

# Maternal, fetal, and perinatal outcomes of COVID-19-infected pregnancies in Saudi Arabia: a meta-analysis and systematic review

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## ABSTRACT

The SARS-CoV-2 pandemic has been researched in various conditions to know the extent of its damage. During pregnancy, there is a placental exchange of blood between mother and fetus. This meta-analysis aimed to investigate the prevalence of maternal, fetal, and perinatal outcomes of COVID-19-positive pregnancy cases in Saudi Arabia. PubMed, Google Scholar, and Web of Science were searched for the period 2019-2024. Pregnancy cases only from Saudi Arabia and reverse transcription polymerase chain reaction confirmed COVID-19 positive were included. Women with any other diseases were excluded. Six studies were selected for meta-analysis with a total of 1065 COVID-19-infected pregnancies. Among the maternal conditions, preterm rupture of membrane (PROM) had the highest prevalence [odds ratio (OR)=4.21; 95% confidence interval (CI): 1.4-7]. Among fetal outcomes, the odds of postpartum anomalies were 4.8 (95% CI: 1.3-11). Intrapartum complications among perinatal outcomes were most likely to occur (OR=2.11; 95% CI: 120.9-125.1). No factual trend for a particular condition can be declared. PROM, postpartum, and intrapartum complications were more likely to occur in COVID-19-infected pregnancies.

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## Introduction

SARS-CoV-2, also known as severe acute respiratory syndrome coronavirus, is responsible for the onset of COVID-19.<sup>1</sup> The first instances of novel COVID-19-associated pneumonia were documented in December 2019 in Wuhan City, China.<sup>1</sup> The World Health Organization officially declared the ongoing COVID-19 pneumonia outbreak as a pandemic on March 11, 2020.<sup>2</sup> In light of the increasing mortality rate, it is imperative to identify and protect the most susceptible segments of society. There have been reports of a case fatality rate of up to 35%, and there are frequent hospitalizations for critical care.<sup>3,4</sup> Transmission from mothers to babies mostly occurs during and immediately after childbirth; however, the use of infection control measures may help mitigate the risk. There are case reports of severe neonatal SARS-CoV-2 infection, including cardiorespiratory failure and death, even though the majority of infected newborns are asymptomatic or only minimally symptomatic.<sup>5,6</sup> There is little data available about the likelihood of neonatal infection after discharge from the hospital, and the evidence regarding the factors during childbirth and after childbirth that influence this risk is inconclusive.<sup>7</sup> The physiological changes that occur during pregnancy make the woman more vulnerable to severe diseases.<sup>8</sup> Maternal tolerance to hypoxia is diminished by morphological modifications such as an increase in the thoracic cage's transverse diameter and an increased elevation of the diaphragm.<sup>9</sup> Increased secretions in the upper respiratory tract and mucosal edema could occur due to vasodilation and changes in lung capacity. Furthermore, alterations in cell-mediated immunity contribute to pregnant women's heightened sensitivity to intracellular infections, including viruses.<sup>10</sup> The innate and adaptive immune systems of fetuses and infants are still growing, which renders them particularly susceptible to infection.<sup>11</sup> The development and function of the brain may be severely influenced by the dysregulation of components like cy-

tokines and the complement cascade.<sup>12</sup> Therefore, it is particularly necessary to identify whether an infectious agent may infect a fetus or baby *via* vertical transmission.<sup>13</sup> It is vital to identify whether expecting moms and their unborn infants could be at risk for developing the current COVID-19 pandemic. Given the little data available on the novel coronavirus and the steeply expanding disease burden, it is vital that scientific facts about the illness be distributed in an accessible and effective fashion.<sup>14</sup> Few case studies and series offer information on the maternal and perinatal outcomes of pregnant women infected with SARS-CoV-2. The findings are variable, and the sample sizes are modest. The results of this research are tough to assess owing to changes in health policy in pandemic-affected countries, continuing changes in clinical care standards, and doubts regarding the quality of the data.

## Methods

### Study strategy and selection criteria

The meta-analysis was conducted using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guiding principles and Meta-Analysis of Observational Studies in Epidemiology (MOOSE).

### Research questions

What was the prevalence of maternal, fetal, and perinatal outcomes of COVID-19-positive pregnancy cases in Saudi Arabia? Were there any statistically significant differences between the COVID-19-positive and healthy pregnancies with respect to the three pregnancy outcome groups?

### Search strategy and data sources

Pub-Med, Google Scholar, and Web of Science were searched for extracting relevant studies published between 2019 and 2024. The string of “pregnancy outcomes”, “COVID-19”, “Saudi Arabia”, “retrospective”, “case-control”, “cohort studies”, “cross-sectional”, “maternal”, “neonatal”, and “fetal” was used. Articles were filtered for duplication and full-text availability using Endnote 21<sup>®</sup> software. Manual screening was performed on titles and abstracts and then on full text to obtain the eligible studies.

### Inclusion criteria

Studies that incorporated Saudi pregnant women who had given or gave birth during the research and were declared COVID-19-positive through reverse transcription polymerase chain (RT-PCR) were included.

### Exclusion criteria

Studies in which pregnant women were not from Saudi Arabia and had diseases or syndromes other than COVID-19 were excluded.

### Data extraction

From the selected studies, the extracted data included authors' names, study types, gestational ages, sample sizes,

and events of selected maternal, fetal/neonatal, and perinatal outcomes. Conditions of each outcome discussed directly or indirectly in at least two of the studies were extracted.

### Outcome of interest

Maternal outcomes encompassed cesarean section, normal vaginal delivery, assisted vaginal delivery, preterm rupture of membrane (PROM), intensive care unit (ICU) admission, and pre-eclampsia. Fetal/neonatal outcomes were low heart rate (beat/minute), stillbirth, low birth weight, premature births, respiratory complications, and postpartum anomalies. Among the perinatal outcomes, gestational sac abnormalities, intrapartum complications, miscarriage/abortion, and intrauterine fetal death were extracted.

### Statistical analysis

A random effects model was used for measuring the pooled prevalences (odds ratios) with a 95% confidence interval (CI). Qualitative risk of bias assessment of the studies was done through the New Castle Ottawa Scale (NOS). Heterogeneity between studies was evaluated using the  $I^2$  test for all three outcomes and reported as a percentage. Forest plots were used for the schematic representation of meta-analysis results. Publication bias for each outcome was checked through funnel plots. JASP 0.19 software was used for statistical analysis.

## Results

Through literature research, 369 studies were identified. Removal of duplications resulted in 277 studies. Full-text availability filter further removed 88 articles. The remaining 189 were skimmed for COVID-19, pregnancy cases, and Saudi Arabia, concluding with 20 studies. Manual scrutinization resulted in six eligible studies (Figure 1).

Table 1 shows NOS scoring for and effect size measurements.<sup>15-20</sup> A total of 1065 pregnant women were part of the meta-analysis. The gestational age at the time of delivery was no more than 40 weeks. Among the COVID-19-positive pregnant women, 326 (58.5%) were delivered through normal vaginal delivery and 11 (1.6%) suffered preeclampsia. Among fetal outcomes, 60.2% were born with low heart rates, and 4.8% of cases had gestational sac abnormalities. Only postpartum complications in fetuses were statistically significant between COVID-19-exposed and unexposed mothers ( $p=0.04$ ), with 4.8 times more likelihood of their occurrence in COVID-19-infected pregnancies. Excessive bleeding/PROM was the second largest maternal outcome in terms of occurrence, with a 4.2 times higher chance in COVID-19-affected mothers. Among perinatal conditions, intrapartum complications were 2.1 times more likely to occur in cases of COVID-19-infected pregnancies.

Rank test for funnel plot asymmetry revealed that there was no publication bias for maternal ( $p=1$ ), fetal ( $p=0.2$ ), and perinatal outcomes ( $p=0.7$ ). The heterogeneity ( $I^2$ ) between studies for maternal and perinatal outcomes was moderate, while for fetal outcomes was low (Figure 2).

