Review Article
Obstet Gynecol Sci 2023;66(4):270-289
https://doi.org/10.5468/ogs.22323
eISSN 2287-8580

Obstetrics & Gynecology Science

The coronavirus disease 2019 infection in pregnancy and adverse pregnancy outcomes: a systematic review and meta-analysis

Yeonsong Jeong, MD, Min-A Kim, MD, PhD

Department of Obstetrics and Gynecology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

The coronavirus disease 2019 (COVID-19) outbreak which started in December 2019 rapidly developed into a global health concern. Pregnant women are susceptible to respiratory infections and can experience adverse outcomes. This systematic review and meta-analysis compared pregnancy outcomes according to COVID-19 disease status. The MEDLINE, EMBASE, and Cochrane Library databases were searched for relevant articles published between December 1, 2019, and October 19, 2022. Main inclusion criterion was any population-based, cross-sectional, cohort, or case-control study that assessed pregnancy outcomes in women with or without laboratory-confirmed COVID-19. Sixty-nine studies including 1,606,543 pregnant women (39,716 [2.4%] diagnosed with COVID-19) were retrieved. COVID-19-infected pregnant women had a higher risk of preterm birth (odds ratio [OR], 1.59; 95% confidence interval [CI], 1.42-1.78), preeclampsia (OR, 1.41; 95% CI, 1.30-1.53), low birth weight (OR, 1.52; 95% CI, 1.30-1.79), cesarean delivery (OR, 1.20; 95% CI, 1.10-1.30), stillbirth (OR, 1.71; 95% CI, 1.39-2.10), fetal distress (OR, 2.49; 95% CI, 1.54-4.03), neonatal intensive care unit admission (OR, 2.33; 95% CI, 1.72-3.16), perinatal mortality (OR, 1.96; 95% CI, 1.15-3.34), and maternal mortality (OR, 6.15; 95% CI, 3.74-10.10). There were no significant differences in total miscarriage, preterm premature rupture of membranes, postpartum hemorrhage, cholestasis, or chorioamnionitis according to infection. This review demonstrates that COVID-19 infection during pregnancy can lead to adverse pregnancy outcomes. This information could aid researchers and clinicians in preparing for another pandemic caused by newly discovered respiratory viruses. The findings of this study may assist with evidence-based counseling and help clinicians manage pregnant women with COVID-19.

Keywords: Coronavirus disease 2019; Pregnancy outcomes; Pregnancy complications; Respiratory tract infections; Viral infection

Introduction

Coronavirus disease 2019 (COVID-19) is a viral respiratory disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It has been a global threat to public health owing to its high mortality and morbidity rates since the first outbreak in Wuhan, China, in December 2019. According to the World Health Organization, as of November 30, 2022, there were 639,132,486 confirmed cases of COVID-19 globally, including 6,614,082 deaths.

The experience of patients infected with COVID-19 varies significantly, ranging from asymptomatic to acute respiratory distress syndrome accompanied by high fever and severe respiratory symptoms, similar to those of the Middle East respiratory syndrome (MERS) and the SARS outbreak in 2003. Pregnant women undergo immunological and physiological changes that prevent fetal allograft rejection. These changes also increase their susceptibility to viral respiratory infections.

Received: 2022.12.11. Revised: 2023.03.13. Accepted: 2023.04.11.
Corresponding author: Min-A Kim, MD, PhD
Department of Obstetrics and Gynecology, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea
E-mail: makim302@yuhs.ac
https://orcid.org/0000-0002-6199-2010

The SARS outbreak in 2003 and MERS were associated with high fatality rates, with one-third of the infected pregnant women dying.

During the pandemic, pregnant women experienced considerable fear of the respiratory virus, besides anxiety regarding outcomes because it was unknown how the new viral outbreaks would affect pregnancy and neonatal prognosis, and vaccine safety has not been verified. Previous studies have reported increased rates of miscarriage, intrauterine growth retardation (IUGR), premature delivery, and fetal death during MERS. Furthermore, viral respiratory infections are a leading cause of maternal mortality [1,2].

The pregnancy and neonatal outcomes associated with COVID-19 are inconsistent and diverse. Some studies have indicated that SARS-CoV-2 infection is not associated with adverse pregnancy outcomes [3,4]. Large-scale data analyses have stressed the urgency of establishing strategies to help clinicians manage pregnancies and ensure safe maternal and childcare deliveries. This systematic review and meta-analysis were based on a thorough review of the existing literature. We investigated the association between COVID-19 infection during pregnancy and adverse pregnancy outcome to aid clinicians and researchers in managing pregnant women infected with COVID-19 currently and contribute to preparations for future respiratory virus outbreaks.

Search strategy

We searched the literature to identify articles that compared obstetrical and neonatal outcomes between COVID-19-infected and non-infected mothers. This systematic review and meta-analysis were conducted using the PROSPERO protocol (CRD42023402238). We performed a systematic online search of the MEDLINE, EMBASE, and Cochrane Library databases for relevant articles published until October 19, 2022. The databases were searched using a combination of Medical Subject Headings and text terms related to COVID-19 and pregnancy outcomes. The detailed search strategy used for each database is presented in Supplementary Table 1. Two reviewers (M.A.K. and Y.J.) independently selected studies. They first performed title and abstract screening and then assessed the full texts of the selected studies for eligibility according to the inclusion criteria. They cross-checked previously published review articles to identify additional studies that were missed during our online searches. Discrepancies were resolved by consensus-based discussions.

Study selection

We selected full-text articles that reported the impact of COVID-19 on obstetrical and neonatal outcomes by comparing infected and non-infected mothers and those that met the inclusion criteria as follows. 1) A population-based, cross-sectional, cohort, or case-control study design. 2) Inclusion of laboratory-confirmed non-infected pregnant women or pregnant women before the pandemic as a control group. 3) The study population included pregnant women with laboratory-confirmed COVID-19 infection at any stage of gestation, or pregnant women with assigned codes for COVID-19 based on the International classification of disease 10th version and related health problems. 4) Results included pregnancy or neonatal outcomes according to the COVID-19 infection status.

Outcomes, such as miscarriage, preterm birth, preeclampsia, cesarean section, intrauterine fetal death (IUFD) or stillbirth, preterm premature rupture of membranes (PPROM), placental abruption, placenta previa, postpartum hemorrhage, and maternal mortality were assessed as obstetric outcomes. IUGR, small for gestational age (SGA), low birth weight (LBW), neonatal intensive care unit (NICU) admission, and perinatal mortality were assessed as neonatal outcomes. Studies that met the following criteria were excluded: case reports, case series, review articles, editorials or letters to the editor, conference abstracts, lack of a control group, publications other than English, and inadequate information for data extraction.

Data extraction

We reviewed the full-text articles for complete data extraction and clarity if the details were not explicitly mentioned in the abstracts. The information extracted from each study included the first author's name, publication year, journal name, study design, country, study period, inclusion and exclusion criteria, and the number of women included in the case and control groups.

Quality assessment

The Newcastle-Ottawa scale (NOS) was used to assess the quality of the included studies. The NOS evaluates studies from three perspectives: study group selection, group comparability, and exposure or outcome of interest for case-control or cohort studies. According to the NOS, each study was awarded a maximum of nine points with scores for various questions in each domain. Studies were considered of high quality if they had a NOS score ≥6.

Statistical analysis

This systematic review and meta-analysis were conducted according to the protocols established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and the Cochrane handbook for systematic reviews. We used a random-effects model to calculate the pooled odds ratios (ORs) and 95% confidence intervals (CIs) for adverse pregnancy outcomes experienced by women with or without COVID-19 infection. Heterogeneity was assessed using the I^2 statistic; values of >25%, >50%, and >75% were considered evidence of low, moderate, and considerable statistical heterogeneity, respectively. A sensitivity analysis was conducted to evaluate the influence of individual studies on the meta-analysis by restricting the studies individually and assessing the effect on the main summary estimate. Significance levels were set at $P<0.05$ if the 95% CI did not include 1. All statistical analyses were performed using RevMan (version 5.4; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Study characteristics

The database search identified 4,279 citations, of which 4,108 were excluded from the title and abstract review. The remaining 171 citations were considered eligible for full-text screening, of which 69 met the inclusion criteria and were considered eligible for inclusion in the meta-analysis (Fig. 1). Table 1 presents the baseline characteristics of the 69 includ-

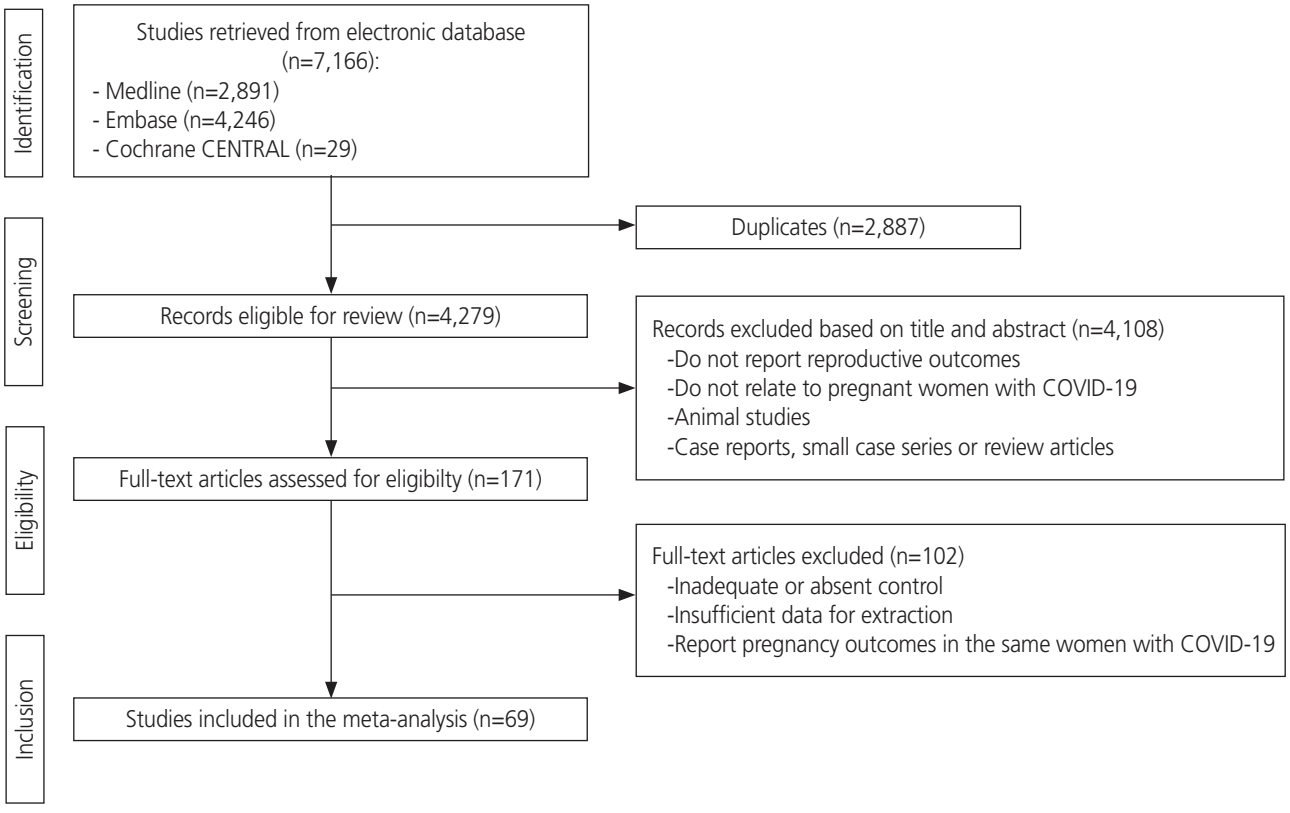


Fig. 1. Flowchart of the study selection process. COVID-19, coronavirus disease 2019.

