First-, Second-, and Third-Trimester Screening for Preeclampsia and Intrauterine Growth Restriction

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KEYWORDS

• Preeclampsia • Intrauterine growth restriction • Screening

KEY POINTS

- Preeclampsia and intrauterine growth restriction may result in adverse perinatal outcome; therefore, early detection and management could improve the outcome.
- Clinical characteristics, ultrasonography and Doppler parameters, and biochemical markers individually have been used in an attempt to predict these conditions with poor results.
- Predictive models combining different biochemical markers and uterine artery Doppler in every trimester have shown mixed results, although some show promise as potential screening tools.

INTRODUCTION

Preeclampsia and intrauterine growth restriction (IUGR) are major contributors to perinatal mortality and morbidity.[1] Although there is an increasing understanding of the pathophysiology of these conditions, their prevention remains a considerable challenge in obstetrics. It is now well-understood that, although the symptoms of preeclampsia and IUGR generally manifest in the second to third trimesters of pregnancy, their underlying pathology largely takes place in the first trimester.[2] This phenomenon has sparked great interest in the search for tests to predicting them early in pregnancy before these complications occur.

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Several individual clinical factors, Doppler ultrasound parameters, and serum analytes have been evaluated for prediction of preeclampsia and/or IUGR. On their own, these tests generally have poor predictive value. This result may reflect the multifactorial nature of the preeclampsia syndrome. However, a combination of selected parameters and results of recent novel measures seem to be promising. The aim of this paper is to review the first-, second-, and third-trimester screening tests for preeclampsia and IUGR.

PATHOPHYSIOLOGY

Although the precise origin of preeclampsia remains elusive, it is believed to be multifactorial, with the placenta playing a central role. During the last several years, a clearer picture of the pathophysiology has begun to emerge.[3] A 2-stage model has been proposed in which poor placentation, the central initiating event, is thought to occur early. This first stage results from failure of the normal physiologic process in early pregnancy where endovascular trophoblast invades the maternal vasculature and replaces the smooth muscle normally present in the spiral arterioles with a noncontractile matrix material. The result of this normal but seemingly destructive event is a high flow, low resistance vascular conduit that perfuses the intervillous space.[4] This is reflected by a decrease in the uterine artery resistance with increasing gestation. Failure of the trophoblast invasion leaves a high resistance vasculature with persistent smooth muscle histology of the maternal blood vessels. This lack of transformation predisposes to hypoperfusion, hypoxia reperfusion injury, oxidative stress, and signs of placental maldevelopment in the second trimester.[5] Recent evidence suggests that a significant part of placental injury is mechanical damage resulting from intermittent perfusion as a result of persistence of smooth muscle in the spiral arterioles.[6]

The second stage of preeclampsia pathogenesis is the maternal response to abnormal placentation, which is initially adaptive, but subsequently results in widespread systemic injury. Key features of this second phase are systemic endothelial dysfunction[3,7] and an imbalance of circulating vasoactive factors.[8–10] Of note, many of the resulting features can be detected before clinical signs of pathology (preeclampsia or IUGR) appear, creating an opportunity for potential predictive tests.

There is emerging evidence that the pathophysiology described is more consistent with preterm preeclampsia with coexisting IUGR than term preeclampsia.[11] For example, placental pathologic studies indicate that preeclampsia or IUGR resulting in preterm delivery before 34 weeks has high rates of thrombotic placental pathologic findings of the villous trees.[12] In contrast, term preeclampsia and/or IUGR was associated with either normal or minimal pathologic findings.[13] Doppler studies also suggest that preterm preeclampsia/IUGR is associated with defective invasion of the spiral arteries, whereas the spiral artery defect plays a much smaller role in the cases nearer term.[14] Thus, term preeclampsia and IUGR seem to be associated with normal trophoblast transformation in the first trimester and late atherosclerotic changes in spiral arterioles. Such late changes may be the consequence of increased placental mass as occurs in diabetic and twin pregnancies, senescence of the placenta as in prolonged pregnancy or placental edema, and necrosis as in fetal hydrops.[15]

SCREENING TESTS FOR PREECLAMPSIA AND INTRAUTERINE GROWTH RESTRICTION

Screening tests are commonly used in clinical practice, yet the underlying principles of screening are widely misunderstood.[16] This overview assumes some basic understanding of the principles of screening, including use of receiver operating