Outcomes in low PAPP-A pregnancies: are we under-investigating?

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Declaration of interests – none to declare.
Background

Pregnancy-associated plasma protein A:
- IGF-binding protein protease, produced by the placenta
- Forms part of the first trimester combined screening test

Low PAPP-A in first trimester independently associated with adverse pregnancy outcome,\(^1,2\) including:
- Intrauterine growth restriction
- Development of pre-eclampsia
- Preterm delivery
- Stillbirth
Background

RCOG Green-top guideline no. 31 – The Investigation and Management of the Small-for-Gestational Age Fetus⁴:

- “A low level of the first trimester marker PAPP-A should be considered a major risk factor for delivery of an SGA neonate”
- Suggests a cut-off of <0.40 MoM (multiples of the mean) to define ‘low’

Local guidance⁴:

- Low PAPP-A defined as <0.30 MoM
- Maternal uterine artery Doppler assessment, fetal growth surveillance, nulliparous schedule of care for blood pressure monitoring
Background

So if national guidance defines low PAPP-A as <0.40 MoM,

but we are using <0.30 MoM,

are we missing an opportunity to monitor a high-risk group?
Aims

To investigate pregnancy outcome and rates of small-for-gestational age, preterm delivery and stillbirth in those women with a first trimester PAPP-A result of <0.30 MoM in our unit.

To investigate the same outcomes in those women with a first trimester PAPP-A result of 0.30 – 0.39 MoM, and compare the two groups.
Methods

All women with PAPP-A <0.40 MoM between October 2013 to September 2016 inclusive were retrospectively identified from screening records.

Those not yet delivered were excluded.

Data collected from electronic records (PAPP-A, screening risk and outcome of any prenatal testing, pregnancy outcome, gestation at delivery, birthweight).

Birthweight centiles were calculated using the Hadlock formula.
## Results - summary

<table>
<thead>
<tr>
<th></th>
<th>PAPP-A &lt;0.30 MoM</th>
<th>PAPP-A 0.30 – 0.39 MoM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>49</td>
<td>98</td>
</tr>
<tr>
<td><strong>Live births</strong></td>
<td>43 (88%)</td>
<td>90 (92%)</td>
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<tr>
<td><strong>Miscarriages</strong></td>
<td>2 (16/40 abruption, 18/40 infection)</td>
<td>3 (13/40 Turners, 15/40 hydrops, 16/40 infection)</td>
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<tr>
<td><strong>Terminations</strong></td>
<td>3 (2 x T21, severe hydrops)</td>
<td>4 (Chr3 deletion, renal agenesis, T18)</td>
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<tr>
<td><strong>Stillbirths</strong></td>
<td>1 (39/40)</td>
<td>1 (30/40 abruption)</td>
</tr>
<tr>
<td><strong>Preterm deliveries</strong>*</td>
<td>6 (14%)</td>
<td>6 (7%)</td>
</tr>
<tr>
<td><strong>Birthweight &lt;10th centile</strong></td>
<td>11 (25%)</td>
<td>20 (22%)</td>
</tr>
</tbody>
</table>

* Percentage of live births.

† Percentage of live births and stillbirths.
Results - birthweights

Percentage of sample by birthweight centile

<table>
<thead>
<tr>
<th>Birthweight centile</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>25.00</td>
</tr>
<tr>
<td>10-19</td>
<td>10-19</td>
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<tr>
<td>20-29</td>
<td>20-29</td>
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<td>30-39</td>
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<td>40-49</td>
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<td>50-59</td>
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<td>60-69</td>
<td>60-69</td>
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<tr>
<td>70-79</td>
<td>70-79</td>
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<tr>
<td>80-89</td>
<td>80-89</td>
</tr>
<tr>
<td>≥90</td>
<td>≥90</td>
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</tbody>
</table>

Median: 30.5

PAPP-A <0.30
Results - birthweights

Percentage of sample by birthweight centile

- Median 30.5 for PAPP-A <0.30
- Median 28.0 for PAPP-A 0.30-0.39
Discussion

• 8% of pregnancies in the sample ended by miscarriage or termination

• Small-for-gestational age rate was similar between the two groups, at 25% with PAPP-A <0.30 MoM and 22% with PAPP-A 0.30-0.39 MoM

• 1 stillbirth in each group, but sample size small

• Recent move to using customised growth charts
Conclusions

• High-risk pregnancies

• Difficult to justify ongoing use of the lower cut-off in our unit based on these data

• Discussion is needed at the regional level regarding further investigation in a larger sample, and whether the regional definition of low PAPP-A needs to be brought into line with national guidance
References


Thank you

Any questions?