Table 1. Baseline characteristics of included studies

Author	Year	Study design	Study location	Study period	COVID test result (positive)	Sample size	COVID test method
Hanna M. Shepard	2022	Retrospective	USA	From 2020-03-01 to 2021-03-31	3,119	69,960	RT-PCR
Helga Vera von Bargen	2022	Prospective, cross-sectional	Chile	From 2020-04-15 to 2020-06-15	68	701	RT-PCR
Ian Griffin	2020	Prospective observational	USA	From 2020-04-21 to 2020-05-05	27	62	RT-PCR
Wei Liu	2020	Retrospective	China	From 2020-01-17 to 2020-03-04	32	48	Nasopharynx swab, chest CT
Oscar Martinez Perez	2020	Population-based, longitudital observational and anlaytic	Spain	From 2020-03-01 to 2020-05	246	1,009	RT-PCR
Amanda Dhyvetter	2021	Retrospective	USA	From 2020-04-12 to 2020-07-11	23	208	RT-PCR
Rong Yang	2020	Retrospective, population-based cohort	China	From 2020-01-13 to 2020-03	65	11,078	RT-PCR
Charles M'poca Charles	2022	Prospective cohort study	Mozambique	From 2020-10-20 to 2021-07-22	22	239	RT-PCR
Arun Harishchandra Nayak	2020	Restrospective observational analytical	India	From 2020-04-01 to 2020-05-15	141	977	
Seyed-Abdolvahab	2021	Retrospective case-control	Iran	From 2020-03-01 to 2020-11-01	55	110	
Jack Milln	2021	Retrospective cross-sectional	UK	From 2020-03-12 to 2020-04-22	32	1,316	
Emily H. Adhikari	2020	Observational cohort	USA	From 2020-03-18 to 2020-08-22	252	3,374	RT-PCR
Mia Ahlberg	2020	Retrospective case-control	Sweden	From 2020-03-25 to 2020-07-24	155	759	RT-PCR
M Prabhu	2020	Prospective cohort study	USA	From 2020-03-22 to 2020-03-24	70	675	RT-PCR
Na Li	2020	Restrospedtive case control	China	From 2020-01-24 to 2020-02-29	16	137	RT-PCR
Valerie J. Flaherman	2021	Prospective cohort study	USA	From 2020-03-22 to 2020-06-22	179	263	RT-PCR
Francesca Crovetto	2021	Prospective population-based cohort	Spain	From 2020-03-15 to 2020-05-31	317	2,225	RT-PCR
Andrea G. Edlow	2020	Propective cohort	USA	From 2020-04-02 to 2020-06-13	64	127	RT-PCR
Marta Rodriguez-Diaz	2021	Propective cohort	Spain	From 2020-03-23 to 2020-10-14	29	620	RT-PCR
Karola S. Jering	2020	Population-based, longitudital observational and anlaytic	USA	From 2020-04-01 to 2020-11-23	6,380	406,446	RT-PCR
Annette K. Regan	2021	National cohot study	USA	From 2020-04-30 to 2020-03-11	2,655	78,283	RT-PCR
Seyit A. Erol	2020	Prospective case-control	Turkey	From 2020-06-26 to 2020-08-27	60	99	RT-PCR
Carolina Loyola Prest Ferrugini	2022	Cross-sectional	Brazil	From 2020-07-01 to 2020-10-01	86	265	RT-PCR
Sumaya Binte Masud	2021	Group-comparison cross-sectional	Bangladesh	From 2020-03-01 to 2020-08-01	70	210	RT-PCR
Justin S. Brandt	2021	Matched case-control study	USA	From 2020-03-11 to 2020-06-11	61	183	RT-PCR

Table 1. Baseline characteristics of included studies (Continued)

Author	Year	Study design	Study location	Study period	COVID test result (positive)	Sample size	COVID test method
Najeh Hcini	2021	Observational prospective cohort	France	From 2020-06-16 to 2020-08-16	137	507	RT-PCR
Elizabeth T. Patberg	2021	Retrospective cohort study	USA	From 2020-03-31 to 2020-06-17	77	133	RT-PCR
Allie Sakowicz	2020	Retrospective cohort study	USA	From 2020-03-19 to 2020-05-31	101	1,418	RT-PCR
Beth L. Pineles	2020	Retrospective cohort study	Houston, USA	From 2020-04-22 to 2020-07-22	77	935	RT-PCR
Zaheera Saadia	2021	Observational study	Pakistan	From April to May 2020	48	94	RT-PCR
Pilar Diaz-Corvillon	2020	Cross-sectional	Chile	From 2020-04-27 to 2020-06-07	37	586	RT-PCR
Noga Fallach	2022	Retrospective large, population-based cohort study	Israel	From 2020-02-21 to 2021-07-02	2,753	43,061	RT-PCR
Desmond Sutton	2021	Retrospective cohort study	USA	From 2020-03-22 to 2020-04-18	79	454	RT-PCR
Darios Getahun	2022	Retrospective cohort study	USA	From 2020-04-06 to 2021-02-28	2,203	35,123	RT-PCR
Monica Cruz-Lemini	2021	Multicenter prospective study	Spain	From 2020-03-01 to 2020-05-31	174	604	RT-PCR
Sara Cruz Meguizo	2021	Multicenter prospective study	Spain	From 2020-03-01 to 2020-05-31	1,347	2,954	RT-PCR
Maria de Lourdes Benamor Teixeira	2021	Multicenter prospective study	Spain	From 2020-04-13 to 2020-06-17	33	115	RT-PCR
Michelle J. Wang	2020	Retrospective cohort study	USA	From 2020-04-01 to 2020-07-22	53	813	RT-PCR
Abedzadeh-Kalahroudi	2021	Cohort study	Iran	From March to November 2020	56	94	RT-PCR
Alipour	2021	Retrospective analytical cohort study	Iran	Between March 15, 2020 to November 15, 2020	133	165	RT-PCR
Bender	2020	Observational study	USA	Between April 13, 2020 and April 26, 2020	53	135	RT-PCR
Cardona-Pe´rez	2021	Retrospective case-control study	Mexico	Between April 22, 2020 and May 25, 2020	70	170	RT-PCR
Chornock	2021	Retrospective cohort study	USA	From 2020-04-08 to 2020-07-31	73	935	RT-PCR
Cosma	2021	Prospective, observational cohort study	Italy	Between April 16, 2020 and June 22, 2020	16	105	RT-PCR
Melguizo	2021	Multicenter prospective observational study	Spain	Between February 26, 2020 and November 5, 2020	1,347	1,607	PCR
Cuñarro-López	2020	Observational, analytic, retrospective cohort study	Spain	From 2020-03-10 to 2020-05-12	43	68	RT-PCR
Farghaly	2020	Retrospective cohort study	USA	From March to May 2020	15	64	RT-PCR
Gulersen	2020	Retrospective cohort study	USA	From 2020-04-09 to 2020-04-27	50	50	RT-PCR

Table 1. Baseline characteristics of included studies (Continued)

Author	Year	Study design	Study location	Study period	COVID test result (positive)	Sample size	COVID test method
Gupta	2021	Retrospective cohort study	India	Between September 1, 2020 and November 30, 2020	108	3,057	RT-PCR
Gurol-Urganci	2021	Population-based cohort study	England	Between May 29, 2020 and January 31, 2021	3,527	338,553	RT-PCR
Smithgall	2020	Retrospective cohort study	USA	From 2020-03-23 to 2020-04-29	51	25	RT-PCR
Katz	2021	Retrospective cohort study	USA	From 2020-03-19 to 2020-05-31	490	964	RT-PCR
Ko	2021	Retrospective cohort study	USA	From March to September 2020	6,550	482,921	ICD-10-CM code U07.1 (COVID-19, virus identified)
Laresgoiti-Servitje	2021	Retrospective case-control study	Mexico	From mid-April 2020 to mid-September 2020	298	828	RT-PCR
Liao	2020	Retrospective analysis	China	Between January 20, 2020 and March 2, 2020	10	53	RT-PCR
Liu	2021	Retrospective cohort study	USA	From 2020-04-10 to 2020-06-10	56	279	RT-PCR
Norman	2021	Nationwide, prospective cohort study	Sweden	Between March 11, 2020, and January 31, 2021	2,286	84,719	RT-PCR
Papageorghiou	2021	Large, longitudinal, prospective, unmatched diagnosed and not-diagnosed observational study	18 countries	Between March 2, 2020 and February 2, 2021	725	1,401	RT-PCR
Pirjani	2020	Prospective cohort study	Iran	From 2020-03-01 to 2020-09-01	66	133	RT-PCR
Ríos-Silva	2020	Retrospective cohort study	Mexico	From the beginning of the epidemic in Mexico until May 25, 2020	448	17,942	RT-PCR
Rosenbloom	2021	Retrospective cohort study	USA	From 2020-06-01 to 2020-11-30	83	166	RT-PCR
Ruggiero	2021	Prospective cohort study	Italy	Between April 7, 2020 to May 6, 2020	28	287	RNA PCR, anti-envelope anti-nucleoprotein
Savir´on-Cornudella	2021	Observational cohort study	Spain	Between March 31, 2020 and September 30, 2020	22	1,146	PCR test and by detection of serum immunoglobulins G and M.
SOTO-TORRES	2021	Retrospective case-control study	USA	Between May 1, 2020 and August 31, 2020	106	103	RNA PCR, rapid antigen tests
Steffen	2021	Prospective cohort study	USA	Between May 1, and September 2020	61	939	RT-PCR

Table 1. Baseline characteristics of included studies (Continued)

Author	Year	Study design	Study location	Study period	COVID test result (positive)	Sample size	COVID test method
Timircan	2021	Prospective cohort study	Romania	Between August 30, 2020 and January 31, 2021	101	938	RT-PCR
Trahan	2021	Prospective	Canada	Between March 22, 2020 and July 31, 2020	45	225	RT-PCR
Villar	2021	Prospective, longitudinal, observational study	18 countries	From March to October 2020	706	1,424	Real-time polymerase chain reaction and antibody tests
Vousden	2021	National, prospective cohort study	UK	From 2020-03-01 to 2020-08-31	722	694	Not mentioned
Yadav	2020	Retrospective comparative study	India	Between March 23, 2020 till July 23, 2020	28	112	RT-PCR

RT-PCR, reverse transcriptase–polymerase chain reaction; CT, computed tomography; ICD-10-CM, international classification of diseases, tenth revision, clinical modification; COVID-19, coronavirus disease 2019; RNA, ribonucleic acid.

ed studies. These studies included 39,716 pregnant women with COVID-19 and 1,566,827 pregnant women without COVID-19. Reverse transcriptase-polymerase chain reaction was used as a diagnostic method to confirm COVID-19 in most studies [3,5-71].

Preterm birth

Fifty studies reported the incidence of preterm births in 2,687 (10.3%) women with COVID-19 infection versus 58,203 (6.1%) women without the infection, demonstrating a significant difference (P<0.001). The risk of preterm birth was significantly (1.6-fold) higher among women with COVID-19 than those without (OR, 1.59; 95% CI, 1.42-1.78; I^2=69%; Fig. 2A). Most studies did not accurately describe the indications for preterm birth. When only the eight studies that classified spontaneous preterm births were analyzed, the odds were 1.3-fold higher in women with COVID-19 than those without (OR, 1.33; 95% CI, 1.20-1.48; I^2=22%; Fig. 2B).

Preeclampsia

Thirty-four studies reported that preeclampsia occurred in 2,214 of 27,732 women with COVID-19 (8.0%) versus 78,429 of 1,358,619 women without COVID-19 (5.8%), demonstrating a significant difference (OR, 1.41; 95% CI, 1.30-1.5; I^2=31%; Fig. 3A).

Low birth weight

Twelve studies reported that 987 neonates had LBW, including 407 born to women with COVID-19 and 580 born to women without COVID-19. The risk of LBW was significantly higher among the offspring of women with COVID-19 infection than those born to women without the infection (OR, 1.52; 95% CI, 1.30-1.79; I^2=6%; Fig. 3B).

Cesarean section

Fifty-seven studies reported the incidence of cesarean sections in 1,484,791 pregnant women. Women who experi-

A

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	19	55	12	94	1.4%	3.61 [1.59, 8.21]
Adhikari, 2020	27	245	328	3,035	3.1%	1.02 [0.67, 1.55]
Ahlberg, 2020	14	155	45	604	2.0%	1.23 [0.66, 2.31]
Alipour, 2021	25	53	18	135	1.6%	5.80 [2.79, 12.08]
Brandt, 2021	7	61	10	122	1.0%	1.45 [0.52, 4.02]
Cardona-Perez, 2021	14	64	38	157	1.8%	0.88 [0.44, 1.76]
Cosma, 2021	1	16	9	105	0.3%	0.71 [0.08, 6.02]
Crovetto, 2021	20	317	81	1,908	2.6%	1.52 [0.92, 2.52]
Cruz-Lemini, 2021	13	174	28	430	1.8%	1.16 [0.59, 2.29]
Cruz-Meguizo, 2021	149	1,347	94	1,607	4.0%	2.00 [1.53, 2.62]
Cunarro-Lopez, 2020	13	68	2	43	0.5%	4.85 [1.04, 22.66]
Diaz-Corvillon, 2020	4	37	27	549	0.9%	2.34 [0.77, 7.09]
Edlow, 2020	10	64	5	63	0.8%	2.15 [0.69, 6.69]
Erol, 2020	1	60	0	36	0.1%	1.84 [0.07, 46.38]
Fallach, 2022	93	2,753	75	2,753	3.8%	1.25 [0.92, 1.70]
Farghaly, 2020	2	15	3	64	0.3%	3.13 [0.47, 20.64]
Ferrugini, 2022	7	61	10	122	1.0%	1.45 [0.52, 4.02]
Flaherman, 2021	21	179	9	84	1.4%	1.11 [0.48, 2.53]
Getahun, 2022	186	2,203	2,210	32,920	4.8%	1.28 [1.10, 1.50]
Gupta, 2021	31	108	446	3,057	3.0%	2.36 [1.53, 3.62]
Gurol-Urganci, 2021	369	3,047	18,572	322,494	5.0%	2.25 [2.02, 2.52]
Hcini, 2021	11	137	36	370	1.7%	0.81 [0.40, 1.64]
Jering, 2020	459	6,380	23,234	400,066	5.0%	1.26 [1.14, 1.38]
Katz, 2021	72	490	98	964	3.7%	1.52 [1.10, 2.11]
Laresgoiti-Servitje, 2021	39	298	129	828	3.3%	0.82 [0.55, 1.20]
Li, 2020	3	16	41	121	0.5%	3.76 [0.86, 16.33]
Liao, 2020	1	10	7	53	0.2%	1.07 [0.11, 10.24]
Liu, 2021	8	56	5	279	1.4%	0.97 [0.43, 2.19]
M'poca Charles, 2020	3	21	49	202	0.7%	0.52 [0.15, 1.84]
Martinez-Perez, 2020	34	246	51	763	2.8%	2.24 [1.41, 3.55]
Masud, 2021	37	70	42	140	2.2%	2.62 [1.45, 4.73]
Millin, 2021	6	30	117	1268	1.2%	2.46 [0.99, 6.14]
Nayak, 2020	38	141	239	836	3.2%	0.92 [0.62, 1.38]
Norman, 2021	205	2,323	4,719	85,836	4.8%	1.66 [1.44, 1.93]
Papageorghiou, 2021	152	725	191	1,459	4.3%	1.76 [1.39, 2.23]
Pineles, 2020	5	77	90	858	1.2%	0.59 [0.23, 1.51]
Prabhu, 2020	11	70	57	605	1.7%	1.79 [0.89, 3.61]
Regan, 2021	335	2,655	6,053	75,628	5.0%	1.66 [1.48, 1.87]
Ruggiero, 2021	2	28	22	287	0.5%	0.93 [0.21, 4.16]
Saadia, 2021	1	48	0	46	0.1%	2.94 [0.12, 73.95]
Seyed-Abdolvahab, 2021	5	20	2	20	0.4%	3.00 [0.51, 17.74]
Smithgall, 2020	10	51	4	25	0.7%	1.28 [0.36, 4.57]
Sutton, 2021	10	79	37	375	1.6%	1.32 [0.63, 2.79]
Teixeira, 2021	7	33	10	82	0.9%	1.94 [0.67, 5.62]
Timircan, 2021	15	101	75	938	2.1%	2.01 [1.10, 3.65]
Trahan, 2021	7	45	21	225	1.2%	1.79 [0.71, 4.50]
Villar, 2021	159	706	194	1,424	4.3%	1.84 [1.46, 2.33]
Wang, 2020	9	53	66	760	1.6%	2.15 [1.01, 4.60]
Yadav, 2020	8	28	13	112	1.0%	3.05 [1.12, 8.31]
Yang, 2020	9	65	579	11,013	1.7%	2.90 [1.43, 5.88]
Total (95% CI)		26,084				
Total events	2,687		58,203	955,965	100.0%	1.59 [1.42, 1.78]

Heterogeneity: Tau^2=0.06; Chi^2=155.89; df=49 (P<0.00001); I^2=69%
Test for overall effect: Z=8.07 (P<0.00001)

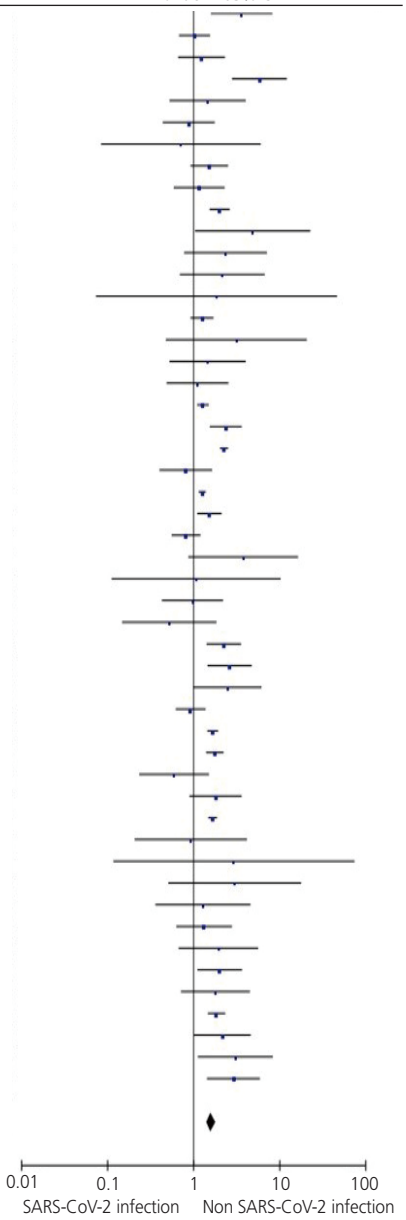


Fig. 2. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and preterm delivery (A) and spontaneous preterm delivery (B). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval.

enced the COVID-19 infection during pregnancy were 1.2-fold more likely to deliver by a cesarean section than those without (OR, 1.20; 95% CI, 1.10-1.30; I^2=79%; Fig. 4A).

IUFD or stillbirth

Twenty-seven studies reported the incidence of IUFD or stillbirth in 256 women with COVID-19 and 6,730 women without COVID-19. The odds of IUFD or stillbirth were higher in women with COVID-19 than those without (OR, 1.71; 95% CI, 1.39-2.10; I^2=27%; Fig. 4B).

B

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Alipour, 2021	7	53	10	135	1.0%	1.90 [0.68, 5.29]
Cruz-Meguizo, 2021	78	1,347	74	1,607	8.4%	1.27 [0.92, 1.77]
Getahun, 2022	99	2,203	1,134	32,920	17.1%	1.32 [1.07, 1.63]
Hcini, 2021	11	137	36	370	2.0%	0.81 [0.40, 1.64]
Ko, 2021	315	6,550	17,392	482,921	35.1%	1.35 [1.21, 1.52]
Martinez-Perez, 2020	15	246	36	763	2.6%	1.31 [0.71, 2.44]
Regan, 2021	231	2,655	4,574	75,628	29.1%	1.48 [1.29, 1.70]
Villar, 2021	27	706	66	1,424	4.6%	0.82 [0.52, 1.29]
Total (95% CI)		13,897		595,768	100.0%	1.33 [1.20, 1.48]
Total events	783		23,322			

Heterogeneity: Tau^2=0.00; Chi^2=8.95; df=7 (*P*=0.26); I^2=22%
Test for overall effect: Z=5.53 (*P*<0.00001)

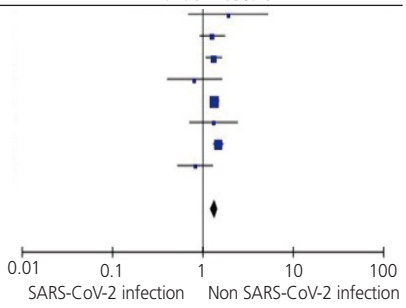


Fig. 2. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and preterm delivery (A) and spontaneous preterm delivery (B). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval. (Continued)

Fetal distress, NICU admission, and perinatal mortality

Seven studies reported the incidence of fetal distress in 169 women with COVID-19 and 577 women without COVID-19. We observed a statistically significant increase in fetal distress among women with COVID-19 than those without (OR, 2.49; 95% CI, 1.54-4.03; I^2=69%; Fig. 5A). Thirty-one studies reported the NICU admissions of 12,397 neonates (1,187 with COVID-19 and 11,210 without COVID-19). The overall risk of NICU admission was significantly higher among women with COVID-19 infection than those without (OR, 2.33; 95% CI, 1.72-3.16; I^2=89%; Fig. 5B). Perinatal mortality occurred in 27 of 4,123 (0.65%) cases with COVID-19 versus 105 of 14,474 (0.73%) cases without COVID-19 among a total of 21 studies (OR, 1.96; 95% CI, 1.15-3.34; I^2=0%; Fig. 5C).

Maternal mortality

Twelve studies reported the incidence of maternal mortality in 39 of 9,633 women (0.40%) with COVID-19 versus 90 of 494,811 women (0.02%) without COVID-19, revealing a significant difference between the two (*P*<0.05). COVID-19 infection during pregnancy resulted in an increased risk of maternal mortality relative to those who were not infected (OR, 6.15; 95% CI, 3.74; I^2=62%; Fig. 5D).

Other outcomes

Pregnant women with COVID-19 had a higher risk of placental abruption (OR, 1.40; 95% CI, 1.02-1.92; I^2=19%; 12 studies), IUGR or SGA (OR, 1.12; 95% CI, 1.0-1.26; I^2=48%; 27 studies), gestational diabetes mellitus (OR, 1.13; 95% CI, 1.04-1.23; I^2=45%; 40 studies), and congenital anomalies (OR, 1.45; 95% CI, 1.04-2.01; I^2=0%; eight studies) (Supplementary Fig. 1). No significant differences were observed in the total miscarriage rates (OR, 1.04; 95% CI, 0.64-1.60; I^2=74%; 13 studies), the incidences of PPROM (OR, 1.36; 95% CI, 0.96-1.93; I^2=26%; 10 studies), postpartum hemorrhage (OR, 0.98; 95% CI, 0.78-1.24; I^2=70%; 22 studies), cholestasis (OR, 1.34; 95% CI, 0.83-2.18; I^2=0%; seven studies), or chorioamnionitis (OR, 1.26; 95% CI, 0.93-1.72; I^2=38%; 14 studies) between women with and without the COVID-19 infection (Supplementary Fig. 2).

