Review Article

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A Meta-Analysis for Prevalence of Cesarean Section, Preterm Birth, Stillbirth, and Low Birth Weight Deliveries in Infected Pregnant Women with COVID-19

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ABSTRACT

Background: The aim of this meta-analysis was to estimate the prevalence of cesarean section (CS), preterm birth, stillbirth, and low birth weight deliveries (LBWD) in pregnant women with SARS-COV-2 infection.

Methods: All relevant studies were searched up to 30 February 2021.

Results: A total of 47 studies with 5970 infected pregnant women were included. There were 1010 CS, 55 stillbirths, 524 preterm birth, and 82 with LBWD. Pooled data showed that the prevalence of CS, preterm birth, stillbirth, and LBWD among women with SARS-COV-2 infection was 29.6% (95% CI 0.081-0.160), 2.1% (95% CI 0.081-0.160), 11.5% (95% CI 0.081-0.160), and 2.1% (95% CI 0.081-0.160), respectively. Stratified analysis revealed that these pregnancy outcomes among Asian women were higher than Caucasians.

Conclusion: Our combined data revealed that the CS prevalence (29.6%) was the highest followed by preterm birth (11.5%), stillbirth (2.1%), and LBWD (2.1%) among women with COVID-19.

Introduction

Following the recognition of coronavirus disease 2019 (COVID-19) in Wuhan, China in December 2019, pregnant women were reported to acquire the virus, termed SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), both in this and other regions in the country.[1-6] Initial reports suggested that clinical disease in most infected pregnant women was either non-existent or mild,[1,7] and significant maternal complications appeared to be rare. Similar to such previous coronavirus diseases as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS),[8] and some other pathogenic RNA respiratory viruses 9, there was no proven mother-to-neonate (vertical) transmission recognized at that time.[9,10] However, following the subsequent spread of COVID-19 to involve countries in the Western Hemisphere, Europe, and the Middle East, the situation changed. Reports of clinical disease among pregnant women became more frequent and the spectrum of complications and the severity of their infections appeared to become worse. These findings included the development of severe and critical pneumonia, thrombosis, cardiomyopathy, multiorgan disease, need for intensive care, and mechanical ventilation which, in a small number of cases, led to maternal deaths.[11-14] Besides the reports of increases in maternal morbidity and mortality, there were increasing descriptions of newborn infants who tested positive for SARS-CoV-2.[15-17] Some of whom were symptomatic. More recently, the occurrence of intrauterine maternal-fetal transmission of the virus across the placenta has been described in a small number of cases,[18-21] adding a new and worrisome aspect to SARS-CoV-2 infection occurring during pregnancy.

As the COVID-19 pandemic has spread throughout the world, some of the most challenging and complex questions concern the effects of the virus on the pregnant mother, fetus and neonate. Multiple clinical studies have now demonstrated that pregnant women with COVID-19 are at an increased risk for severe disease as well as such poor perinatal outcomes as preterm birth, stillbirth and LBW infants.[22] In this communication, we have conducted a meta-analysis of published studies to assist in estimating the prevalence of preterm births, stillbirths, CS and LBW infants occurring among pregnant women with SARS-COV-2 infection.

Materials and Methods

Search Strategies: We performed a meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (http://www.prismastatement.org). A comprehensive search on PubMed/MEDLINE, Google Scholar, EMBASE, Cochrane Library database, SciELO, Springer Link, Technology Journal database and Egyptian Knowledge Bank (EKB)Chinese Biomedical Database (CBD), China National Knowledge Infrastructure (CNKI) platforms, VIP, Chinese literature (Wan Fang) and China Science to identify all relevant studies on the incidence of preterm birth, stillbirth, cesarean section and low birth weight in women with SARS-COV-2 infection up to 30 February 2021. The following medical subject headings (MeSH) terms was used to search: (‘’COVID-19 virus disease’’ OR ‘’Severe Acute Respiratory Syndrome Coronavirus 2’’ OR ‘’SARS-CoV-2’’ OR ‘’2019 novel coronavirus infection’’ OR ‘’2019-nCoV infection’’ OR ‘’coronavirus disease’’ OR ‘’coronavirus disease-19’’ OR ‘’2019-nCoV disease’’ OR ‘’COVID-19 virus infection’’) AND (‘’Death’’ OR ‘’Mortality’’ OR ‘’Pregnancy Outcome’’ OR ‘’Fetus Outcomes’’ OR ‘’Outcome’’) AND (‘’Preterm Birth’’ OR ‘’Premature Birth’’) AND (‘’Stillbirth ‘’ OR ‘’Fetal Death’’ OR ‘’Fetal Demise’’) AND (‘’Cesarean Section’’ OR ‘’ C-section’’ OR ‘’Cesarean Birth’’ OR ‘’Surgical Delivery’’) AND (‘’neonate weight’’ OR ‘’low birth weight’’). We restricted our search to human studies and published articles in English and

Chinese. Moreover, a manually screened references of relevant articles for additional relevant articles was carried out by two authors. Articles included in the current meta-analysis had no obvious overlap of subjects with other studies.

Inclusion and Exclusion Criteria: The full text of primary studies was selected according to the following inclusion and exclusion criteria: 1) cross-sectional studies and consecutive case series; 2) studies on pregnancy outcomes among women with SARS-CoV-2 infection; 3) studies with sufficient data to calculate the odds ratio (OR) with 95% confidence interval (CI). The following exclusion criteria were also used: 1) insufficient data; 2) non-human or in vitro studies; 3) abstracts, case report, posters, editorials, reviews, conference papers, and previous meta-analyses and non-standard data presentation; and 4) overlapping and duplicated data.

Data Extraction: Two authors independently reviewed all titles and abstracts of the selected studies in the primary search in order to extract the necessary data into a standardized form. When the authors were not in agreement, a third author was involved to reach an agreement. According to the inclusion and exclusion criteria, two authors independently screened and selected the studies. Characteristics such as name of first author, year of publication, country, ethnicity, total numbers of women with SARS-COV-2 infection, preterm birth, stillbirth, CS and LBWD were data extracted from each study. If a duplicate publication was found or the same population was used in multiple studies, the publication with the larger sample size was included in the meta-analysis. We contacted the corresponding author through email for any missing data.

