72nd American Diabetes Association. scientific sessions

JUNE 8-12, 2012 • PHILADELPHIA, PA

Control/Tracking Number: 2012-A-3180-Diabetes
Activity: Abstract
Current Date/Time: 1/6/2012 2:52:39 PM

First-trimester Maternal Serum Biomarkers for Prediction of Gestational Diabetes

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Abstract:
Gestational diabetes (GDM) confers an increased risk for pregnancy complications and development of subsequent type-2 diabetes. In this case-control study, we evaluated glycoproteins as alternative GDM biomarkers based on the hypothesis that increased hexosamine biosynthetic pathway flux secondary to hyperglycemia in GDM may affect the levels of serum analyte glycosylation. Maternal serum samples were collected between 9-11 and 16-27 gestational weeks from 150 Finnish women participating in a prospective observational cohort. GDM was diagnosed by a standard oral glucose tolerance test. Fibronectin glycosylation associated with Sambucus nigra lectin binding (FN-SNA), adiponectin, SHBG, and CRP levels were determined by immunoassay and analyzed using Receiver Operating Characteristic (ROC) curves from logistic regression modeling. First-trimester FN-SNA, adiponectin, and CRP levels were all significantly associated with subsequent development of GDM in 50 GDM subjects compared to 50 trimester-matched controls. The mean FN-SNA concentration was greater in participants who later developed GDM than in controls (102+30 mg/L vs. 56+15 mg/L; $p<0.0001$). At a false-positive rate of 4%, FN-SNA alone detected 84% of 1st-trimester GDM cases. The detection rate increased to 92% with addition of adiponectin and CRP. FN-SNA, adiponectin, and SHBG were all significantly associated with GDM in the 2nd trimester ($p<0.01$). The area under the ROC curve for FN-SNA alone was 0.92 (95% CI: 0.86, 0.98), which increased to 0.99 (95% CI: 0.98, 1.00) with the addition of adiponectin and SHBG. Similar discrimination was achieved with Aleuria aurantia lectin-reactive pregnancy-specific glycoprotein (PSG-1). Our data demonstrate that maternal serum FN-SNA represents a promising single-marker test for early identification of women at risk for GDM. Reliable early diagnosis using maternal serum glycoprotein biomarkers can facilitate new intervention strategies to prevent the complications of GDM.
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Author Disclosure Information: J.P. Rasanen: None. S.R. Nagalla: *Employee*; *Author*; DiabetOmics. *Stock/Shareholder*; *Author*; DiabetOmics. C.A. Snyder: *Employee*; *Author*; DiabetOmics. C.T. Roberts: *Stock/Shareholder*; *Author*; DiabetOmics. V. Paturi: *Stock/Shareholder*; *Author*; DiabetOmics.
Category (Complete): 01-A Clinical Therapeutics/New Technology - Glucose Monitoring and Sensing
Presentation Preference (Complete): Oral Preferred

Sponsor (Complete):

* At least one (1) author listed on this abstract is a current member of the ADA and therefore a sponsor is not required.: Yes

Financial Support (Complete):

* ADA Support: No

Keywords (Complete): gestational diabetes ; glycoproteins

Payment (Complete): Your credit card order has been processed on Friday 6 January 2012 at 2:49 PM.

Status: Complete

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