Maternal and neonatal complications in pregnancy with COVID-19: a systematic review

Wisam Nabil Ibrahim
Qatar University
Fawziya Al-Baker
Qatar University
Sara Awwad
Qatar University
Saja A Abdallah
University of Birmingham Medical School
Abdulhadi H Al-Mazroea
Taibah University
Atiyeh M Abdallah
Qatar University
Amal Al-Haidose (amalah@qu.edu.qa)
Qatar University

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Abstract

The COVID-19 pandemic has had a profound impact on global health, leading to significant morbidity and mortality. Pregnancy can weaken the maternal immune response to the SARS-CoV-2 virus and increase the risk of severe adverse outcomes for both mother and fetus or newborn. Despite the well-known effects of viruses on pregnancy and the potential association with congenital anomalies, the impact of COVID-19 on pregnancy is still not fully understood. Here we systematically gathered and analyzed data from studies reporting the effects of maternal COVID-19 infection on mothers and their newborns. Through a comprehensive search of the PubMed, EMBASE, and Cochrane Library databases, 20 relevant studies were identified. Our analysis revealed that pregnant women with COVID-19 are at higher risk of morbidity and mortality and are more likely to require admission to the intensive care unit. Their newborns are also at increased risk of premature birth, low birth weight, and admission to neonatal intensive care unit. Our findings highlight the vulnerability of pregnant women and their newborns to COVID-19 complications and underscore the need for further research to better understand modes of neonatal SARS-CoV-2 transmission and the potential for congenital anomalies in early pregnancy infections.

INTRODUCTION

Coronaviruses belong to the family Coronaviridae and are characterized by their single-stranded, enclosed, and non-segmented RNA genomes. While many coronavirus infections in humans are mild and cause symptoms similar to the common cold such as fever, cough, and fatigue, some virus strains - such as Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV) - can result in severe respiratory illness and significantly impact public health [1, 2].

An initial outbreak of coronavirus-associated pneumonia was documented in Wuhan, China in December 2019, and after the virus disseminated rapidly both domestically and internationally, the World Health Organization (WHO) designated a novel coronavirus disease (Coronavirus Disease 19; COVID-19, caused by the new SARS-CoV-2 virus) on February 11, 2020 and declared it a pandemic on March 11, 2020 [3]. As of May 15, 2022, there were over 600 million cumulative confirmed cases of COVID-19 and 6 million reported deaths attributed to the SARS-CoV-2 virus [4].

Pregnant women are more susceptible to adverse outcomes from COVID-19, which represents a complex and incompletely understood phenomenon that depends on multiple factors including maternal immunity, gestational age, and the specific viral infection. During gestation, embryonic growth and development cause various physiological and anatomical adaptations that have both positive and negative impacts on maternal health [1, 5]. For instance, the alterations in lung capacity and increased oxygen demand of pregnancy can reduce maternal respiratory system tolerance to hypoxia and increase the risk of respiratory infections, including with SARS-CoV-2 [6]. Pregnancy-related changes in vascular permeability and vasodilation can promote the development of mucosal edema and reduce gas exchange efficiency, exacerbating the risk of respiratory compromise [7]. Furthermore, pregnancy is associated with changes in cell-mediated immunity, which can increase the susceptibility of pregnant women to various types of infections, including viral infections, and alter their response to SARS-CoV-2. Outcomes from viral infections during pregnancy therefore vary widely and depend on multiple factors including maternal immunity, gestational age, vaccination, and the specific viral infection, with respiratory morbidities ranging from mild to severe [8–10].

It is also important to consider the interplay between pregnancy and underlying health in the context of viral infections [11]. The presence of comorbidities in pregnancy such as diabetes and hypertension can further complicate and increase the risk of severe outcomes related to viral infections. These comorbidities are well established risk factors for infection in non-pregnant individuals and may lead to more severe infections in pregnant women. Diabetes and hypertension are associated with an increased risk of vertical transmission of SARS-CoV-2 to fetuses, as evidenced by the detection of the virus in placental tissue samples obtained in the second trimester; however, results from RT-PCR testing of amniotic fluid and vaginal wall samples were negative for the virus [12]. Nevertheless, SARS-CoV-2-infected pregnancies have been reported to be associated with more severe symptoms and increased fetal complications, including a significant reduction in placental volume and weight compared with non-infected pregnancies.

Fetal health is a critical concern during pregnancy and the potential impact of viral infections on fetal development must be thoroughly evaluated. The immature fetal immune system, including both the innate and adaptive arms, makes fetuses

particularly susceptible to the adverse effects of viral infections. Additionally, complement system and cytokine imbalances can interfere with fetal development and cause significant harm *in utero* [13, 14]. The pathophysiology of COVID-19 is particularly concerning in this context, as the virus is known to unbalance immune responses, including promoting the development of a “cytokine storm” (cytokine release syndrome), which can increase the risk of harm to both fetus and mother and may result in premature birth, abortion, and other fetal anomalies. The altered cytokine response to SARS-CoV-2 infection may also disrupt the normal inflammatory responses of pregnancy, increasing the risk of placental and fetal hypoxia, which can have significant consequences including decreased fetal growth and increased risk of premature birth, stillbirth, altered brain development, and consequent long-term cognitive and behavioral effects [15, 16]. Given these concerns, understanding the full impact of COVID-19 on fetal health is essential to develop strategies to mitigate the risk of harm to fetuses and mothers. It is important to thoroughly investigate the possibility of vertical transmission (VT) of the virus during pregnancy, labor, or shortly thereafter [17–19], and the evaluation of critical maternal and neonatal outcomes such as lifelong disability, sepsis, multiple organ failure, and death is essential to understand the full impact of COVID-19 on mothers and their children [20–22].

Other coronaviruses (e.g., SARS-CoV and MERS-CoV) are associated with moderate to severe morbidities in pregnant women including admission to the intensive care unit (ICU) and death. [17, 23]. However, the full impact of SARS-CoV-2 on pregnant women and their newborns during delivery is poorly understood [24]. Therefore, the objective of this systematic review was to comprehensively analyze all published literature on COVID-19 infection in pregnancy. The aim was to gather and assess all available clinical data on both the mother and fetus to determine the incidence of VT and to evaluate maternal and fetal indicators of morbidity and mortality in response to the infection. This analysis also sought to identify any potential complications associated with COVID-19 infection in pregnancy.

MATERIALS AND METHODS

Search Strategy

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement was followed, and the PRISMA_S checklist is included in **Supplementary Table S1** [25]. Four researchers (W.N.I., F.A.B., S.A., and S.A.A.) conducted a systematic literature search from inception until January 2023 of the PubMed, EMBASE, and Cochrane Library databases to identify relevant studies on COVID-19 in pregnancy. The search focused on maternal complications, VT, and outcomes of COVID-19-positive pregnancies using the keywords "pregnancy," "newborn," "COVID-19," and "vertical transmission". The primary objective was to determine evidence of VT of the virus from infected mothers to their newborns. The secondary objective was to assess the prevalence of maternal and neonatal complications including symptoms, mode of delivery, morbidity, and admission to the ICU. Newborns were evaluated for prematurity, low birth weight, and admission to the neonatal ICU (NICU). The study was registered with OSF Registries (identifier: DOI 10.17605/OSF.IO/EU75C).

Study selection

The main inclusion criterion was any article reporting the impact of COVID-19 during pregnancy. Records from other sources such as books, systematic reviews, guidelines, and other types of study were excluded. The remaining articles were reviewed after deleting duplicates, and studies were further excluded if the article was not fully within the scope of the study, selection bias was expected, or if the studies included unrelated records. Each record was screened by two authors to ensure eligibility. The shortlisting process was followed as described in the PRISMA flowchart (Fig. 1).

Quality assessment

The QUADAS-2 tool was used to assess the quality of the included studies in conjunction with primary data extraction to avoid bias in study selection (for example, study design and outcomes). The QUADAS tool is divided into four primary domains: patient selection, index test, reference standard, and flow and timing [26], where each domain is rated as a “low”, “high”, or “unclear” risk of bias. Quality assessment was performed by two authors and, in the case of discrepancy, a senior author was consulted.

Data extraction and statistical analysis

Using a pre-designed extraction sheet (Excel spreadsheet), two authors separately extracted data from the included articles. The extracted information included: author names, publication year, location, sample size, age, clinical presentation of COVID-19, maternal characteristics, neonatal parameters, characteristics, and neonatal COVID-19 complications. The McGrath et al. [27] method was used to estimate means and to standardize the measures among the selected studies (https://smcgrath.shinyapps.io/estmeansd/).

RESULTS

Identification and selection of records

A total of 3285 research articles were obtained from all databases using specific keywords, of which 518 met the inclusion criteria of being cohort studies. The remainder were excluded because they were systematic reviews, bibliographies, books, or guidelines or because they were duplicates. The remaining 271 articles were subjected for evaluation including availability of full access to the article, the scope of the study, records, and selection bias. Consequently, 250 articles were excluded. One article was later removed due to insufficient information related to the study. Finally, 20 articles were eligible for analysis. Quality assessment outcomes are shown in **Table S2** and Fig. 2. Patient selection had the highest risk of bias, as some articles were retrospective studies.

Study characteristics

The studies were published between 2020 and January 2023 and included 31,317 participants from different countries. 4399 women had confirmed COVID-19 (14%) by testing, while 26,918 women were negative on COVID-19 testing (86%). The number of participants and mean age varied in each study, although the mean age of COVID-19 patients and controls were relatively similar (30.4 and 29.6 years, respectively). The study details are shown in Table 1.

Table 1
Demographics of the included studies.

	Reference	Country	Study design	Study duration (months)	Women positive for COVID-19			Women negative for COVID-19			
					Patient number	Age		Patient number	Age		Total patients
						Mean	SD		Mean	SD	
1	Villar et al. 2021 [28]	Multiple	Prospective	8	706	30.2	6.1	1424	30.2	6.1	2130
2	Metz et al. 2021 [29]	USA	Retrospective	5	1219	29	6.3	0			1219
3	Edlow et al. 2020 [30]	USA	Prospective	4	64	31.6	5.6	63	33.9	5.4	127
4	Oncel et al. 2021 [31]	Turkey	Retrospective	4	125			0			125
5	Salvatore et al. 2020 [32]	USA	Prospective	3	78			0			78
6	Moreno et al. 2020 [33]	Jamaica	Retrospective	2	19	31.7	6.7	0			19
7	Antoun et al. 2020 [34]	UK	Prospective	3	23	29	2.9	0			23
8	Pirjani et al. 2020 [35]	Iran	Prospective	7	66	30.97	6.38	133	28.79	6.42	199
9	Carrasco et al. 2021 [36]	Spain	Prospective	5	105	34	1.7	0			105
10	Gupta P et al. 2021 [37]	India	Retrospective	3	108	24.7	2.4	3057	25.1	2.6	3165
11	Remaeus K et al. 2020 [38]	Sweden	Retrospective	1	67	32	5.3	0			67
12	Dumitriu et al. 2021 [39]	USA	Retrospective	1	100	29.7	2.4	0			100
13	Prabhu M el al. 2020 [40]	USA	Prospective	1	70	31.2	2.5	605	34	1.1	675
14	WAPM working group 2020 [41]	Multiple	Prospective	3	388	32.2	6.1	0			388

	Reference	Country	Study design	Study duration (months)	Women positive for COVID-19			Women negative for COVID-19			
15	Yang R et al. 2020 [42]	China	Retrospective	3	65			11013			11078
16	Solis-Garcia et al. 2020 [43]	Spain	Prospective	3	73	33.3	2.3	0			73
17	Hcini N et al. 2020 [44]	France	Prospective	6	137	25.4	2.1	370	25.4	1.8	507
18	Seaton L et al., 2023 [45]	USA	Retrospective	1.5	638	30.3	5.9	8345	30.1	6	8983
19	Adam A. et al., 2022 [46]	Romania	Retrospective	1	31	26.7	4.5	0			31
20	Crovetto F. et al., 2022 [47]	Spain	Prospective	2.5	317	33.2	2.3	1908	33.2	2.3	2225
	Total				4399			26918			31317

Analysis outcome

In pregnant women with COVID-19, reported symptoms included cough (22%; the most common symptom) followed by fever (21%) and shortness of breath or dyspnea (13%). These three symptoms were reported in most of the studies. By contrast, muscle ache or myalgia (9%), vomiting (5%) and diarrhea (4%) were less common in infected participants in most studies. The clinical presentations of infected pregnant women are presented in Fig. 3.

