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













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## Invited Editorial



# Placental growth factor as a screening tool of preeclampsia

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Preeclampsia (PE) is one of the most serious pregnancy-specific multisystem disorders defined by the onset of hypertension accompanied by significant proteinuria after 20 weeks of pregnancy.<sup>(1)</sup> The prevalence of PE is estimated to be around 2%-8% worldwide but varies greatly depending on racial or ethnic origin and geographic region, and prevalence is higher in some developing countries. In addition, women in low-resource countries are at higher risk of developing PE compared to those in high-resource countries. Previous studies have shown that there is a lower frequency of PE among Asian women.<sup>(2,3)</sup> Preeclampsia is the leading cause of maternal and perinatal morbidity and mortality and is associated with approximately 80,000 maternal deaths and more than 500,000 infant deaths each year.<sup>(4)</sup>

Although a complete understanding of the pathogenesis remains unclear, current theories suggest a two-step process. The first stage is caused by superficial trophoblastic invasion resulting in inadequate spiral artery remodeling. This is thought to lead to the second stage, which involves the maternal response to endothelial dysfunction and the imbalance between angiogenic and antiangiogenic factors, resulting in the clinical picture of the disorder. In late-onset disease, the placenta is usually normal; however, fetoplacental demand exceeds supply, resulting in a placental response that triggers the clinical phenotype.<sup>(5)</sup>

Although not yet clear, several biochemical, biophysical, and sonographic parameters have

been investigated as potential tools for identifying women at high risk of PE that can help us on our long journey.<sup>(1)</sup> Several studies have been conducted by examining first-trimester maternal serum markers to evaluate placental growth factor (PIGF) levels in the first trimester to predict the incidence of preeclampsia. Placental growth factor is a protein from the family of vascular endothelial growth factors (VEGF), which promotes the blood vessels formation. The substance is present in high concentrations in the villous cytotrophoblast and syncytiotrophoblast tissues. Placental growth factor has been shown to have a very important role in the prediction of first trimester PE and has a good diagnostic capacity in symptomatic women after 20 weeks of gestation.<sup>(6)</sup>

Boutin et al.<sup>(7)</sup> conducted a study to evaluate the performance of first trimester PIGF for predicting PE in nulliparous women. Of the 4,652 participants, they observed 232 (4.9%) PE cases including 202 (4.3%) term and 30 (0.6%) preterm PE. Placental growth factor was associated with the risk of term PE (AUC=0.61, 95% confidence interval [CI] 0.57–0.65) and preterm PE (AUC=0.73, 95% CI 0.64–0.83). The model was improved with the addition of maternal characteristics (AUC for term PE 0.66, 95% CI 0.62–0.71; AUC for premature PE 0.81, 95% CI 0.72–0.91;  $p < 0.01$ ). At a 10% false positive rate, PIGF combined with maternal characteristics predicts 26% term PE and 55% preterm PE.

Agrawal, et al.<sup>(8)</sup> conducted a meta-analysis to study the predictive accuracy of PIGF

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in asymptomatic women. Their analysis included 40 studies with 3189 cases of preeclampsia and 89,498 controls. The overall predictive odds ratio of this test is 9 (6-13). Subgroup analysis evaluating different PIGF thresholds showed that the highest predictive value for PIGF levels was between 80 and 120 pg/mL with a high predictive odds ratio of 25 (7–88), sensitivity of 0.78 (95% CI, 0.67–0.86), specificity 0.88 (95% CI, 0.75–0.95).

The now widely recommended alternative approach to PE screening is based on the Fetal Medicine Foundation's (FMF) multi-marker prediction algorithm, which is the first trimester combined test for PE, which has been supported by the International Federation of Gynecology and Obstetrics (FIGO).<sup>(1,9)</sup>

Global implementation of an effective first trimester program to screen for and prevent preterm PE will provide an opportunity to reduce the risk of maternal and perinatal morbidity and mortality in the short term. Traditional screening methods as recommended in the past have limited predictive performance, so they need to be updated to reflect the latest scientific evidence that the target should be for preterm PE. To achieve optimal screening performance, the key is to establish a standard method for measuring biomarkers and assessing the quality of biomarkers on a regular basis, because each biomarker is prone to inaccurate measurements, thereby affecting screening performance.

Although the National Institute for Health and Care Excellence (NICE) recommends PIGF as an exclusion test for preeclampsia, it is not currently recommended for routine adoption to exclude or diagnose preeclampsia due to insufficient evidence. Further research is needed about repeat PIGF-based testing in women with suspected preeclampsia who have previously negative results and about how positive PIGF-based tests used to rule out preeclampsia will influence management decisions at the time of delivery and outcome. related to this.<sup>(10)</sup>

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