Statistical Analysis: The prevalence of CS, stillbirth, preterm birth, and LBWD in infected pregnant women with SARS-CoV-2 infection was assessed by odds ratios (ORs) with 95% confidence intervals (CIs). A between-study heterogeneity was tested using the Q-statistic test, which $P \leq 0.10$ indicated a significant between-study heterogeneity. In order to qualify the heterogeneity, the I^2 statistic was used (range of 0 to 100%: I^2 = 0-25%, no heterogeneity; I^2 = 25-50%, moderate heterogeneity; I^2 = 50-75%, large heterogeneity; I^2 = 75-100%, extreme heterogeneity). A random effect model (DerSimonian and Laird method) was adopted If between-study heterogeneity existed statistically; otherwise, affixed effect model (Mantel-Haenszel method) was used in the absence of heterogeneity. A visual inspection of the funnel plot was used to assess potential publication bias. Moreover, Egger's test was performed to assess the publication bias statistically, in which $P < 0.05$ was considered statistically significant. If the publication bias tests indicated bias existed, the Duval and Tweedie ''trim and fill'' method was used to adjust the bias.[23] Using Comprehensive Meta-Analysis (CMA) software version 2.0 (Biostat, USA), all of the statistical calculations were performed. Two-sided $P < 0.05$ were considered statistically significant.

Results

Our initial search yielded 819 studies up to 30 February 2021 as shown in Figure 1. After the removal of duplicate articles, the search retrieved 583 items. Upon a check of the article titles and abstracts, 379 articles were excluded due to irrelevance to the current meta-analysis scope. Of the remaining 204 articles that were assessed for eligibility in full-text screening, 157 did not meet inclusion criteria. Finally, a total of 47 studies [2-5, 24-64] with 2410 pregnant women with SARS-COV-2 infection were selected. The characteristics of studies included in the present meta-analysis are presented in table 1. Among them, there were 1010 CS, 55 stillbirth, 524 preterm birth, and 82 neonates with LWBD. The studies were performed in China (n = 16), United States (n = 12), France (n = 5), Spain (n = 2), Italy (n = 2), United Kingdom (n = 2), India (n = 2), Iran (n = 2), Denmark (n = 1), Netherlands (n = 1), Turkey (n = 1), and Kuwait (n = 1). All selected studies were published between 2020 and 2021 and in English and Chinese.

Data Synthesis

Cesarean Section: The summaries for the prevalence of CS among pregnant women with SARS-COV-2 infection are listed in Table 2.

In the current meta-analysis, there was significant heterogeneity for CS, thus a random-effect meta-analysis was selected to estimate its prevalence among pregnant women with SARS-COV-2 infection. Combined data revealed that the prevalence of CS was 29.6% (95% CI 0.223-0.380, Figure 2) overall. Stratified analysis by ethnicity showed that the prevalence of CS in the Asian and Caucasian women with SARS-COV-2 infection was 63.0% and 14.3%, respectively. Moreover, stratified analysis by country of origin revealed that the prevalence of CS was highest in China (74.4%) followed by Iran (45.3%), united kingdom (45.1%), Italy (33.9%), India (37.4%), Spain (22.1%), USA (16.6%) and France (3.6%).