Figure 4 compares prognostic indicators for women with infected and non-infected pregnancies including admission to ICU, morbidity, and mortality. Most studies reported an increased risk of admission to ICU for COVID-19 pregnancies. There was a slight increase in mortality in infected mothers, and morbidity was higher in COVID-19 patients, indicating that morbidities such as diabetes or hypertension were higher in infected pregnancies.

Cesarian deliveries were reported in 19 of 20 studies for women positive for COVID-19 (all except Pirjani et al. [35]). In the systematic analysis, there appeared to be a slight increase in the percentage of cesarian deliveries in mothers infected with SARS-CoV-2 compared with non-infected mothers. Differences in delivery mode according to the infection status are presented in Fig. 5.

An analysis of perinatal complications (Fig. 6) showed an increase in the rates of preterm birth, fetal distress, low birth weight, and admissions to the NICU in neonates of mothers testing positive for COVID-19. Mortality was slightly higher in neonates from mothers who tested positive for COVID-19 (4%) compared with mothers testing negative for COVID-19 (2%). This might indicate that maternal COVID-19 infection is associated with fetal distress and death. However, this observation was based on only a few studies, as most did not report information regarding NICU admission and mortality in pregnancies without COVID-19 infection.

In the pooled analysis, COVID-19 was negative in 98.84% of neonates and positive in 1.14% of neonates up to 15 days post-delivery. In all studies, confirmation of COVID-19 positivity was by RT-PCR laboratory testing based on pharyngeal swabbing. Nevertheless, VT of COVID-19 infection was not evident in the majority of neonates. Table 2 summarizes the results of neonatal infections with COVID-19 in this analysis.

Table 2
Neonatal results for COVID-19.

	Reference	Positive COVID-19 at birth	Positive COVID-19 1–15 days	Negative for COVID-19	Number of neonates tested
1	Villar et al. 2021 [28]	0	54	362	416
2	Metz et al. 2021 [29]	0	118	1151	1269
3	Edlow et al. 2020 [30]	0	0	77	77
4	Oncel et al. 2021 [31]	0	4	121	125
5	Salvatore et al. 2020 [32]	0	0	120	120
6	Moreno et al. 2020 [33]	0	0	21	21
7	Antoun et al. 2020 [34]	0	0	20	20
8	Pirjani et al. 2020 [35]	1	0	42	43
9	Carrasco et al. 2021 [36]	0	1	104	105
10	Gupta P et al. 2021 [37]	0	0	108	108
11	Remaeus K et al. 2020 [38]	0	3	65	68
12	Dumitriu et al. 2021 [39]	0	2	99	101
13	Prabhu M el al. 2020 [40]	0	0	71	71
14	WAPM working group 2020 [41]	1	0	250	251
15	Yang R et al. 2020 [42]	0	0	11078	11078
16	Solis-Garcia et al. 2020 [43]	0	1	72	73
17	Hcini N et al. 2020 [44]	0	4	104	108
18	Seaton L et al., 2023 [45]	0	0	N/A	N/A
19	Adam A. et al., 2022 [46]	0	0	N/A	N/A
20	Crovetto F. et al., 2022 [47]	0	0	2225	2225
	Total	2	187	16090	16279
	Percentage	0.01%	1.14%	98.84%	

DISCUSSION

Pregnancy induces numerous anatomical and physiological changes including alterations to the immune system, which may affect the body's response to infections. Specifically, the immune system adapts to tolerate the fetus, leading to a state of relative immunosuppression [48, 49]. This altered immune response might influence the susceptibility to, and severity of, respiratory viral infections like COVID-19, potentially exacerbating maternal and fetal complications.

Angiotensin-converting enzyme 2 (ACE2) has been identified as the main receptor for SARS-CoV-2. Increased expression of ACE2 has been observed in pregnant women, which might contribute to their susceptibility to the virus. Furthermore, pregnancy has been associated with increased levels of certain pro-inflammatory cytokines that might exacerbate the cytokine storm seen in

severe COVID-19, leading to critical complications such as acute respiratory distress syndrome (ARDS) and multi-organ failure. In this systematic review, we analyzed 20 articles from nine countries spanning Africa, Asia, Europe, and North America. The average age of women diagnosed with COVID-19 during pregnancy did not differ significantly from that of non-infected pregnant women (30.4 and 29.6 years, respectively). It is worth noting that COVID-19 infections are more common in older individuals or those with chronic illnesses or obesity [50].

As demonstrated in the pooled sample, the most common symptoms experienced by pregnant women with COVID-19 infection were similar to those experienced by the general population. These symptoms included shortness of breath, fever, and cough, which were reported in over 56% of pregnancies, while vomiting, diarrhea, and myalgia were less commonly described in the pooled sample [51]. We found that more pregnant women were admitted to the ICU and experienced increased morbidities, consistent with other studies [52]. Since infected mothers had more morbidities, it was difficult to attribute these admissions solely to COVID-19, as maternal ICU admissions are also common in mothers with preeclampsia, gestational diabetes, hypothyroidism, and placenta previa. COVID-19 might exacerbate the severity of these disorders; however, this observation requires further clarification. A Swedish study of data extracted from the Swedish National Quality Registry reported that pregnant women with COVID-19 had a five-fold increased risk of being admitted to the ICU and a four-fold increased risk of intubation compared with non-pregnant women of the same age [53].

We found that maternal mortality among COVID-19 pregnancies was higher than in non-infected mothers, consistent with previous reports. This observation highlights the potential risks and complications associated with COVID-19 during pregnancy and the importance of continued research, preventative measures, and targeted treatment strategies for pregnant women contracting the disease [54, 55]. In a large cohort study in the USA, there was a reported an increase in maternal mortality from 19 per 100,000 before the pandemic to 25.5 per 100,000 during the pandemic, implicating COVID-19 in maternal mortality and underscoring the importance of implementing effective preventative measures and providing appropriate care for pregnant women during these challenging times [56]. Another report from Wuhan, China detected no significant increase in maternal mortality during the COVID-19 pandemic [57]. These discrepancies in observed maternal mortality in different regions may be influenced by several factors including genetics, local healthcare practices, and the demographics of the study population.

