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Comments
Aylin Sert participated in this study as a medical student in the Senior Scholars research program at the University of Massachusetts Medical School.

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Background: 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 its unique metalloprotease PAPP-A (**P**regnancy **A**ssociated **P**lasma **P**rotein-A) may play mechanistic roles in GDM development by regulating functional IGF-1 levels and lipid storage and metabolism.

Aim: 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: A retrospective cohort of women delivering singleton gestations at UMass Memorial Healthcare (2009, 2010, 2014, 2015) was assembled by abstracting electronic medical records. PAPP-A was measured in first trimester (11-14 weeks), and reported as quartiles of multiples of the mean (MoM) based on gestational age and adjusted for maternal weight and race/ethnicity. GDM diagnosis based on standard 2-step protocol (~24-28 weeks; failed 50g 1hr glucola screen then ≥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: Women (N=1,251) were 29.7 (SD:5.7) years old and 12.5 (SD:0.6) weeks gestation at PAPP-A measurement. 7.6% (n=95) developed GDM. Median PAPP-A MoM were 0.7 (inter-quartile range [IQR]=0.5-1.0) among women with GDM and 0.9 (IQR=0.6-1.3) among controls; 39% versus 23% were in the 1st quartile, respectively. After adjusting for pre-pregnancy body mass index, 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 GDM compared to women in the 1st quartile.

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

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