Association between First Trimester Pregnancy Associated Plasma Protein–A (PAPP-A) and Gestational Diabetes Mellitus Development

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Pregnancy Associated Plasma Protein, PAPP-A, Gestional diabetes mellitus, IGFBP-5, IGF-1

Comments
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Background

- Affecting 5-6% of pregnancies, Gestational Diabetes (GDM) is a common pregnancy complication with significant cardiometabolic consequences for mothers and offspring.
- Previous research from our group suggests that adipose tissue IGFBP-5 and the metalloprotease PAPP-A (Pregnancy Associated Plasma Protein-A) may play a mechanistic role in GDM development by regulating functional IGF-1 levels and lipid storage and metabolism.

Objective

To examine the relationship between circulating PAPP-A levels and GDM development. We hypothesized that high first trimester PAPP-A levels would be associated with decreased GDM risk.

Methods

- Retrospective cohort from EMR data of 1,251 women delivering singleton gestations during the years 2009, 2010, 2014 and 2015
- PAPP-A was measured in the first trimester (11-14 weeks) as part of routine aneuploidy screen, and reported as quartiles of multiples of the mean (MoM) based on gestational age and adjusted for maternal weight and race/ethnicity.
- GDM diagnosis was based on a standard 2-step protocol (~24-28 weeks; failed 50g 1hr glucola screen followed by ≥2 abnormal values per Carpenter-Coustan criteria on 100g 3hr glucose tolerance test).
- Crude and multivariable-adjusted logistic regression models estimated the association between PAPP-A MoM quartiles and GDM.

Results

<table>
<thead>
<tr>
<th>Normal (N=1,156)</th>
<th>GDM (N=95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at lab visit (mean, SD)</td>
<td>29.5 (5.7)</td>
</tr>
<tr>
<td>Gestational age at lab visit (mean, SD)</td>
<td>12.5 (0.6)</td>
</tr>
<tr>
<td>Pre-Pregnancy BMI</td>
<td>615 (53%)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>317 (27%)</td>
</tr>
<tr>
<td>Obese</td>
<td>224 (19%)</td>
</tr>
<tr>
<td>Cigarette smoker No</td>
<td>1019 (88%)</td>
</tr>
<tr>
<td>No</td>
<td>76 (7%)</td>
</tr>
<tr>
<td>Parity Nulliparous</td>
<td>473 (41%)</td>
</tr>
<tr>
<td>Multiparous</td>
<td>683 (59%)</td>
</tr>
<tr>
<td>Crown Rump Length (median, p25,p75)</td>
<td>1.3 (1.1, 1.6)</td>
</tr>
<tr>
<td>Nuchal Translucency (median, p25,p75)</td>
<td>6.5 (5.7, 55.7)</td>
</tr>
</tbody>
</table>

- 7.6% (n=95) of women developed GDM.

- Median PAPP-A MoM levels were 0.7 (interquartile range [IQR]=0.5-1.0) among women with GDM & 0.9 [IQR=0.6-1.3] among women who did not develop GDM.

- Adjusting for pre-pregnancy BMI, nuchal translucency, crown rump length, smoking status, and parity, women with PAPP-A MoM in 2nd, 3rd, and 4th quartiles had 52% (OR=0.48, 95%CI=0.26-0.88), 45% (OR=0.55, 95%CI=0.30-0.99) and 73% (OR=0.27, 95%CI=0.13-0.53) lower odds of developing GDM vs women in the 1st quartile.

Conclusions

- Higher PAPP-A MoM levels were associated with lower GDM risk.
- Future studies should assess whether higher PAPP-A levels are associated with enhanced IGF-1 signaling and improved pregnancy metabolic homeostasis.

Acknowledgements

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