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Brief Report

Rates of Successful Conceptions According to COVID-19 Vaccination Status: Data from the Czech Republic

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Abstract: Background/Objectives: Adverse effects of COVID-19 vaccination on human menstrual cycle characteristics have been observed, but limited data are available on the relationship between COVID-19 vaccination status and birth rates. Therefore, we used nationwide data from the Czech Republic to examine rates of successful conceptions (SCs), i.e., conceptions leading to live births 9 months later, for women who were either vaccinated or unvaccinated against COVID-19 before SC. Methods: Summary monthly COVID-19 vaccination and birth data for women aged 18-39 years in the Czech Republic were retrieved for the period from January 2021 to December The numbers of SCs per month per 1,000 women were calculated for preconception-vaccinated or unvaccinated women, respectively, as well as the number of SCs per month per 1,000 women for all women aged 18-39 years. Results: During the study period, there were approximately 1,300,000 women aged 18-39 years in the Czech Republic, and the proportion of COVID-19-vaccinated women increased until reaching a steady state of around 70% by the end of During the entire study period, SCs per 1,000 women were considerably lower for women who were vaccinated, compared to those that were unvaccinated, before SC. Furthermore, SC rates for the vaccinated group were generally much lower than expected based on their proportion of the total population. Conclusions: In the Czech Republic, SC rates were substantially lower for women vaccinated against COVID-19 before SC than for those who were not vaccinated. These hypothesis-generating and preliminary results call for further studies of the potential influence of COVID-19 vaccination on human fecundability and fertility.

Key words COVID-19; vaccine; fecundability; fertility

Introduction

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Decreased birth rates have been reported in the Czech Republic and many other countries following the COVID-19 pandemic.¹⁻³ Although studies have indicated that COVID-19 vaccination has no appreciable effect on human fertility and that COVID-19 vaccines are safe during pregnancy,^{4,5} adverse effects of COVID-19 vaccines on menstrual characteristics are well-documented, suggesting that COVID-19 vaccination may influence fecundability, i.e., the probability of achieving successful conception (SC) within a single menstrual cycle.^{6,7} Unfortunately, the potential influence on reproductive health was not assessed in randomized preauthorization trials of COVID-19 vaccines

and investigations aimed at the influence of individual COVID-19 vaccines on human fecundability are encumbered by methodological challenges including, for example, temporal variation in vaccinerelated factors (vaccine characteristics, accessibility, eligibility, hesitancy, policies etc.), healthy vaccine and selection bias of available preconception cohorts (pregnancy planners, women undergoing invitro fertilization etc.), and inherent limitations of electronic health care data that are not designed to measure SCs (left-truncation bias, inability to capture early pregnancy loss without registered medical contact etc.).⁸ However, data that may add to evidence on the potential influence of COVID-19 vaccination on human fecundability are obviously of great importance to public health. The Czech Republic is one of the few countries where nationwide birth data are available for women who were vaccinated or unvaccinated for COVID-19, and we therefore used these data to compare rates of SCs resulting in live births for these two groups.

Material and Methods

Data for the number of live births by women in the Czech Republic aged 18-39 years (hereafter referred to as 'women') were retrieved from the Institute of Health Information and Statistics of the Czech Republic (IHIS). The data contained the number of births per month between January 2021 and December 2023 by women who were vaccinated, i.e., had received at least one COVID-19 vaccine dose by the date of delivery, and by women who were unvaccinated, respectively. Furthermore, the number of births per months by women vaccinated during pregnancy was provided. A SC was defined as one that resulted in a live birth 9 months later. Accordingly, the obtained data enabled us to calculate the number of births per month by women who were vaccinated prior to SC, i.e., the number of women vaccinated by the date of delivery 9 months later, minus the number of women who were vaccinated during pregnancy, as well as the number of women who were unvaccinated before SC, respectively. The total number of women vaccinated against COVID-19 per month was also obtained from IHIS, and the total number of women in the population was obtained from the public database of the Czech Bureau of Statistics. Consequently, the numbers of SCs per month per 1,000 women were calculated for women that were pre-SC-vaccinated and pre-SC-unvaccinated, respectively, as well as the number of SCs per month per 1,000 women for all women aged 18-39 years in the Czech Republic. The study relied solely on secondary anonymized data and was, therefore, exempt from research ethics board review.

Results

The data for vaccinated and unvaccinated women are shown in Figure During the study period (January 2021–March 2023), there were approximately 1,300,000 women aged 18-39 years in the Czech Republic, and the proportion of vaccinated women increased until reaching a steady state of around 70% of all women by the end of 2021 (Figure 1A). The Comirnaty (Pfizer-BioNTech) and Spikevax (Moderna) mRNA vaccines comprised 96% of all administered COVID-19 vaccine doses, with a 11:1 ratio in the use of these two vaccines. Notably, during the entire study period, monthly numbers of SCs per 1,000 women were considerably lower for women that were vaccinated before SC, compared to those that were not. SC rates for women vaccinated before SC were generally much lower than expected based on their share of the total population of women (Figure 1A and B). For example, at the end of June 2021, where 39% of all women had been vaccinated, those vaccinated before SC contributed only 7% of all SCs. In June 2021, a sharp increase in the rate of SC was observed for women unvaccinated before SC, and this higher rate was maintained over the succeeding 6-month period. During 2022, rates of SCs stabilized in both women that were vaccinated and unvaccinated before SC. However, throughout 2022, SC rates remained about 1.5 times higher for women that were unvaccinated before SC compared with those that were vaccinated before SC (Figure 1B).



