Reviewer's report

Title: Serum 25(OH)D concentrations and atopic diseases at age 10: Results from the GINIplus and LISAplus birth cohort studies

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Reviewer: Ting Fan Leung

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Wawro et al. measured serum levels of 25-hydroxyvitamin D [25(OH)D] in 2,815 10-year-old German children who participated in the GINIplus and LISAplus studies and attempted to analyze their relationship to current and ever presence of atopic disorders. They observed a significant positive relationship between serum 25(OH)D levels and current and ever eczema as well as aeroallergen and food sensitizations. This research topic is controversial and under hot debate. The sample size of this study appeared to be adequate to address the research question, and analytical approach also seemed to be acceptable. However, the authors need to consider the following issues to improve this manuscript.

Major compulsory revisions

My main concern about this manuscript is the lack of accurate documentation for subjects’ dietary intakes and average sunlight exposure (or outdoor activities). The authors did mention vitamin D supplementation during infancy among subjects from LISAplus, but such could not reflect their current vitamin D intakes. It would be impossible to address without such dietary data the important issue of reverse causation as suggested also by the authors.

Although this study analyzed 25(OH)D data from a seemingly large group of 2,815 children, this sample size only represented less than one-third of the initial GINI and LISA cohorts (2815/9100 = 30.9%). I wonder whether the current 10-year-old children were representative of the overall study population, and such data must be provided beside that listed in Table 1 in order for readers to judge about possible biases.

Given that the authors commented their serum 25(OH)D levels to be higher than expected, did they measure 25(OH)D in such samples (at least a subset) by methods other than Roche assay such as ELISA and mass spectrometry? They should also discuss about these laboratory and analytical issues to possibly highlight such as a limitation of this study.

The large number of subjects being analyzed made the statistical analysis much more powerful, and which might lead to the detection of statistically significant yet small effect size of the association between serum 25(OH)D levels and various atopy phenotypes. These ORs were ranged 1.05-1.09, and the authors need to discuss about the clinical significance of such findings.
Regarding logistic regression analyses, why did the authors adjust for single parent status as a confounder? Did they collect any dietary vitamin D intake data so that they could include such in their models? How about subjects’ social class?

Minor essential revisions

The authors need to provide details on the storage condition for serum samples prior to 25(OH)D measurement, and whether all such samples were first-thawed for the present study. In addition, what is the sensitivity and lower detection limit of the Roche assay? Were the samples analyzed for 25(OH)D in duplicates, triplicates or only one assay per sample?

The authors need to update the reference list as there were some newer studies on the topic.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.