25 FIRST-TRIMESTER SERUM ANGIOGENIC FACTORS AND THE RISK OF INTRAUTERINE FETAL DEMISE

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OBJECTIVE: The purpose of this study was to determine whether increased maternal serum levels of soluble fms-like tyrosine kinase -1 (sFlt-1) and decreased levels of placental growth factor (PlGF) measured during the first trimester are associated with a subsequent increased risk of intrauterine fetal demise (IUFD).

STUDY DESIGN: We performed a prospective, nested case-control study of the Massachusetts General Hospital Obstetric Maternal Study (MOMS). This cohort included 34 cases of IUFD, as well as 246 randomly selected control women who delivered a healthy baby at term. First-trimester serum samples were assayed for circulating levels of sFlt-1 and PlGF by ELISA. We used logistic regression to assess the risk of IUFD according to baseline levels of angiogenic factors and to adjust for potential confounders.

RESULTS: Women with IUFD had significantly increased first-trimester levels of sFlt-1 (1178 +/− 530 vs. 889 +/− 562 pg/ml; $p<0.01$) but there were no significant differences in PlGF levels according to pregnancy outcome (38.6 +/− 20.8 vs. 40.0 +/− 28.4 pg/ml; p=NS). In the unadjusted analysis, there was a 7% increase in risk of IUFD (RR 1.07; 95% CI 1.01- 1.14; p=0.02) with each 100 pg/ml increase in sFlt-1. There was no association between PlGF and IUFD. When sFlt-1 was analyzed according to tertiles based on women in the control group, the highest tertile (OR 9.59; 95% CI 1.92 - 48.0; $p<0.01$) was associated with a markedly increased risk of IUFD compared to the lowest tertile.

CONCLUSION: Increased maternal serum levels of sFlt-1 measured in the first trimester are independently associated with increased risk of IUFD.

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26 THE SOLUBLE FORM OF THE RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS (SRAGE), A DECOY FOR RAGE, IS INCREASED IN THE SERUM LEVEL OF WOMEN WITH SEVERE PREECLAMPSIA

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OBJECTIVE: RAGE-dependent cellular activation is known to cause inflammatory and oxidative damage in various cells via NF-κB transactivation. A truncated form of RAGE (sRAGE) has been shown to bind RAGE ligands, thereby preventing downstream RAGE signaling. This study was conducted to identify changes in systemic sRAGE levels in normal pregnancy as well as in pathological states of excess oxidative stress such as pre-eclampsia.

STUDY DESIGN: In a nested case-control study, we analyzed serum specimens obtained throughout pregnancy, but before labor, from 57 healthy pregnant women (CRL), and 34 severe preeclamptic women (sPE). Serum samples from 11 non-pregnant reproductive age women were used to identify the effect of pregnancy on sRAGE. sRAGE levels were measured by sensitive immunoassay.

RESULTS: 1) Pregnancy is associated with a significant decrease in serum sRAGE as compared to the non-pregnant state (p=0.007); **2**) The analysis of the healthy pregnant CRL group demonstrates that the serum sRAGE system is not gestational age regulated (r= −0.117, p=0.387); **3**) Compared with gestational age matched CRL specimens, preeclamptic women had significantly higher serum sRAGE concentrations reaching levels 2-fold higher between 24-33 weeks of gestation (median [IQR] sPE: 671 [482-1477] vs CRL: 367 [310-479] pg/mL, $p<0.001$).

CONCLUSION: Lower levels of sRAGE in pregnancy compared to the non-pregnant state may render pregnant women vulnerable to obstetrical pathogenic processes associated with oxidative stress and inflammation. An elevation in serum concentrations of sRAGE observed in sPE may reflect the existence of a protective mechanism against oxidative stress.

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