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# Association of SARS-CoV-2 infection during late pregnancy with maternal and neonatal outcomes

Ting Du[1], Yawen Zhang[1], Xueli Zha[1] and Qin Huang[1*]

## Abstract

**Background** Limited data on the impact of the coronavirus disease 2019 (COVID-19) during pregnancy on newborn outcomes are available. This study aimed to characterize and compare the clinical outcomes of newborns from women with and without the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection during late pregnancy.

**Method** This was a retrospective cohort study of women who were either infected or not infected with the SARS-CoV-2 virus during late pregnancy. The neonatal complications associated with COVID-19-positive pregnant women were investigated and analyzed.

**Results** Among 2063 pregnant women over 28 weeks of gestation, 1.2%, 3.3%, and 18.7% of patients with multiple pregnancies, abnormal fetal positions, and lack of maternal or neonatal follow-up data, respectively, were excluded. Patients who were COVID-19-negative (60.6%) and -positive (16.2%) remained for further analysis. SARS-CoV-2 infection was significantly associated with higher SARS-CoV-2 infection rates in newborns (0% vs. 1.49%, $P < 0.01$) and longer duration of hospital stay ($6.39 \pm 2.2$ vs. $4.92 \pm 1.6$, $P < 0.01$). However, comparing neonatal complications, including Apgar score, preterm birth, low birth weight, cesarean section rate, newborn hearing, neonatal congenital heart defects, and height and weight compliance rate of 6-month-old children, between non-infected and infected participants did not reach statistical significance.

**Conclusion** SARS-CoV-2 infection in late pregnancy has no significant impact on neonatal outcomes. After six months of follow-up of the neonates, we observed that SARS-CoV-2 infection in the third trimester of pregnancy did not affect their growth and development. Hopefully, these findings will guide management strategies and clinical practice.

**Keywords** SARS-CoV-2 infection, COVID-19, Neonatal outcome, Pregnant women, Infant development

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The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spread rapidly around the world, causing a pandemic that affected millions of people after the pandemic outbreak. Many countries, including China, tightened anti-epidemic restrictions to prevent the spread of the virus. By the end of 2022, as the toxicity and transmission of the virus declined, the Chinese government downgraded the COVID-19 epidemic prevention policy. Hence, the number of SARS-CoV-2-infected people increased dramatically within a short period. Concurrently, many pregnant women were infected during this period [1]. Previous studies reported that maternal SARS-CoV-2 infection during pregnancy was associated with neonatal morbidity and maternal mortality [2–10], and premature birth [11, 12]., in the post-pandemic era, the pathogenicity and mortality rate of the virus has decreased [13]. The answer to whether infection in pregnant women will still result in adverse outcomes for both mothers and infants remains unclear. Furthermore, the majority of existing information pertains to the consequences of perinatal pregnancy outcomes, while relatively little is known about the growth and development of newborns in the later postnatal period. In this study, we characterized and compared the clinical outcomes of newborns from women with and without SARS-CoV-2 infection during late pregnancy between December 2022 and June 2023. We used infected and non-infected participants and their infants in Suzhou City, a well-developed city in Jiangsu province of eastern China, to assess the growth and development of newborns from mothers with SARS-CoV-2 infection during late pregnancy. Our cohort studies with 1585 pregnant women and over 1500 cases of live births provide reliable results and will help guide healthcare strategies and clinical practice.

## Methods

### Study Design and participants

We conducted a retrospective cohort study of pregnant women who delivered between December 2022 and June 2023 and were at least 28 weeks pregnant. Using oropharyngeal and nasopharyngeal swabs, real-time polymerase chain reaction (RT-PCR) screening was conducted to divide all pregnant women who delivered at the hospital during the study period into a COVID-19-positive group and a COVID-19-negative group, regardless of whether they were admitted for obstetrical or medical reasons. COVID-19 disease severity was classified according to World Health Organization criteria. We included two groups in our study, based on the severity of COVID-19: asymptomatic-mild and moderate groups. Severe patients who received treatment in other hospitals and did not have information about pregnant-baby data were not included in the study. The clinical severity levels were assessed at hospital admission. Neonates of COVID-19-positive mothers underwent RT-PCR tests 24 and 48 h after delivery, with retesting at 72 h if one of the previous tests was positive or inconclusive. The hospital's electronic medical record system provided delivery and neonatal data. Women with multiple pregnancies, abnormal fetal positions, additional medical problems, or insufficient information regarding SARS-CoV-2 infection, pregnancy follow-up data, periodical antenatal examination, or clear neonatal prognosis were excluded from the study. No participant had a history of smoking., and mode of delivery. The final Dataset included age, pregnancy status, delivery method, complications, and neonatal outcomes. Infants were required to have at least one outpatient visit within six months to assess their growth and development. Because of the fear of vertical mother-to-child transmission, late umbilical cord amputation was not used in all cases.

