

Concurrent and contingency strategies using first trimester markers for the prediction of pre-eclampsia in women with a priori high risk

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Objective: To evaluate concurrent and contingent strategies for assessing the risk of pre-eclampsia (PE) in women at high-risk, using first trimester serum PP13, uterine artery Doppler Pulsatility Index (PI) and pulse wave analysis (augmentation index at heart rate 75/min, AIx-75).

Methods: Women between 11+0 and 13+6 weeks' gestation at increased risk of PE were recruited to this nested case control study. Uterine artery Doppler and pulse wave analysis were measured, and venous samples assayed for PP13 using enzyme-linked immunosorbent assay. Gestation specific medians were calculated to obtain Multiples of Medians which were then adjusted for body mass index, ethnicity, smoking, maternal age and parity. For each case of PE (n=42), five controls were randomly selected from the study group. PP13, mean PI and AIx-75 were compared between women who developed PE and controls using the Wilcoxon rank sum test. Sensitivities and specificities were derived from receiver operating characteristic curves.

Results: Compared with controls, women who developed PE had significantly lower PP13, higher mean PI and higher AIx-75 (P<0.001). For a fixed false positive rate of 10%, the best detection rate for all PE (85.7%) and PE before 34 weeks' gestation (92.9%) was achieved by concurrent testing with PP13, mean PI and AIx-75. In contingency screening, the best two orders of testing were (AIx-75:PP13:mean PI) and (PP13:AIx-75:mean PI). Both yielded similar results: 86% detection rate for a 9% and 10% false positive rate respectively. These two sequences would require 410 and 414 tests respectively, compared with 756 tests (252 each) in concurrent testing.

Conclusion: Concurrent first trimester testing with PP13, pulse wave analysis and mean PI can achieve clinically useful prediction of PE in women at increased a priori risk. Contingency screening achieves similar detection rates but requires almost 50% fewer tests, making it a more cost-effective option.