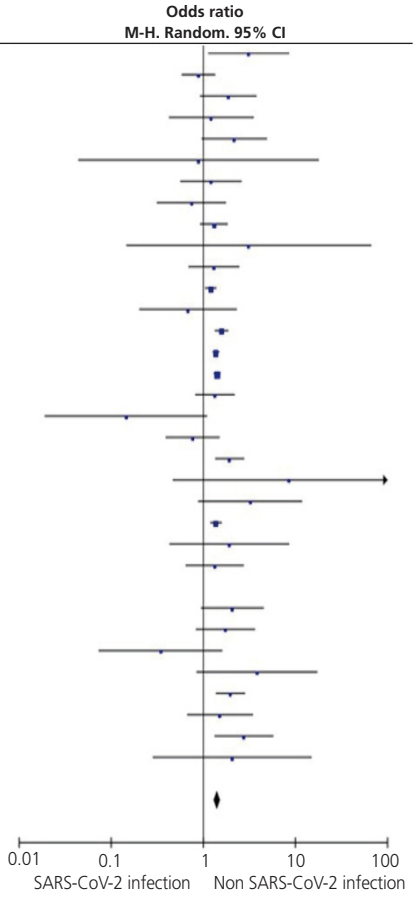
Conclusion

COVID-19 has spread rapidly worldwide and become a global health concern. It is associated with various complications, including high mortality and morbidity rates ranging from pulmonary distress to death. Pregnant women are susceptible to respiratory infections and can experience adverse outcomes. In this updated systematic review and meta-analysis, we described the obstetric and neonatal outcomes of COVID-19-infected versus non-infected pregnant women. We also investigated the effects of COVID-19 infection dur-

A

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	11	55	7	94	0.7%	3.11 [1.13, 8.57]
Adhikari, 2020	26	245	359	3,035	3.2%	0.88 [0.58, 1.35]
Ahlberg, 2020	12	155	26	604	1.3%	1.87 [0.92, 3.79]
Brandt, 2021	6	61	10	122	0.6%	1.22 [0.42, 3.53]
Cardona-Perez, 2021	12	67	15	164	1.0%	2.17 [0.95, 4.92]
Cosma, 2021	0	16	3	105	0.1%	0.89 [0.04, 17.98]
Crovetto, 2021	8	317	40	1,908	1.1%	1.21 [0.56, 2.61]
Cruz-Lemini, 2021	7	174	23	430	0.9%	0.74 [0.31, 1.76]
Cruz-Meguizo, 2021	69	1,347	64	1,607	4.4%	1.30 [0.92, 1.84]
Erol, 2020	2	60	0	36	0.1%	3.12 [0.15, 66.83]
Ferrugini, 2022	19	86	32	179	1.6%	1.30 [0.69, 2.46]
Getahun, 2022	222	2,203	2,802	32,920	11.9%	1.20 [1.04, 1.39]
Gulersen, 2020	5	50	7	50	0.5%	0.68 [0.20, 2.32]
Gurol-Urganci, 2021	139	3,527	8,591	338,553	10.4%	1.58 [1.33, 1.87]
Jering, 2020	605	6,380	28,355	400,066	15.5%	1.37 [1.26, 1.49]
oll;lkKo, 2021	616	6,550	33,078	482,921	15.5%	1.41 [1.30, 1.54]
Laresgoiti-Servitje, 2021	25	298	53	828	2.5%	1.34 [0.82, 2.20]
M'poca Charles, 2020	1	21	52	202	0.2%	0.14 [0.02, 1.10]
Martinez-Perez, 2020	11	246	44	763	1.4%	0.76 [0.39, 1.51]
Papageorghiou, 2021	59	725	64	1,459	4.1%	1.93 [1.34, 2.78]
Patberg, 2021	59	77	04	56	0.1%	8.57 [0.46, 158.29]
Pirjani, 2020	5	66	4,406	133	0.4%	3.23 [0.88, 11.85]
Regan, 2021	6	2,655	22	75,628	11.9%	1.37 [1.19, 1.59]
Rodriguez-Diaz, 2021	208	29	22	591	0.3%	1.92 [0.43, 8.57]
Rosenbloom, 2021	2	83	22	166	1.2%	1.33 [0.64, 2.75]
Saadia, 2021	14	48	0	46		Not estimable
Soto-Torres, 2021	0	106	11	103	1.1%	2.07 [0.94, 4.54]
Steffen, 2021	21	61	85	939	1.2%	1.74 [0.83, 3.65]
Teixeira, 2021	9	33	13	82	0.3%	0.34 [0.07, 1.61]
Timircan, 2021	2	19	28	938	0.3%	3.82 [0.84, 17.35]
Villar, 2021	2	706	63	1,424	4.0%	1.97 [1.36, 2.84]
Vousden, 2021	59	1,148	8	694	1.0%	1.52 [0.67, 3.47]
Wang, 2020	20	53	59	760	1.2%	2.76 [1.32, 5.78]
Yang, 2020	10	65	83	11,013	0.2%	2.06 [0.28, 15.01]
	1					
Total (95% CI)		27,732		1,358,619	100.0%	1.41 [1.30, 1.53]
Total events	2,214		78,429			

Heterogeneity: Tau^2=0.01; Chi^2=46.18; df=32 (*P*=0.05); I^2=31%
Test for overall effect: Z=8.06 (*P*<0.00001)



B

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	11	55	14	94	3.2%	1.43 [0.60, 3.41]
Alipour, 2021	16	53	20	135	4.3%	2.49 [1.17, 5.29]
Fallach, 2022	96	2,753	72	2,753	21.7%	1.35 [0.99, 1.83]
Li, 2020	3	17	3	121	0.9%	8.43 [1.55, 45.84]
Masud, 2021	17	70	27	140	5.1%	1.34 [0.67, 2.67]
Millin, 2021	5	30	121	1,268	2.6%	1.90 [0.71, 5.04]
Saadia, 2021	96	2,753	72	2,753	21.7%	1.35 [0.99, 1.83]
Seyed-Abdolvahab, 2021	2	20	1	20	0.4%	2.11 [0.18, 25.35]
Sutton, 2021	9	79	37	375	4.1%	1.17 [0.54, 2.54]
Teixeira, 2021	2	33	10	82	1.0%	0.46 [0.10, 2.25]
Trahan, 2021	5	47	22	227	2.4%	1.11 [0.40, 3.10]
Villar, 2021	145	706	181	1,424	32.5%	1.77 [1.40, 2.26]
	1					
Total (95% CI)		6,616		9,392	100.0%	1.52 [1.30, 1.79]
Total events	407		580			

Heterogeneity: Tau^2=0.01; Chi^2=11.74; df=11 (*P*=0.38); I^2=6%
Test for overall effect: Z=5.19 (*P*<0.00001)

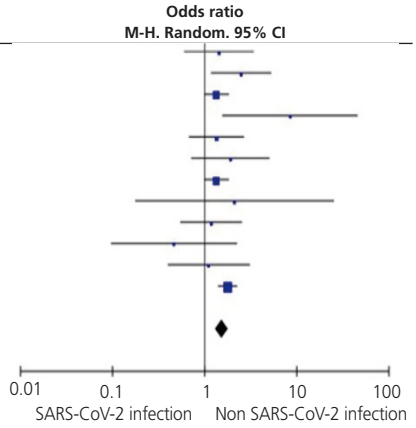


Fig. 3. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and preeclampsia (A) and low birth weight (B). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval.

ing pregnancy on adverse pregnancy outcomes by comparing the obstetric and neonatal outcomes of COVID-19-infected versus non-infected pregnant women.

Adverse pregnancy outcomes were more common in pregnant women with COVID-19 than in those without. This review revealed that COVID-19 during pregnancy is associated with an increased risk of cesarean delivery, preterm birth, preeclampsia, IUFD or stillbirth, gestational diabetes mel-

A

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	37	55	45	94	1.1%	2.24 [1.12, 4.48]
Adhikari, 2020	65	245	1,011	3,035	2.9%	0.72 [0.54, 0.97]
Ahlberg, 2020	36	155	159	604	2.1%	0.85 [0.56, 1.28]
Alipour, 2021	33	53	88	135	1.2%	0.88 [0.46, 1.70]
Bender, 2020	0	8	95	310	0.1%	0.13 [0.01, 2.32]
Brandt, 2021	14	61	40	122	1.1%	0.61 [0.30, 1.24]
Cardona-Perez, 2021	51	63	113	154	1.0%	1.54 [0.75, 3.18]
Chornock, 2021	28	73	342	935	1.8%	1.08 [0.66, 1.76]
Cosma, 2021	5	16	26	105	0.5%	1.38 [0.44, 4.35]
Crovetto, 2021	54	317	311	1,908	2.7%	1.05 [0.77, 1.45]
Cruz-Lemini, 2021	36	174	74	430	2.0%	1.25 [0.80, 1.96]
Cruz-Meguizo, 2021	373	1,347	328	1,607	3.8%	1.49 [1.26, 1.77]
Cunarro-Lopez, 2020	19	68	4	43	0.5%	3.78 [1.19, 12.03]
Diaz-Corvillon, 2020	18	37	272	549	1.2%	0.96 [0.50, 1.88]
Edlow, 2020	21	64	39	63	1.0%	0.30 [0.15, 0.62]
Farghaly, 2020	10	15	27	64	0.5%	2.74 [0.84, 8.94]
Ferrugini, 2022	57	86	100	179	1.6%	1.55 [0.91, 2.65]
Flaherman, 2021	63	179	34	84	1.6%	0.80 [0.47, 1.36]
Getahun, 2022	615	2,203	9,264	32,920	4.2%	0.99 [(0.90, 1.09]
Griffin, 2020	10	27	10	35	0.5%	1.47 [10.50, 4.29]
Gupta, 2021	63	108	914	3,057	2.3%	3.28 [2.22, 4.85]
Gurol-Urganci, 2021	1,355	3,527	109,322	338,553	4.3%	1.31 [1.22, 1.40]
Hcini, 2021	19	137	62	370	1.5%	0.80 [0.46, 1.39]
Jering, 2020	1,847	6,380	109,865	400,066	4.4%	1.08 [1.02, 1.14]
Katz, 2021	171	490	331	964	3.3%	1.03 [0.82, 1.29]
Ko, 2021	2,193	6,550	154,401	482,921	4.4%	1.07 [1.02, 1.13]
Laresgoiti-Servitje, 2021	124	298	368	828	3.1%	0.89 [0.68, 1.16]
Li, 2020	14	16	57	121	0.3%	7.86 [1.71, 36.08]
Liu, 2020	29	32	13	16	0.2%	2.23 [0.40, 12.57]
Liu, 2021	16	56	97	279	1.3%	0.75 [0.40, 1.41]
M'poca Charles, 2020	3	21	48	202	0.4%	0.53 [0.15, 1.89]
Martinez-Perez, 2020	55	246	143	763	2.5%	1.25 [0.88, 1.77]
Masud, 2021	50	70	59	140	1.3%	3.43 [1.85, 6.36]
Millin, 2021	12	30	359	1,268	1.0%	1.69 [0.80, 3.54]
Nayak, 2020	67	141	376	836	2.5%	1.11 [0.77, 1.58]
Norman, 2021	495	2,286	15,450	84,719	4.2%	1.24 [1.12, 1.37]
Patberg, 2021	20	77	42	56	0.9%	0.12 [0.05, 0.26]
Pineles, 2020	21	77	233	858	1.6%	1.01 [0.60, 1.70]
Prabhu, 2020	32	70	187	605	1.7%	1.88 [1.14, 3.11]
Regan, 2021	712	2,655	15,609	75,628	4.2%	1.41 [1.29, 1.54]
Rodriguez-Diaz, 2021	8	29	104	591	0.8%	1.78 [0.77, 4.14]
Rosenbloom, 2021	26	83	43	166	1.4%	1.30 [0.73, 2.33]
Ruggiero, 2021	10	28	108	287	0.9%	0.92 [0.41, 2.07]
Saadia, 2021	20	48	17	46	0.8%	1.22 [0.53, 2.79]
Saviron-Comudella, 2021	3	22	156	1,146	0.4%	1.00 [0.29, 3.43]
Seyed-Abdolvahab, 2021	9	20	8	20	0.4%	1.23 [0.35, 4.31]
Smithgall, 2020	25	51	15	25	0.6%	0.64 [0.24, 1.69]
Soto-Torres, 2021	29	106	41	103	1.4%	0.57 [0.32, 1.02]
Sutton, 2021	36	79	168	375	1.8%	1.03 [0.63, 1.68]
Teixeira, 2021	10	33	26	82	0.8%	0.94 [0.39, 2.25]
Timircan, 2021	30	101	159	938	1.9%	2.07 [1.31, 3.28]
Trahan, 2021	13	45	76	225	1.1%	0.80 [0.39, 1.61]
Villar, 2021	346	706	547	1,424	3.7%	1.54 [1.28, 1.85]
Vousden, 2021	467	1,148	201	694	3.5%	1.68 [1.37, 2.06]
Wang, 2020	23	53	257	760	1.5%	1.50 [0.85, 2.64]
Yadav, 2020	18	28	40	112	0.8%	3.24 [1.37, 7.69]
Yang, 2020	52	65	6,020	11,013	1.3%	3.32 [1.80, 6.10]
Total (95% CI)		31,158		1,453,633	100.0%	1.20 [1.10, 1.30]
Total events	9,968		428,304			