### Variables definitions

Various factors were considered in this study to investigate the influence of COVID-19 during pregnancy on maternal and neonatal outcomes. Obesity was defined as a body mass index (BMI) of 30 or above for the mother. Pregnancy-related hypertension was defined as a blood pressure reading of 140/90 mmHg or more after the 20th week of gestation, along with or without proteinuria, occurring for the first time during the second half of the pregnancy. A live birth was defined as the delivery of a live newborn after the 28th week of gestation. Preterm birth, as determined by clinical assessment, was defined as a live birth prior to 37 weeks of gestation. Macrosomia was defined as a birth weight of over 4000 g, while low birth weight was defined as a newborn's weight of less than 2500 g. Pathological fetal position referred to a non-vertex presentation, which included breech, oblique, and transverse positions. We defined a 6-month-old child's length and weight as standard between the 3rd and 97th percentiles.

### Statistical analysis

All statistical analyses were carried out using SPSS version 23.0 (IBM Inc., U.S.A.). Normally distributed quantitative data were expressed as means±standard deviations, and comparisons between different groups were made using the student's *t*-test or the one-way ANOVA where appropriate. The Mann–Whitney U test was used for data that were not normally distributed. Qualitative data were expressed as percentages, and comparisons of frequencies and proportions between groups were made by using the chi-square test. A *P*-value of less than 0.05 was considered statistically significant.

### Ethical considerations

The study protocol was approved by the ethics committee of The First Affiliated Hospital of Soochow University, and each patient gave written informed consent.

## Results

### Overview of the entire cohort

During the study period, 2063 pregnant women, with an average age of 28.3 years, were enrolled. Out of these participants, we excluded 24 (1.16%), 68 (3.30%), and 386 (18.71%) due to multiple pregnancies, abnormal fetal positions (breech presentation and transverse position), and lack of maternal or neonatal follow-up data, respectively. In the remaining cohort, 1250 (60.59%) participants tested negative for COVID-19, while 335 (16.24%) tested positive. The status of SARS-CoV-2 infection was determined using RT-PCR analysis over 28 weeks of gestation (as shown in Fig. 1).

### Key findings

Table 1 illustrates the comparison of maternal characteristics between the COVID-19- positive and -negative groups, revealing no statistically significant differences between the two groups for the mentioned parameters. However, it is worth noting that the mean duration of hospital stay was significantly longer in the COVID-19-positive group compared to the COVID-19-negative group (6.39±2.2 vs. 4.92±1.6, $P<0.01$).

Subsequently, we compared the neonatal characteristics between the COVID-19-positive and -negative groups. Per our inclusion criteria, all neonates were delivered at or after the 28th week of gestation, as per our inclusion criteria. The status of SARS-CoV-2 infection in neonates was determined using the RT-PCR test twice. Table 2 presents the comparison results of neonatal outcome parameters between COVID-19-positive and -negative groups. Among the 335 COVID-19-positive patients, there were 5 COVID-19-positive neonates compared to no infected neonates from 1250 COVID-19-negative participants ($P<0.01$) (as shown in Table 2).

In addition, we compared newborn outcomes between the two groups at 6-month follow-up after birth. Our results showed no significant differences in outcomes stratified by anticipated Apgar score, low birth weight, neonatal intensive care unit admission, stillbirth, a true knot of the umbilical cord, fetal intrauterine distress, placental abruption, neonatal death, neonatal asphyxia, neonatal hearing screening, neonatal congenital heart defects, and height and weight compliance rate of 6-month-old children (as shown in Table 2). This suggests

