Author's response to reviews

Title: Vitamin-D status and neurodevelopment and growth in young North Indian children: a secondary data analysis

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Author’s response to reviews:

Reviewer #1

1. This is a potentially very important publication. However there are major deficiencies that require attention. The definition for vitamin D deficiency is not what is accepted by most of the literature. The Institute of medicine concluded that for maximum bone health a blood level should be at least 20 ng/mL and the Endocrine Society's Practice Guidelines recommended for maximum bone health a level should be above 30 ng/mL.

Response: Thanks for the acknowledgement.


2. It would be very important to note what percent of these children had blood levels <10, 11-20, 21-29 and those above 30 ng/mL. They should then relate their outcome measures to these quartiles.
34.6% children were <10, 42.4% were 11-20, 17% were 21-29 and 6% were above 30 ng/ml. We have run analyses for all outcomes as per this new category of vitamin D level. None of the neurodevelopment outcomes (Total ASQ-3, sub scales of ASQ-3 i.e. communication, Gross motor, Fine motor, problem solving, personal social) and growth outcomes (wasting, stunting and underweight at baseline and end study) were significantly associated with any of these quartiles.

3. The authors provide no information on the range of blood levels. It's quite possible that all of these infants were vitamin D deficient or insufficient raising questions about their conclusion.

Response:

The mean (SD) and median (IQR) of vitamin-D level were 14.82 (8.7) ng/ml and 13.15 (8.31, 19.2) ng/ml. We have incorporated this information in the manuscript.

4. Did the authors measure PTH which would have been very helpful?

Response:

We did not measure PTH in this study.

5. The authors used the term vitamin D levels when presumably they mean vitamin D status or 25-hydroxyvitamin D levels since they did not measure vitamin D levels? This should be corrected throughout the manuscript.

Response:

Thanks for the suggestion. We have changed the term vitamin D levels to vitamin D status.

Reviewer #2:

1. This manuscript evaluates the vitamin D status in North Indian children in relation to the neurodevelopment and growth. The paper is well written. The statistical analysis seems adequate.

Response:

Thanks for the acknowledgement.
2. The study is performed in 960 children for growth and 401 for neurodevelopment. A substantial portion of the children is underweight, at baseline about 31% and after 6 months the prevalence has increased to about 34%. What was the cause of the increase of the percentage of children who are underweight?

Response:

This is the natural course of undernutrition. There tend to be fewer malnourished children in the younger age groups and then this number increases throughout childhood.


3. The vitamin D level has been assessed at baseline and 34.5% of the children had a vitamin D level below < 10 ng/ml. During the 6 months of the study more children got underweight so the percentage of vitamin D deficient children may also have increased. The vitamin D level should also be assessed after 6 month. Only on a baseline assessment of vitamin D the authors cannot conclude that vitamin D deficiency is not associated with poor growth and neurodevelopment.

Response:

Thanks for the comments.

We had vitamin D level after 6 months for only 243 children. Out of the 243 children vitamin-D <10 ng/ml was 38.3%.

Of the 243 children, neurodevelopment data were available for 92 children. None of the neurodevelopment outcomes (Total ASQ-3, sub scales of ASQ-3 i.e. communication, Gross motor, Fine motor, problem solving, personal social) were significantly associated with vitamin D level after 6 months.

Even the growth outcomes (wasting, stunting and underweight at baseline and end study) were not significantly associated with vitamin D level after 6 months.

We have added this in results section.

4. At baseline, about 70% of the children were anemic. For growth both calcium and vitamin D are needed. Do the authors have data of the calcium intake of the children? This should be discussed. In the discussion it should be added that the study was performed in a population with a poor feeding status. The majority of the children is anemic which may negatively influence the development. Other deficiencies also negatively influence growth and development.
Response:

Thanks for the comments.

We don’t have data on calcium intake. We have adjusted baseline anemia status for all the outcomes.

We have included the following sentence in the discussion:

There may be deficiencies other growth-limiting macro and micronutrients such as calcium, zinc, vitamin –B12 etc. Poor quality of food i.e. lower proportion of animal source protein may also contribute to poor growth. The influence of vitamin D might be negibile in the light of other growth limiting factors.

5. Growth and neurodevelopment are assessed 6 month after the assessment of vitamin D status which is rather short.

Response:

This a secondary data analysis from a randomized controlled trial (RCT) of daily supplementation with folic acid and/or vitamin B12 or placebo for six months in 6 to 30 months old children. In the main trial growth was assessed at baseline and after 6 months follow up. Neurodevelopment was assessed after 6 months follow up. We had the opportunity to assess whether the baseline vitamin-D status was associated with neurodevelopment measured by the Ages and Stages Questionnaire-3 (ASQ-3) after 6 months as well as the association between vitamin-D deficiency and physical growth (wasting, stunting and underweight) at baseline and 6 months later. However, we agree that this could be a limitation to our study and have modified the discussion accordingly.

6. Table 1: change rupees in American Dollars.

Response:

Thanks for the suggestion. We have changed rupees in American Dollars.