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Keywords

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

Comments

Aylin Sert participated in this study as a medical student as part of the Senior Scholars research program at the University of Massachusetts Medical School. This poster was presented on Senior Scholars Program Poster Presentation Day at the University of Massachusetts Medical School, Worcester, MA, on April 27, 2016.

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



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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.

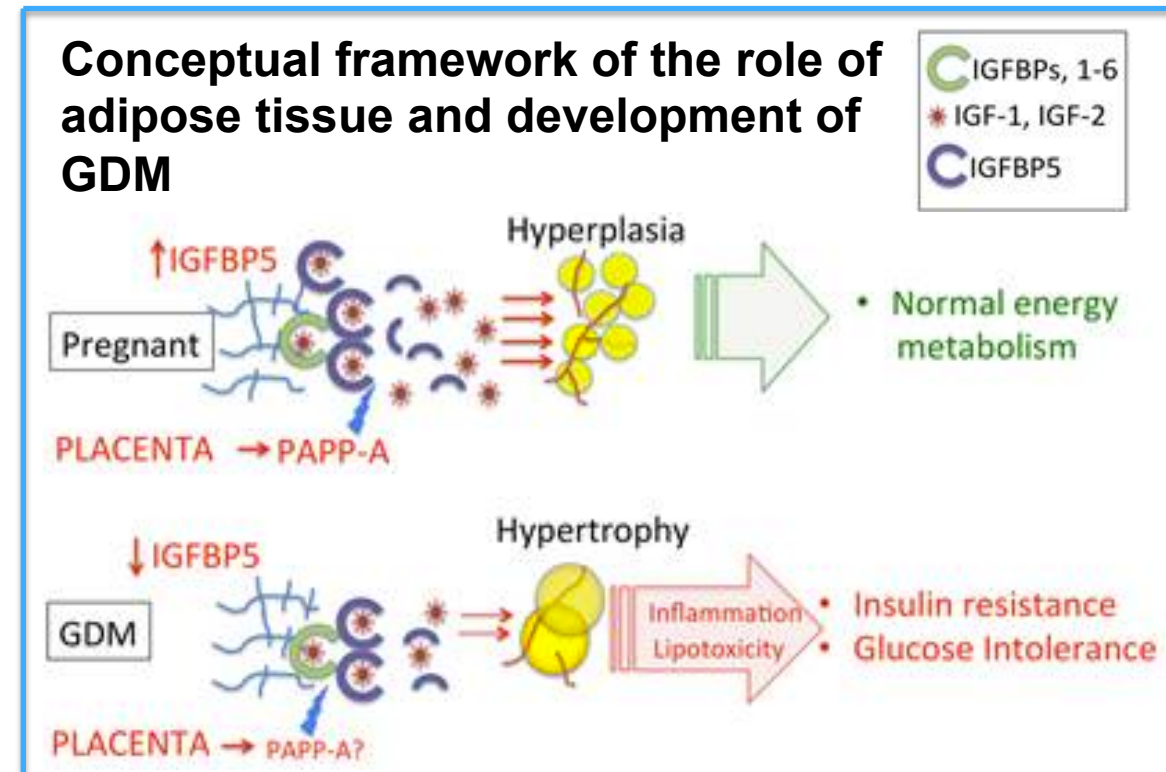


Figure. In normal pregnancy, induction of IGFBP-5 increases the amount of sequestered IGF-1 and IGF-2 and PAPP-A degrades IGFBP-5 to release IGFs which in turn promote angiogenesis and hyperplastic expansion. In women with GDM, insufficient levels of IGFBP-5 and possibly decreased levels of PAPP-A, lead to decreased bioavailability of IGF which prevents proper angiogenesis resulting in adipocyte hypertrophy and decreased capillary density.