During pregnancy, hormonal changes can affect various aspects of a woman's immune system. For instance, increased progesterone levels are thought to suppress immune responses, which may contribute to the severity of respiratory viral infections like COVID-19. Elevated estrogen levels can also affect immune cell function and cytokine production, potentially influencing the body's response to SARS-CoV-2 infection [58]. Moreover, pregnant women experience physiological adaptations in their respiratory systems including an increase in tidal volume, minute ventilation, and oxygen consumption, which can reduce functional residual capacity and increase susceptibility to respiratory infections [58, 59]. Consequently, pregnant women might experience more severe respiratory distress during COVID-19 infection, increasing their risk of complications.

One possible explanation for the discrepancy in maternal mortality rates between different regions could be related to the prevalence of particular viral strains. Indeed, some SARS-CoV-2 strains may cause more severe disease than others, and the distribution of these strains can vary geographically. Additionally, variations in public health measures, access to healthcare, and treatment practices might also impact maternal mortality rates during the pandemic. Understanding these diverse factors will help inform the development of effective preventative measures, targeted treatment strategies, and evidence-based guidelines for the management of COVID-19 in pregnant women.

In the pooled sample, pregnancies with confirmed COVID-19 infection had higher rates of cesarean deliveries compared with non-infected pregnancies. This might be due to the increased morbidity rates in infected mothers or the higher observed incidence of neonatal complications. In another retrospective study of 2,474 pregnancies, there was no significant increase in cesarean delivery rates after controlling for variables such as hypertension or diabetes, suggesting that the cause of our observation of increased cesarean deliveries might be due to comorbidities [60]. In some studies, pregnancies with severe COVID-19 infection were at higher risk of maternal distress and hypoxia, which might increase the need for cesarean delivery [57].

Vertical transmission is defined as the direct transmission of pathogens, such as viruses or bacteria, from mothers to embryos, fetuses, or babies during pregnancy, delivery, or immediately after labor through breastfeeding. The study of VT is important for

understanding the potential risks and consequences of maternal infections on newborn health and development [61]. The potential for VT depends on the specific pathogen involved as well as the timing and route of transmission. Some infections, like cytomegalovirus (CMV), Zika virus, and rubella, cause congenital infections, crossing the placental barrier to infect the fetus during pregnancy and resulting in congenital abnormalities, developmental delays, or other complications [41, 42]. We could not confirm VT in our analysis, as most of the neonatal pharyngeal swabs were negative for COVID-19, although some might have had elevated levels of IgM antibodies against the virus [57]. Interestingly, some neonates who tested positive for COVID-19 had normal Apgar scores and no evident abnormalities apart from low lymphocyte counts and abnormal liver function tests. Only a very small percentage of newborns were infected at birth, 0.01% of the total newborns. Most reported neonatal infections occurred in the days following birth and prior to hospital discharge, accounting for approximately 1.14% of total neonates. This finding suggests that transmission could occur through breastfeeding or other postnatal interactions between the infected mother and the newborn. Further studies are now needed to confirm the specific routes of transmission and to establish guidelines for safe breastfeeding and postnatal care practices for mothers with COVID-19.

Breast milk provides essential nutrients and immune factors that support the infant's growth and development while protecting against pathogens. Therefore, it is crucial to carefully balance the risk of viral transmission with the benefits of breastfeeding. Studies investigating the presence of SARS-CoV-2 in breast milk have reported mixed results. Some studies have detected the virus in breast milk samples from infected mothers, while others have not [62–64]. The risk of transmission through breastfeeding remains uncertain, and further research is needed to determine whether SARS-CoV-2 can be consistently transmitted via this route.

SARS-CoV-2 may also undergo postnatal transmission via respiratory droplets from the mother during close contact or contact with contaminated surfaces in the environment. Implementing precautions such as wearing masks, practicing hand hygiene, and maintaining a clean environment can help to minimize the risk of postnatal transmission. Current WHO and Centers for Disease Control and Prevention (CDC) guidelines recommend that mothers with COVID-19 continue breastfeeding while taking appropriate precautions including wearing a mask while breastfeeding, practicing hand hygiene before and after touching the infant, and cleaning any surfaces that may have come into contact with respiratory secretions [65].

In several studies documenting neonatal infections with COVID-19, certain infants exhibited not only abnormal blood test results but also developed severe complications such as disseminated intravascular coagulation and multiple organ failure, ultimately leading to fatalities [52]. Considering these observations, it is crucial not to dismiss the potential for vertical maternal-fetal transmission, as the fetus and neonate might be affected by the mother's infection, which might be subclinical. A more comprehensive understanding of VT and its impact on neonatal health is required.

Interestingly, no congenital anomalies were reported in neonates born to mothers infected with COVID-19 in the examined studies [65–67]. Furthermore, the exact timing of neonatal COVID-19 infection remains uncertain, as it is unclear whether the infection occurred *in utero*, during delivery, or immediately after labor. This observation underscores the need for further research to ascertain the mode of VT.

Despite the relatively low risk of neonatal infection and the lack of congenital anomalies, it remains crucial to implement appropriate protective measures for mothers who test positive for COVID-19 at the time of delivery. Employing proper hygiene procedures and aseptic techniques during delivery is vital. Mothers should be advised to reduce close contact with their infants by utilizing personal protective equipment during interactions such as breastfeeding and skin-to-skin contact [65].

Early studies indicated that the pandemic period was characterized by a significant decrease in premature births [68]. Our findings suggest that 19% of pregnancies complicated by COVID-19 infection were associated with premature birth, compared with 9% in non-infected pregnancies. Consistent with this, neonates born to infected mothers were more likely to have low birth weight, increased chances of NICU admission, and higher mortality rates compared with those born to mothers negative for COVID-19 (Fig. 6). However, most of these newborns tested negative for the virus, and, in many cases, the cause of death was attributed to other known risk factors for neonatal mortality such as prematurity, low birth weight, asphyxiation, and distress.

It remains crucial to identify high-risk pregnancies and regularly monitor them for any signs of COVID-19. Standardizing monitoring for all pregnant women entering inpatient or outpatient facilities is also essential, along with the careful management of all suspected and confirmed COVID-19 cases. Strict maternal and neonatal monitoring should be implemented when infection is confirmed.

