Reviewer's report

Title: Maternal hyperuricemia in normotensive singleton pregnancy, a prenatal finding with continues perinatal and postnatal effects, a prospective cohort study

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Reviewer: T Lee-Ann Hawkins

Reviewer's report:

This study provides novel data concerning the effect of maternal hyperuricemia on neonatal outcome independent of maternal hypertensive disease. The authors use of a prospective study design with adequate sample size (and appropriate sample size calculation) further strengthen their results. In addition, the authors appreciate the importance of using a “gestational age corrected uric acid” when determining hyperuricemia in pregnancy.

MAJOR COMPULSORY REVISIONS:

Given the authors objective of creating a non-hypertensive cohort of deliveries, further description of how they excluded maternal hypertensive disorders is required. They state that 61 of 559 (11%) were excluded for pre-existing and/or hypertensive disorders of pregnancy. Given that a significant proportion of women will manifest their hypertensive disorder of pregnancy in the early postpartum period (reported rates as high as 30% in some studies), how were these patients followed postpartum, and does the exclusion population of 61 include those that presented with de novo postpartum preeclampsia? It would be prudent to include data to prove that this population was indeed normotensive if available (i.e. blood pressure in first trimester, blood pressure between day 3-5 postpartum). This data along with that presented in the “descriptive statistics” could be presented more easily in tabular format.

MINOR ESSENTIAL REVISIONS:

1. The prevalence of admission to NICU in this cohort was 19.5%. Can the authors please provide additional commentary in the discussion regarding this? My specific questions include:
   a) although this percentage seems rather high (where the incidence in my country averages 10% (range 5-23%)), is this considered normal in Iran? If not, further discussion is needed. If so, then mention of this with appropriate reference to published local data is needed.
   b) I note that the authors do not include inclusion criteria in the description of this cohort. With the possible higher than expected prevalence of poor neonatal outcome, could this be due to selection bias of women who were deemed study appropriate? It is critical for this study to describe in detail the inclusion criteria used so that readers do not assume that those included in the study are somehow biased.
2. The authors statement “Maternal blood samples were drawn up to 24 hours before delivery…” needs to be clarified with more specific detail. It would be useful to know when labs were drawn with respect to delivery in this population (i.e. in ___% of participants, labs were drawn within 1 week of delivery, and for the remainder, labs were drawn within 2-___ weeks)

3. The use of Lind’s data to define hyperuricemia is appreciated! Could the authors please include a table detailing the levels of uric acid for each gestational age used in this definition? Alternatively, perhaps the authors used the same gestational age corrected values published elsewhere, and if this is the case, then this could be referenced.

4. The statement “One standard deviation was chosen because it is shown that this value of uric acid elicit(s) a concentration-dependent attenuation of trophoblast invasion and integration into a uterine microvascular endothelial cell monolayer” should be adjusted to instead reflect that: use of the gestation corrected uric acid was chosen because the value of uric acid in normal pregnancy is dynamic and fluctuates in a consistent pattern (Lind). The authors choice of using “one-standard deviation” above this level is consistent with other published studies and also with standard laboratory protocols to determine “abnormal” values. The negative effect of maternal hyperuricemia on placental/fetal development explanation needs to remain in the Interpretation section of the paper.

5. Table 1 is difficult to interpret as the meaning of the “yes”/”no” characteristic is vague - does is represent yes/no to preterm delivery OR yes/no to maternal age <26? Why do the N values not equal either n=72 for preterm delivery, n=404 for total population, n=103 for hyperuricemia or another pre-specified number. I do not fault the statistics, only the manner in which it is presented. I would also prefer to see the statistical p values rather than a * to signify statistical significance.

DISCRETIONARY REVISIONS:
1. Figure 1 could be omitted as the results are easily described in the written results.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests.