Reviewer's report

Title: Folic Acid Supplementation, Dietary Folate Intake during Pregnancy and Risk for Spontaneous Preterm Delivery: A Prospective Observational Cohort Study

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Reviewer: Bridget S. Mosley

Reviewer's report:

Review of manuscript: “Folic Acid Supplementation, Dietary Folate Intake during Pregnancy and Risk for Spontaneous Preterm Delivery: A Prospective Observational Cohort Study”

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Summary:
The aim of this study was to evaluate the association between folic acid intake (both dietary and supplement use) and the risk for prematurity, stratified by early and late spontaneous preterm delivery. The investigators used data from the Norwegian Mother and Child Study, which is a cohort study assessing multiple exposures and pregnancy outcomes among a large (100,000+) number of participants. The study is well positioned to address this research question.

Only 38.5% of invited women agreed to participate in the study.

The analysis excluded women with diabetes mellitus, hypertension, autoimmune diseases, inflammatory bowel diseases, systemic lupus erythematosus, rheumatoid arthritis, scleroderma, other immune-compromised conditions and those that underwent in-vitro fertilization, as well as those with pregnancy-related complications such as preeclampsia, hypertension, gestational diabetes, placental abruption, placenta previa, cervical cerclage and serious fetal malformations. In addition, only women with index singleton pregnancies and probable energy intake (between 4.5-20 MJ) reported from the food frequency questionnaire were included.

Measures of both prematurity outcome (timing of birth as measured by 2nd trimester ultrasound) and folic acid exposures (maternal interview and food frequency questionnaire during pregnancy) are appropriate for this type of analysis.

The observed results indicated little or no protective effect from folic acid on the risk for prematurity. Surprisingly, folic acid supplement use prior to pregnancy (8 weeks prior to conception) was found to be a risk factor for early spontaneous preterm birth. From the measurements taken in this study, a small percentage (<3%) of the women were receiving the recommended daily levels folic acid (500
ug/d) in their diet.

Comments:
Overall, this is a well designed analysis using appropriate data to address this research question. These results can be added to a body of literature showing inconsistent results evaluating the relationship between folic acid and prematurity.

I would recommend that an additional statement be added in the discussion regarding the uniqueness of population being evaluated. With so many adverse conditions being excluded from the analysis, this study population was a relatively healthy group of women. If folic acid truly does have any protective effect on the risk of prematurity, it may very well be most effective for the group of women that were excluded from this analysis.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests