Reviewer’s report

Title: Development and validation of prediction models for risk of adverse outcomes in women with early onset pre-eclampsia: protocol of the prospective cohort PREP study

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Reviewer: Sebhat Erqou

Reviewer's report:

Allotey JA et al herein present a protocol for prospective cohort aimed at developing and validating a predicting risk of adverse outcomes in early onset pre-eclampsia. The project is of importance in its field and the article is well written. The authors have developed a well thought out protocol for the project. I think the article is acceptable for publication with some clarifications.

1. in Table 2, in candidate predictor variables - have you considered including the following variables: pre-existing proteinuria (in history), those presenting with single seizure (under examination) and evidence of hemolysis (e.g. haptoglobin, LDH) under labs --> which also be combined with ALT and platelet into HEELP syndrome as single predictor.

2. in Table 3, under outcomes, authors indicate hepatic dysfunction and provide definition of DIC. Are the authors planning to combine definition of DIC and hepatic dysfunction together. Should you have two categories, one for hepatic dysfunction, defined by hepatic enzymes and perhaps albumin levels and INR; and another for DIC defined by fibrinogen level, INR, PTT, etc?

3. Sample size calculations - authors rightly indicate they need to 10 events per variable plan to recruit 500 women to assess 10 predictor variables. After adding pre-term delivery in their outcomes, the authors increase their putative variables to 22. Do you expect that pre-term delivery rate will increase your event by 40%? One consideration in model building if you do not have sufficient number of events to fit all variables in the same model, may be to use forward stepwise model building approach.

4. In statistical analyses, authors indicate they will plan to do backward selection procedure as well as fractional polynomial procedure for non linear trends. Is the plan to perform backward selection first and then assess for non linear trend those selected variables using polynomial models? Or are you planning to assess each variable for polynomial trend simultaneously while doing backward selection?
**Level of interest**
Please indicate how interesting you found the manuscript:

An article of importance in its field

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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