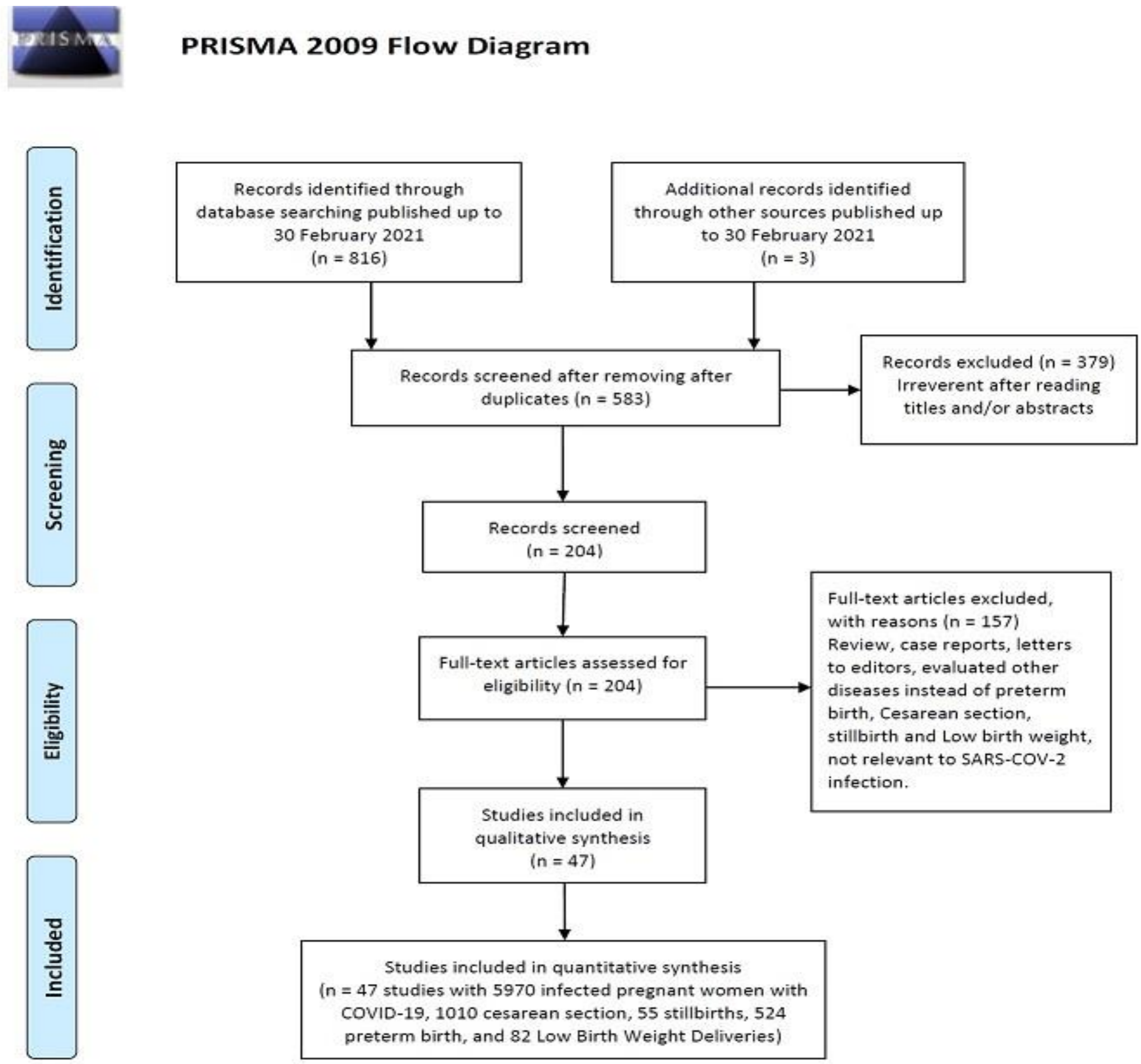

Figure 1. The study selection and inclusion process

Table 1. Details of included studies in the current meta-analysis

First Author	Country (Ethnicity)	Women with SARS-COV-2	Cesarean Section	Preterm Birth	Stillbirth	Low Birth Weight
Chen et al.,	China(Asian)	9	9	4	0	2
Chen et al.,	China(Asian)	5	3	0	0	0
Yu et al.,	China(Asian)	7	7	0	0	0
Wu et al.,	China(Asian)	23	18	3	3	0
Wu et al.,	China(Asian)	8	6	0	0	0
Liu et al.,	China(Asian)	15	10	3	0	0
Liu et al.,	China(Asian)	13	10	6	1	0
Liu et al.,	China(Asian)	19	18	2	0	1
Liu et al.,	China(Asian)	41	0	0	0	0
Zhu et al.,	China(Asian)	9	9	6	1	7
Khan et al.,	China(Asian)	17	17	3	0	3
Yan et al.,	China(Asian)	116	85	99	0	0
Zeng et al.,	China(Asian)	16	12	3	0	2
Zhang et al.,	China(Asian)	16	10	3	5	0
Li et al.,	China(Asian)	16	14	4	0	3
Liao et al.,	China(Asian)	10	0	1	0	0
Mahajan et al.,	India(Asian)	879	248	61	10	0
Nayak et al.,	India(Asian)	141	68	0	3	39
Hantoushzadeh et al.,	Iran(Asian)	9	6	8	5	7
Jenabi et al.,	Iran(Asian)	90	39	18	0	16
Ayed et al.,	Kuwait(Asian)	185	0	0	1	0
Sahin et al.,	Turkey(Caucasian)	533	0	0	1	0
Egerup et al.,	Denmark(Caucasian)	28	6	2	0	0
Ferrazzi et al.,	Italy(Caucasian)	42	18	11	0	2
Savasi et al.,	Italy(Caucasian)	77	22	12	0	0
Govind et al.,	UK(Caucasian)	9	8	2	0	0
Knight et al.,	UK(Caucasian)	427	42	66	3	0
Pereira et al.,	Spain(Caucasian)	60	5	2	0	0
Preze et al.,	Spain(Caucasian)	82	37	15	0	0
NVOG	Netherlands(Caucasian)	528	25	7	0	0
Sentilhes et al.,	France(Caucasian)	54	9	3	0	0
Kayem et al.,	France(Caucasian)	617	0	0	7	0
Hcini et al.,	France(Caucasian)	137	0	0	7	0
Vivanti et al.,	France(Caucasian)	100	16	20	0	0
Tsatsaris et al.,	France(Caucasian)	25	0	0	3	0
Blitz et al.,	USA(Caucasian)	13	6	5	2	0
London et al.,	USA(Caucasian)	68	22	9	1	0
Lokken et al.,	USA(Caucasian)	46	3	1	1	0
Qadri et al.,	USA(Caucasian)	16	0	1	0	0
Andrikopoulou et al.,	USA(Caucasian)	158	2	2	0	0
Pierce-Williams et al.,	USA(Caucasian)	64	24	19	0	0
Malhotra et al.,	USA(Caucasian)	131	41	41	0	0
Prabhu et al.,	USA(Caucasian)	70	32	11	0	0
Ahlberg et al.,	USA(Caucasian)	155	15	14	1	0
Breslin et al.,	USA(Caucasian)	43	8	1	0	0
Delahoy et al.,	USA(Caucasian)	598	15	56	0	0
Adhikar et al.,	USA(Caucasian)	245	65	0	0	0

Preterm Birth: The summaries for the prevalence of preterm birth among pregnant women with SARS-COV-2 infection are presented in Table 3. There was significant heterogeneity for preterm birth in the current meta-analysis, thus a random-effect meta-analysis was selected to estimate its prevalence among pregnant women with SARS-COV-2 infection. Pooled data indicated that the prevalence of preterm birth was 11.5% (95% CI 0.081-0.160, Figure 3) in overall.

Table 2. Summary for prevalence of cesarean section among pregnant women with COVID-19

Subgroup	Type of Model	Heterogeneity		Odds Ratio		Publication Bias	
		I^2 (%)	P_H	Prevalence	95% CI	P_{Beggs}	P_{Eggers}
Overall	Random	93.59	≤ 0.001	0.296	0.223-0.380	0.934	0.818
By ethnicity							
Asians	Random	90.28	≤ 0.001	0.630	0.491-0.750	0.672	0.009
Caucasian	Random	93.19	≤ 0.001	0.143	0.094-0.211	0.145	0.225
By country of origin							
China	Random	59.94	0.001	0.744	0.621-0.837	0.321	0.894
USA	Random	93.53	≤ 0.001	0.166	0.094-0.278	0.086	0.261
France	Random	83.28	≤ 0.001	0.036	0.009-0.133	0.462	0.022
Italy	Fixed	59.29	0.117	0.339	0.259-0.430	NA	NA
UK	Random	93.75	≤ 0.001	0.451	0.012-0.982	NA	NA
Spain	Random	94.48	≤ 0.001	0.221	0.032-0.711	NA	NA
India	Random	95.43	≤ 0.001	0.374	0.204-0.582	NA	NA
Iran	Fixed	41.01	0.193	0.453	0.357-0.552	NA	NA

Stratified analysis by ethnicity showed that the prevalence of preterm birth in the Asian and Caucasian women with SARS-COV-2 infection was 17.5% and 8.5%, respectively. Then, subgroup analysis by country of origin showed that the prevalence of preterm birth was highest in China (21.9%) followed by Iran (54.8%), Italy (19.8%), UK (15.6%), USA (10.3%), Spain (9.0%), India (2.2%), and France (2.1%).

