

Detection rate (10% FPR)
- early PE $\sim 40\%$
- late PE $\sim 30\%$

Maternal cardiovascular assessment

- Cardiac output
- Cerebral hemodynamics
- Pulse wave analysis

**Blood pressure**

*Detection rate (10% FPR)*

- early PE ~50%
- late PE ~35%

Pregnant women 12 weeks

Age: 35 years

Blood test 11.2 wks: \( PAPP-A = 1 \text{ MoM} \), \( bHCG = 0.7 \text{ MoM} \)

US 11.5 wks: normal anatomy, \( NT 1.2 \text{ mm } (0.8 \text{ MoM}) \)

Risk for Down’s syndrome 1/1200

¿Risk for preeclampsia?
European, nullipara, BMI 28, no previous disease
BP: 125/85

¿Uterine artery Doppler?
Uterine artery Doppler

Gómez O 2008, UOG 32:128-32
NORMAL PLACENTATION

ABNORMAL PLACENTACIÓN
EARLY PE/IUGR
At first trimester, detection rate for early PE **40-50 %** (5-10% FP)

Maternal history + uterine Doppler, detection rate for early PE **70-80 %** (10% FPR)
Pregnant women 12 weeks

Age: 35 years

Blood test 11.2 wks: \( PAPP-A = 1 \text{ MoM}, \ bHCG = 0.7 \text{ MoM} \)

US 11.5 wks: normal anatomy, \( NT = 1.2 \text{ mm (0.8 MoM)} \)

Risk for Down’s syndrome 1/1200

¿Risk for preeclampsia?

European, nullipara, BMI 28, no previous disease

BP: 125/85

Uterine artery Doppler: mean PI 1.8

¿Biochemical markers?
Biochemical markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Area under ROC curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIGF</td>
<td>0.654</td>
</tr>
<tr>
<td>PAPP-A</td>
<td>0.570</td>
</tr>
<tr>
<td>free bHCG</td>
<td>0.548</td>
</tr>
<tr>
<td>Inhibin-A</td>
<td>0.546</td>
</tr>
<tr>
<td>PP13</td>
<td>0.517</td>
</tr>
<tr>
<td>ADAM-12</td>
<td>0.500</td>
</tr>
</tbody>
</table>

Audibert et al. AJOG 2010
angiogenic proteins

vascular growth
angiogenesis

VEGF+

VEGF−

VEGF ++

VEGF +/−
## Biochemical markers

<table>
<thead>
<tr>
<th></th>
<th>early PE</th>
<th>late PE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIGF</strong></td>
<td>60%</td>
<td>-</td>
</tr>
<tr>
<td><strong>PAPP-A</strong></td>
<td>60%</td>
<td>45%</td>
</tr>
<tr>
<td><strong>sEng</strong></td>
<td>47%</td>
<td>-</td>
</tr>
<tr>
<td><strong>Inhibin A</strong></td>
<td>40%</td>
<td>17%</td>
</tr>
<tr>
<td><strong>PP13</strong></td>
<td>38%</td>
<td>-</td>
</tr>
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Pregnant women 12 weeks

Age: 35 years

Blood test 11.2 wks: \( \text{PAPP-A} = 1 \text{ MoM}, \text{bHCG} = 0.7 \text{ MoM} \)

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Risk for Down’s syndrome 1/1200

¿Risk for preeclampsia?

European, nullipara, BMI 28, no previous disease

BP: 125/85

Uterine artery Doppler: mean PI 1.8

Blood test: PAPP-A 1 MoM

COMBINED SCREENING
Combined first trimester screening

Detection rate (10% FP)

- early PE ~90%
- late PE ~60%

Poon LC, Hypertension 2009
Khalil A, Ultrasound Obstet Gynecol 2010
Poon LC, J Hum Hypertens 2010
Performance of a first-trimester screening of preeclampsia in a routine care low-risk setting.

Population
N=5170
early PE  0.5%
late PE   2.1%

Detection rate (10% FPR)
early PE  81%
late PE   40%

Scazzocchio AJOG 2013
## Preeclampsia risk

### Epidemiological data

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Parity</strong></td>
<td>Nullipara</td>
</tr>
<tr>
<td><strong>Previous PE</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Renal disease</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Coagulopathy</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td>European</td>
</tr>
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</table>

### Data at first TM US

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>CRL (mm)</strong></td>
<td>65</td>
</tr>
<tr>
<td><strong>PAPP-A (MoMs)</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td>125</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td>85</td>
</tr>
<tr>
<td><strong>mean UtAPI</strong></td>
<td>1.8</td>
</tr>
</tbody>
</table>

### Data at booking

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<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>35</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>165</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>65</td>
</tr>
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</table>

- **Calculate**
# Preeclampsia risk

<table>
<thead>
<tr>
<th>Parity</th>
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<tbody>
<tr>
<td>Previous PE</td>
<td>No</td>
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<tr>
<td>Hypertension</td>
<td>No</td>
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<tr>
<td>Renal disease</td>
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<td>No</td>
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<td>Diabetes</td>
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</table>

- **Age (years)**: 35
- **Height (cm)**: 165
- **Weight (kg)**: 65

- **CRL (mm)**: 65
- **PAPP-A (MoMs)**: 1
- **Systolic BP (mmHg)**: 125
- **Diastolic BP (mmHg)**: 85
- **Mean UtAPI**: 1.8

**PE risk**: 1/17  
**Early PE risk**: 1/37  
**Late PE risk**: 1/32
Information + monitoring symptoms

Monitoring BP (1-2 times per week)

Specific blood test
  (urine prot/creat ratio, liver & renal profile)

Maternal follow-up
  (every 2-3 weeks until 34w/ every 1-2 weeks > 34 wks)

Fetal US follow-up
  (fetal US 28, 32 +/- 36 weeks)

AAS 100 mg / day ?

<table>
<thead>
<tr>
<th></th>
<th>AAS</th>
<th>Control</th>
<th>OR (IC 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanio</td>
<td>2/43</td>
<td>10/43</td>
<td>0.16 [0.03, 0.79]</td>
</tr>
<tr>
<td>Ebrashy</td>
<td>26/74</td>
<td>40/65</td>
<td>0.34 [0.17, 0.68]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>117</td>
<td>108</td>
<td>0.29 [0.16, 0.55]</td>
</tr>
</tbody>
</table>

Van den Elzen 95, Martin 01, Vainio 05, Ebrashy 05, Gómez 05, Parra 05, Plasencia 07
prediction of PE & IUGR

EARLY-ONSET

1 %

LATE-ONSET

4-8 %

PREECLAMPSIA

1 %

PREECLAMPSIA + IUGR

1 %

IUGR

4-8 %

20 25 30 35 40

www.fetalmedicinebarcelona.org/
early IUGR

AUC 0.848 (0.768 – 0.928)

ethnicity, maternal disease, previous PE/IUGR, blood pressure, uterine Doppler

late IUGR

AUC 0.652 (0.623 – 0.680)

maternal age, smoking, parity, maternal disease, uterine Doppler.

Detection rate (10% FP)

early IUGR  60%
late IUGR  23%

67% PE

8% PE
combined screening

11-14 wks

early PE/IUGR

late PE/IUGR

COMBINED SCREENING
maternal data + US + blood test

high predictive for EARLY PE/IUGR
DR 60-90%
(PFR 10%)

limited for LATE PE/IUGR
DR 20-60%
(FPR 10%)

Crispi UOG 2007, Poon Hypertens 209, Scazzochio AJOG 2013, Crovetto UOG 2013
thank you