Our findings of increased maternal and neonatal morbidity and mortality are consistent with the published literature. Although COVID-19 appears to have a minor direct impact on infant mortality, there is still a need for research to gather more data to corroborate these findings. A comprehensive understanding of the pathophysiological processes contributing to maternal and fetal mortality is crucial for developing effective preventive strategies against these outcomes in pregnant women who test positive for COVID-19.

The limitations of this study include the analysis of a limited number of studies and potential weaknesses in the included studies such as study quality and possible methodological biases, as well as limited clinical data on maternal or fetal health. More studies are needed to examine comprehensive parameters of neonatal wellbeing during and after labor. This might include assessing neonatal conditions immediately after delivery, such as estimating the rates of neonates small for gestational age (SGA) and evaluating Apgar scores. More studies with complete biodata would enhance the analytical power to draw robust conclusions about neonates born to infected mothers. Multivariate analyses and controlling for covariates that contribute to prematurity, low birth weight, and other neonatal complications are essential. Moreover, controlling for maternal confounding factors, such as chronic morbidities and their severity, is necessary to confirm the association between maternal complications and COVID-19.

CONCLUSIONS

In conclusion, we identified 20 studies evaluating pregnant women with COVID-19 and their newborns. COVID-19 infection had a significant impact on maternal and fetal morbidity and mortality and was detected in 1.14% of newborns. Preterm births and admission to ICU were reported in some cases; however, the extent to which this was related to the clinical course of the disease remains unclear. Occasional but serious complications of infection affect both mothers and newborns. The timing and rate of infection (intrauterine, during, or after delivery) were not reported in most of the studies so more research is needed to better understand the relationship between COVID-19 and pregnancy outcomes.

Declarations

- **Ethics approval and consent to participate: Not applicable**
- **Consent for publication: Not applicable**
- **Availability of data and materials:** The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.
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Figures

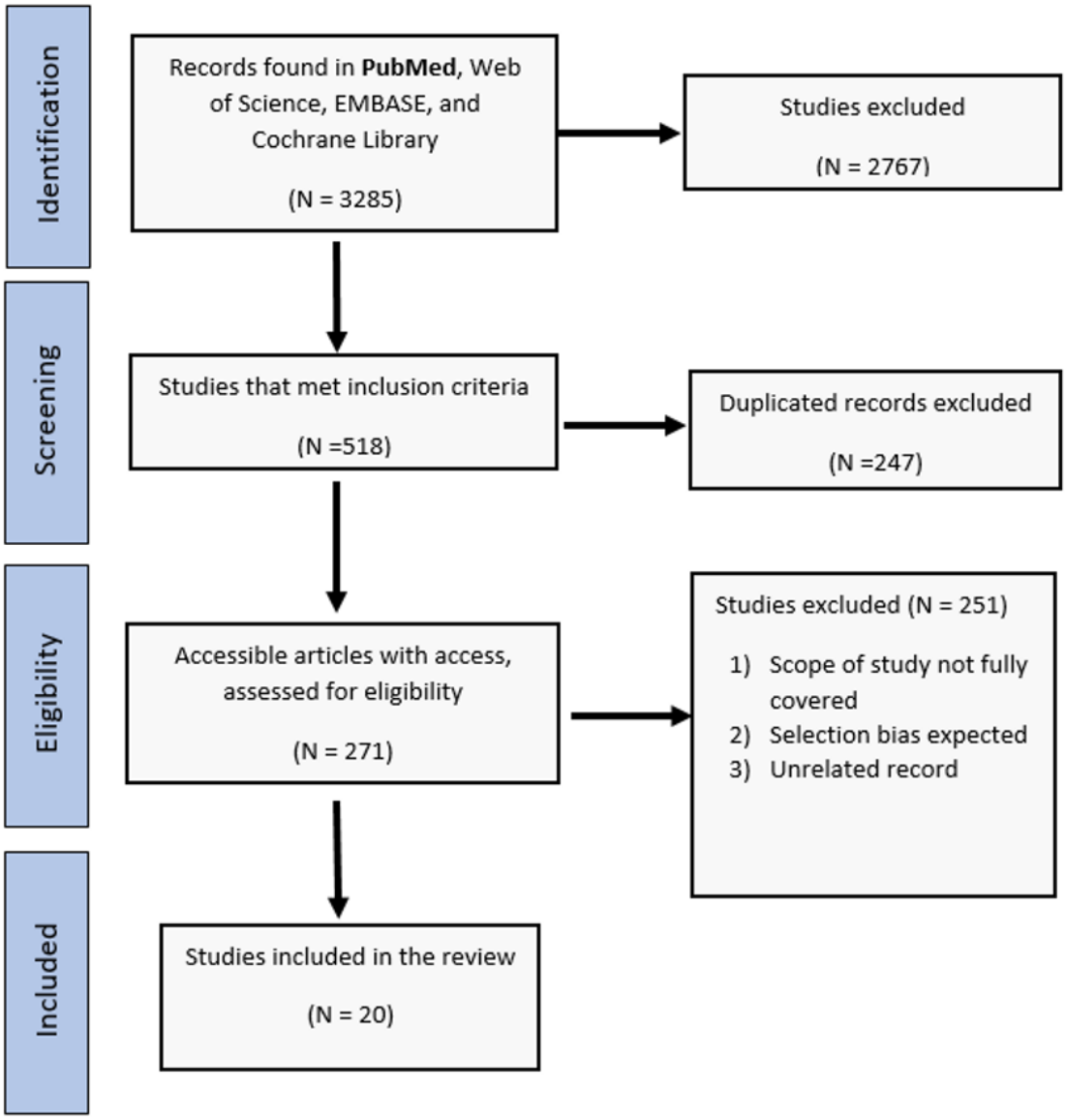

Figure 1

PRISMA flowchart of the literature review.