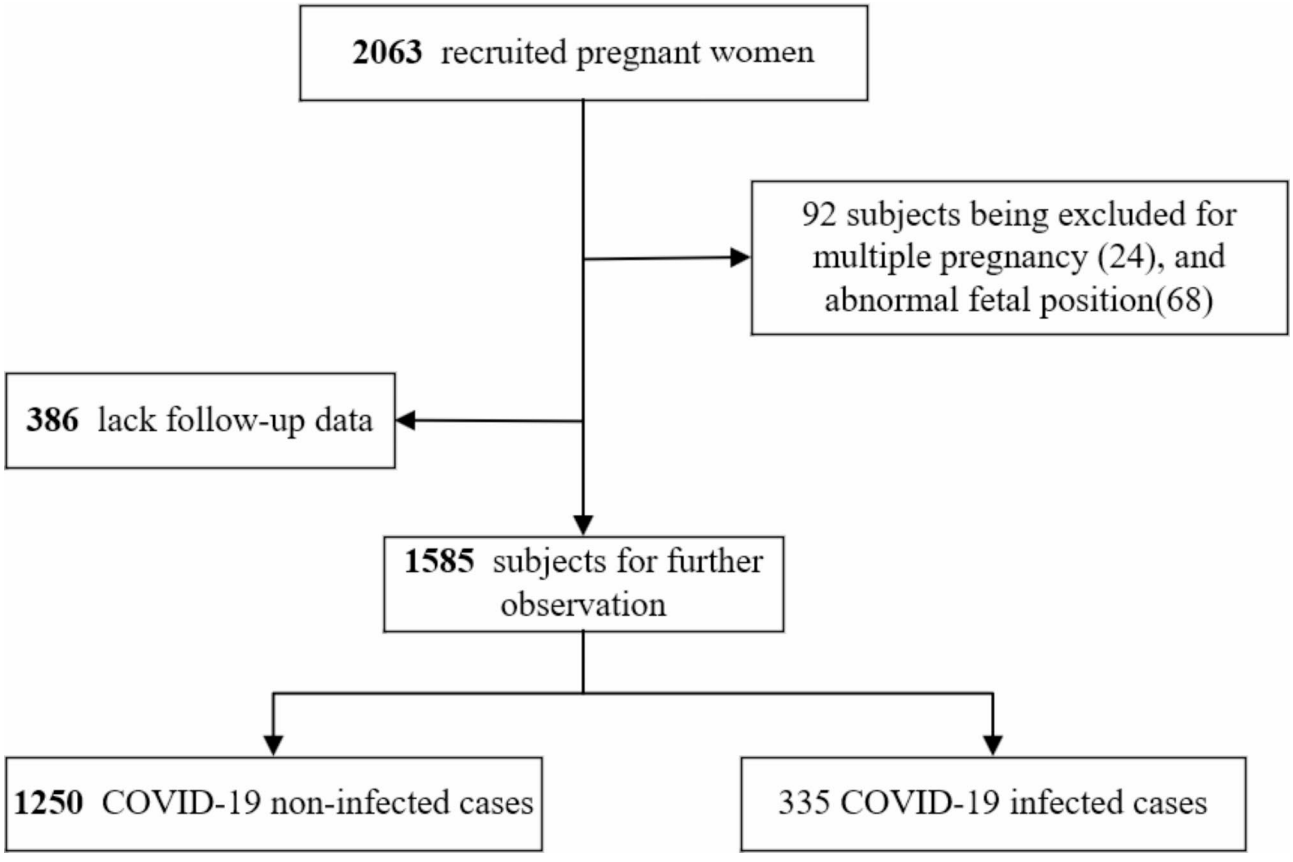


**Fig. 1** The Flowchart of the cohort study

**Table 1** Comparison of pregnancy and labor related data between COVID-9 infection and non-infection groups

| Variables(*n*/%) | COVID-19 non-infection (*n* = 1250) | COVID-19 infection (*n* = 335) | *P* value |
|---|---|---|---|
| **Maternal background characteristics** | | | |
| Maternal age at delivery (y) | 28.91 ± 4.16 | 29.26 ± 3.84 | 0.164 |
| Primigravida | 512 | 156 | 0.082 |
| Vaccination Status | | | 0.089 |
| not vaccinated | 610 | 181 | |
| Vaccinated ≥ 1 dose | 640 | 154 | |
| Education ≥ 12 (y) | 536 | 154 | 0.311 |
| Obesity | 107 | 35 | 0.283 |
| Delivery mode | | | 0.891 |
| Vaginal | 771 | 208 | |
| Cesarean section | 479 | 127 | |
| **Pregnancy-related complications** | | | |
| Gestational hypertension | 57 | 19 | 0.398 |
| Gestational diabetes mellitus | 69 | 19 | 0.914 |
| Premature rupture of membranes | 123 | 39 | 0.334 |
| Oligohydramnios | 60 | 22 | 0.195 |
| Polyhydramnios | 28 | 10 | 0.429 |
| Preterm live birth | 138 | 44 | 0.286 |
| Perineum wound infection or surgical site infection | 9 | 4 | 0.393 |
| Postpartum hemorrhage ≥ 1000 ml | 94 | 22 | 0.552 |
| Hospitalization days | 4.92 ± 1.6 | 6.39 ± 2.2 | <0.01 |