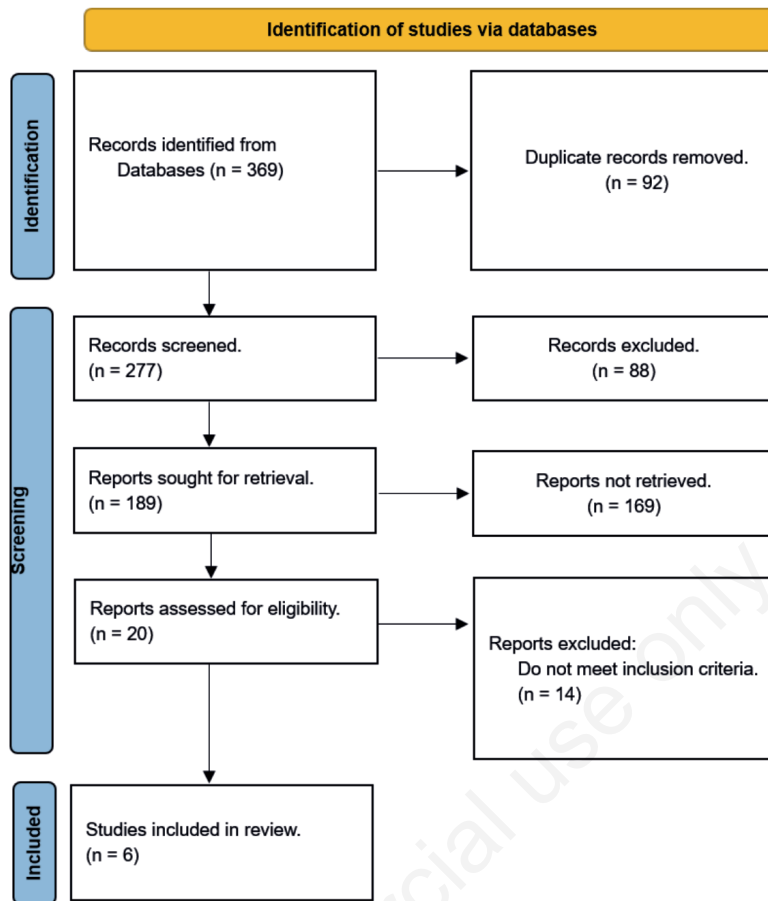


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for the selection process of studies.

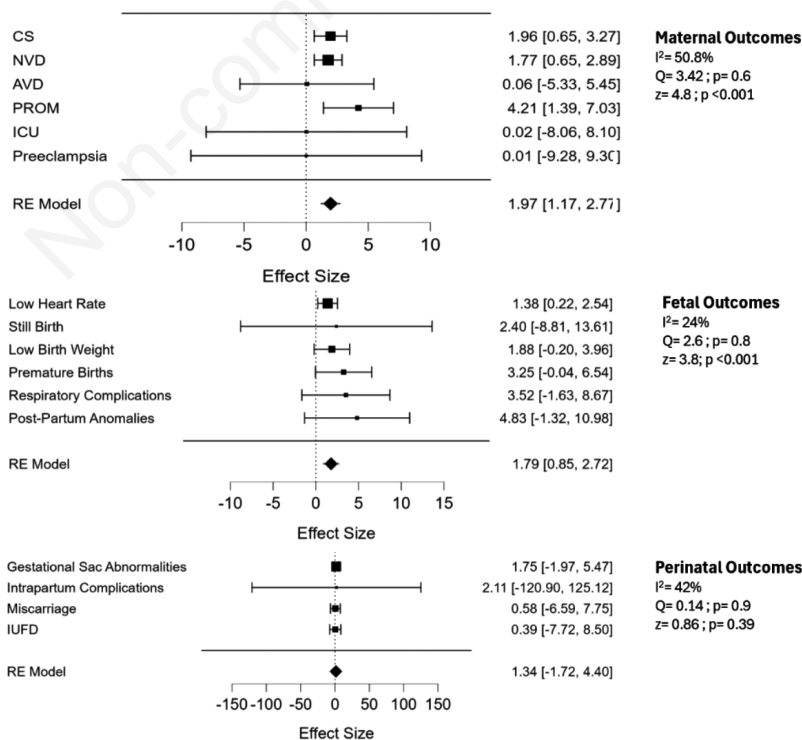


Figure 2. Forest plots constructed for maternal, fetal, and perinatal outcomes using random effects model.