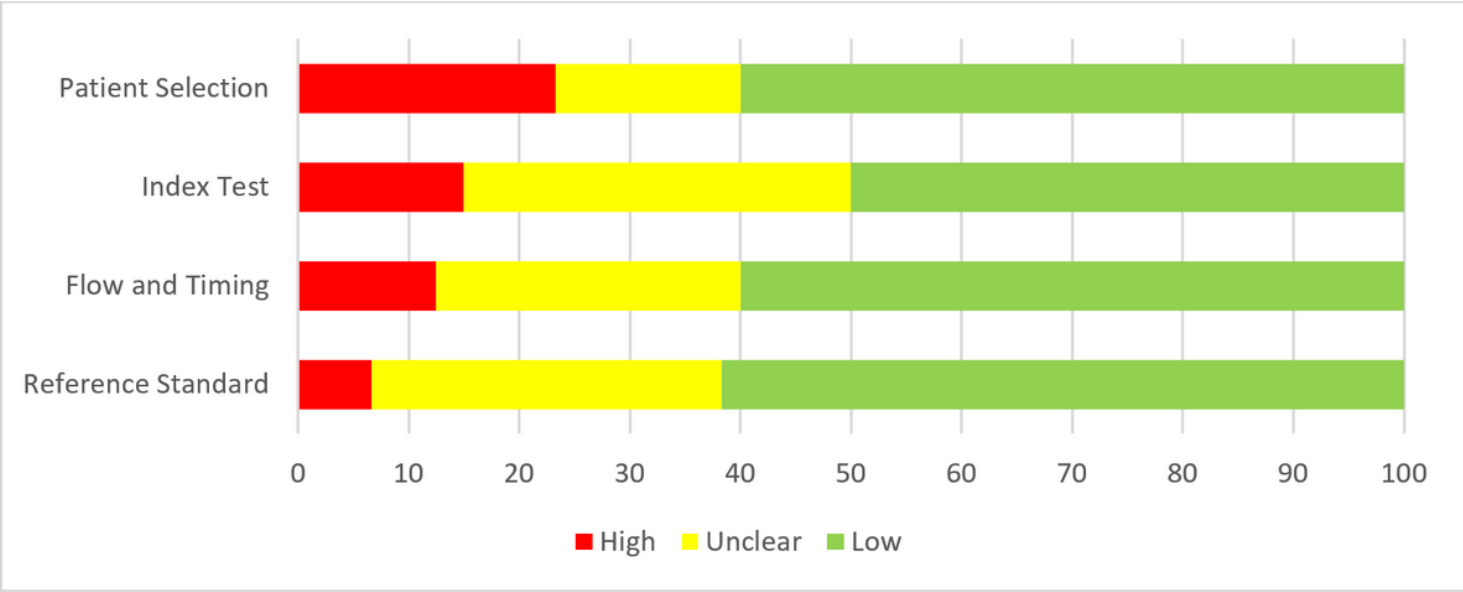

Figure 2

Outcome of the QUADAS-2 quality assessment for the 20 included studies.

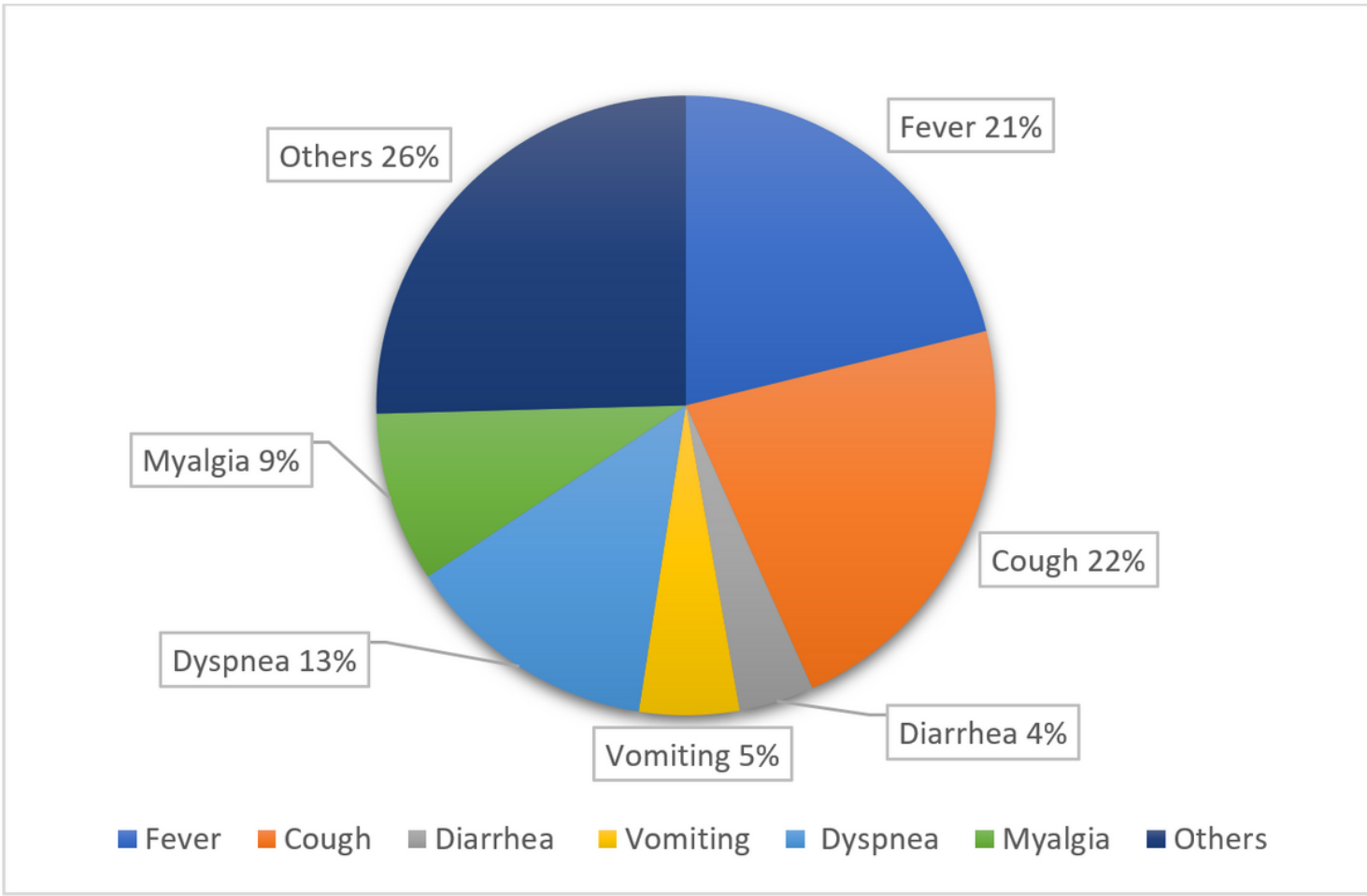

Figure 3

Common symptoms experienced by pregnant women with COVID-19 infection in the pooled sample.