Heterogeneity: Tau^2=0.04; Chi^2=262.94; df=49 (*P*<0.00001); I^2=79%
Test for overall effect: Z=4.20 (*P*<0.0001)

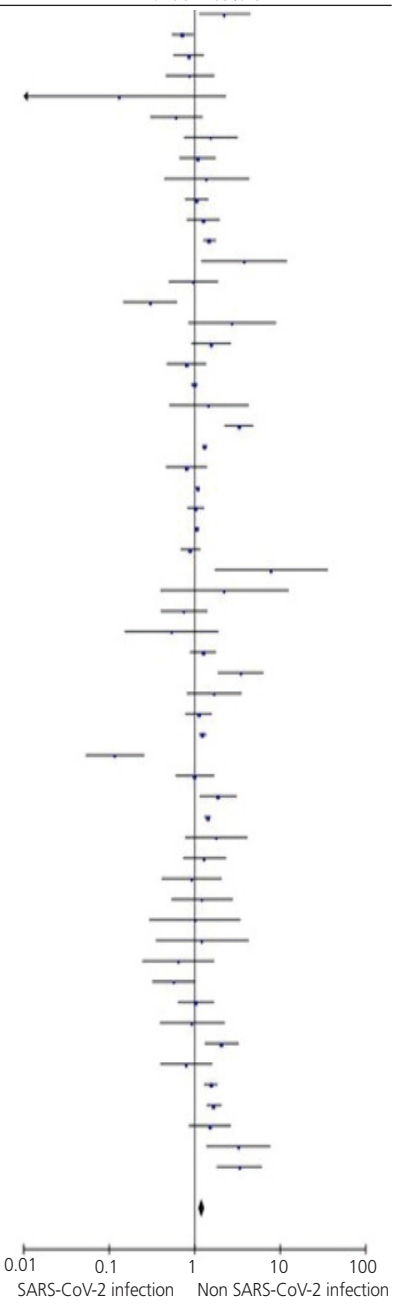


Fig. 4. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and cesarean section (A) and IUFD or stillbirth (B). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval; IUFD, intrauterine fetal death.

litus, IUGR or SGA, and LBW. Moreover, COVID-19 infection during pregnancy can lead to an increased risk of neonatal complications, such as fetal distress, NICU admission, and perinatal mortality. Furthermore, COVID-19 negatively affected maternal mortality.

These findings are consistent with those of previous stud-

B

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Adhikari, 2020	0	245	18	3,035	0.5%	0.33 [0.02, 5.53]
Ahlberg, 2020	1	155	4	604	0.8%	0.97 [0.11, 8.78]
Brandt, 2021	0	61	0	122		Not estimable
Cardona-Perez, 2021	5	70	6	170	2.5%	2.10 [0.62, 7.13]
Cosma, 2021	0	16	0	105		Not estimable
Cruz-Lemini, 2021	2	174	0	430	0.4%	12.48 [0.60, 261.25]
Cruz-Meguizo, 2021	10	1,347	3	1,607	2.3%	4.00 [1.10, 14.56]
Fallach, 2022	16	2,753	11	2,753	5.4%	1.46 [0.68, 3.15]
Getahun, 2022	14	2,203	160	32,920	8.8%	1.31 [0.76, 2.27]
Gurol-Urganci, 2021	30	3,527	1,140	338,553	13.5%	2.54 [1.76, 3.65]
Hcini, 2021	7	137	4	370	2.4%	4.93 [1.42, 17.11]
Jering, 2020	34	6,380	1,289	400,066	14.2%	1.66 [1.18, 2.33]
Ko, 2021	63	6,550	3,439	482,921	17.4%	1.35 [1.05, 1.74]
Laresgoiti-Servitje, 2021	19	298	38	828	8.4%	1.42 [0.80, 2.50]
M'poca Charles, 2020	2	21	202	1	1.3%	5.21 [0.90, 30.33]
Martinez-Perez, 2020	3	246	763	3	0.8%	9.41 (0.97, 90.86]
Masud, 2021	4	70	140	10	1.7%	2.77 [0.60, 12.72]
Millin, 2021	0	30	1,268	31	0.5%	1.96 [0.11, 34.30]
Nayak, 2020	3	141	836	535	2.6%	0.56 [0.17, 1.87]
Regan, 2021	25	2,655	75,628	0	12.3%	1.33 [0.89, 2.00]
Rodriguez-Diaz, 2021	0	29	591	0		Not estimable
Ruggiero, 2021	28	0	287	2		Not estimable
Saviron-Comudella, 2021	22	20	1,146	21,202	0.4%	10.17 [0.47, 218.04]
Seyed-Abdolvahab, 2021	1,148	68	20	694	0.4%	0.32 [0.01, 8.26]
Soto-Torres, 2021	9	1,148	633	694	1.7%	2.73 [0.59, 12.69]
Von Bargen, 2022						Not estimable
Vousden, 2021					1.7%	2.73 [0.59, 12.69]
Total (95% CI)		29,542		1,347,386	100.0%	1.71 [1.39, 2.10]
Total events	256		6,703			

Heterogeneity: Tau^2=0.05; Chi^2=28.65; df=49 (*P*<0.12); I^2=27%
Test for overall effect: Z=5.13 (*P*<0.00001)

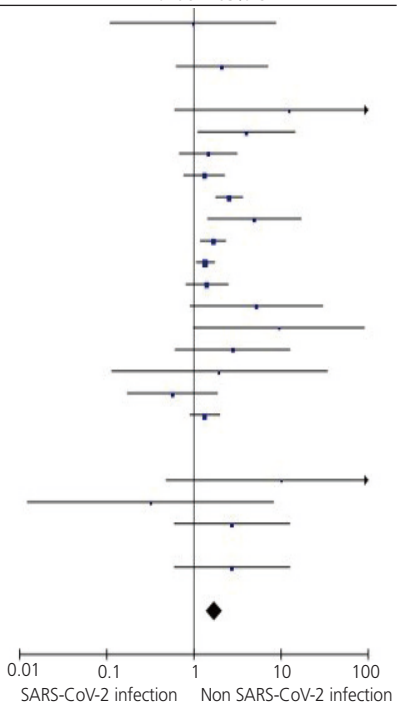


Fig. 4. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and cesarean section (A) and fetal death (B). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval. (Continued)

ies [72]. Allotey et al. [2] reported that COVID-19 infection during pregnancy increases the risk of preterm birth, LBW, NICU admission, and stillbirth. Lassi et al. [73] reported a 2-fold increased risk of preterm birth in women with severe symptomatic COVID-19. Pathirathna et al. [74] suggested that pregnant women with COVID-19 have an increased risk of maternal death, preeclampsia, cesarean delivery, fetal distress, preterm birth, LBW, NICU admission, and stillbirth. In contrast, Huntley et al. [75], and Wei et al. [76] reported that COVID-19 infection during pregnancy did not increase the risk of cesarean delivery. Nevertheless, Wei et al. [77] reported that the risk of preterm birth, cesarean delivery, and preeclampsia increased with the presence and severity of COVID-19 symptoms.

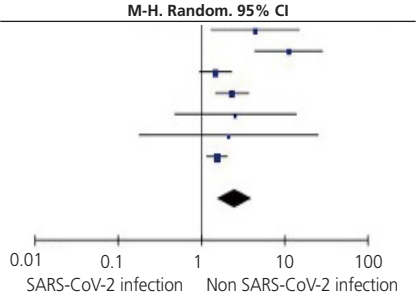
Previous studies have reported that the most common obstetric complications associated with COVID-19 are PPROM, postpartum hemorrhage, cesarean delivery, and preterm birth [78,79]. The inflammatory reaction associated with infection can lead to the destruction of placental function and the subsequent development of adverse pregnancy outcomes [18,58,80]. Cesarean section is the preferred delivery route in COVID-19-positive pregnancies. The higher rate of cesarean sections compared to the current cesarean delivery rate of 30% could be due to changes in the obstetric management protocols influenced by the infectious disease management policy of the institution; this could also be attributed to disease progression caused by COVID-19. This finding is consistent with the results of another meta-analysis. Since most studies examined did not specify the indications for cesarean sections, this could not be accurately analyzed.

The present review demonstrates that COVID-19 infection during pregnancy is associated with an increased risk of preeclampsia. Pérez-López et al. [81] reported that preeclampsia and hypertensive disorders of pregnancy were more common in COVID-19-infected pregnant women regardless of the presence or severity of their symptoms. Other studies reported a positive association between preeclampsia and COVID-19 during pregnancy [74,77,82,83]. Multiple mechanisms are involved in the pathogenesis of preeclampsia in pregnant women with COVID-19. SARS-CoV-2 binds to cell

A

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	9	55	4	94	9.7%	4.40 [1.29, 15.06]
Alipour, 2021	20	53	7	135	13.2%	11.08 [4.32, 28.43]
Crovetto, 2021	25	317	105	1,908	21.7%	1.47 [0.93, 2.31]
Gupta, 2021	24	108	334	3,057	21.4%	2.33 [1.46, 3.72]
Li, 2020	2	17	6	121	6.2%	2.56 [0.47, 13.83]
Seyed-Abdolvahab, 2021	2	20	1	20	3.3%	2.11 [0.18, 25.35]
Villar, 2021	87	706	120	1,424	24.4%	1.53 [1.14, 2.05]
Total (95% CI)		1,276		6,759	100.0%	2.49 [1.54, 4.03]
Total events	169		577			

Heterogeneity: Tau^2=0.22; Chi^2=19.48; df=6 (*P*=0.003); I^2=69%
Test for overall effect: Z=3.72 (*P*=0.0002)



B

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	9	55	20	94	3.4%	0.72 [0.30, 1.73]
Alipour, 2021	18	53	10	135	3.4%	6.43 [2.72, 15.18]
Bender, 2020	0	8	25	310	0.9%	0.66 [0.04, 11.74]
Brandt, 2021	53	61	14	122	3.3%	51.11 [20.19, 129.37]
Chomock, 2021	12	73	113	935	3.9%	1.43 [0.75, 2.74]
Cosma, 2021	1	16	6	105	1.4%	1.10 [0.12, 9.79]
Cruz-Lemini, 2021	12	174	7	430	3.2%	4.48 [1.73, 11.57]
Cruz-Meguizo, 2021	137	1,347	39	1,607	4.4%	4.55 [3.16, 6.55]
Cunarro-Lopez, 2020	14	68	3	43	2.5%	3.46 [0.93, 12.84]
Farghaly, 2020	10	15	16	64	2.7%	6.00 [1.78, 20.19]
Ferrugini, 2022	34	86	25	179	4.0%	4.03 [2.20, 7.37]
Flaherman, 2021	31	179	13	84	3.8%	1.14 [0.56, 2.32]
Getahun, 2022	191	2,203	2,684	32,920	4.7%	1.07 [0.92, 1.25]
Gupta, 2021	14	108	254	3,057	4.0%	1.64 [0.92, 2.92]
Hcini, 2021	3	137	12	364	2.6%	0.66 [0.18, 2.36]
M'poca Charles, 2020	2	21	36	202	2.2%	0.49 [0.11, 2.18]
Martinez-Perez, 2020	23	246	18	763	3.9%	4.27 [2.26, 8.05]
Nayak, 2020	24	141	202	836	4.2%	0.64 [0.40, 1.03]
Norman, 2021	271	2,323	7,351	85,386	4.7%	1.40 [1.23, 1.59]
Patberg, 2021	6	77	6	56	2.7%	0.70 [0.21, 2.31]
Pineles, 2020	74	77	107	858	2.8%	173.13 [53.63, 558.89]
Prabhu, 2020	13	73	68	614	3.9%	1.74 [0.91, 3.33]
Ruggiero, 2021	5	28	21	287	3.0%	2.75 [0.95, 7.98]
Saadia, 2021	3	48	2	46	1.7%	1.47 [0.23, 9.21]
Seyed-Abdolvahab, 2021	2	20	3	20	1.6%	0.63 [0.09, 4.24]
Soto-Torres, 2021	39	106	15	103	3.8%	3.41 [1.74, 6.71]
Sutton, 2021	14	79	46	375	3.9%	1.54 [0.80, 2.96]
Timircan, 2021	6	101	27	938	3.3%	2.13 [0.86, 5.29]
Trahan, 2021	6	47	22	227	3.2%	1.36 [0.52, 3.57]
Vousden, 2021	156	1,148	37	694	4.4%	2.79 [1.93, 4.05]
Yadav, 2020	4	28	8	112	2.6%	2.17 [0.60, 7.79]
Total (95% CI)		9,146		131,966	100.0%	2.33 [1.72, 3.16]
Total events	1,187		11,210			

