Reviewer’s report

Title: First trimester ultrasound measurements and maternal serum biomarkers as prognostic factors in monochorionic twins: a cohort study

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Reviewer: Christiana Naaktgeboren

Reviewer’s report:

This study investigates the individual predictive value of several first trimester markers for poor outcome in monochorionic twin pregnancies in a cohort of 177 twins. In reviewing it, I have focused on primarily on the methodology.

Major comments

It may not be entirely clear to the reader how predictive markers for adverse outcomes in twin pregnancies during the first trimester could improve clinical care. In the second paragraph, the authors mention that intensive surveillance associated with MC twin pregnancies has costs and burdens. Is the idea that low risk pregnancies could be identified where surveillance could be reduced or is it the hope that high risk pregnancies could be identified so that interventions can be taken. Maybe both are possibilities, but it would be helpful to have a little more on this in the introduction.

I don’t agree with the choice of the wording "clinical utility" as I think this should be reserved when looking at the impact on health and cost outcomes when a predictor is implemented in practice. What the authors refer to as "clinical utility" is just dichotomization of the prognostic factor to help simplify the results for the reader.

The exclusion of twins without aneuploidy screening may make the results less generalizable if a large percentage of women don't participate (e.g. younger women). Please reflect on this in the discussion.

The authors did not adjust for gestational age at sampling because it was perfectly correlated with a factor under investigation, crown rump length. I don’t think that gestational age should have been excluded for this reason if it thought to be an important confounder.

In terms of the maternal complications and composite outcomes, I wonder why you included gestational diabetes (half of all the complications) and hypertensive disorders. Do they occur more often in twin pregnancies? If not, you may just have the same findings as any study trying to predict these disorders (e.g. same findings as a study looking at biomarkers to predict GDM in all pregnancies). I think the more important outcomes to focus on are the ones that are specifically related to twin pregnancies.
Minor comments

Ln 171. Do you mean that you used WHO growth curves? It's not entirely clear from this sentence.

Ln 178-179. The neonatal and maternal composite outcomes should be specified in the text, not in an additional file. It's also not clear if the neonatal outcome in this sentence is defined the same as the primary outcome, which is also a neonatal outcome.

Ln 196-199. It is not entirely clear from this sentence that you looked at the "added" value of the prognostic markers on top of the "existing factors". Please reword.

Ln 211-214. While I can understand that dichotomizing the prognostic factors at commonly used thresholds makes the results clinically interpretable, I think I would have preferred to have (also) seen a decision curve analysis.

Ln 220-222. It's not clear why the patient characteristics were dichotomized when looking at clinical utility.

Table 2. Include total N. It should also be obvious what the composite outcomes are in the table. Some outcomes could have some more definition (e.g. spontaneous ptb), for example in footnotes.

Line 361. I wouldn't describe TTTS as a confounder of the association between biomarkers and IUFD, but rather an intermediate. Explain that if TTTS is detected and treatable, then this would weaken the association observed between biomarkers and IUFD. I also didn't find this a logical following sentence. "This is an interesting finding as consequently PlGF could be viewed as a marker of severity of TTTS."

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