Reviewer’s report

Title: Association between Pre-and Postnatal Growth and Longitudinal Trends in Serum Uric Acid Levels and Blood Pressure in Children aged 3 to 7 years

Version: 1 Date: 18 Mar 2019

Reviewer: Research Square

Reviewer's report:

"STATISTICAL REVIEWER ASSESSMENT:

Is the study design appropriate for the research question (considering whether the analyzed population accurately reflects the design and whether you see any problems with control/comparison groups, e.g., likely confounders)?
Yes - overall design, population, and control groups are appropriate

Are methodologies adequate and well implemented (considering whether assumptions are addressed and whether analyses are robust)?
No - there are major issues

Are the analyses adequately communicated (considering whether reporting details are adequate and whether figures and tables are well labeled and described)?
No - there are minor issues

Does the interpretation accurately reflect the analyses without overstatement (considering whether limitations/bias are acknowledged and whether accurate descriptors, e.g., 'significant', are used?)
No - there are minor issues

Could an appropriately REVISED version of this work represent a statistically sound contribution?
Probably - with minor revisions

STATISTICAL REVIEWER COMMENTS:

Uric acid is an organic compound which resulted from purine catabolism, through the catalytic effect of xanthine oxidase. Causes of variation in serum Uric acid level is multidimensional and these mainly emerge from some environmental and genetic factors. This is an interesting paper and its contents have public health importance. The study adopts the use of a class of cohort study in its design where the subjects were followed-up for some time to see the influence of pre-and postnatal growth on the serum uric acid levels and blood pressure. The conceptualization of this idea was in order but there are few clarifications that the authors will have to make to ensure that everything is practically okay with the implementation of the study. Here under listed are my few concerns.

REQUESTED REVISIONS:
Statistical Analysis
Page 7: 164-165: The authors said that "Means and standard deviations were calculated for continuous variables". How did they ensure that Mean is the correct descriptive statistics to be used for the analysis and not median which is peculiar to the case of non-normality?
Linear mixed models are an extension of simple linear models that allows both fixed and random effects, and are particularly used when there is non-independence in the data, such as arises from a hierarchical structure. The model has both fixed effects and random effects and are useful in a wide variety of disciplines but of more importance in settings where repeated measurements are made on the same statistical units (longitudinal study), or where measurements are made on clusters of related statistical units. Therefore, the use of linear mixed models in this study is in order. However, there are various assumptions that must be satisfied before the models can be used correctly and effectively. I encourage the authors to address in their paper how these assumptions were handled to prevent them from being violated. This is pertinent to the analysis, the results and findings from this study.

1. In the application of any mixed model, its random variables add the assumption that observations within a level, the random variable groups, are correlated. The assumption can only be relaxed if observations are independent of other observations except where there is correlation specified by the random variable groups.

2. Independence assumption: Independence shows the effects connected with the random variable groups that are uncorrelated with the means of the fixed effect from the random variable groups.

3. Linearity: For each of the independent variables in a mixed model, there is an assumption that the models are similar. This assumption can be checked with plots of the residuals versus each of the variables.

4. Normality of the residuals: This is often addressed with a quantile-quantile plot where a substantial deviation from linearity of the observations is an indication of a deviation from residuals normality.

Diagnostic check:
Appropriate diagnostic check must be used to ascertain that the model built is not influenced by one or a small set of observations, an evidence that the model over fits or sensitive to those observations included in the model.

Inter Class Correlation must also be checked to show how much of the variation in the response variable, that is not attributed to fixed effects, but accounted for by a random effect. This is done by computing the ratio of the variance of the random effect to the total random variation.

Mixed models function by providing some contraction to the random effects and the amount of this contraction is based on how much information is domicile in a random effect groups. In order to know which of the observations used in the model constitutes stress to the model, creating both the fixed effect model and the model with the random effects is necessary. There might be need to evaluate both models for those observations with high leverage or Cook's distance. Thereafter, it is also necessary to evaluate the coefficients' change in the mixed model by dropping some observations marked by the linear or generalized model.

The authors are to provide statistical evidence in the paper on how these diagnostic checks were accomplished.

ADDITIONAL REQUESTS/SUGGESTIONS:
Title: The design of the study does not provide any indication that can convince the scientific world that pre- and postnatal growth are the main causes of the change in the longitudinal trends in Serum Uric Acid Levels (a product of purine catabolism, and hyperuricemia) and Blood Pressure in Children as emphasized in the title. Therefore, the use of the word "effects" in the title should be revised.

Abstract
Problem statement and objectives of the study are missing in the background section.

The author should specify whether the study is retrospective or prospective cohort study. The specific type of generalized linear model used should be mentioned. The word catch-up must be defined clearly in the method since a result was generated based on the word in the abstract.

The conclusion must include a statement that depicts the main finding from this study. The included sentences as currently presented are recommendations which ought to have come from the main finding. Consequently, this section should be revised.

Introduction
Despite the importance of this study and its associated relevance to the scientific world, many studies have been conducted using the same approach in some settings around the world. I doubt if the findings from this new study will significantly vary from those obtained from these previous studies. It is understood that cultural differences in terms of food intake and environmental conditions can make a difference in Uric Acid Levels and Blood Pressure in Children between settings. It is essential that the authors make a good case for the motivation and justification for this study in Ewha. The possible explanation could be in terms of the design of the study, in terms of study subjects including modes of selection and data analyses approaches utilized. The gap in knowledge should be essentially indicated in the introduction.

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Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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