18 CLASSIC RISK FACTORS PREDICTIVE OF FIRST CARDIOVASCULAR EVENTS IN WOMEN WITH A HISTORY OF EARLY-ONSET PREECLAMPSIA: OPPORTUNITIES FOR PRIMARY PREVENTION

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OBJECTIVE: Women with a history of early-onset preeclampsia are at increased risk of developing major cardiovascular disease (CVD) related events, that have a detrimental effect on their long-term health and life expectancy. In this follow-up study, we measured established risk factors predictive of first CVD events after early-onset preeclampsia.

STUDY DESIGN: Over a 10-year interval, 243 primiparous women with a history of early-onset preeclampsia (delivery <34 weeks gestation) were included and tested for major cardiovascular risk factors at least six months after delivery, in addition to a population-based control group of 374 healthy non-pregnant women. Women with chronic hypertension were excluded.

RESULTS: Mean age was 30.5 years for cases compared to 28.3 years for controls (P<.001). After adjustment for age, we observed significantly increased mean values for weight (P=.002), body-mass index (P<.001), systolic blood pressure (P<.001), diastolic blood pressure (P<.001), total cholesterol (P=.006), LDL cholesterol (P<.001), triglycerides (P=.027), fasting blood glucose (P<.001), and lower HDL cholesterol (P<.001) in women with previous early-onset preeclampsia. No difference was found for height, smoking, diabetes, and ethnicity. Estimated 10-year risk of first CVD events by Framingham Risk Scores remained <10% for all women (low-risk). Nonetheless, at mean (SD) 0.7 (1.0) years after early-onset preeclampsia, 15% of women met the criteria for metabolic syndrome. Additionally, 89% of women exhibited >=1, 51% of women >=2 and 19% of women >=3 major CVD risk factors.

CONCLUSION: The majority of women with a history of early-onset preeclampsia exhibit at least one modifiable risk factor for future CVD. Although most of these women are classified as low-risk according to the current AHA guidelines, this is mainly due to their young age masking other, mostly modifiable, major risk factors. Our data thus support life-style intervention programs aimed at primary prevention of CVD in women with a history of early-onset preeclampsia.

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19 EFFECT OF SFLT-1 OVER-EXPRESSION ON BLODD PRESSURE OF MICE IN THEIR SECOND PREGNANCY

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OBJECTIVE: sFlt-1 is believed to play a role in the pathogenesis of preeclampsia. Over-expression of sFlt-1 in pregnant mice produces a preeclampsia-like condition. Given that the rate of preeclampsia in nulliparous women is higher than in women who have had a prior pregnancy, we hypothesized that over-expresion of sFlt-1 in mice in their second pregnancy would not result in the preeclampsia-like condition as in the first. Our aim in this study was to evaluate the effect of sFlt-1 over-expression on blood pressure (BP) using mice in their subsequent pregnancy.

STUDY DESIGN: CD-1 mice at day 8 of gestation were injected with the adenovirus carrying sFlt-1 (10^9 PFU; sFlt-1 group) or the murine IgG2 α Fc fragment (10^9 PFU; mFc group as the virus control). At day 11 of gestation, BP catheters were inserted into the aortic arch and tunneled to a telemetric transmitter. BP was monitor continuously in the conscious unrestrained animals until day 18 of pregnancy, at this time mice were sacrificed, blood was collected and placentas/fetuses were counted and weighted. Student ***t*** test was used for statistical analysis (significance: p<0.05).

RESULTS: Our previous data showed that over-expression of sFlt-1 in mice in their first pregnancy leads to increase in mean BP, fetal growth restriction, low platelet, and higher hematocrit. However, when mice in their second pregnancy were evaluated, mean BP, average pups/placental weight, as well all the maternal hematological parameters (platelet, white cell count, hemoglobin, hematocrit, serum creatinine, uric acid) did not differ between the sFlt-1 and mFc groups.

CONCLUSION: Our results confirm the similarity between the sFlt-1 animal model and preeclampsia in humans. A prior pregnancy appears to confer a protective mechanism against the effect of inhibition of angiogenic factors by sFlt-1. Further evaluation of these mechanisms may improve our knowledge of the pathogenesis of preeclampsia, and provide novel avenues for prevention.

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20 FIRST TRIMESTER MATERNAL SERUM BIOMARKERS FOR PREDICTION OF PREECLAMPSIA

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OBJECTIVE: We conducted a systematic analysis of the maternal first trimester serum proteome to identify predictors of preeclampsia (PE).

STUDY DESIGN: A total of 110 women from a prospective observational cohort were included in this study. Maternal serum samples were collected between 9 and 11 gestational weeks. PE was defined as mild or severe following ACOG classification. Maternal serum proteome analysis was performed by fluorescence 2 D gel analysis, multidimensional liquid chromatography tandem mass spectrometry and label-free quantification. Pair-wise comparison was performed by x2 goodness-of-fit tests and adjusted for multiple comparisons via the false-discovery rate method. Immunoassays were used for accurate quantification and evaluated by the Receiver Operating Characteristic (ROC) curves and logistic regression analysis.

RESULTS: Control group comprised 44 women who delivered at term, 21 subjects developed mild PE at 36 weeks gestation (mean) and 45 severe PE at 31 weeks gestation (mean). There were no significant differences in demographic or reproductive factors between the groups. Proteome analysis revealed 416 unique proteins for label-free quantification including 24 differentially expressed (p<.05) in PE. Differentially expressed proteins included immunoregulators (Lipopolysaccharide-binding protein), cytoskeletal proteins (Tubulin beta, Filamin), vascular and lipid metabolism proteins (Vascular cell adhesion protein, Vasorin, Cathepsin D, Apolioprotein A II) and extracellular matrix proteins. Immunoassay for 5 potential biomarkers demonstrated discriminant capability with AUROCs ranging from 0.66 to 0.89. Logistic Regression analysis showed positive interaction and increased the discriminant ability (AUROC>0.80). Serum markers of active PE such as fibronectin, S-endoglin and VEGFRs were not significant in this analysis.

CONCLUSION: First trimester maternal serum proteome analyses identified a distinct set of positive predictors of PE. This may provide a sensitive maternal serum test to predict PE in first trimester and facilitate early intervention.

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