Heterogeneity: Tau^2=0.51; Chi^2=261.41; df=30 (*P*< 0.00001); I^2=89%
Test for overall effect: Z=5.46 (*P*<0.00001)

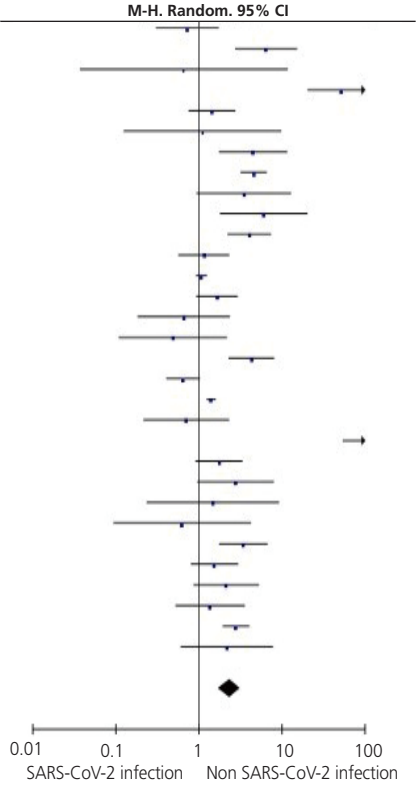


Fig. 5. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and fetal distress (A), NICU admission (B), perinatal mortality (C), and maternal mortality (D). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval; NICU, neonatal intensive care unit.

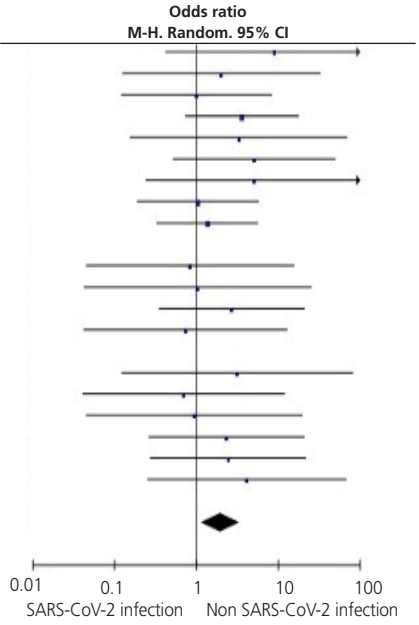
membrane angiotensin-converting enzyme 2, which plays an important role in the renin-angiotensin system (RAS). RAS controls trophoblast proliferation, angiogenesis, and uteroplacental blood flow. COVID-19 can alter RAS function via its downregulation, which induces preeclampsia. Moreover, the infected placenta shows a decreased expression of angiotensin-conversing enzyme 2 receptors concurrent with increased production of soluble fms-like tyrosine kinase-1, which has been implicated in the pathogenesis of preeclampsia. Garrido-Pontnou et al. [84], and Hecht et al. [85] reported that infected COVID-19 term placentas demonstrated villous trophoblast necrosis, inflammatory infiltration, and fibrinoid deposition. The authors suggest that these placental mechanisms against infection could contribute to adverse pregnancy outcomes.

Moreover, COVID-19 infection during pregnancy increases

C

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Abedzadeh-Kalahroudi, 2021	2	55	0	94	3.0%	8.83 [0.42, 187.39]
Brandt, 2021	1	61	1	122	3.7%	2.02 [0.12, 32.80]
Crovetto, 2021	1	317	6	1,908	6.3%	1.00 [0.12, 8.36]
Cruz-Meguizo, 2021	6	1,347	2	1,607	11.1%	3.59 [0.72, 17.82]
Cunarro-Lopez, 2020	2	68	0	43	3.0%	3.27 [0.15, 69.78]
Diaz-Corvillon, 2020	1	37	3	549	5.4%	5.06 [0.51, 49.83]
Edlow, 2020	2	64	0	63	3.0%	5.08 [0.24, 107.95]
Ferrugini, 2022	2	86	4	179	9.6%	1.04 [0.19, 5.80]
Gupta, 2021	2	108	42	3,057	13.9%	1.35 [0.32, 5.67]
Hcini, 2021	0	137	0	364		Not estimable
M'poca Charles, 2020	0	21	5	202	3.3%	0.84 [0.04, 15.62]
Martinez-Perez, 2020	0	246	1	763	2.8%	1.03 [0.04, 25.39]
Millin, 2021	1	30	16	1,268	6.7%	2.70 [0.35, 21.03]
Pineles, 2020	0	77	7	858	3.4%	0.73 [0.04, 12.95]
Ruggiero, 2021	0	28	0	287		Not estimable
Seyed-Abdolvahab, 2021	1	20	0	20	2.7%	3.15 [0.12, 82.16]
Steffen, 2021	0	65	10	971	3.5%	0.70 [0.04, 12.06]
Sutton, 2021	0	79	2	375	3.1%	0.94 [0.04, 19.76]
Timircan, 2021	1	101	4	938	5.9%	2.33 [0.26, 21.09]
Vousden, 2021	47	1,148	1	694	5.9%	2.42 [0.27, 21.72]
Yadav, 2020	1	28	1	112	3.6%	4.11 [0.25, 67.85]
Total (95% CI)		4,123		14,474	100.0%	1.96 [1.15, 3.34]
Total events	27		105			

Heterogeneity: Tau^2=0.00; Chi^2=5.94; df=49 (*P*=1.00); I^2=0%
Test for overall effect: Z=2.48 (*P*=0.01)



D

Study or subgroup	SARS-COV-2 infection Events	Total	Non SARS-CoV-2 infection Events	Total	Weight	Odds ratio M-H. Random. 95% CI
Cruz-Meguizo, 2021	2	1,347	0	1,607	4.4%	5.97 [0.29, 124.53]
Gupta, 2021	1	108	7	3,057	4.6%	4.07 [0.50, 33.39]
Hcini, 2021	0	137	0	370		Not estimable
Ko, 2021	9	6,550	32	482,921	8.3%	20.76 [9.91, 43.51]
Millin, 2021	1	30	0	1,268	0.2%	129.00 [5.15, 3233.01]
Nayak, 2020	3	141	8	836	22.0%	2.25 [0.59, 8.58]
Rios-Silva, 2020	10	448	7	1,216	35.9%	3.94 [1.49, 10.42]
Ruggiero, 2021	0	28	0	287		Not estimable
Saadia, 2021	2	48	0	46	4.7%	5.00 [0.23, 107.01]
Saviron-Comudella, 2021	0	22	35	1,146	13.3%	0.70 [0.04, 11.70]
Villar, 2021	11	706	1	1,424	6.4%	22.52 [2.90, 174.80]
Von Bargen, 2022	0	68	0	633		Not estimable
Total (95% CI)		9,633		494,811	100.0%	6.15 [3.74, 10.10]
Total events	39		90			

Heterogeneity: Tau^2=20.79; Chi^2=8; df=49 (*P*<=0.008); I^2=62%
Test for overall effect: Z=7.17 (*P*<0.00001)

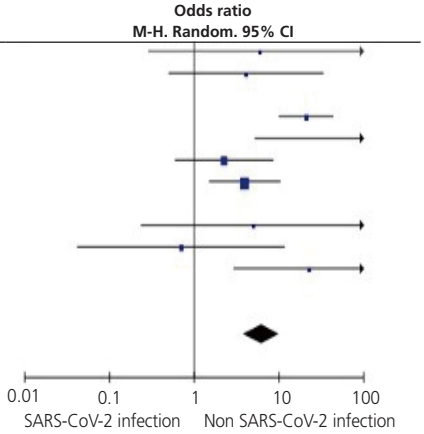


Fig. 5. Forest plots of the summary crude odds ratios and 95% confidence intervals for the association between coronavirus disease 2019 and fetal distress (A), NICU admission (B), perinatal mortality (C), and maternal mortality (D). SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; CI, confidence interval; NICU, neonatal intensive care unit. (Continued)

the risk of preterm birth. However, a previous study reported that the preterm birth rate during the pandemic was lower than that in the pre-pandemic era [86]. In this review, we did not address the causes of preterm birth, whether spontaneous or medically induced. Even when analyzing spontaneous preterm births, we observed that the risk of spontaneous preterm births was significantly higher in women with COVID-19 than in those without. Neonates born to women with COVID-19 had a higher NICU admission risk than those born to non-infected women. This finding is consistent with those of previous studies. Furthermore, COVID-19 increases the risk of fetal distress and perinatal mortality.

Pregnant women are categorized as immunosuppressed because they undergo immunological and physiological changes during pregnancy that prevent fetal allograft rejection [87]. Hence, pregnant women are more susceptible to respiratory infections than does the general population. Moreover, the physiological changes in the cardiopulmonary system in pregnant women can worsen the symptoms of respiratory infections. Furthermore, an elevated diaphragm, increased oxygen demand, and generalized edema, including that in the bronchial mucosa, experienced by pregnant

women are risk factors for hypoxia [88,89]. Previously, influenza A subtype H1N1 virus, SARS-CoV, and MERS infections have demonstrated more systemic complications in pregnant women than in the general population [90,91]. However, unlike other respiratory viruses, the severity of COVID-19 remains relatively low. A previous study reported that the laboratory findings, clinical presentations, and radiological findings of pregnant women with COVID-19 were similar to those of non-pregnant women [11]. Several hypotheses have been proposed to explain these findings. One of them is that COVID-19 is caused by a novel ribonucleic acid mutation. Furthermore, concurrent with pregnancy, adaptive organ changes to offset fetal rejection may have resulted in a protective effect against the virus [92]. The process of immunological adaptation, which starts during pregnancy, may be the key to the milder symptoms of COVID-19 noted during pregnancy.

Vertical transmission was not considered in the present study. A previous review reported that vertical transmission of SARS-CoV-2 was rare and not detected in nasopharyngeal swabs of neonates, cord blood, or amniotic fluid [80]. Other studies have also reported very little evidence to support the vertical transmission of COVID-19 [81,83].

Although a few studies have investigated breastfeeding with COVID-19 infection, previous studies have reported conflicting results. Some researchers do not recommend breastfeeding when a nursing mother is infected, whereas others suggest that breastfeeding while wearing a mask should be practiced. Additionally, the virus is not believed to be transmitted through breast milk. However, further studies to confirm this hypothesis are warranted [80,93-96].

This review has several strengths. As the studies included in this review were extracted from multiple countries, our findings can be generalized globally and interpreted regardless of race or country. The present systematic review compared the pregnancy outcomes of COVID-19-infected and non-infected pregnant women and did not investigate the general population. The selection bias was low owing to the high threshold of the inclusion criteria. This review also included a larger number of studies than previous reports. This review demonstrated that COVID-19 has a worse effect on outcomes, such as preterm birth, cesarean section, and placental abruption, compared with the outcomes reported in previous studies.