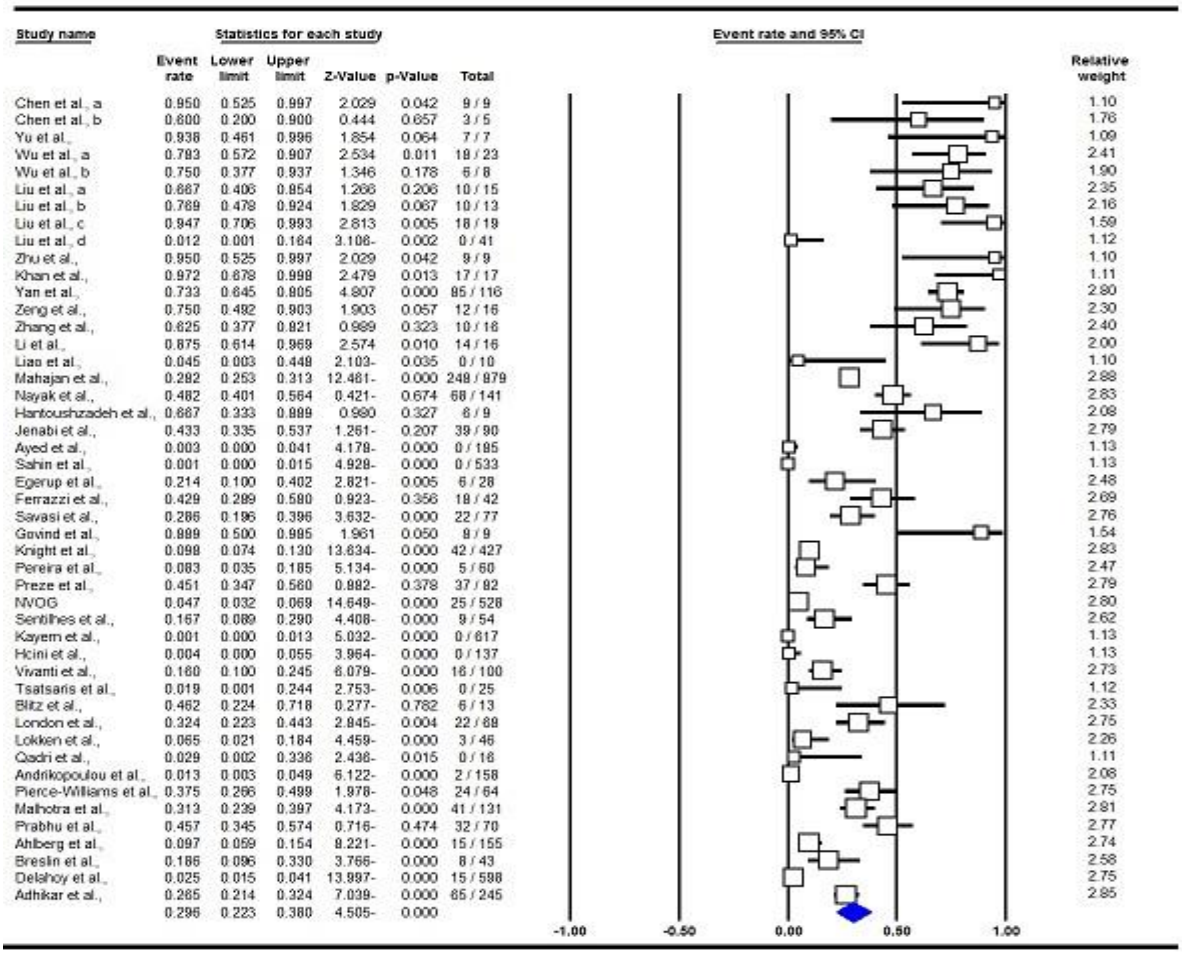

Figure 2. Forest plots for prevalence of cesarean section in infected pregnant women with COVID-19

Table 3. Summary for prevalence of preterm birth among pregnant women with COVID-19

Subgroup	Type of Model	Heterogeneity		Odds Ratio		Publication Bias	
		I^2 (%)	P_H	Prevalence	95% CI	P_{Beggs}	P_{Eggers}
Overall	Random	90.32	≤ 0.001	0.115	0.081-0.160	0.020	0.350
By ethnicity							
Asians	Random	92.83	≤ 0.001	0.175	0.083-0.330	0.102	0.611
Caucasian	Random	86.89	≤ 0.001	0.085	0.058-0.124	0.009	0.012
By country of origin							
China	Random	86.43	≤ 0.001	0.219	0.101-0.410	0.857	≤0.001
USA	Random	88.00	≤ 0.001	0.103	0.059-0.174	0.303	0.305
France	Random	86.30	≤ 0.001	0.021	0.003-0.125	0.806	0.012
Italy	Fixed	48.02	0.165	0.198	0.135-0.281	NA	NA
UK	Fixed	0.00	0.583	0.156	0.125-0.193	NA	NA
Spain	Random	82.88	0.016	0.090	0.016-0.378	NA	NA
India	Random	78.22	0.032	0.022	0.001-0.294	NA	NA
Iran	Random	90.05	0.002	0.548	0.040-0.973	NA	NA

Stillbirth: The summaries for the prevalence of stillbirth in the pregnant women with SARS-COV-2 infection are presented in Table 4. There was a significant heterogeneity for stillbirth, thus a random-effect meta-analysis was selected to estimate its prevalence among pregnant women with SARS-COV-2 infection in overall. Pooled data found that the prevalence of stillbirth was 2.1% (95% CI 0.013-0.034, Figure 4) in overall.