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

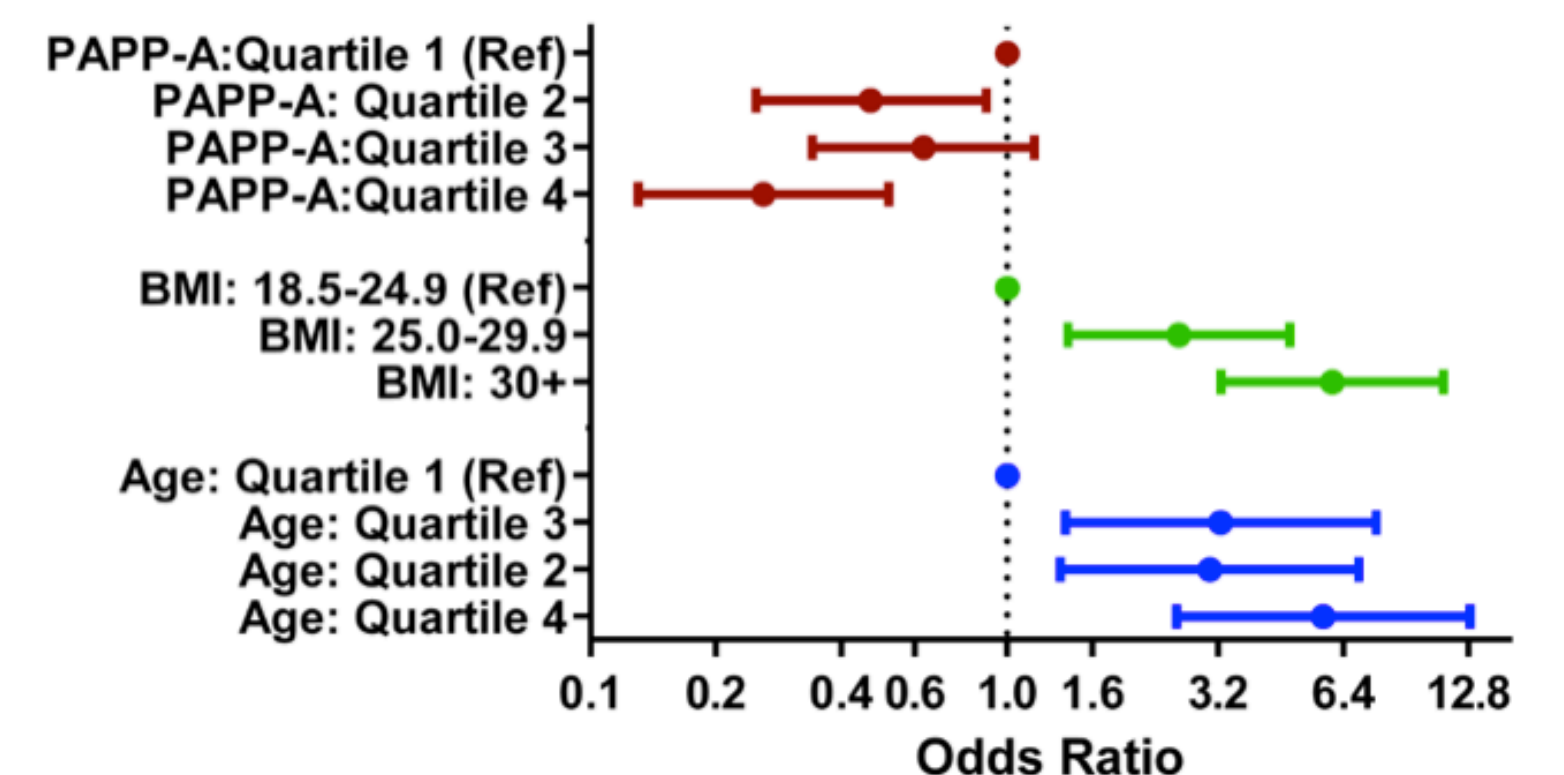
- ◆ Retrospective cohort from EMR data of 1,251 women delivering singleton gestations during the years 2009, 2010, 2014 and 2015
- ◆ PAPP-A was measured in the first trimester (11-14 weeks) as part of routine aneuploidy screen, and reported as quartiles of multiples of the mean (MoM) based on gestational 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

	Normal (N=1,156)	GDM (N=95)
	N	N
Age at lab visit (mean, SD)	29.5 (5.7)	32.4 (5.0)
Gestational age at lab visit (mean, SD)	12.5 (0.6)	12.4 (0.5)
Pre-Pregnancy BMI		
Normal weight	615 (53%)	24 (25%)
Overweight	317 (27%)	32 (34%)
Obese	224 (19%)	39 (41%)
Cigarette smoker		
No	1019 (88%)	87 (91%)
Smoker	76 (7%)	2 (2%)
Parity		
Nulliparous	473 (41%)	26 (27%)
Multiparous	683 (59%)	69 (73%)
Crown Rump Length (median, p25,p75)	1.3 (1.1, 1.6)	1.3 (1.1, 1.7)
Nuchal Translucency (median, p25,p75)	6.5 (5.7, 55.7)	6.4 (5.6, 50.5)

- ◆ 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.

Figure: Incident gestational diabetes mellitus (GDM) in relation to first-trimester PAPP-A, pre-pregnancy BMI, and age, OR (95% CI)



- ◆ 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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