

# Caesarean Section in Preventing Stillbirths in Pregnancy Complicated with COVID-19: a Narrative Review

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## Abstract

**Introduction.** COVID-19 is a complex syndrome caused by SARS-Cov-2. It mainly affects the respiratory system, but it could cause serious harm during pregnancy. An increase in stillbirths and preterm births has been highlighted by many authors. Although WHO and Royal College of Obstetrics and Gynecology don't recommend elective cesarean section in women with confirmed infection, cesarean sections were performed by many clinicians. This short narrative review aims to analyze pieces of evidence found in literature about the effectiveness of cesarean section in preventing stillbirths in COVID-19 positive mothers.

**Methods.** Studies included in the present review were retrieved searching MEDLINE (last access August 5<sup>th</sup>, 2021) with the following keywords: "pregnant woman with covid-19", "Caesarean section", "Abdominal Delivery" and "Stillbirth". Studies regarding the mode of delivery in pregnant women infected with COVID-19 and neonatal outcomes were included. Studies about biology, anesthesiology and necroscopy were excluded. Filters for "human" and "English" were applied.

**Results.** Searching MEDLINE, 24 references were found. Other 103 articles were found searching bibliography. Two references were excluded after duplicate removal, 77 references after the title screen and 27 after the abstract screen. The final number of references included was 23. Most of the included studies were case reports. Most of them were from China.

**Discussion.** Many authors highlighted the increased risk of fetal death in pregnancies complicated with SARS-Cov-2 infection, but it is not clear if Caesarean Section could reduce this risk. Pieces of evidence show that most clinicians choose to perform an elective cesarean section mostly because of maternal conditions or the fear of possible vertical transmission. Data show that mode of delivery doesn't affect the neonatal outcome and Caesarean Section doesn't reduce the positivity rate among neonates. Different opinions were found about the possible infection of amniotic fluid, cord blood and placenta. The risk of vertical transmission is considered moderate or low by most of the authors. Positivity to SARS-Cov-2 isn't an indication of elective cesarean section by itself, but this mode of delivery should be optioned in patients with other obstetrical indications or with severe conditions due to COVID. The recent increase in stillbirths could be related to the overall deterioration of maternal conditions. *Clin Ter 2021; 172 (6):e570-576. doi: 10.7417/CT.2021.2380*

**Key words:** SARS-CoV-2, abdominal delivery, fetal death, pregnancy, alcohol

## Introduction

SARS-Cov-2 was firstly isolated in Wuhan, Hubei region, China at the end of 2019 (1,2) and it causes the syndrome called COVID-19 that mainly affects the respiratory system (3). COVID-19 virus is transmitted from person to person through droplets, fomites, and close interpersonal contact (4). SARS is the acronym for "Severe Acute Respiratory Syndrome" (5). Symptoms of COVID infection include fever, sore throat, dyspnea, and they can be mild during pregnancy. Moreover, some atypical symptoms can occur, like abdominal pain (6).

Many authors highlighted the increase in stillbirths in patients affected with COVID-19 during pregnancy (7–10). Although the World Health Organization (WHO) and Royal College of Obstetrics and Gynecology (RCOG) don't recommend elective cesarean section in women with confirmed COVID-19 (11), cesarean sections were performed by many clinicians. To the best of our knowledge, no samples of vaginal swabs proved positive to SARS-Cov-2 and the risk of vertical transmission is low (12). However, cardiotocography is recommended to monitor fetal wellbeing (11).

A multidisciplinary approach is recommended to treat positive patients (11). The team should include gynecologists, midwives, neonatologists, infectious diseases specialists and nurses (13–18).

This narrative review aims to analyze pieces of evidence found in literature about the effectiveness of cesarean section in preventing stillbirths in COVID-19 positive mothers.

## Methods

The studies included in the present review were retrieved searching MEDLINE (last access August 5<sup>th</sup>, 2021) with the following search string: ((pregnant woman with covid-19 or pregnant women with COVID-19 or pregnant woman with SARS-CoV-2 or pregnant women with SARS-CoV-2) and (Caesarean section or Abdominal Delivery or C-Section or C Section or C-Sections) and (Stillbirth or Fetal Death)).

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The following inclusion and exclusion criteria were applied: studies regarding mode of delivery in pregnant women infected with COVID-19 and neonatal outcomes were included. Studies about biology, anesthesiology and neurosurgery were excluded. Filters for “human” and “English” were applied. Mendeley was used for reference management and duplicate removal.

Although a systematic review on this topic would be interesting, the paucity of retrieved pertinent articles pushed the Authors to write a narrative review. Indeed, only 21 articles from the searched string were strictly pertinent to the topic.