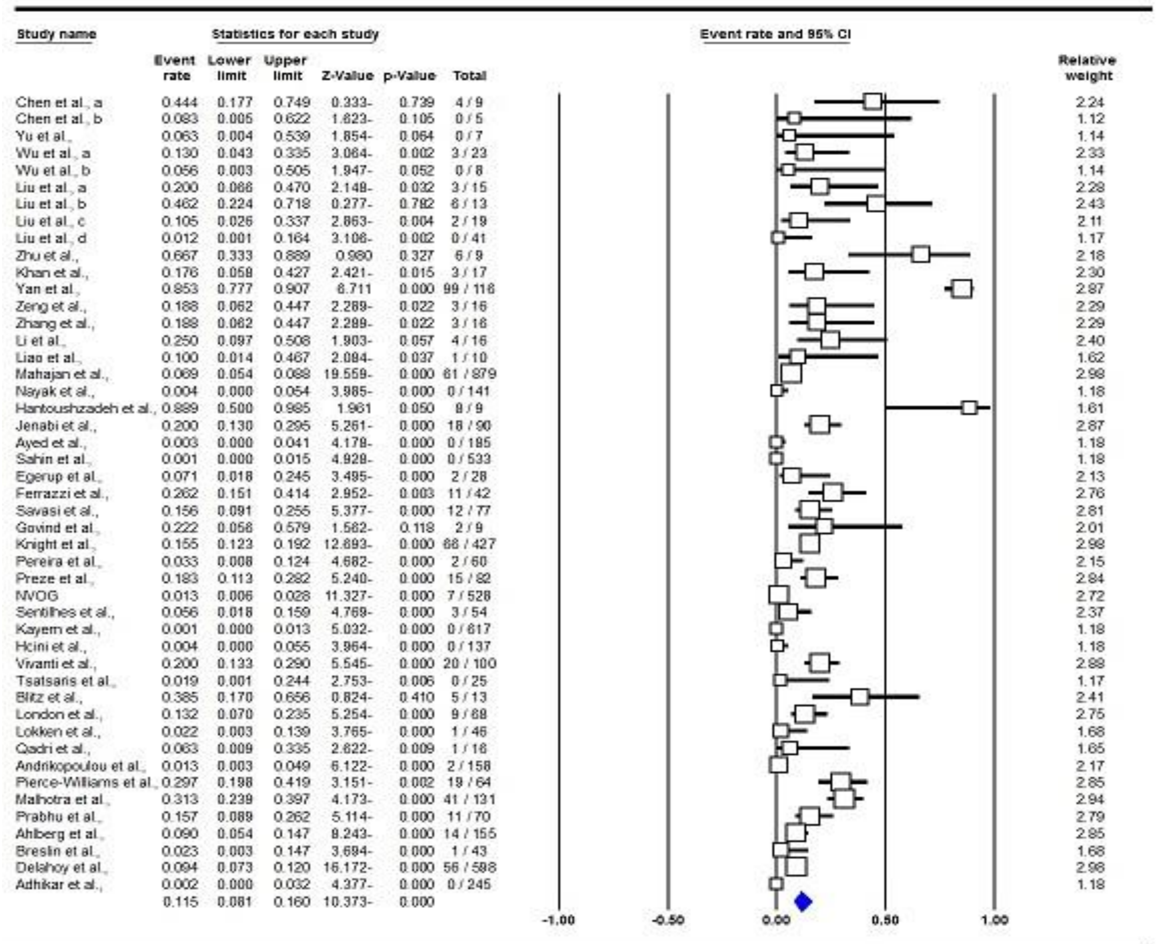

Figure 3. Forest plots for prevalence of cesarean section in infected pregnant women with COVID-19

Table 4. Summary for prevalence of stillbirth among pregnant women with COVID-19

Subgroup	Type of Model	Heterogeneity		Odds Ratio		Publication Bias	
		I^2 (%)	P_H	Prevalence	95% CI	P_{Beggs}	P_{Eggers}
Overall	Random	69.07	≤ 0.001	0.021	0.013-0.034	0.001	0.205
By ethnicity							
Asians	Random	74.66	≤ 0.001	0.044	0.020-0.098	0.131	0.785
Caucasian	Random	55.55	≤ 0.001	0.012	0.007-0.021	0.017	0.021
By country of origin							
China	Fixed	24.47	0.177	0.088	0.054-0.141	0.528	≤0.001
USA	Fixed	41.28	0.059	0.014	0.007-0.026	0.360	0.003
France	Random	76.49	0.002	0.027	0.009-0.081	0.806	0.837
Italy	Fixed	0.00	0.765	0.009	0.001-0.059	NA	NA
UK	Fixed	39.38	0.199	0.009	0.003-0.026	NA	NA
Spain	Fixed	0.00	0.877	0.007	0.001-0.048	NA	NA
India	Fixed	0.00	0.339	0.013	0.008-0.022	NA	NA
Iran	Random	91.62	0.001	0.088	0.001-0.951	NA	NA

Subgroup analysis by ethnicity showed that the prevalence of stillbirth in the Asian and Caucasian pregnant women with SARS-COV-2 infection was 4.4% and 1.2%, respectively. Then, subgroup analysis by country of origin showed that the prevalence of stillbirth was highest in China (8.8%) and Iran (8.8%) followed by France (2.7%), India (1.3%), USA (1.4%), Italy (0.9%), UK (0.9%), and Spain (0.7%).

