



Encourage women to receive COVID-19 vaccination before, during and after pregnancy

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The outbreak of coronavirus disease 2019 (COVID-19), the novel severe acute respiratory syndrome (SARS)-coronavirus (CoV)-2 pathogen-related disease, pandemic results in a catastrophic shock to the world, and subsequently contributes to significant changes in daily life and social activity, and harms to personal health and wealth worldly.¹⁻⁵ As a new disease, evidence-based knowledge, such as prevention, diagnosis, and management about COVID-19 in pregnant women is still scarce, although some can follow previous experience in facing influenza, SARS, and Middle East respiratory syndrome in women before, during, and after pregnancy.¹⁻⁵ A recent Canadian Surveillance of COVID-19 in pregnancy tried to clarify whether SARS-CoV-2 infection during pregnancy is associated with an increased risk of adverse maternal and perinatal outcomes or not, and they used the strategy to compare 6012 pregnant women with COVID-19 and cases of COVID-19 among the general Canadian population of reproductive-age female individuals to respond to the above question.⁶ As expected, the results showed that there was a significantly increased risk of COVID-19-related hospitalization (7.75% vs. 2.93%, relative risk [RR], 2.65; 95% confidence interval [CI], 2.41–2.88) as well as an increased risk of intensive care unit/critical care unit admission (2.01% vs. 0.37%; RR, 5.46; 95% CI, 4.50–6.52), and also strongly associated with the risk of preterm birth (11.05% vs. 6.76%; RR, 1.63; 95% CI, 1.52–1.76), further supporting the negative impact on reproductive outcome in pregnant women infected by SARS-CoV-2.⁶

Additionally, the study also confirmed our previous review showing that increasing age, preexisting hypertension, and greater gestational age at diagnosis were significantly associated with worse maternal outcomes.^{1,2} In fact, Canada's information seems to be not new, as there are many studies that show the untoward outcomes of pregnancy and perinatal outcomes in pregnant

women when they get COVID-19 infection.^{1,7,8} However, one of the critical findings about their study is that 98.7% of pregnant women with COVID-19 (3318/3361) did not receive any one dose of vaccination.⁶ Therefore, the issue of addressing the COVID-19 vaccination for pregnant women appears important. It is urgent to reconsider the need of application of COVID-19 vaccination to the pregnant women who are vulnerable to infectious disease. Therefore, the recent publication of the May issue of the *Journal of the Chinese Medical Association* entitled "Pharmacological consideration of COVID-19 infection and vaccines in pregnancy" is worthy of further discussion.⁹

In this review, the authors have mentioned that both Pfizer/BioNTech and mRNA-1273 Moderna/National Institute of Health have been approved as vaccines for pregnancy.⁹ The authors also mentioned that US Food and Drug Administration, the Advisory Committee on Immunization Practices, and other regulatory professional authorities left open the choice for pregnant and lactating women to take the vaccine.⁹ The following comments did not argue the policy about the aforementioned important issue as a shared decision-making between health providers and pregnant women—open the choice for pregnant and lactating women to receive the COVID-19 vaccination. Some opinions are worthy of presentations.

It is fully understood for vaccine hesitancy during pregnancy when COVID-19 vaccines were first authorized because pregnant people were excluded from the initial COVID-19 vaccine trials.¹⁰ However, similar to the question as shown by McClymont conducting the study to clarify the association between COVID-19 and pregnancy outcome,⁶ the audience may be interested in whether COVID-19 vaccination during pregnancy is associated with adverse peripartum or pregnancy outcomes or not? Although the question remains whether the evidence from the following two studies will convince those who remain unvaccinated to receive a COVID-19 vaccine during pregnancy, the strength of their results should be claimed, including the large and well-defined population-based cohorts, the availability of validated data on vaccine exposures and birth outcomes through regional and national registries, and the thoughtful approaches addressing the following common sources of bias in observational studies of maternal vaccination: healthy vaccinee bias and confounding by indication, immortal time bias, and cohort truncation.¹⁰⁻¹²

In terms of the association of COVID-19 vaccination in pregnancy with adverse peripartum outcomes, the authors enrolled 97 590 pregnant women, containing 22 660 (23%) who received at least one dose of COVID-19 vaccine during pregnancy (63.6% received the first dose in the third trimester; 99.8% received an mRNA vaccine) and 44 815 women who were vaccinated after pregnancy, and the results showed that the vaccination against SARS-CoV-2 was not significantly associated with

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increased risk of postpartum hemorrhage (3% vs. 3%; adjusted risk ratio [aRR] 0.91; 95% CI, 0.82–1.02), chorioamnionitis (0.5% vs. 0.5%; aRR 0.92; 95% CI, 0.70–1.21), cesarean delivery (30.8% vs. 32.2%; aRR 0.92; 95% CI, 0.89–0.95), neonatal intensive care unit admission (11.0% vs. 13.3%; aRR 0.85; 95% CI, 0.80–0.90), or low Apgar score (1.8% vs. 2.0%; aRR 0.84; 95% CI, 0.72–0.97).⁹ Based on the aforementioned finding, the authors highly recommended that COVID-19 vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimester.¹¹

In terms of the association of COVID-19 vaccination in pregnancy with adverse pregnancy outcomes, the authors included 157 521 singleton pregnancies, consisting of 28 506 (18.1%) who received at least one dose of COVID-19 vaccine during pregnancy (3.9%, 45.9%, and 50.2% received the first dose in the first, second and third trimester, respectively; 98.3% received an mRNA vaccine) and the remaining women who were not vaccinated during pregnancy, and the results showed that there were no significantly increased risks of preterm birth (adjusted hazard ratio [aHR], 0.98; 95% CI, 0.91–1.05), stillbirth (aHR, 0.86; 95% CI, 0.63–1.17), small for gestational age (adjusted odds ratio [aOR], 0.97; 95% CI, 0.90–1.04), low Apgar score (aOR, 0.97; 95% CI, 0.87–1.08), or neonatal care admission (aOR, 0.97; 95% CI, 0.86–1.10).¹² Based on the absence of association between COVID-19 vaccination and pregnancy outcomes, their study is also in agreement with Dr. Fell's recommendation that mRNA vaccines during the second and third trimesters of pregnancy should be considered.¹¹

Additionally, data from the US Vaccine Safety Datalink can inform strategies to increase booster dose vaccinations and effective messaging COVID-19 vaccinations significantly lower the risk of serious illness from COVID-19 in pregnant individuals, and data indicate potential benefits to the developing fetus.^{11–13}

Taken together, some authors claimed that the COVID-19 vaccine is a safety weapon against the COVID-19 pandemic for pregnant women,¹⁴ as well as our previous review² and current comment favoring the COVID-19 vaccination to the pregnant women or other populations vulnerable to infectious disease;^{2,15} however, there is no doubt that we are eagerly looking forward to learning more work attempting to achieve equity in the availability, acceptance, and administration of life-saving interventions, such as the COVID-19 vaccines.

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