Reviewer’s report

Title: Screening models for early detection of late-onset preeclampsia with various markers in low-risk pregnant population

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Reviewer: Stefan Verlohren

Reviewer’s report:

The manuscript of Park et al evaluated the performance of different screening protocols for late onset preeclampsia. The authors found that a serial measurements of the sFlt-1/PIGF-ratio in the second trimester combined with PAPP-A provided best prediction for late onset PE. The study is well conceived, topic is of high interest and the paper is well written. However, the reviewer has some concerns.

The authors might discuss recent publications of Ajkolekar et al, who retrieved detections rates of around 90% of early onset PE employing a first trimester algorithm. The authors might discuss that the detection rates for late onset preeclampsia are much lower with those algorithms and might point out the advantages of repeated measurements.

The authors used repeated measurements of sFlt-1/PIGF. They might employ calculations of the slope of repeated measurements in order to enhance predictive accuracy and to optimize their algorithm.

Did the authors look for concomitant SGA / IUGR? In the unaffected group, the median of the sFlt-1/PIGF in 34-37 weeks is low but has a very high range of values: 8 (0.8-156). Did the authors look into patients with high values (e.g. >85) for components of placental insufficiency other than uterine doppler?

The biggest flaw of the study is the low number of case subjects, only n=8 out of the n=262 prospectively enrolled patients developed preeclampsia. Please discuss these limitations more intense, also methodologically and compare to other studies on that subject (=late onset PE).

Please check spelling carefully throughout the manuscript.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
served as speaker and/or consultant to Roche Diagnostics, ThermoFisherScientific and Novartis