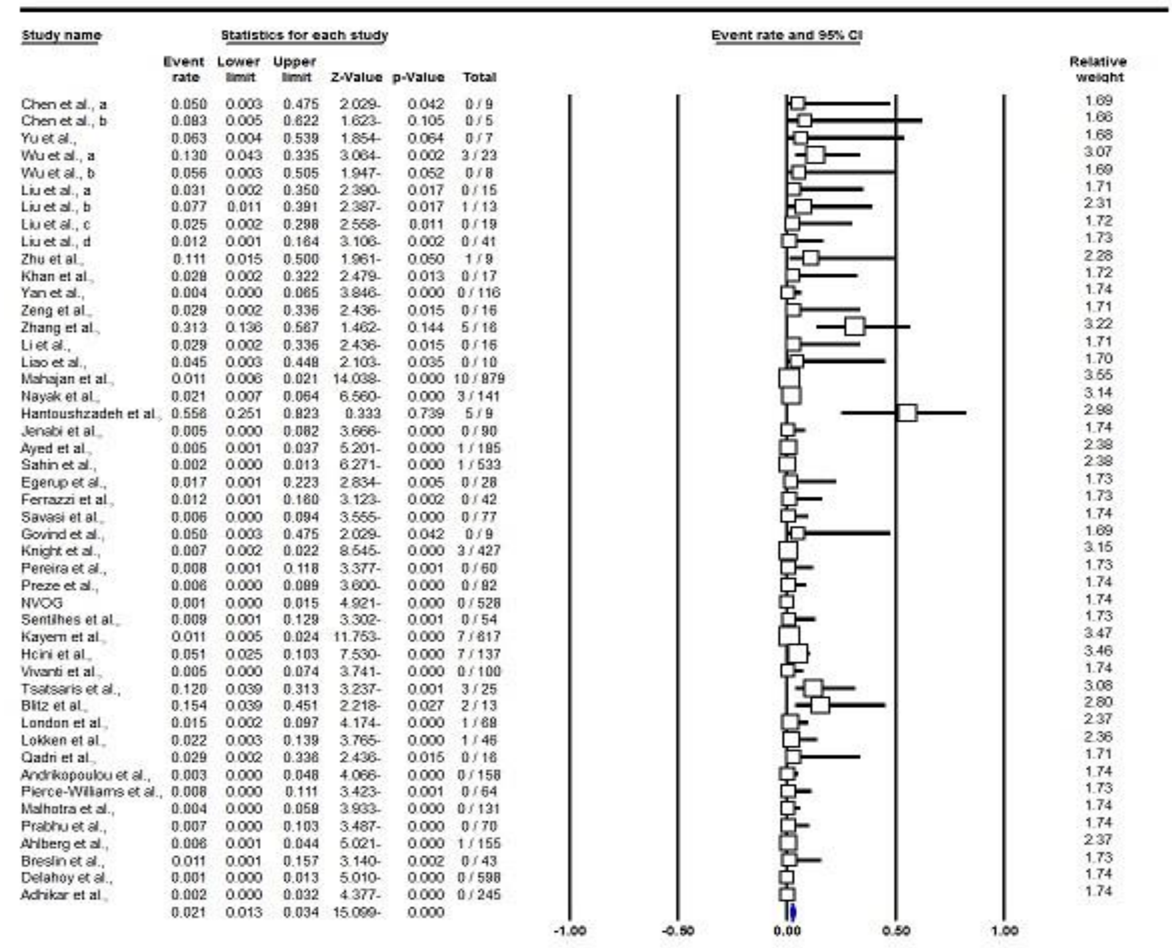

Figure 4. Forest plots for prevalence of stillbirth in infected pregnant women with COVID-19

Table 5. Summary for prevalence of low birth weight among pregnant women with COVID-19

Subgroup	Type of Model	Heterogeneity		Odds Ratio		Publication Bias	
		I^2 (%)	P_H	Prevalence	95% CI	P_{Beggs}	P_{Eggers}
Overall	Random	81.79	≤ 0.001	0.021	0.011-0.039	0.003	≤ 0.001
By ethnicity							
Asians	Random	76.14	≤ 0.001	0.092	0.048-0.168	0.432	0.005
Caucasian	Random	0.00	0.468	0.007	0.004-0.012	≤ 0.001	0.003
By country of origin							
China	Random	55.64	0.004	0.086	0.041-0.174	0.787	0.003
USA	Fixed	0.00	0.850	0.006	0.003-0.014	0.001	≤0.001
France	Fixed	0.00	0.592	0.005	0.001-0.016	0.027	0.043
Italy	Fixed	39.47	0.199	0.032	0.009-0.104	NA	NA
UK	Fixed	71.65	0.060	0.007	0.001-0.052	NA	NA
Spain	Fixed	0.00	0.877	0.007	0.001-0.048	NA	NA
India	Random	95.19	≤ 0.001	0.017	0.001-0.910	NA	NA
Iran	Random	90.72	0.001	0.440	0.049-0.923	NA	NA

Low birth weight Deliveries: The summaries for the prevalence of LBWD in pregnant women with COVID-19 are presented in Table 5. There was significant heterogeneity for LBWD, thus a random-effect meta-analysis was selected to estimate its prevalence among pregnant women with SARS-COV-2 infection overall. Pooled data found that the prevalence of LBWD was 2.1% (95% CI 0.011-0.039, Figure 5) overall.

