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Associations between pregnancy and symptoms of COVID-19 are worth further analysis

Dear Editor,

We read with interest a recent article entitled "*The association between pregnancy and COVID-19: A systematic review and meta-analysis*" by Wang et al. in the *American Journal of Emergency Medicine*, and the study synthesized eight observational studies to reveal the association of pregnancy and the risk of mortality, intensive care unit (ICU) admission, as well as ventilation uses. The synthesis has clearly demonstrated that pregnancy was associated with significantly higher risk of ICU admission (risk ratio [RR], 2.23; 95% confidence interval [CI]: 1.58 to 3.16) and ventilation (RR, 2.13; 95% CI: 1.06 to 4.28), but not with the risk of mortality [1]. In addition to the terminal outcomes, the article also reported symptoms of COVID-19 between pregnant and non-pregnant women, and we recognize that these information are also valuable and meaningful to clinical practice. Unfortunately, the study has neither analysis on the association of pregnancy and symptoms of COVID-19 nor further discussion on them. The purpose of this letter aimed to have more understandings on the association between pregnancy and symptoms among cases with COVID-19.

We, here, proposed two examples using two commonly discussed symptoms of COVID-19 [2-4], and would like to depict the associations between pregnancy and diarrhea and headache. Data of the two examples were extracted from the article by Wang et al. Pooled analysis was based on random-effects model, and results were presented in RR and 95% CI with heterogeneity test (I-square). Threshold of statistical heterogeneity was I-square > 50%, and leave-one-out sensitivity analysis was further performed for heterogeneous synthesis.

On the basis of four previous studies with 804,264 cases, pregnancy was associated with significantly lower risk of diarrhea (RR, 0.70; 95% CI: 0.61 to 0.79) among the women with COVID-19 (Fig. 1A). The pooled result was not affected by any single study although the heterogeneity was relatively high (I-square = 55%). With regard to headache, the risk seemed to be similar with the risk in both pregnant and non-pregnant women (RR, 0.85; 95% CI: 0.72 to 1.01; Fig. 1B), while a serious heterogeneity raised concerns in this data synthesis (I-square = 93%). Leave-one-out analysis showed that no single study can change the trend of meta-analysis, but the pooled result reached statistical significance after removing the study by BahaaEldin et al. (RR, 0.81; 95% CI: 0.68 to 0.96) [5].

This letter tries to set two examples for others to follow, and some meaningful findings could be observed in our brief analysis in both statistics and clinical perspectives. Statistical significance is evident in abovementioned results, wherefore we focus on clinical importance in the following discussion. It has been known that signs and symptoms are associated severity and clinical outcomes of COVID-19 [6,7]. Besides, severity and symptoms of COVID-19 among pregnant women are significantly associated with preterm birth even with increased risk of severe neonatal morbidity [2,8,9]. Specifically, pregnant women with diarrhea have higher risk of preterm birth [8]. To have more understandings on the associations of pregnancy and symptoms of COVID-19, therefore, is important to clinical practice. The present letter is a glance of this issue, and we encourage further studies to have a full review with more accurate data to provide an overview on the associations of pregnancy and symptoms and clinical outcomes of COVID-19. Further review ought to be carefully synthesized data after checking the definition of each clinical outcome and symptom among studies.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analysed during this study are included in this published article.

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Competing interests

Chia-Yi Sun, Chen Hsin Ping, and Yi-No Kang declare that they have no competing interests.

CRediT authorship contribution statement

Chia-Yi Sun: Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Hsin-Ping Chen:** Writing – review & editing, Investigation, Formal analysis, Data curation, Conceptualization. **Yi-No Kang:** Writing – review & editing, Visualization, Supervision, Methodology, Formal analysis.

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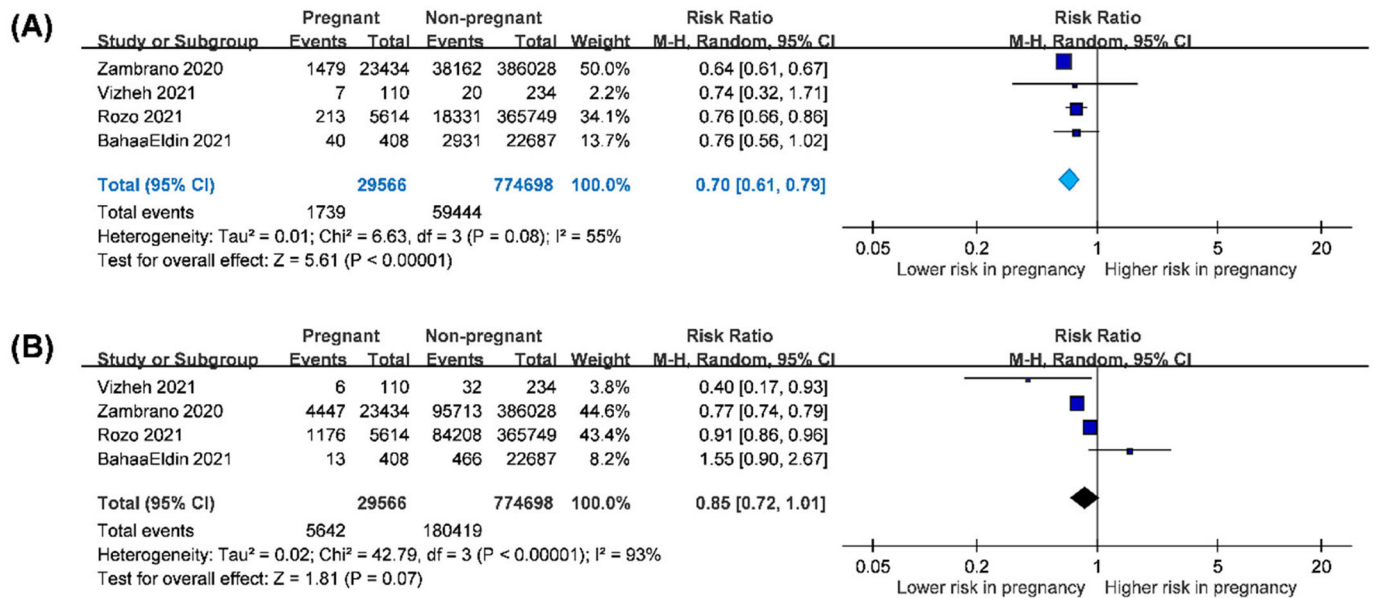
Fig. 1. Forest plot of the association of pregnancy and (A) diarrhea and (B) headache. CI, confidence interval.

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