New pathways to diagnose preeclampsia. (Mini-commentary on BJOG-19-1876.R1)

Ignacio Herraiz[1]

[1]Hospital Universitario 12 de Octubre

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Mini-commentary on BJOG-19-1876.R1: Glycosylated fibronectin point-of-care test for diagnosis of preeclampsia in a low-resource setting: a prospective Southeast Asian population study

New pathways to diagnose preeclampsia

Ignacio Herraiz

Fetal Medicine Unit, Maternal and Child Health and Development Network (Red SAMID-RD12/0026/0016). Department of Obstetrics and Gynaecology. Hospital Universitario 12 de Octubre. Instituto de Investigación Hospital 12 de Octubre (imas12). Av. de Córdoba, s/n, 28041 Madrid, Spain.

[2] Universidad Complutense de Madrid. Av. Séneca, 2, 28040 Madrid, Spain.

Email: ignacio.herraiz@salud.madrid.org

The diagnosis of preeclampsia is a major obstetric challenge that we face daily. In the success differentiating what it is and what it is not, rests the correct decision making that avoids unnecessary complications for the mother and the child.

The first step is to always keep this condition in mind. There is no point in having the most up-to-date guidance if we do not recognize the palpebral edema of a pregnant woman that enters through our office door while looking at the computer screen.

The second step is to achieve a diagnostic confirmation as soon as possible. Rivers of ink have flowed about the inaccuracy of the used diagnostic criteria that are not based on the etiopathogenic knowledge. Thus, the definition has been changing over the years. From the classic triad of "edema, proteinuria, and hypertension", edema disappeared more than 20 years ago due to its unspecificity. Nowadays, proteinuria is no longer considered a *sine qua non* criterion, due to the diagnostic delays that its demonstration may cause. However, the room for improvement is poor if we still deny the role of the biomarkers in preeclampsia, as in many other areas of modern medicine. The pathway was opened with the discovery of the angiogenic imbalance between anti-angiogenic (e.g. sFlt-1) and pro-angiogenic (e.g. PlGF) factors in the past decade. They are especially useful for ruling-out early-onset preeclampsia (Zeisler H et al. NEJM 2016 ;374:13-22). and its implementation in clinical practice has been shown to translate into earlier and more accurate diagnosis, with less maternal complications associated with misdiagnosis (Duhig KE et al. Lancet 2019;393:1807-18). These biomarkers also have weaknesses as they are less useful in late-onset forms and its availability depends on the use of expensive platforms. In this paper (Nagalla SR et al. BJOG 2020), a new biomarker that should raise our attention is proposed: the glycosylated fibronectin (GlyFn). This case-control study has obvious weaknesses when compared with the abovementioned studies on angiogenic-related biomarkers. In particular, cases and controls slightly differ on gestational age at sample collection, new criteria for diagnosing non-proteinuric preeclampsia has not been adopted, fetal growth restriction has not been analyzed and relevant

maternal and perinatal adverse outcomes are missing. However, the performance of the GlyFn test shown in this study is impressive, even for late-onset presentations, with an area under the curve of 0.992 (95% CI 0.988 – 0.997).

The final step is forgoing shortcuts. Immediately after the diagnosis is made, the patient should be referred to a specialized center with adequate resources to attend the mother-fetus bionomial. This is of most relevance in low-resource settings where preeclampsia strikes hardest. The future availability of this reliable point-of-care test would facilitate a prompt diagnosis in regions without central laboratory processing. It will allow timely allocation of these women and hopefully avoiding severe morbidity and mortality. Therefore, the promising GlyFn test deserves the development of further studies inspired in those conducted for PlGF and the sFlt-1/PlGF ratio to validate the results.

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