## Results

Twenty-four references were retrieved by searching MEDLINE. Other 103 articles were found through manual search.

Two references were excluded after duplicate removal, 77 references after the title screen and 27 after the abstract screen. The final number of references included is 23. Fig. 1 (19) shows the search strategy.

Among the 23 studies, 12 were case series (8 from China, 2 from Brazil, 1 from Poland, 1 from Iran), 5 case reports (1 from Iran, 1 from Korea, 1 from Portugal, 1 from USA and 1 from Australia), 5 cohort studies (1 from China, 2 from the UK, 1 from Italy and 1 international study), 2 retrospective studies (1 from Italy, 1 from China).

Table 1 summarizes the main findings of included studies.

## Discussion

COVID-19 can cause a severe syndrome that can affect women during pregnancy with an important impact on both maternal and fetal wellbeing (20). Many authors highlighted the increased risk of fetal death in pregnancies complicated with SARS-CoV-2 infection (8–10,21).

This narrative review aims to analyze pieces of evidence about the effectiveness of cesarean section in preventing stillbirths in COVID-19 positive mothers.

Few studies included in the present review specifically focus on the mode of delivery. No studies were found focusing on the correlation between cesarean section and the prevention of stillbirths. Available data are mostly from case reports and case series from different countries of the World and from the first outbreak of the COVID pandemic (between March and July 2020).

The included pieces of evidence show that most clinicians choose to perform an elective cesarean section instead of vaginal birth. Indications were diverse and mostly related to worsening of maternal conditions (22–28) or the fear of possible transmission through contact with the vaginal mucosa (29–31). In the UK a large cohort study (28) reported that of the 722 women admitted to hospital with symptomatic SARS-CoV-2, 640 had completed their pregnancy. Sixteen women with symptomatic SARS-CoV-2 had a pregnancy loss before 24 weeks of gestation. Around 314 women gave birth by cesarean section, with 64 being for maternal com-

promise secondary to SARS-CoV-2. The risk of cesarean section for women with symptomatic SARS-CoV-2 almost doubled compared to the historical comparison cohort without SARS-CoV-2. Operative vaginal births were also increased. However, data show that the mode of delivery doesn't affect neonatal outcomes.

Some studies reported different opinions about the possible infection of amniotic fluid (32), cord blood (33) and placenta (34). Zamaniyan and colleagues (2020) reported a negative PCR test for SARS-CoV-2 on those tissues, but the baby in their case developed a COVID-19 related syndrome after birth. Zhu and colleagues (2020) reported 9 neonates who developed SARS-CoV-2 related symptoms after birth.

Based on current knowledge, breast milk of COVID-19 positive mothers proved safe and it should be administered to the baby. Breastfeeding was safe for both mother and baby (36). If maternal general conditions do not allow breastfeeding, she should be encouraged to express breast milk (37). If it is not possible, a donor's milk could be a good option (38). Midwives should support COVID-19 positive mothers in early breastfeeding their nurslings. In order to reduce the risk of transmission to the child, the Italian National Institute of Health (2020) advises preventive procedures, such as hand cleaning and the use of a face mask during feeds. Moreover, the RCOG suggests keeping the mother and baby together, unless the mother is critically ill (40).

The increase in fetal deaths was reported only by three studies (21,24,41). Moreover, the cause of such deaths was not investigated in deep. Although many doubts are still questioning mother-to-child transmission (42), the risk of vertical transmission is considered moderate or low by the majority of authors (21,22,43–45).

Placental transmission seems difficult because of the immunological barrier to the entry of pathogens (46). Indeed, the presence of diverse inflammatory cells of the innate immune system including natural killer cells (70%), CD4 T cells (15%), and decidual macrophages (15%) in the decidua basalis as the maternal component of the placenta was proven (47). Nevertheless, the pathological alterations of the placenta following COVID-19 in pregnant women can lead to fetal-neonatal consequences. It has been reported that chronic inflammation result from viral infections can induce placental lesions characterized by the infiltration of plasma cells, lymphocytes, and/or macrophages. These lesions include chronic chorioamnionitis, villitis, and chronic deciduitis (48). This inflammatory state and cytokines release could impact placental function and disrupt maternal-fetal perfusion (49).

Positivity to SARS-CoV-2 isn't an indication of elective cesarean section by itself, but this mode of delivery should be optioned in patients with other obstetrical indications or with severe conditions due to COVID-19 (23,26,28,39,50–52).