**Table 2** Comparison of newborn characteristics between COVID-19 infection and non-infection groups

| Variables(*n*/%) | COVID-19 negative (*n* = 1250) | COVID-19 positive (*n* = 335) | *P* value |
|---|---|---|---|
| Newborn COVID-19 infection | 0 | 5 | <0.01 |
| Apgar score < 7 at 5 min | 15 | 5 | 0.67 |
| Low birth weight (< 2500 g) | 23 | 9 | 0.328 |
| NICU | 20 | 7 | 0.539 |
| Stillbirth | 6 | 2 | 0.798 |
| *A True knot of the umbilical cord* | 2 | 0 | |
| *Fetal intrauterine distress* | 2 | 1 | |
| *Placental abruption* | 2 | 1 | |
| Neonatal death | 2 | 0 | 0.464 |
| *Neonatal asphyxia* | 2 | 0 | |
| Neonatal congenital heart defects | 16 | 6 | 0.478 |
| Height compliance rate of 6-month-old children | 5 | 3 | 0.256 |
| Weight compliance rate of 6-month-old children | 8 | 4 | 0.229 |

Abbreviation: NICU, neonatal intensive care unit

that SARS-CoV-2 infection in late pregnancy has no significant impact on neonatal outcomes.

## Discussion

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has profoundly impacted the world since its emergence in late 2019. Throughout this period, scientific research and clinical investigations have been conducted extensively. Pregnant women and neonates may be particularly susceptible to COVID-19 due to the physiologic changes that occur in pregnancy, which affect cardiorespiratory and immune systems [14]. However, the nature of the association between COVID-19 and pregnancy outcomes is unclear, and further investigation is needed to understand the impact of COVID-19 on maternal and neonatal health.

To assess the maternal and neonatal outcomes of mothers with COVID-19 during late pregnancy, we conducted a comprehensive case-control study at the First Affiliated Hospital of Soochow University between January 2021 and January 2022. The study included 1585 pregnant women, of whom 335 were diagnosed with COVID-19 during the third trimester of their pregnancy. The cases group consisted of 335 mothers with positive results for

COVID-19, while the control group included 1250 mothers who were not diagnosed with COVID-19 after the 28th week of their pregnancy. The COVID-19 infection rate (335 vs. 1585, infected women vs. pregnant women) was higher than previously reported [15], which may be attributed to the liberalization of the COVID-19 epidemic prevention policy in China at the end of December 2022, as well as the low vaccination rate of COVID-19 among pregnant women [16].

Our findings suggest that the clinical presentation of COVID-19 in late pregnancy did not appear to impact the neonatal outcomes in our cohort study. This finding is consistent with previous research that reported no significant differences in maternal or neonatal outcomes between pregnant women with and without COVID-19 [17, 18]. However, these results may not be generalizable to all populations, and further research is needed to fully understand the impact of COVID-19 on maternal and newborn health.

The current study demonstrated that individuals in the COVID-19-positive group experienced longer hospital stays than those in the COVID-19-negative group (4.92±1.6 vs. 6.39±2.2, $P<0.01$). These findings align with the research of Nachega et al., which included 1315 hospitalized women: 510 pregnant women with SARS-CoV-2, 403 nonpregnant women with SARS-CoV-2, and 402 pregnant women without SARS-CoV-2 infection. In their research, among pregnant women, SARS-CoV-2 infection was found to increase the risk of ICU admission, and they reported a statistically significant difference in hospital stay duration between SARS-CoV-2–infected and –uninfected pregnant women ($P<001$) [19]. Racine et al. also reported similar findings [20]. In our study, the prolonged hospital stays of pregnant women with SARS-CoV-2 infection may be attributed to the fact that COVID-19 can cause fever or other respiratory symptoms in pregnant women, necessitating extended hospital stays for observation and healthcare. Some patients are admitted to the hospital in advance of labor due to a fever caused by SARS-CoV-2 infection.