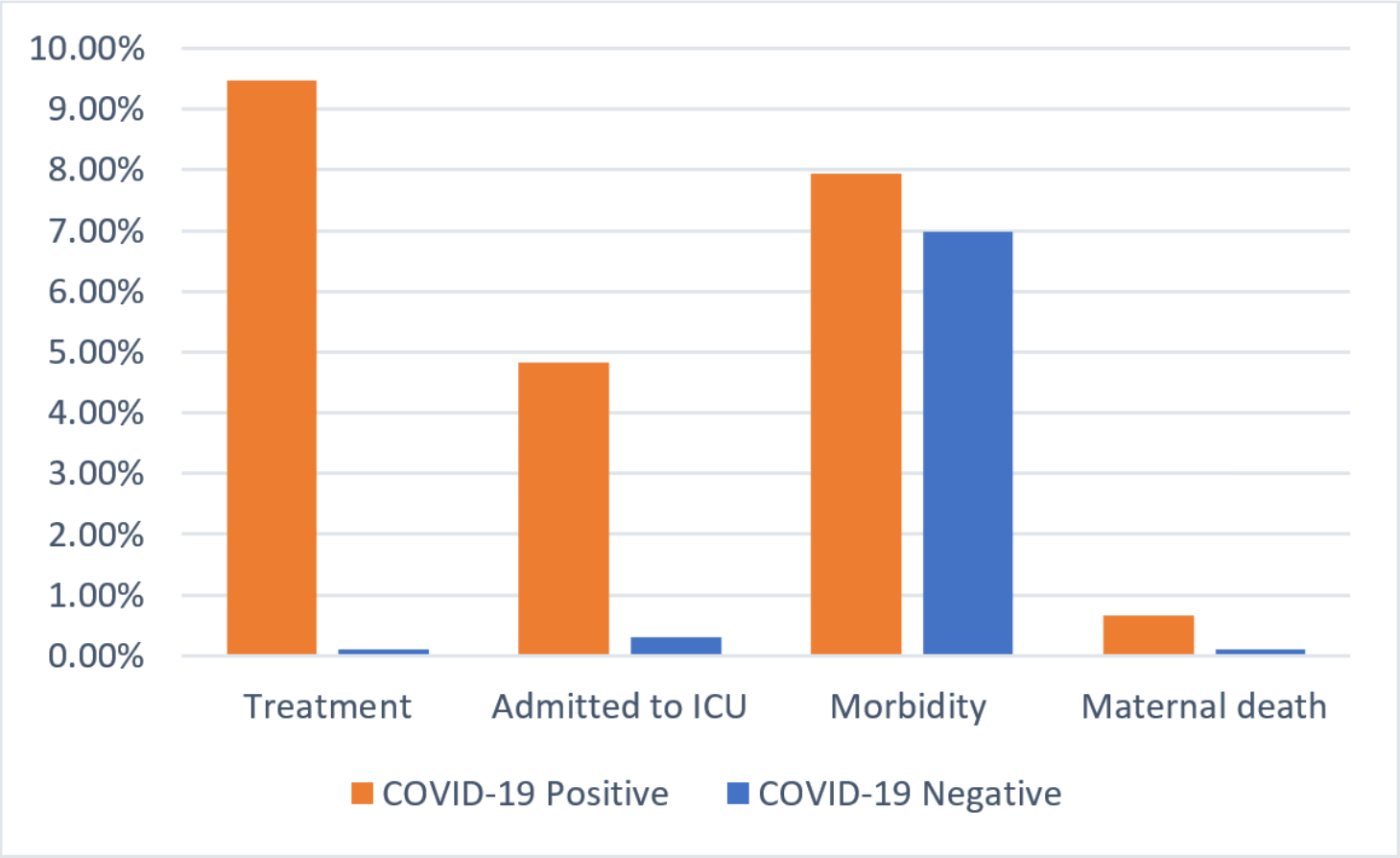

Figure 4

Maternal admission to ICU, morbidity, and mortality of pregnant women with COVID-19 infection compared with pregnancies without COVID-19 infection.

