Robust Early Pregnancy Prediction of Later Preeclampsia Using Metabolomic Biomarkers

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Abstract—Preeclampsia is a pregnancy-specific syndrome that causes substantial maternal and fetal morbidity and mortality. The etiology is incompletely understood, and there is no clinically useful screening test. Current metabolomic technologies have allowed the establishment of metabolic signatures of preeclampsia in early pregnancy. Here, a 2-phase discovery/validation metabolic profiling study was performed. In the discovery phase, a nested case-control study was designed, using samples obtained at 15±1 weeks’ gestation from 60 women who subsequently developed preeclampsia and 60 controls taking part in the prospective Screening for Pregnancy Endpoints cohort study. Controls were proportionally population matched for age, ethnicity, and body mass index at booking. Plasma samples were analyzed using ultra performance liquid chromatography-mass spectrometry. A multivariate predictive model combining 14 metabolites gave an odds ratio for developing preeclampsia of 36 (95% CI: 12 to 108), with an area under the receiver operator characteristic curve of 0.94. These findings were then validated using an independent case-control study on plasma obtained at 15±1 weeks from 39 women who subsequently developed preeclampsia and 40 similarly matched controls from a participating center in a different country. The same 14 metabolites produced an odds ratio of 23 (95% CI: 7 to 73) with an area under receiver operator characteristic curve of 0.92. The finding of a consistent discriminatory metabolite signature in early pregnancy plasma preceding the onset of preeclampsia offers insight into disease pathogenesis and offers the tantalizing promise of a robust presymptomatic screening test.

Key words: preeclampsia • metabolomics • biomarkers • screening • hypertension