**Table 1.** Summary of included studies and effect size calculations of maternal, fetal, and perinatal outcomes.

Author (year)	Al-Zahrani <i>et al.</i> , 2023	Babic <i>et al.</i> , 2022	Abdulghani <i>et al.</i> , 2021	Shams <i>et al.</i> , 2022	Al-Matary <i>et al.</i> , 2021	Eltayab <i>et al.</i> , 2023	Total, n (%)	p	OR
Study type	Retro- spective	Retro- spective	Retro- spective cohort	Cross- sectional	Retro- spective	Retro- Case-			
Gestational age (weeks)	35-40	37±3	37.67±6.4.78	38	38	34			
COVID-19-positive pregnant women (n)	82	209	62	394	204	114			
New Castle Ottawa Scale									
Selection	2	4	3	2	3	1			
Comparability	0	1	2	2	0	2			
Outcome	1	1	1	2	1	3			
Total	3/9	6/9	6/9	6/9	4/9	6/9			
Maternal outcomes									
COVID-19 exposed, n (%)									
Cesarean section	43 (9.4)	136 (30)	20 (4.4)	102 (22.4)	73 (16)	81 (17.8)	455 (42.7)	0.1	1.96 (0.7-3.3)
NVD	38 (11.7)	120 (36.8)	37 (11.3)	-	131 (40.2)	-	326 (58.5)	0.08	1.77 (0.7-2.9)
AVD	1 (16.7)	-	5 (83.3)	-	-	-	6 (4.2)	0.06	0.06 (-5.3-5.5)
Excessive bleeding/PROM	3 (5.3)	-	38 (66.7)	-	16 (28)	-	57 (16.4)	0.3	4.21 (1.4-7)
ICU admission	12 (30.8)	22 (56.4)	-	5 (12.8)	-	-	39 (5.7)	0.5	0.02 (-8.1-8.1)
Preeclampsia	2 (18.2)	-	-	5 (45.5)	4 (36.410)	-	11 (1.6)	0.5	0.01 (-9.3-9.3)
Fetal outcomes, n (%)									
Low heart rate	4 (3.4)	-	-	-	-	114 (96.6)	118 (60.2)	0.2	1.38 (0.2-2.5)
Stillbirth	10 (38.5)	3 (11.5)	-	7 (26.9)	5 (19.2)	1 (3.8)	26 (2.6)	0.1	2.4 (-8.9-13.6)
Low birth weight	-	1 (1.2)	62 (74.7)	20 (24)	-	-	83 (12.5)	0.3	1.88 (-0.2-4)
Premature births	-	39 (21.8)	62 (34.6)	47 (26.3)	31 (17.3)	-	179 (20.6)	0.3	3.25 (-0.04-6.5)
Respiratory complications	-	-	57 (58.8)	17 (17.5)	14 (14.4)	9 (9.3)	97 (12.5)	0.2	3.52 (-1.6-8.7)
Postpartum anomalies	-	-	4 (4.7)	82 (95.3)	-	-	86 (18.9)	0.04	4.8 (-1.3-11)
Perinatal outcomes, n (%)									
GSA	-	6 (18.8)	10 (31.3)	16 (50)	-	-	32 (4.8)	0.2	1.75 (-2-5.5)
IC	-	-	10 (71.4)	4 (28.6)	-	-	14 (3)	0.4	2.11 (-120.9-125.1)
Miscarriage	-	2 (13.3)	-	13 (86.7)	-	-	15 (2.5)	0.2	0.58 (-6.6-7.8)
IUFD	-	6 (85.7)	-	-	1 (14.31)	-	7 (1.7)	0.1	0.39 (-7.7-8.5)

OR, odds ratio; NVD, normal vaginal delivery; AVD, assisted vaginal delivery; PROM, preterm rupture of membrane; ICU, intensive care unit; GSA, gestational sac abnormalities; IC, intrapartum complications; IUFD, intrauterine fetal death.

## Discussion

This meta-analysis is the first of its kind that investigated the maternal, neonatal/fetal, and perinatal outcomes of COVID-19-affected pregnancies. Among the maternal outcomes, PROM had the highest coincidence in infected women. Among the fetal/neonatal outcomes, low heart rate penetrated greatly among the neonates born through infected pregnancy. In the case of perinatal outcomes, intrapartum complications were more likely to occur. Mothers with other diseases were excluded so that only COVID-19 complications could be evaluated. Prospective observational research conducted in North India by Agarwal *et al.* investigated the maternal and perinatal outcomes of 65 RT-PCR-confirmed pregnant women.<sup>21</sup> Not a single premature birth or premature membrane rupture was observed, which is contrary to the prevalence of 20.6% and 16.4%, respectively. In comparison to another retrospective descriptive study formulated by Yildiz *et al.*, there were 5.7% of cases of ICU admissions due to gestational diabetes and not due to COVID-19 respiratory complications.<sup>22</sup> This proportion is less than that inferred in our study, which is 5.7%, with multiple reasons for admission. A meta-analysis performed by Di Toro *et al.* on

the impact of COVID-19 on maternal and neonatal outcomes stated, among many findings, that there was a prevalence of 8% ICU-admitted mothers, three stillbirths, and a pooled prevalence of 85% for cesarean deliveries.<sup>23</sup> All these proportions contradict our findings of the mentioned outcomes, with percentages of 5.7%, 1.79%, and 42.7%, respectively. The results of a meta-analysis performed by Marchand *et al.* up till June 3, 2021, on the maternal and neonatal clinical features and pregnancy outcomes reported the incidence odds of premature delivery (1.48; 95% CI, 1.22-1.8), preeclampsia (1.6; 95% CI, 1.2-2.1), and stillbirth (2.36; 95% CI, 1.24-4.46).<sup>24</sup> Comparatively, according to our review, the relative risk of stillbirth in fetuses of the case-cohort was 1.55 (95% CI, 0.13-17.3); premature births and preeclampsia were not likely to occur in pregnancies infected with COVID-19 as compared to healthy pregnancies with relative risks less than 1.

## Conclusions

No factual trends for a particular condition can be declared, especially for Saudi Arabia. Babies born from COVID-19 pregnant women significantly face challenging

postpartum complications in Saudi Arabia. PROM is more likely to occur among maternal outcomes. Intrapartum complications have a higher chance of occurrence among perinatal conditions. More intervention-based research is needed in the area for more accurate and reliable results.

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