Re: First-trimester screening for pre-eclampsia: moving from personalized risk prediction to prevention

The recent Editorial by Dr Baschat[1] highlighted seminal concepts regarding the controversies surrounding the prediction of pre-eclampsia[2]. Thanks to the adjusted proportional distribution of individual variables contributing to pre-eclampsia risk, calculated from eight studies that adopted multivariate prediction models, we are informed that body mass index (BMI) and uterine artery Doppler velocimetry rank uppermost among the risk factors for pre-eclampsia.

This might be interpreted either as a controversial finding or, conversely, as strong evidence that these risk factors are associated with different clinical phenotypes of pre-eclampsia. The 'early placental' risk factors, epitomized by abnormal uterine artery Doppler velocimetry, yield a clinical phenotype of pre-eclampsia that is characterized by a well-known shallow trophoblastic invasion, small placenta and growth-restricted fetus. The maternal risk factors, epitomized by increased BMI and the cluster of risk factors that also happen to constitute metabolic syndrome, yield a clinical phenotype of pre-eclampsia that is more frequently associated with normal-weight or large fetuses and placental damage characterized typically by 'terminal villi … overcrowded with diminished intervillous pore size impeding intervillous perfusion with increasing intervillous hypoxia and syncytiotrophoblast stress. This type of syncytiotrophoblast stress has no antecedent pathology, so fetuses are well-grown …'[3]. We should interpret the placental origin of pre-eclampsia with these two distinctions in mind.

The impact of obesity as a maternal risk factor is exemplified by another paper of Baschat and co-workers[4]: algorithms for pre-eclampsia derived from populations with an average prevalence of maternal BMI > 30 of less than 20% (such as in many European countries), achieve at their best a sensitivity that is half that when applied to a population in which more than 45% of the female population is obese. It is logical that the two conditions (increasing trend for obesity and early abnormal trophoblastic invasion) might encroach on one another and lead to different clinical expressions, since obesity might interfere with the immune system, and severe dyslipidemia might enhance oxidative stress and endothelial dysfunction[5], and worsen decidual atherosis near term[6].

This changing scenario of human health further increases the challenge of prediction and prevention of pre-eclampsia, yet it should be borne in mind that the influence of a small placenta from shallow trophoblastic invasion does not suddenly 'end' at $33 + 6$ weeks' gestation, while the metabolic impact of obesity on endothelial and placental dysfunction does not suddenly start at $34 + 0$ weeks of gestation. Classification of pre-eclampsia based on time domains should be replaced by classification based on pathophysiology, which can be evaluated objectively using bedside diagnostics such as uterine artery Doppler velocimetry, fetal ultrasound biometry and early changes in placental vascular growth factors.

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