Increased incidence of first-trimester miscarriage during the COVID-19 pandemic

There is limited research on the first-trimester outcomes of women with coronavirus disease 2019 (COVID-19). Recent meta-analyses demonstrated the detrimental effect of COVID-19 on preterm birth, Cesarean section rates and maternal morbidity\(^1,2\). However, the effect of first-trimester severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on early pregnancy outcome is still unknown. Recently, Cosma et al. reported that the cumulative incidence of COVID-19 did not differ significantly between women who experienced a miscarriage during the first trimester of pregnancy and those who did not\(^3\). However, their findings were limited by the small sample size and case–control study design. A recent global review investigating the effects of the COVID-19 pandemic on maternal and pregnancy outcomes found increased stillbirth rates in low- and middle-income countries but did not report on miscarriage rates\(^4\).

This was a retrospective cohort study comparing the incidence of miscarriage between a 13-week period in 2019 and the same epoch in 2020, at Ankara University Hospital, Turkey. Women who had their first perinatal visit for a new pregnancy with a verified pregnancy outcome record were included in the study. All women admitted for miscarriage in 2020 were screened for SARS-CoV-2 infection by reverse transcription polymerase chain reaction (RT-PCR) testing of nasopharyngeal samples. The difference between the two epochs (in 2019 vs in 2020) was modelled using mixed-effects Poisson regression with random intercepts. Intercepts were allowed to vary between the same months of 2019 and 2020 to account for the dependency structure. Results were reported as incidence rate ratios (IRR) with 95% CI. The dependent variable was the number of miscarriages and the independent variables were the number of new pregnancies and SARS-CoV-2 screening result.

A total of 1269 pregnant women were included in the study. Between 29 June and 30 September 2019, 727 women had their first prenatal visit, of whom 67 (9.2%) had a miscarriage. During the corresponding period in 2020, 542 women had their first prenatal appointment, of whom 64 (11.8%) had a miscarriage before 12 weeks’ gestation. All women who had a miscarriage in 2020 were tested for SARS-CoV-2 before admission and 4.7% (3/64) tested positive. A mixed-effects Poisson regression model with random intercepts for matching months was used to adjust for seasonality. The results indicated that the number of miscarriages per 100 new pregnancies was significantly higher in 2020 compared with 2019 (IRR, 1.25 (95% CI, 1.16–1.35); \(P < 0.0001\)). However, the rate of positive SARS-CoV-2 test results did not have a significant effect on the miscarriage rate (\(P = 0.810\)). The observed increase in miscarriage rate (Figure 1a) was modified by the reduced number of new pregnancies in 2020 (IRR, 0.75 (95% CI, 0.66–0.84); \(P < 0.0001\)) (Figure 1b). The absolute number of miscarriages admitted per week was
similar between the studied epochs in 2019 and 2020 (IRR, 0.95 (95% CI, 0.86–1.06); P = 0.407) (Figure 1c).

Limitations of the study include its retrospective design, single-centre setting and limited sampling period. Although we matched the months of the epochs and used a mixed-effects model to account for seasonality, a time series analysis to check for trend was not performed. Furthermore, serological data to document previous SARS-CoV-2 infection were not available. Strengths of the study include the adequate sample size and availability of RT-PCR results for all miscarriage cases. The number of new pregnancies was lower during the study period in 2020 compared with the same epoch before the pandemic in 2019. This finding is in line with recent reports showing the negative effect of the COVID-19 pandemic on fertility behavior. Another reason for fewer new pregnancy diagnoses could be reduced healthcare-seeking behavior among pregnant women due to the pandemic or lockdown measures. However, there were no stringent lockdown measures in effect in Turkey during the study period.

The incidence of miscarriage was increased by 25% during the COVID-19 pandemic in our population. More extensive studies, including multiple hospitals from the same region, are needed to avoid sampling bias. Serological data to document previous SARS-CoV-2 infection would be useful to demonstrate a causal link between miscarriage and SARS-CoV-2 infection.

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