We conducted a study to compare the outcomes of neonates between COVID-19 positive and negative groups. Our findings revealed an increase in positive cases in the case group (0 vs. 5, $P<0.01$). However, the overall rate was relatively low (5 vs. 335, 1.49%), suggesting that mother-to-infant viral transmission may be occurring. The increase in newborn positivity rate may be attributed to mother-infant cohabitation, where these neonates were not immediately isolated from their mothers after delivery, and skin-to-skin contact was allowed. As neonates are cared for in the same room as mothers and neonates after birth, the positive rate of COVID-19 in the positive mothers group increases. However, we do not have evidence to suggest that these infections were congenitally acquired [21–24], and they should be classified as possible neonatal-acquired infections. During the study period, the Chinese government's guidance for postnatal management of neonates born to mothers with confirmed or suspected SARS-CoV-2 infection was to keep mother and infant together and to encourage breastfeeding.

The incidence of preterm birth in our study was significantly lower (13.13%) than the rates reported by Villar et al. [10] and Jering et al. [25]. Their studies found that maternal SARS-CoV-2 infection was associated with an increased risk of preterm birth, but our results aligned with the findings of Yalçin et al., who found no difference in the preterm birth rate between women with and without SARS-CoV-2 infection [26]. Furthermore, we observed no significant difference in the cesarean section rates between pregnant women with and without SARS-CoV-2 infection. The cesarean section rate did not increase due to SARS-CoV-2 infection, which may be attributed to increased awareness of COVID-19 in the post-pandemic era, reducing the transmission of SARS-CoV-2 from mothers to infants.

Our study demonstrated that COVID-19 infection during late pregnancy did not increase the risk of neonatal ICU admission and was not significantly associated with an increased risk of neonatal complications, including Apgar score(less than 7 at 5 min), birth weight, stillbirth, and neonatal death. There were eight cases of stillbirth (6 vs. 2, $P=0.798$) and two cases of neonatal death (2 vs. 0, $P=0.464$), but the direct cause of all adverse outcomes was not SARS-CoV-2 infection. These findings are consistent with the research conducted by Stowe et al. [27], They indicate that postpartum mother-infant cohabitation is feasible since the neonatal infection rate is low, symptoms are mild, and the prognosis is favorable. The consequences of maternal exposure to SARS-CoV-2 during pregnancy on child development remain unclear [28–30]. Our study, which followed the growth and development of infants six months after birth, found no significant difference in the rate of achieving standard height and weight milestones between the two groups. Tianchen et al. conducted a prospective, observational cohort study in China from May 1 to October 31, 2020, enrolling 135 mother-infant pairs, 57 in the infection cohort and 78 in the non-infection cohort. The study concluded that SARS-CoV-2 exposure during late pregnancy did not increase the risk of developmental delay of the offspring three months after delivery. However, SARS-CoV-2 may indirectly affect early childhood development by lengthening the duration of maternal-infant separation [31]. Similarly, the findings of Pinheiro et al. indicated that SARS-CoV-2 gestational exposure did not increase the risk of developmental delay [32], suggesting that a SARS-CoV-2 infection during late pregnancy may

not impact postnatal growth and development. In our study, we conducted a cohort study that included more than 1,500 live birth cases with reliable follow-up data to evaluate the growth and development of infants, providing more robust, dependable results. Our study may help offer guidance following maternal SARS-CoV-2 exposure during the third trimester. However, it is essential to consider multiple factors, not just SARS-CoV-2 exposure during the third trimester; they can influence neonatal growth and development. Consequently, further research studies are needed to make precise predictions.

## Conclusion

Our research reveals that contracting SARS-CoV-2 during the late stages of pregnancy has no significant impact on maternal and neonatal outcomes. Following a six-month neonatal monitoring period, it was discovered that infants born to mothers with the SARS-CoV-2 infection during their third trimester showed no disruptions to their growth and development. Our findings guide healthcare professionals in caring for newborns whose mothers have confirmed or suspected COVID-19. It is essential to conduct further investigations to assess the long-term effects of SARS-CoV-2 infection during the third trimester of pregnancy on the well-being of neonates.

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**Author contributions**
Ting Du conducted the research and drafted the manuscript. Xueli Zha and Yawen Zhang analyzed the data. Qin Huang reviewed and revised the manuscript. Ting Du and Qin Huang designed the study, verified the authenticity of the raw data, and conceptualized the study. All authors have read and approved the final manuscript and significantly contributed to the work reported. They agree to take responsibility and be accountable for the article's contents and to share responsibility for resolving any questions raised about the accuracy or integrity of the published work.

**Data availability**
No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate**
This study was approved by the Institutional Review Board of the First Affiliated Hospital of Soochow University (approval no. [2024] Ethical Research NO.237). Informed consent was obtained from all patients or their legal surrogates.

**Conflicts of interest**
The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

**Competing interests**
The authors declare no competing interests.

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