Unbiased metabolomics reveals polycyclic aromatic hydrocarbon exposure is associated with alterations in placental glutamate metabolism

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OBJECTIVE: Prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) is associated with adverse outcomes including small for gestational age infants. Exposure to PAHs largely comes from tobacco smoke, consumption of grilled meat and through the environment due to the incomplete combustion of fossil fuels. We have previously shown that PAH exposure disrupts the placental transcriptome. In this study we utilized unbiased metabolomics of the placenta to measure alterations of the placental metabolome with PAH exposures.

STUDY DESIGN: Placental levels (N=30) of the PAHs benzo[a]pyrene (BaP), and benzo[b]fluoranthene (BbF) were measured using gas chromatography followed by quadrupole mass spec. Quantitation was performed using external calibration curves. Metabolites were extracted from 100mg of placenta tissue, and subjected to liquid chromatography-mass spectrometry. Identified metabolites were quantified by normalizing against their respective internal standard. Metabolites which were identified from differential analyses between high and low PAH exposures were mapped to the Human Metabolome Database (HMDB) using CAS numbers and uploaded to MetaboAnalyst.

RESULTS: Six metabolites were found to be differentially regulated between the high and low exposure groups including 4-hydroxy-L-glutamic acid (0.97 log fold change, p=0.001), D-gluconic acid (1.34 log fold change, p=0.002) and D-saccharic acid 1,4-lactone (-2.52 log fold change, p<0.01). Analysis of pathways which are enriched for these metabolites revealed an alteration in "D-glutamine and D-glutamate metabolism," p=0.018 and "Alanine, aspartate and glutamate metabolism," p=0.039.

CONCLUSION: We found alterations of metabolites in the glutamine and glutamate metabolism pathways by virtue of PAH exposure level in the placenta. Glutamine and glutamate exchange in the placenta is important to supply the growing fetus with the appropriate amino acids for growth. Such alterations in metabolism due to environmental exposures warrant further study to determine underlying causes of the growth restriction observed in these infants.

Do maternal characteristics affect nuchal translucency variation?: Analysis of five million cases from NTQR Program

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OBJECTIVE: First-trimester screening for Down syndrome is dependent on the quality of the nuchal translucency (NT) measurement. The Nuchal Translucency Quality Review (NTQR) program of the Pregnancy Quality Foundation has provided standardized education, credentialing, and external quality monitoring of NT measurements for over 9000 providers since 2005. The objective of this study was to assess the effect of maternal characteristics on NT measurement.

STUDY DESIGN: Distributions were derived from NT data submitted to NTQR by screening laboratories between 01/2005 and 03/2019 for each of the three primary performance indicators of NT (median MoM, SD of log10 MoM and slope of NT on CRL). The relationship between NT median MoM and maternal age, weight, ethnicity/race, number of fetuses, and IVF vs. non-IVF conception was evaluated using the Wilcoxon Rank Sum Test and ANOVA. Multiple regression analysis was performed to control for potential confounders.

RESULTS: NT measurements were performed in a total of 5,234,950 scans by 9340 providers at 3319 sites. Providers reported varying levels of complete data to the laboratories for maternal characteristics: maternal age (81%), maternal weight (58%), race/ethnicity (50%), number of fetuses (98%) and IVF vs non-IVF (36%). There was a steady increase in NT median MoM with advancing maternal age and weight, lower levels for multiple pregnancies and higher levels for IVF (Table). After multiple regression analysis all variables remained statistically significant except for IVF (P=0.28). For the subset of 2,547,258 results with complete information on the remaining variables, MoMs were recalculated dividing the observed NT MoM by the expected NT MoM, from the regression equation, with the overall median reduced by 2%.

CONCLUSION: Maternal characteristics including maternal age, weight, race/ethnicity and fetal number significantly affect NT median MoMs. It is critical that providers submit complete data for these variables to laboratories in conjunction with the NT to optimize the calculation of Down syndrome risk.
Predictive modeling of postpartum readmission for hypertension: A retrospective study
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OBJECTIVE: Hypertension is the most common reason for postpartum hospital readmission. We aimed to evaluate clinical predictors of readmission through 42-days postpartum using a novel statistical model.

STUDY DESIGN: We conducted a retrospective cohort study from a single Midwestern academic center of all women who delivered between 2009-2015. The primary outcome was to establish a predictive model for hypertension-related postpartum readmission. We used a cost-sensitive random forest method to determine variable predictors of postpartum readmission.

RESULTS: Our study included 19,820 women who delivered from 2009-2015; 102 were readmitted in the postpartum period due to a hypertension-related diagnosis. Random forest method achieved a sensitivity of 86% and a specificity of 72% for predicting readmission. The fifteen most important variables for predicting readmission included mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP) in labor and at 24 and 48 hours postpartum; body mass index; gestational age at delivery; and maternal age (Figure 1). Less important variables included meeting criteria for a diagnosis of hypertension, mode of delivery, and antihypertensive medication use during labor or postpartum.

CONCLUSION: There are no available composite models using clinical variables to help predict or prevent postpartum readmission due to hypertension. This study highlights that timing of SBP, DBP, MAP, and PP at all points throughout the labor course and through 48 hours postpartum should be included in a predictive model and can be combined with other variables to increase sensitivity and specificity for predicting women at risk for postpartum readmission. Further analysis with a larger dataset is needed to validate the most promising variables and determine the best timing of blood pressure measurements and threshold blood pressure values to use to better allocate interventions that may prevent postpartum readmission.

The association of pathological nuchal translucency to placental complications in cases of normal microarray analysis
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OBJECTIVE: To identify placental pathology related complications, labor and neonatal outcomes in pregnancies complicated by pathological nuchal translucency (NT) with normal microarray analysis.

STUDY DESIGN: Retrospective study designed to compare women with singleton pregnancies who presented nuchal translucency above 3 mm and had a normal microarray analysis to women with normal nuchal translucency and normal microarray analysis (2013-2019). The following placental pathology related parameters were measured: pre-eclampsia, oligohydramnios, suspected intrauterine growth restriction or small for gestational age. Primary outcome was defined as composite of complications related to placental pathology including pre-eclampsia and small for gestational age neonate. Secondary outcomes were labor and neonatal complications.

RESULTS: One hundred eighty-five women were included in the study: of them, 47 with abnormal NT (study group) and 138 (ratio