Figure A: Histogram showing the percentage of women aged 18-39 years in the Czech Republic who were vaccinated with at least one dose of a COVID-19 vaccine by the end of the respective month (January-December = 1-12 on the abscissa). **B:** Histogram showing the number of successful conceptions per 1,000 women aged 18-39 years according to their preconception COVID-19 vaccination status.

Discussion

In this study, we used simple descriptive statistics and data visualization to analyze summary COVID-19 vaccination and birth data for all women aged 18-39 years in the Czech Republic and found that from January 2021 to December 2022, monthly numbers of SCs per 1,000 women were markedly lower for women vaccinated before SC compared to those that were unvaccinated before SC. Furthermore, the contribution of women vaccinated before SC to the total monthly rate of SCs was substantially lower than to be expected according to the proportion of vaccinated women in the total population of women.

Declining birth rates have been reported in many countries following the COVID-19 pandemic and have been linked with economic instability, social inequality, and the stringency of pandemicrelated social restrictions.¹⁻³ An association between declining birth rates and onset of COVID-19 vaccinations has also been suggested and thought to indicate that women postponed conception until after vaccination.²⁻³ Indeed, concern about COVID-19 vaccine safety has been a major reported reason for remaining unvaccinated, and reproductive adults appear particularly anxious about potential adverse effects of COVID-19 vaccination on fertility.⁹⁻¹⁰ In this regard, although the overall safety of COVID-19 vaccination during pregnancy has been well documented, vaccination may be associated with menstrual pain and changes in menstrual flow and cycle length, and direct effects of the Comirnaty vaccine (Pfizer-BioNTech) on the ovarian follicle were reported recently.⁵⁻⁷ However, to date very little data on birth rate linked to COVID-19 vaccination status have been reported.

To our knowledge, the relationship between COVID-19 vaccination status and rates of SCs has not been examined previously on a population level. However, a prospective cohort study of pregnancy planners (n=2,126 women) in the US and Canada indicated that preconception COVID-19 vaccination did not influence the probability of SC, albeit that study only included women who were trying to conceive and was also limited by use of self-reported vaccination status.¹¹ Contrary to these findings, our current real-world population data from the Czech Republic indicated that COVID-19 vaccination was linked with substantial decreases in SC rates compared to non-vaccinated women.

While the strength of our study is its nationwide unselected sample of fertile women, the observed association between decreased SC rates and COVID-19 vaccination is, of course, not proof of a causal relationship between vaccination and fecundability. For example, it is possible that more women who wished to become pregnant, i.e., achieve SC, chose not to be vaccinated, and/or that more women who did not plan to become pregnant opted for vaccination. Indeed, such self-selection bias is compatible with the decrease in SC observed amongst women vaccinated before SC in the first months of the vaccination campaign as well as the sudden increase in SCs of the women unvaccinated before SC in June 2021 (Figure 1B). However, to defer vaccination was against sanctioned national public recommendations in the Czech Republic at the time, and if this type of self-selection bias had

been the predominant underlying factor for the observed reduction in SC rates in vaccinated women, the total fertility rate would have remained relatively constant throughout the study period. However, the total fertility rate in the Czech Republic decreased from 1.83 births per 1000 women in 2021, to 1.62 in 2022, and 1.45 in 2023,¹² and self-selection bias, therefore, does not seem to fully explain the observed link between vaccination status and SC rates. Notably, we and others have previously found a batch-dependent safety signal for the Comirnaty vaccine (Pfizer-BioNTech) in the Czech Republic, Denmark, Sweden, and the US, and the possibility of a disproportionate influence of early batches of this vaccine on SC rates remains to be investigated.¹³⁻¹⁶

The current study should be interpreted in view of other limitations that include, for example, unmeasured confounders such as socioeconomic factors, comorbidities, effects of individual COVID-19 vaccination boosters, concurrent COVID-19 infection specifics, preconception fertility, contraception use, pregnancy loss, stillbirths, and paternal vaccination status. In addition, the Czech Republic population is almost exclusively Caucasian, and results may not apply to other ethnicities.

Conclusions

We conclude that during the study period, SC rates in the Czech Republic for all women vaccinated against COVID-19 before SC were substantially lower than for those who were unvaccinated before SC. These hypothesis-generating and preliminary results call for further studies of the influence of COVID-19 vaccination on human fecundability and fertility.

Author Contributions: Conceptualization: TF, VM; Methodology: TF, VM; Investigation: TF, VM, PRH; Data curation: TF, MS; Formal analysis: TF, VM, MS, JDG, PRH; Writing-Original draft: VM, TF, JDG, PRH; Writing-Review and editing; VM, TF, MS, JDG, PRH; Project administration: VM; Funding acquisition: VM.

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Data Availability Statement: The original data presented in the study are openly available at https://github.com/Schmeling-M/C-19-Conception.

Conflicts of interest: None.

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