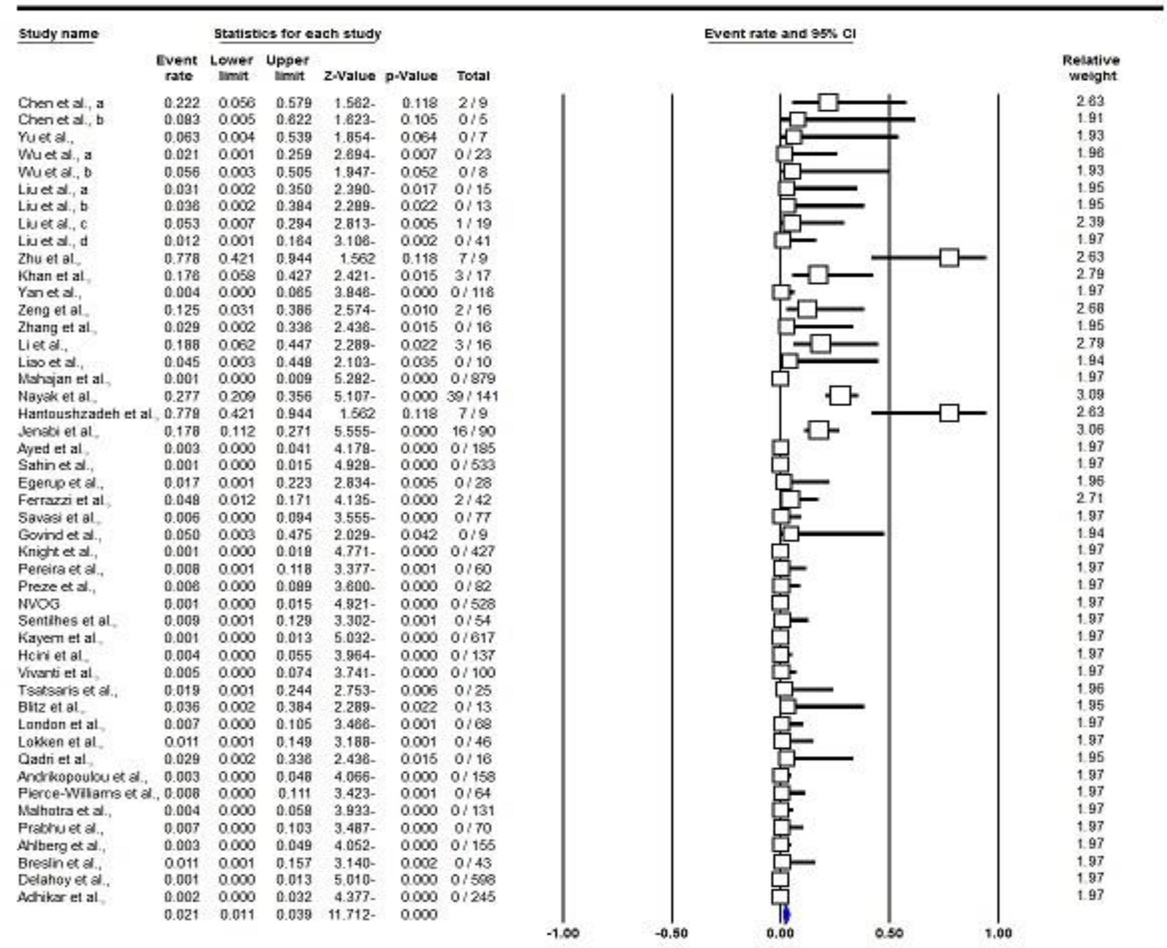

Figure 5. Forest plots for prevalence of low birth weight deliveries in infected pregnant women with COVID-19

Subgroup analysis by ethnicity showed that the prevalence of LBWD in the Asian and Caucasian pregnant women with COVID-19 was 0.92% and 0.07%, respectively. Then, subgroup analysis by country of origin showed that the prevalence of LBWD was highest in Iran (4.4%) followed by China (8.6%), Italy (3.2%), India (1.7%), UK (0.7%), Spain (0.7%), USA (0.6%), and France (0.5%).

Heterogeneity Test: There was significant heterogeneity among these studies for CS (I^2 = 93.59, $P_H \leq 0.001$), preterm birth (I^2 = 90.32, $P_H \leq 0.001$), stillbirth (I^2 = 69.07, $P_H \leq 0.001$), and LBWD (I^2 = 81.79, $P_H \leq 0.001$). Then, we assessed the source of heterogeneity by ethnicity and country of origin. We found that country of origin might be contribute to substantial heterogeneity for stillbirth, but not for stillbirth and LBWD (Tables 2-5).

Publication Bias: Both Begg's funnel plot and Egger's test were used to examine the publication bias of literatures. The Egger's test results and Begg's funnel plots showed an evidence of publication bias for preterm birth (P_{Beggs} = 0.020; P_{Eggers} = 0.350) and stillbirth (P_{Beggs} = 0.001; P_{Eggers} = 0.205), and LBWD (P_{Beggs} = 0.003; $P_{Eggers} \leq 0.001$), but not for CS (P_{Beggs} = 0.934; P_{Eggers} = 0.818). Thus, we used the Duval and Tweedie ''trim and fill'' method to adjust for possible publication bias in the current meta-analysis. Figure 6A-C showed the Duval and Tweedie nonparametric ''trim and fill'' methods funnel plot for preterm birth, stillbirth and LBWD. This method results did not change for the complications, suggesting that our combined data are reliable.

Discussion

Most pregnant infected women with SARS-CoV2 preferred early delivery by CS to avoid a prolonged labor, which may worsen COVID-19 for women and increase the risk of infection for the medical staff.[65,66] Dixon et al. found that the number of CS increased by 4.3% (95% CI 1.3-7.4; P = 0.015) in the United Kingdom between 1 April and 31, 2020.

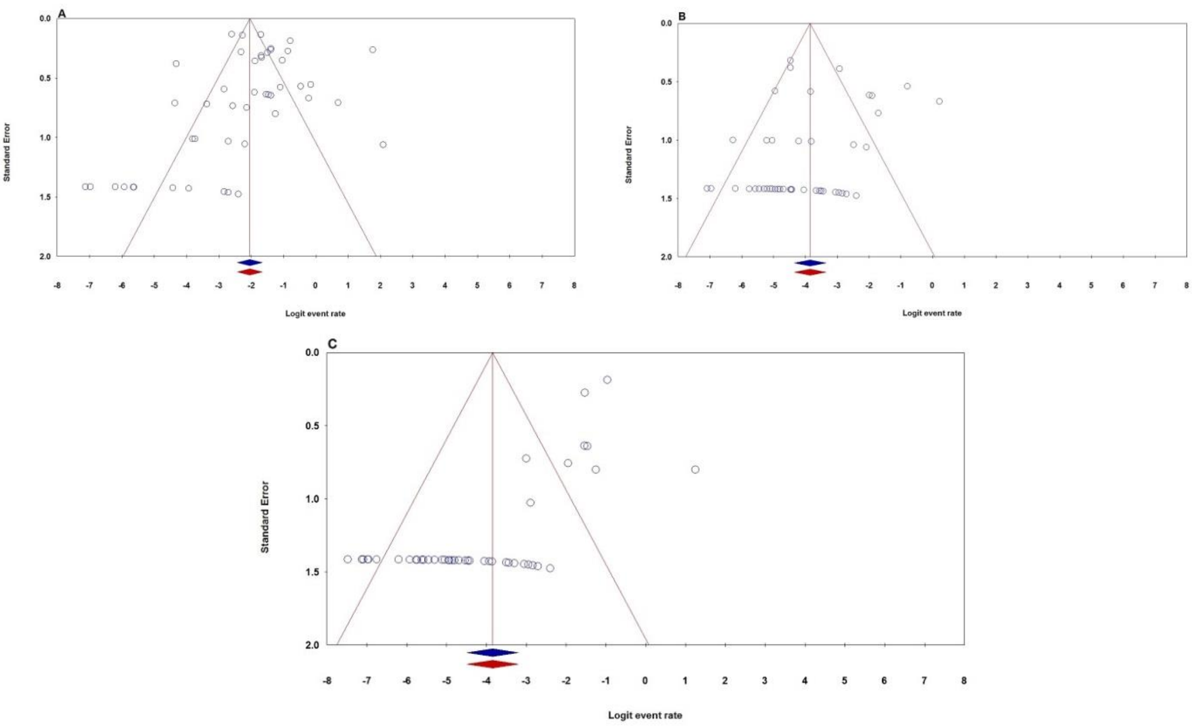

Figure 6. Begg's funnel plot for publication bias test for prevalence of preterm birth, stillbirth, and low birth weight deliveries in infected pregnant women with COVID-19