This study also has several limitations. First, the disease remains prevalent globally, causing additional alterations in public health restrictions. However, prospective randomized studies on viral infections are not applicable to pregnant women. Therefore, we included only retrospective, nonrandomized studies in this review. Second, the studies included in this report were conducted in multiple countries, and their baseline characteristics were highly heterogeneous including the types of COVID-19 variants. Third, we were unable to access the raw data analyzed in these studies. Fourth, this study did not analyze infections according to pregnancy trimesters. The pregnancy trimester at the infection time could be a significant factor in adverse pregnancy outcomes, as respiratory infections in early pregnancy can critically impact organogenesis. Fifth, this review did not assess indications for the delivery route.

As the global spread of COVID-19 continues, it is imperative to determine further its impact on pregnancy outcomes to prepare for future outbreaks. Pregnant women are particularly susceptible to respiratory infections, which can lead to high pregnancy morbidity and mortality rates. The findings of this review and meta-analysis provide sufficient information to enable evidence-based counseling and help clinicians manage pregnant women with COVID-19.

Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

The study is not applicable to Institutional Review Board.

Patient consent

No informed consent was obtained from the patients because the study was retrospective.

Funding information

None.

References

1. Khoury R, Bernstein PS, Debolt C, Stone J, Sutton DM, Simpson LL, et al. Characteristics and outcomes of 241 births to women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at five New York City medical centers. Obstet Gynecol 2020;136:273-82.
2. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020;370:m3320.
3. Adhikari EH, Moreno W, Zofkie AC, MacDonald L, McIntire DD, Collins RRJ, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. JAMA Netw Open 2020; 3:e2029256.
4. Melo GC, Araújo KCGM. COVID-19 infection in pregnant women, preterm delivery, birth weight, and vertical transmission: a systematic review and meta-analysis. Cad Saude Publica 2020;36:e00087320.
5. Shephard HM, Manning SE, Nestoridi E, Brown C, Yazdy MM. Characteristics of people with and without laboratory-confirmed SARS-CoV-2 infection during pregnancy, massachusetts, March 2020-March 2021. Public Health Rep 2022;137:782-9.
6. Vera von Bargen H, Espinosa Serrano M, Martin Navarrete D, Ahumada Droguett P, Méndez Benavente C, Flores Castillo M, et al. Analysis of prevalence and sociodemographic conditions among women in labor with and without COVID-19 in public hospitals in Chile. J Perinat Med 2021;50:132-8.
7. Griffin I, Benarba F, Peters C, Oyelese Y, Murphy T, Contreras D, et al. The impact of COVID-19 infection on labor and delivery, newborn nursery, and neonatal intensive care unit: prospective observational data from a single hospital system. Am J Perinatol 2020;37:1022-30.
8. Wei L, Gao X, Chen S, Zeng W, Wu J, Lin X, et al. Clinical characteristics and outcomes of childbearing-age women with COVID-19 in Wuhan: retrospective, single-center study. J Med Internet Res 2020;22:e19642.
9. Martinez-Perez O, Prats Rodriguez P, Muner Hernandez M, Encinas Pardilla MB, Perez Perez N, Vila Hernandez MR, et al. The association between SARS-CoV-2 infection and preterm delivery: a prospective study with a multivariable analysis. BMC Pregnancy Childbirth 2021;21:273.
10. Dhuyvetter A, Cejtin HE, Adam M, Patel A. Coronavirus disease 2019 in pregnancy: the experience at an urban safety net hospital. J Community Health 2021;46:267-9.
11. Yang H, Wang C, Poon LC. Novel coronavirus infection and pregnancy. Ultrasound Obstet Gynecol 2020;55: 435-7.
12. Charles CM, Osman NB, Arijama D, Matingane B, Sitoé T, Kenga D, et al. Clinical and epidemiological aspects of SARS-CoV-2 infection among pregnant and postpartum women in Mozambique: a prospective cohort study. Reprod Health 2022;19:164.
13. Nayak AH, Kapote DS, Fonseca M, Chavan N, Mayekar R, Sarmalkar M, et al. Impact of the coronavirus infection in pregnancy: a preliminary study of 141 patients. J Obstet Gynaecol India 2020;70:256-61.
14. Taghavi SA, Heidari S, Jahanfar S, Amirjani S, Aji-ramkani A, Azizi-Kutenaee M, et al. Obstetric, maternal, and neonatal outcomes in COVID-19 compared to healthy pregnant women in Iran: a retrospective, case-control study. Middle East Fertil Soc J 2021;26:17.
15. Milln J, Heard S, Gunganah K, Velauthar L, Saeed F. Clinical characteristics and pregnancy outcomes of women diagnosed with SARS-CoV-2 in London's most ethnically diverse borough: a cross-sectional study. Obstet Med 2021;14:164-9.
16. Pasternak B, Neovius M, Söderling J, Ahlberg M, Norman M, Ludvigsson JF, et al. Preterm birth and stillbirth during the COVID-19 pandemic in Sweden: a nationwide cohort study. Ann Intern Med 2021;174:873-5.
17. Prabhu M, Cagino K, Matthews KC, Friedlander RL, Glynn SM, Kubiak JM, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study. BJOG 2020;127:1548-56.
18. Li N, Han L, Peng M, Lv Y, Ouyang Y, Liu K, et al. Maternal and neonatal outcomes of pregnant women with coronavirus disease 2019 (COVID-19) pneumonia: a case-control study. Clin Infect Dis 2020;71:2035-41.
19. Flaherman VJ, Afshar Y, Boscardin WJ, Keller RL, Mardy AH, Prahl MK, et al. Infant outcomes following maternal infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): first report from the pregnancy coronavirus outcomes registry (PRIORITY) study. Clin In-

fect Dis 2021;73:e2810-3.
20. Crovetto F, Crispi F, Llurba E, Pascal R, Larroya M, Trilla C, et al. Impact of severe acute respiratory syndrome coronavirus 2 infection on pregnancy outcomes: a population-based study. Clin Infect Dis 2021;73:1768-75.
21. Edlow AG, Li JZ, Collier AY, Atyeo C, James KE, Boatin AA, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. JAMA Netw Open 2020;3:e2030455.
22. Rodríguez-Díaz M, Alonso-Molero J, Cabero-Perez MJ, Llorca J, Dierssen-Sotos T, Gómez-Acebo I, et al. Pregnancy and birth outcomes during the early months of the COVID-19 pandemic: the MOACC-19 cohort. Int J Environ Res Public Health 2021;18:10931.
23. Jering KS, Claggett BL, Cunningham JW, Rosenthal N, Vardeny O, Greene MF, et al. Clinical characteristics and outcomes of hospitalized women giving birth with and without COVID-19. JAMA Intern Med 2021;181:714-7.
24. Regan AK, Arah OA, Fell DB, Sullivan SG. SARS-CoV-2 infection during pregnancy and associated perinatal health outcomes: a national US cohort study. J Infect Dis 2022;225:759-67.
25. Sahin D, Tanacan A, Erol SA, Anuk AT, Eyi EGY, Ozgu-Erdinc AS, et al. A pandemic center's experience of managing pregnant women with COVID-19 infection in Turkey: a prospective cohort study. Int J Gynaecol Obstet 2020;151:74-82.
26. Ferrugini CLP, Boldrini NAT, Costa FLS, Salgueiro MAOB, Coelho PDP, Miranda AE. SARS-CoV-2 infection in pregnant women assisted in a high-risk maternity hospital in Brazil: clinical aspects and obstetric outcomes. PLoS One 2022;17:e0264901.
27. Binte Masud S, Zebeen F, Alam DW, Hossian M, Zaman S, Begum RA, et al. Adverse birth outcomes among pregnant women with and without COVID-19: a comparative study from bangladesh. J Prev Med Public Health 2021;54:422-30.
28. Brandt JS, Fell DB. SARS-CoV-2 infection in pregnancy: lessons learned from the first pandemic wave. Paediatr Perinat Epidemiol 2021;35:34-6.
29. Hcini N, Maamri F, Picone O, Carod JF, Lambert V, Mathieu M, et al. Maternal, fetal and neonatal outcomes of large series of SARS-CoV-2 positive pregnancies in peripartum period: a single-center prospective comparative study. Eur J Obstet Gynecol Reprod Biol 2021;257:11-8.
30. Patberg ET, Adams T, Rekawek P, Vahanian SA, Akerman M, Hernandez A, et al. Coronavirus disease 2019 infection and placental histopathology in women delivering at term. Am J Obstet Gynecol 2021;224:382.e1-382.e18.
31. Sakowicz A, Ayala AE, Ukeje CC, Witting CS, Grobman WA, Miller ES. Risk factors for severe acute respiratory syndrome coronavirus 2 infection in pregnant women. Am J Obstet Gynecol MFM 2020;2:100198.
32. Pineles BL, Goodman KE, Pineles L, O'Hara LM, Nadimpalli G, Magder LS, et al. In-hospital mortality in a cohort of hospitalized pregnant and nonpregnant patients with COVID-19. Ann Intern Med 2021;174:1186-8.
33. Saadia Z, Farrukh R, Kanwal S, Shahzad Q. Clinical profiles, demographic features, and maternal outcomes among coronavirus disease positive pregnant women: a cross-sectional study. Open Access Maced J Med Sci 2021;9:486-91.
34. Díaz-Corvillón P, Mönckeberg M, Barros A, Illanes SE, Soldati A, Nien JK, et al. Routine screening for SARS CoV-2 in unselected pregnant women at delivery. PLoS One 2020;15:e0239887.
35. Fallach N, Segal Y, Agassy J, Perez G, Peretz A, Chodick G, et al. Pregnancy outcomes after SARS-CoV-2 infection by trimester: a large, population-based cohort study. PLoS One 2022;17:e0270893.
36. Sutton D, Wen T, Staniczenko AP, Huang Y, Andrikopoulou M, D'Alton M, et al. Clinical and demographic risk factors for COVID-19 during delivery hospitalizations in New York City. Am J Perinatol 2021;38:857-68.
37. Getahun D, Peltier MR, Lurvey LD, Shi JM, Braun D, Sacks DA, et al. Association between SARS-CoV-2 infection and adverse perinatal outcomes in a large health maintenance organization. Am J Perinatol 2022 Jun 23 [Epub]. https://doi.org/10.1055/s-0042-1749666.
38. Cruz-Lemini M, Ferriols Perez E, de la Cruz Conty ML, Caño Aguilar A, Encinas Pardilla MB, Prats Rodríguez P, et al. Obstetric outcomes of SARS-CoV-2 infection in asymptomatic pregnant women. Viruses 2021;13:112.
39. Cruz Melguizo S, de la Cruz Conty ML, Carmona Payán P, Abascal-Saiz A, Pintando Recarte P, González Rodríguez L, et al. Pregnancy outcomes and SARS-CoV-2 infection: the Spanish Obstetric Emergency Group study. Viruses 2021;13:853.
40. Teixeira MLB, Costa Ferreira Júnior OD, João E, Fuller