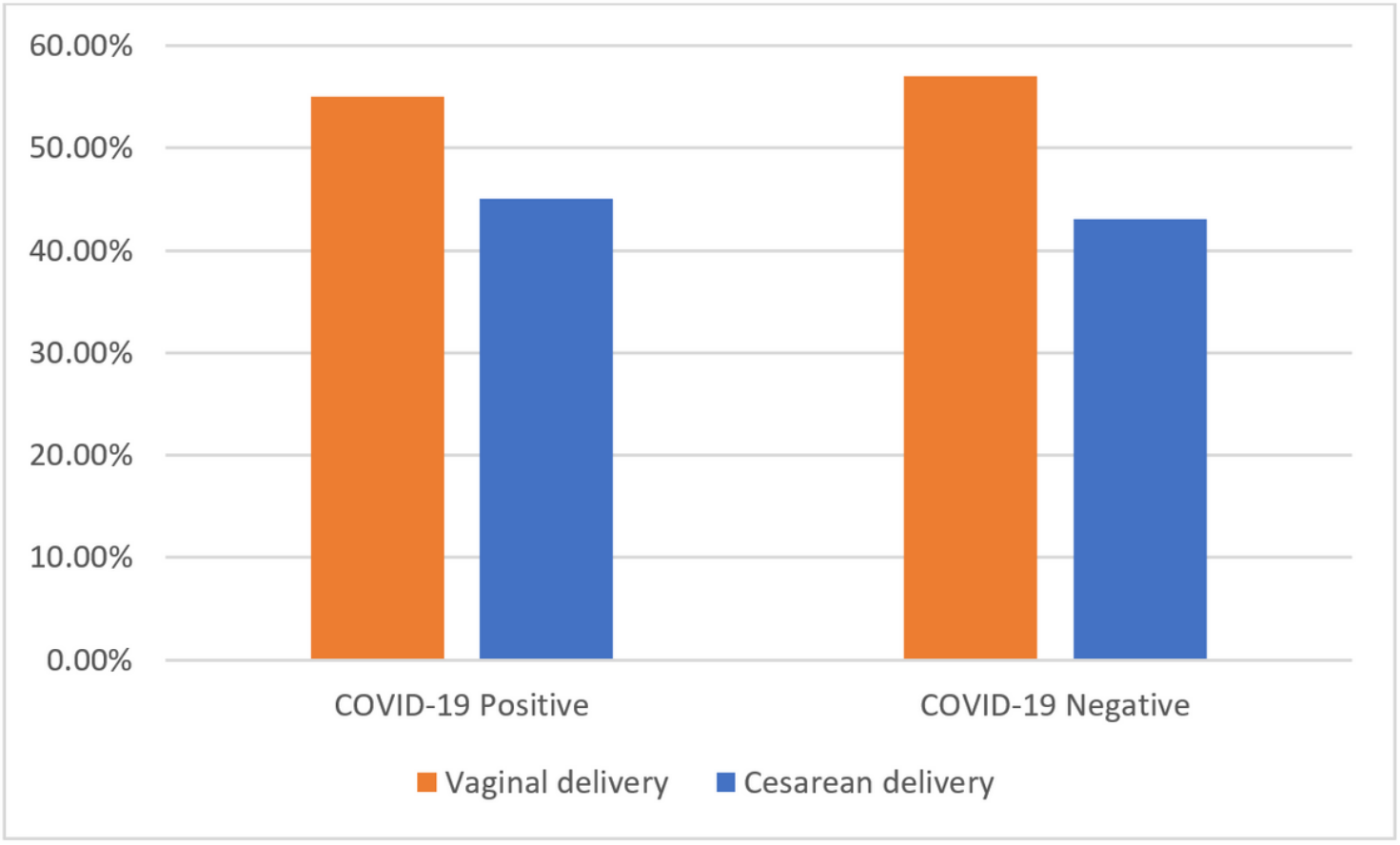

Figure 5

Pooled analysis of the differences in mode of delivery for pregnancies testing positive or negative for COVID-19.

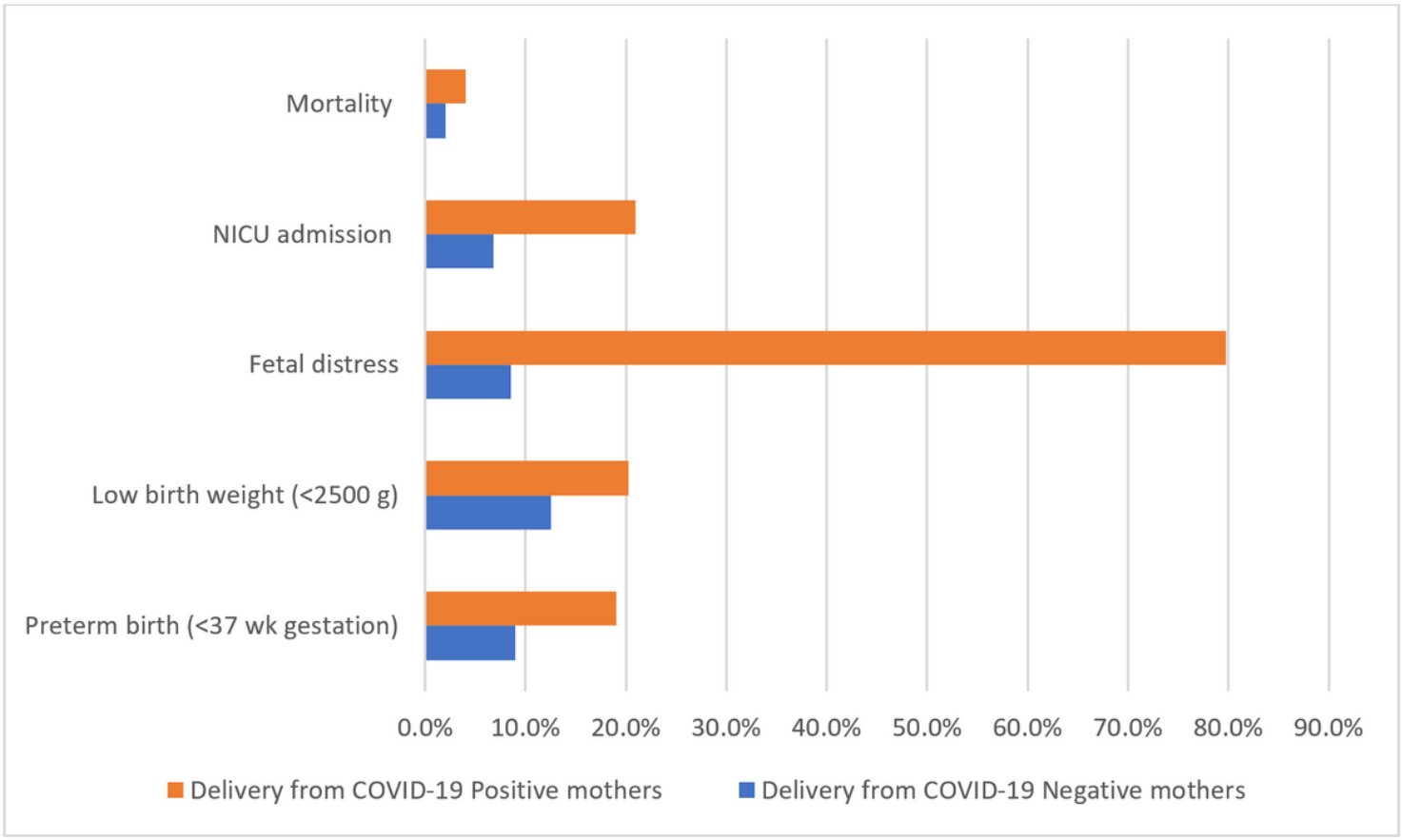

Figure 6

Neonatal complications of maternal COVID-19 infection, comparing pregnancies with mothers testing positive for COVID-19 compared with pregnancies with negative test results.

Supplementary Files

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