Author's response to reviews

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

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Author's response to reviews: see over
Dear Sir/Madam

Thank you very much for your kind consideration of our paper entitled "Maternal hyperuricemia in normotensive singleton pregnancy, a prenatal finding with continues perinatal and postnatal effects, a prospective cohort study" with the manuscript number of "MS: 4511397921179460". Here I am submitting the revised version of the paper that was changed according to the recommendations of the reviewers and the editor. The following changes were made to the paper:

• **Answers and changes according to the comments of Dr. Hawkins:**

**Major compulsory revisions:**

1. In the "method – study population and study design" section of the paper, it is mentioned that women with "any hypertensive disorder including both pre-existing and gestational related hypertensive disorders" were excluded of the study, postpartum hypertensive disorders were considered as a subgroup of gestational related hypertensive disorders. In our study upon admission blood pressure was measured for the participants, in which 34 of them had high blood pressure (6.08 %). After delivery as mentioned in the paper we followed the neonates for one month, when the mothers referred for the postnatal visits their blood pressure was measured in which, 27 of our participants developed hypertension in the postpartum period (4.83 %). As the reviewer recommended this sentence was added to the "method – data and specimen collection" part of the
paper: "The mothers were also followed and examined in the postpartum period for one week for the detection of post partum hypertensive disorders.". Unfortunately we do not have reliable data regarding the blood pressure of all the participants in the first gestational trimester.

**Minor essential revisions:**

1. **a.** This percentage is rather high in Iran too, because the samples were gathered from two referral centers with high percentage of high risk pregnancies (where NICU admission rate is as high as 30% and more). We were also concerned about selection bias that could happen and affect the study results. After consulting the university's statistical center, they proposed the use of strict inclusion / exclusion criteria and using multivariate logistic regression analysis to minimize the selection bias. This was added to the paper in the "Discussion – Strengths and Limitations" part of the paper as " Another limitation of the study was that the study was conducted in two referral centers with high percentage of high risk pregnancies; the percentage of poor neonatal outcome in this study was rather high. However by using strict inclusion / exclusion criteria and applying multivariate logistic regression analysis we tried to minimize the selection bias that could affect the study."

1. **b.** We added the inclusion criteria that were used to the "Methods – Study population and study design" section of the paper as follows: " Pregnant
women were considered eligible for the study if they had the following criteria: singleton pregnancy, normal blood pressure upon enrolment, nonsmokers, nonalcoholic, no history of substance abuse, intact fetal membranes, no history of fever or antibiotic use and / or any site of infection in the previous two weeks, no vaginal bleeding upon admission."

2. It seems that there is a misunderstanding regarding the statement of "Maternal blood samples were drawn up to 24 hours before delivery" due to language editing problems. This was corrected as follows: "Maternal blood samples were drawn within 24 hours preceding delivery"

3. As the reviewer recommended a table was added to the paper (table2.)

4. In the "Results – The association of maternal hyperuricemia and preterm birth with maternal factors" section of the paper, as the reviewer recommended the second paragraph was changed as follows: "Hyperuricemia was defined as a serum uric acid level one standard deviation greater than the appropriate for gestational age as defined by Lind et al. (Table2) [12] 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, [12] the 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. [13]"

5. As the reviewer recommended for a better understanding and interpretation table 1. was changed.
DISCRETIONARY REVISIONS:

1. Figure 1. Was omitted of the paper.

• Answers and changes according to the comments of Dr. Javadian:

There were no major or minor essential problems with the paper as Dr. Javadian mentioned, so no change was made to the paper.

• Answers and changes according to comments of editorial office:

1. The email addresses of all the authors have been added to the title page.

2. Acknowledgements section was added to the paper.

3. The heading "Interpretation" was changed to "Discussion".

4. We had obtained a written informed consent of the participants and this was corrected in the manuscript.

Thank you again for your kind consideration

Yours Sincerely

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