Moreover, their single-center study revealed a reduction in the frequency of administration of general anesthesia for all categories of CS during the COVID-19 pandemic, which might be associated with increased maternal morbidity and mortality.[67] Our data revealed that the prevalence of CS was 29.6% in women with SARS-CoV2 infection. Its prevalence in the Asian and Caucasian women with SARS-COV-2 infection was 63.0% and 14.3%, respectively. Khalil et al., in a meta-analysis based on 17 studies with 2567 pregnancies, reported that 48.3% of women with SARS-CoV2 have delivered by CS.[68] Malhotra et al., reported that there were no changes in CS rate during the COVID-19 pandemic in New York City. Their results revealed 31.3% of pregnant women with SARS-CoV-2 infection underwent of CS, which was not different from the expected average rate of 31% from previous years. Moreover, they reported the rate of CS in non-tested women was 31.4% and was 33.9% in woman with a negative test for SARS-CoV2.[59] However, Gao et al., in a meta-analysis based on 14 studies including 236 pregnant women with SARS-CoV2, reported that the prevalence of CS among these women was 65% (95% CI = 0.42-0.87, $P \leq 0.001$).[69] In another meta-analysis based on 13 studies, the pooled prevalence of reported CS was 88.0% (95% CI = 0.82-0.94).[70] A meta-analysis performed by Dubey et al. revealed that the frequency of CS performance was 72%.[71]

The impact of the SARS-CoV2 infection on timing of delivery is still unclear.[72] Several studies showed that preterm birth rates have been increased in pregnant women with SARS-CoV-2 infection.[60,61,73] A study from China reported a 46% preterm labor rate between 32 and 36 weeks of gestation in 10 women with SARS-CoV-2 infection.[27] The prevalence of preterm labor in normal pregnant women who are healthy and uninfected with any virus world-wide is approximately 11%, a metric that varies by ethnicity and country.[74] For example, two meta-analyses demonstrated that the prevalence of preterm delivery in Iran and Ethiopia was 9.2% and 10.48%, respectively.[75,76] Our pooled data showed that the preterm delivery in women with SARS-COV-2 infection was 11.5%. Stratified analysis by ethnicity showed that the prevalence of preterm birth in the Asian and Caucasian women with SARS-COV-2 infection was 17.5% and 8.5%, respectively. In the meta-analysis by Gao et al. that included 236 pregnant women with SARS-CoV2 infection, the frequency of preterm labor was 23% (95% CI 0.14-0.32; $P \leq 0.001$). Yang et al. reported that among pregnant women with SARS-CoV-2 infection the risk of preterm birth (OR 3.34, 95% CI 1.60-7.00) and CS (OR 3.63, 95% CI 1.95-6.76) was increased when compared with pregnant women without SARS-CoV-2 infection in China.[77]

The World Health Organization (WHO) has cautioned that COVID-19 occurring in pregnant women could worsen the global number of stillbirths,[78] with several studies reporting high rates of preterm birth and stillbirth in women with SARS-CoV-2 infection.[73] Khalil et al. compared the pregnancy outcomes at St George's University Hospital, London during the COVID-19 pre-pandemic and pandemic periods. Their results revealed that the incidence of stillbirth was significantly higher during the pandemic period than during the pre-pandemic period.[73] In the current meta-analysis, our pooled data showed that the incidence of stillbirth was 2.1% in women with SARS-CoV-2 infection. Subgroup analysis by ethnicity showed that its prevalence in the Asian and Caucasian pregnant women with SARS-COV-2 infection was 4.4% and 1.2%, respectively. Wald et al., indicated that the stillbirth rates were significantly increased during the pandemic (1.2% pre-pandemic vs. 7% pandemic).[79] Di Toro et al., in a meta-analysis based on 24 studies examining 1100 pregnancies demonstrated that the fetal and neonatal mortality risk in women with SARS-COV-2 infection was extremely low.[80]

LBW is one of the major public health problems, resulting in perinatal mortality of 15-20% of newborns worldwide.[81,82] However, its prevalence varies in different parts of the world with the highest being 28% in South Asia and the lowest 6% in East Asia and the Pacific region.[83] It is defined as absolute weight of < 2500 g regardless of gestational age.[84] Other pathogenic coronaviruses such as severe acute respiratory syndrome coronavirus (SARS-CoV), and Middle East respiratory syndrome coronavirus (MERS-CoV) are associated with significant rates of LBW in newborns from infected pregnant women.[49] Our pooled data showed that the prevalence of LBWD in women with SARS-COV-2 infection was 2.1%. In a meta-analysis, Dubey et al. analyzed 790 pregnant women with SARS-CoV-2 infection and found the frequency of LBW among their neonates to be 7% (95% CI 0.01-0.15). When examining case reports, the authors found that the rate of LBW was 35%.[71]

Some limitations of this meta-analysis should be taken into account. First, all of the included studies in this meta-analysis were performed in Caucasian and Chinese patients. Moreover, we found only studies published in English or Chinese language which might cause potential selection bias. Second, in this meta-analysis the heterogeneity was high. This may mean that the estimated prevalence is less reliable than would be expected. Third, publication bias can present a serious threat to the validity of conclusions this meta-analysis. This might be a limitation for meta-analysis of CS, stillbirth and LBW. Fourth, the sample size of some included studies to estimates the prevalence of stillbirths and low weight birth were small.

Conclusion

Our pooled data showed that the prevalence of CS, preterm birth, stillbirth, and LBWD among women with SARS-COV-2 infection was 29.6%, 2.1%, 11.5% and 2.1%, respectively. The prevalence of these pregnancy outcomes in the Asian women was higher than Caucasian infected pregnant women with COVID-19. Clinicians should be aware of the high prevalence of these obstetrical complications in pregnant women with SARS-COV-2 infection. Moreover, well-designed, large-scale and multicenter clinical studies are required to improve and validate these results.

Conflict of Interests

Authors have no conflict of interests.

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