T, Silva Esteves J, Mendes-Silva W, et al. Maternal and neonatal outcomes of SARS-CoV-2 infection in a cohort of pregnant women with comorbid disorders. Viruses 2021;13:1277.
41. Wang MJ, Schapero M, Iverson R, Yarrington CD. Obstetric hemorrhage risk associated with novel COVID-19 diagnosis from a single-institution cohort in the United States. Am J Perinatol 2020;37:1411-6.
42. Abedzadeh-Kalahroudi M, Karimian Z, Nasiri S, Khorshidifard MS. Anxiety and perceived stress of pregnant women towards covid-19 disease and its related factors in Kashan (2020). Iran J Obstet Gynecol Infertil 2021;24:8-18.
43. Alipour Z, Samadi P, Eskandari N, Ghaedrahmati M, Vahedian M, Khalajinia Z, et al. Relationship between coronavirus disease 2019 in pregnancy and maternal and fetal outcomes: retrospective analytical cohort study. Midwifery 2021;102:103128.
44. Li WK, Chen XJC, Altshuler D, Islam S, Spiegler P, Emerson L, et al. The incidence of propofol infusion syndrome in critically-ill patients. J Crit Care 2022;71:154098.
45. Cardona-Pérez JA, Villegas-Mota I, Helguera-Repetto AC, Acevedo-Gallegos S, Rodríguez-Bosch M, Aguinaga-Ríos M, et al. Prevalence, clinical features, and outcomes of SARS-CoV-2 infection in pregnant women with or without mild/moderate symptoms: results from universal screening in a tertiary care center in Mexico City, Mexico. PLoS One 2021;16:e0249584.
46. Chornock R, Iqbal SN, Wang T, Kodama S, Kawakita T, Fries M. Incidence of hypertensive disorders of pregnancy in women with COVID-19. Am J Perinatol 2021;38:766-72.
47. Cosma S, Carosso AR, Borella F, Cusato J, Bovetti M, Bevilacqua F, et al. Prenatal biochemical and ultrasound markers in covid-19 pregnant patients: a prospective case-control study. Diagnostics (Basel) 2021;11:398.
48. Cuñarro-López Y, Cano-Valderrama Ó, Pintado-Recarte P, Cueto-Hernández I, González-Garzón B, García-Tizón S, et al. Maternal and perinatal outcomes in patients with suspected COVID-19 and their relationship with a negative RT-PCR result. J Clin Med 2020;9:3552.
49. Farghaly MAA, Kupferman F, Castillo F, Kim RM. Characteristics of newborns born to SARS-CoV-2-positive mothers: a retrospective cohort study. Am J Perinatol 2020;37:1310-6.
50. Gulersen M, Blitz MJ, Rochelson B, Nimaroff M, Shan W, Bornstein E. Clinical implications of SARS-CoV-2 infection in the viable preterm period. Am J Perinatol 2020;37:1077-83.
51. Gupta P, Khatana VP, Prabha R, Jha I, Singh M, Pandey AK, et al. An observational study for appraisal of clinical outcome and risk of mother-to-child SARS-CoV-2 transmission in neonates provided the benefits of mothers' own milk. Eur J Pediatr 2022;181:513-27.
52. Gurol-Urganci I, Waite L, Webster K, Jardine J, Carroll F, Dunn G, et al. Obstetric interventions and pregnancy outcomes during the COVID-19 pandemic in England: a nationwide cohort study. PLoS Med 2022;19:e1003884.
53. Smithgall MC, Liu-Jarin X, Hamele-Bena D, Cimic A, Mourad M, Debelenko L, et al. Third-trimester placentas of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive women: histomorphology, including viral immunohistochemistry and in-situ hybridization. Histopathology 2020;77:994-9.
54. Katz D, Bateman BT, Kjaer K, Turner DP, Spence NZ, Habib AS, et al. The society for obstetric anesthesia and perinatology coronavirus disease 2019 registry: an analysis of outcomes among pregnant women delivering during the initial severe acute respiratory syndrome coronavirus-2 outbreak in the United States. Anesth Analg 2021;133:462-73.
55. Ko JY, DeSisto CL, Simeone RM, Ellington S, Galang RR, Oduyebo T, et al. Adverse pregnancy outcomes, maternal complications, and severe illness among US delivery hospitalizations with and without a coronavirus disease 2019 (COVID-19) diagnosis. Clin Infect Dis 2021;73:S24-31.
56. Laresgoiti-Servitje E, Cardona-Pérez JA, Hernández-Cruz RG, Helguera-Repetto AC, Valdespino-Vázquez MY, Moreno-Verduzco ER, et al. COVID-19 infection in pregnancy: PCR cycle thresholds, placental pathology, and perinatal outcomes. Viruses 2021;13:1884.
57. Liao X, Yang H, Kong J, Yang H. Chest CT findings in a pregnant patient with 2019 novel coronavirus disease. Balkan Med J 2020;37:226-8.
58. Liu S, Dzakpasu S, Nelson C, Wei SQ, Little J, Scott H, et al. Pregnancy outcomes during the COVID-19 pandemic in Canada, March to August 2020. J Obstet Gynaecol Can 2021;43:1406-15.
59. Papageorghiou AT, Gunier RB, Villar J. The link between

COVID-19 and preeclampsia. Am J Obstet Gynecol 2022;226:153-4.
60. Pirjani R, Rabiei M, Abiri A, Moini A. An overview on guidelines on COVID-19 virus and natural and assisted reproductive techniques pregnancies. Int J Fertil Steril 2020;14:264-71.
61. Ríos-Silva M, Murillo-Zamora E, Mendoza-Cano O, Trujillo X, Huerta M. COVID-19 mortality among pregnant women in Mexico: a retrospective cohort study. J Glob Health 2020;10:020512.
62. Rosenbloom JI, Raghuraman N, Carter EB, Kelly JC. Coronavirus disease 2019 infection and hypertensive disorders of pregnancy. Am J Obstet Gynecol 2021;224:623-4.
63. Ruggiero M, Somigliana E, Tassis B, Li Piani L, Uceda Renteria S, Barbara G, et al. Clinical relevance of SARS-CoV-2 infection in late pregnancy. BMC Pregnancy Childbirth 2021;21:505.
64. Savirón-Cornudella R, Villalba A, Esteban LM, Tajada M, Rodríguez-Solanilla B, Andeyro-Garcia M, et al. Screening of severe acute respiratory syndrome coronavirus-2 infection during labor and delivery using polymerase chain reaction and immunoglobulin testing. Life Sci 2021;271:119200.
65. Soto-Torres E, Hernandez-Andrade E, Huntley E, Mendez-Figueroa H, Blackwell SC. Ultrasound and Doppler findings in pregnant women with SARS-CoV-2 infection. Ultrasound Obstet Gynecol 2021;58:111-20.
66. Steffen HA, Swartz SR, Jackson JB, Kenne KA, Ten Eyck PP, Merryman AS, et al. SARS-CoV-2 infection during pregnancy in a rural midwest all-delivery cohort and associated maternal and neonatal outcomes. Am J Perinatol 2021;38:614-21.
67. Timircan M, Bratosin F, Vidican I, Suciu O, Tirnea L, Avram V, et al. Exploring pregnancy outcomes associated with SARS-CoV-2 infection. Medicina (Kaunas) 2021;57:796.
68. Trahan MJ, O'Farrell P, Mitric C, Desilets J, Bastrash MP, Malhame I, et al. 364 obstetrical and neonatal outcomes among pregnancies with SARS-CoV-2. Am J Obstet Gynecol 2021;224:S237.
69. Roffman J, Villarreal J, Pride R, Bazer O, Karmacharya R, Lerou P, et al. Assessing covid-19 effects on neurodevelopment (ACEND): preliminary findings in 12-month-old children exposed to maternal sars-cov-2 infection during pregnancy. Neuropsychopharmacology 2021;46:150-1.
70. Vousden N, Bunch K, Morris E, Simpson N, Gale C, O'Brien P, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: a national cohort study using the UK obstetric surveillance system (UKOSS). PLoS One 2021;16:e0251123.
71. Kathuria P, Khetarpal A, Singh P, Khatana S, Yadav G, Ghuman NK. Role of birth companion in COVID-19: indispensable for her and an auxiliary hand for us. Pan Afr Med J 2020;37:62.
72. Ahn KH, Kim HI, Lee KS, Heo JS, Kim HY, Cho GJ, et al. COVID-19 and vaccination during pregnancy: a systematic analysis using Korea National Health Insurance claims data. Obstet Gynecol Sci 2022;65:487-501.
73. Lassi ZS, Ana A, Das JK, Salam RA, Padhani ZA, Irfan O, et al. A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity. J Glob Health 2021;11:05018.
74. Pathirathna ML, Samarasekara BPP, Dasanayake TS, Saravanakumar P, Weerasekara I. Adverse perinatal outcomes in COVID-19 infected pregnant women: a systematic review and meta-analysis. Healthcare (Basel) 2022;10:203.
75. Huntley BJF, Mulder IA, Di Mascio D, Vintzileos WS, Vintzileos AM, Berghella V, et al. Adverse pregnancy outcomes among individuals with and without severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): a systematic review and meta-analysis. Obstet Gynecol 2021;137:585-96.
76. Wei WH, Mellis S, Geba GP, Sivapalasingam S, Jalbert JJ. Incidence and risk factors for COVID-related urgent medical visits among US patients diagnosed with COVID-19 in the outpatient setting. Pharmacoepidemiol Drug Saf 2021;30:22-3.
77. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. CMAJ 2021;193:E540-8.
78. Bastos SNMAN, Barbosa BLF, Cruz LGB, Souza RP, Silva Melo SSE, Luz CCBDS. Clinical and obstetric aspects of pregnant women with COVID-19: a systematic review. Rev Bras Ginecol Obstet 2021;43:949-60.
79. Jafari M, Pormohammad A, Sheikh Neshin SA, Ghorbani

S, Bose D, Alimohammadi S, et al. Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: a systematic review and meta-analysis. Rev Med Virol 2021;31:1-16.
80. Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, et al. Pregnancy with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases. Zhonghua Bing Li Xue Za Zhi 2020;49:418-23.
81. Pérez-López FR, Savirón-Cornudella R, Chedraui P, López-Baena MT, Pérez-Roncero G, Sanz-Arenal A, et al. Obstetric and perinatal outcomes of pregnancies with COVID 19: a systematic review and meta-analysis. J Matern Fetal Neonatal Med 2022;35:9742-58.
82. Wang H, Li N, Sun C, Guo X, Su W, Song Q, et al. The association between pregnancy and COVID-19: a systematic review and meta-analysis. Am J Emerg Med 2022;56:188-95.
83. Conde-Agudelo A, Romero R. SARS-CoV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. Am J Obstet Gynecol 2022;226:68-89.e3.
84. Garrido-Pontnou M, Navarro A, Camacho J, Crispi F, Alguacil-Guillén M, Moreno-Baró A, et al. Diffuse trophoblast damage is the hallmark of SARS-CoV-2-associated fetal demise. Mod Pathol 2021;34:1704-9.
85. Hecht JL, Quade B, Deshpande V, Mino-Kenudson M, Ting DT, Desai N, et al. SARS-CoV-2 can infect the placenta and is not associated with specific placental histopathology: a series of 19 placentas from COVID-19-positive mothers. Mod Pathol 2020;33:2092-103.
86. Berghella V, Boelig R, Roman A, Burd J, Anderson K. Decreased incidence of preterm birth during coronavirus disease 2019 pandemic. Am J Obstet Gynecol MFM 2020;2:100258.
87. Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. N Engl J Med 2014;370:2211-8.
88. Wastnedge EAN, Reynolds RM, van Boeckel SR, Stock SJ, Denison FC, Maybin JA, et al. Pregnancy and COVID-19. Physiol Rev 2021;101:303-18.
89. Goodnight WH, Soper DE. Pneumonia in pregnancy. Crit Care Med 2005;33:S390-7.
90. Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. Am J Obstet Gynecol 2004;191:292-7.
91. Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle east respiratory syndrome coronavirus (MERS-CoV) infection during pregnancy: report of two cases & review of the literature. J Microbiol Immunol Infect 2019;52:501-3.
92. Jamieson DJ, Theiler RN, Rasmussen SA. Emerging infections and pregnancy. Emerg Infect Dis 2006;12:1638-43.
93. Zhang L, Jiang Y, Wei M, Cheng BH, Zhou XC, Li J, et al. Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei province. Zhonghua Fu Chan Ke Za Zhi 2020;55:166-71.
94. Fan C, Lei D, Fang C, Li C, Wang M, Liu Y, et al. Perinatal transmission of 2019 coronavirus disease-associated severe acute respiratory syndrome coronavirus 2: should we worry? Clin Infect Dis 2021;72:862-4.
95. Ferrazzi E, Frigerio L, Savasi V, Vergani P, Prefumo F, Barresi S, et al. Vaginal delivery in SARS-CoV-2-infected pregnant women in Northern Italy: a retrospective analysis. BJOG 2020;127:1116-21.
96. Damar Çakırca T, Torun A, Hamidanoğlu M, Portakal RD, Ölçen M, Çakırca G, et al. COVID-19 infection in pregnancy: a single center experience with 75 cases. Ginekol Pol 2022;93:410-5.