

Letter to the Editor

Efficacy trials comparing dosages of vitamin D and calcium co-supplementation in gestational diabetes mellitus patients require a methodological revamp

Sumanta Saha. Efficacy trials testing vitamin D and calcium co-supplementation in gestational diabetes mellitus patients.

Sumanta Saha

R. G. Kar Medical College, Kolkata, India

Address for Correspondence: Sumanta Saha

e-mail: sumanta.saha@uq.net.au ORCID: orcid.org/0000-0003-0996-8846

DOI: 10.4274/jtgga.galenos.2019.2021.9-23

Received: 29 September, 2021 **Accepted:** 9 March, 2022

To the Editor

In this letter, I discuss a recently (2021) published clinical trial report by Gunasegaran et al. in the Journal of Obstetrics and Gynaecology Research on the efficacy of prenatal vitamin D and calcium co-supplementation in gestational diabetes mellitus (GDM) patients (1). The report suggests that co-supplementations of vitamin D 1000 IU and calcium 1000 mg are relatively beneficial than co-supplementations of vitamin D 250 IU and calcium 500 mg in achieving blood glucose and lipid homeostasis in GDM patients on medical nutrition therapy (1). The co-supplements were given daily for six weeks (1).

The study is imperative as antenatal glycemic control yields better perinatal outcomes in GDM patients and their neonates. Hyperglycemia in GDM occurs in late pregnancy due to inadequate insulin secretion and consequent failure to counteract the physiologic insulin resistance. Besides, homeostasis of the blood lipid profile in GDM patients is also critical as its derangement is related to diabetes and cardiovascular risk in the long term. Several nutritional supplements have been tested to see their effect on these markers like vitamin D, probiotics, omega-3 fatty acids, etc. Vitamin D is crucial among these as an association between its deficiency and GDM has been reported in observational studies. However, the physiologic role of vitamin D in pregnancy remains poorly understood. Since regular supplementation of vitamin D and calcium in pregnancy is not yet established, it's a hot topic in obstetric medicine, making the trial by Gunasegaran et al. relevant contemporarily (1). It is perhaps the first trial in the Indian subcontinent in this context and an important addition to the existing literature, predominately sourcing from Iran (2,3). The absence of participant attrition from the trial added merit to it. Regarding its limitations, the authors have highlighted its lack of blinding of study participants and personnel and heterogeneity across the participants' baseline vitamin D status (1).

Given the importance of the trial, its scientific appraisal is critical, and I have two viewpoints to share in this regard. First, regarding the statistically significant outcomes, the risk of type 1 error plausibly remains high due to the relatively small sample size of the trial (70

participants data analyzed) (1,4). Second, although the trial (1) depicted statistically how changes in different outcomes post-intervention varied between the compared intervention groups, the inclusion of a placebo arm would have reasonably enhanced its methodological rigor (5). A placebo arm-based juxtaposition is critical before ascertaining comparative efficacy between high and low doses of vitamin D and calcium co-supplementation to investigate if these respective interventions are better than placebo.

To conclude, since every piece of evidence sourced from different clinical trials contributes towards the pool of evidence-based obstetric medicine, future trialists may consider the strengths and limitations of this trial while preparing their trial protocol. Therefore, double-blinded adequately powered trials of factorial design may be the methodological foundation of future trials to disentangle the metabolic effects of prenatal supplementation of vitamin D, calcium, their co-supplemented forms, and the different dosages of the latter in GDM patients.

Acknowledgement: I thank Mr. Chris Nowlan for providing relevant literature to read.

References

1. Gunasegaran P, Tahmina S, Daniel M, Nanda SK. Role of vitamin D-calcium supplementation on metabolic profile and oxidative stress in gestational diabetes mellitus: A randomized controlled trial. *J Obstet Gynaecol Res* [Internet]. 2021 Mar 28;47(3):1016–22. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/jog.14629>
2. Saha S, Saha S. Changes in anthropometric and blood 25-hydroxyvitamin D measurements in antenatal vitamin supplemented gestational diabetes mellitus patients: a systematic review and meta-analysis of randomized controlled trials. *J Turkish Ger Gynecol Assoc* [Internet]. 2021 Mar 31;22(3):217–34. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/33663196>
3. Saha S, Saha S. A comparison of the risk of cesarean section in gestational diabetes mellitus patients supplemented antenatally with vitamin D containing supplements versus placebo: A systematic review and meta-analysis of double-blinded randomized controlled trials. *J Turkish Ger Gynecol Assoc* [Internet]. 2020 Sep 3;21(3):201–12. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32517428>
4. Aguinis H, Vassar M, Wayant C. On reporting and interpreting statistical significance and p values in medical research. *BMJ Evidence-Based Med* [Internet]. 2021 Apr;26(2):39–42. Available from: <https://ebm.bmj.com/lookup/doi/10.1136/bmjebm-2019-111264>
5. Lin C-WC, Day RO, Harris I, Maher CG, McLachlan A. Comparative efficacy trials with no placebo group cannot determine efficacy. *BMJ* [Internet]. 2015 Jun 24;350(jun24 2):h3292–h3292. Available from: <https://www.bmj.com/lookup/doi/10.1136/bmj.h3292>