The cesarean section does not reduce the positivity rate of neonates after birth (53,54). The recent increase in stillbirths could be related to the overall deterioration of maternal conditions. In such cases, a cesarean section could be a valid option but more studies will be needed to clarify its role in preventing stillbirths. Furthermore, quite surprisingly no associations were found between COVID, alcohol consumption during pregnancy (55–62) and stillbir-

Table 1. Main findings of the included studies. The number of the sample (n), Vaginal Birth (VB), Caesarean Section (CS), ICU (Intensive Care Unit), Computerized Tomography (CT).

Reference	n	Study Design	Mode of Delivery	Indications to CS	Neonatal Outcome	Main Conclusions
[35]	9	Case Series	VB (2) CS (7)	Not disclosed	9 neonates with symptoms	COVID-19 infection can cause neonatal harm.
[22]	9	Case Series	VB (0) CS (9)	COVID (9) Obstetric indication (8)	None	There's no evidence of neonatal harm because of COVID-19 infection during the 3 <sup>rd</sup> trimester.
[30]	1	Case Report	VB (0) CS (1)	COVID (1)	1 neonate positive	Amniotic fluid proved positive to COVID-19. Vertical transmission is possible.
[79]	7	Case Series	VB (0) CS (7)	Not disclosed	1 neonate positive	Only 1 neonate proved positive. The maternal outcome was generally good.
[24]	427	Cohort Study	VB (271) CS (156)	COVID (42) Obstetric indication (25) Fetal distress (37)	8 neonates positive 5 stillbirths	It wasn't impossible to determine if stillbirths were related to transmission to COVID-19, either vertical or postnatal transmission.
[50]	10	Case Series	VB (2) CS (8)	Fetal distress (2) Obstetric indication (6)	None	COVID-19 is not a stand-alone indication for performing a CS.
[80]	7	Case Series	VB (0) CS (7)	COVID (5)	None	No adverse neonatal outcomes in women infected with COVID-19 at the end of the pregnancy.
[26]	3	Case Series	VB (0) CS (3)	Serious Maternal conditions (3)	None	CS is indicated when maternal conditions are severely deteriorated.
[51]	5	Case Series	VB (3) CS (2)	Fetal distress (1) Obstetric indication (1)	None	CS should be performed when there is a fetal indication.
[21]	251	Cohort Study	VB (115) CS (136)	Not disclosed	1 neonate positive 15 stillbirths 5 deaths after birth.	COVID infection during pregnancy is associated with 0.8% risk of stillbirth and an 11.1% risk of ICU admission.
[52]	1	Case Report	VB (0) CS (1)	Obstetric indication (1)	None	CS should be performed in a negative-pressure environment with special protective devices to prevent COVID-19 spread.
[41]	5	Case Series	VB (3) CS (2)	Obstetric indication (2)	5 stillbirths	Stillbirths could be caused by COVID-19 harm over the placenta.
[23]	42	Retrospective study	VB (24) CS (18)	COVID (10) Obstetric indication (8)	1 neonate positive	VB is the best choice for patients with COVID-19 positive with mild or no symptoms. CS should be administered for women in severe conditions.
[44]	1	Case Report	VB (0) CS (1)	Obstetric indication (1)	None	In this case, mother and baby were separated after birth to prevent transmission.
[25]	1	Case Report	VB (0) CS (1)	Serious Maternal conditions (1)	None	Induction of labor or CS could be appropriate to prevent the worsening of maternal conditions.
[29]	5	Cohort Study	VB (1) CS (4)	Fetal distress (2)	2 neonates with symptoms	Vaginal swabs proved negative to COVID-19. Vertical transmission seems unlikely.
[36]	1	Case Report	VB (0) CS (1)	Not disclosed	None	Rooming-in and skin-to-skin contact is recommended even for positive patients.
[81]	13	Case Series	VB (4) CS (9)	Not disclosed	1 neonate positive	CT scan could be used during pregnancy to assess COVID-19 progression.

table follows

[82]	67	Cohort Study	VB (36) CS (31)	Not disclosed	1 neonate positive	In 1 case over 5 CS was necessary for worsening of maternal conditions.
[83]	5	Retrospective Study	VB (1) CS (4)	COVID (1) Obstetric indication (3)	None	No evidences of vertical transmission were found.
[28]	722	Cohort Study	CS (314)	Serious Maternal Conditions (64)	None	The risk of CS is doubled for women with symptomatic COVID infection when compared to historical data.
[31]	14	Case Series	CS (3)	Fetal distress (1) Maternal request (2)	None	COVID infection in 3 <sup>rd</sup> trimester can affect maternal health. No neonatal compromise was reported.
[54]	63	Case Series	VB (15) CS (20)	Not disclosed	14 neonates in ICU	Neonates tested for COVID-19 proved negative.

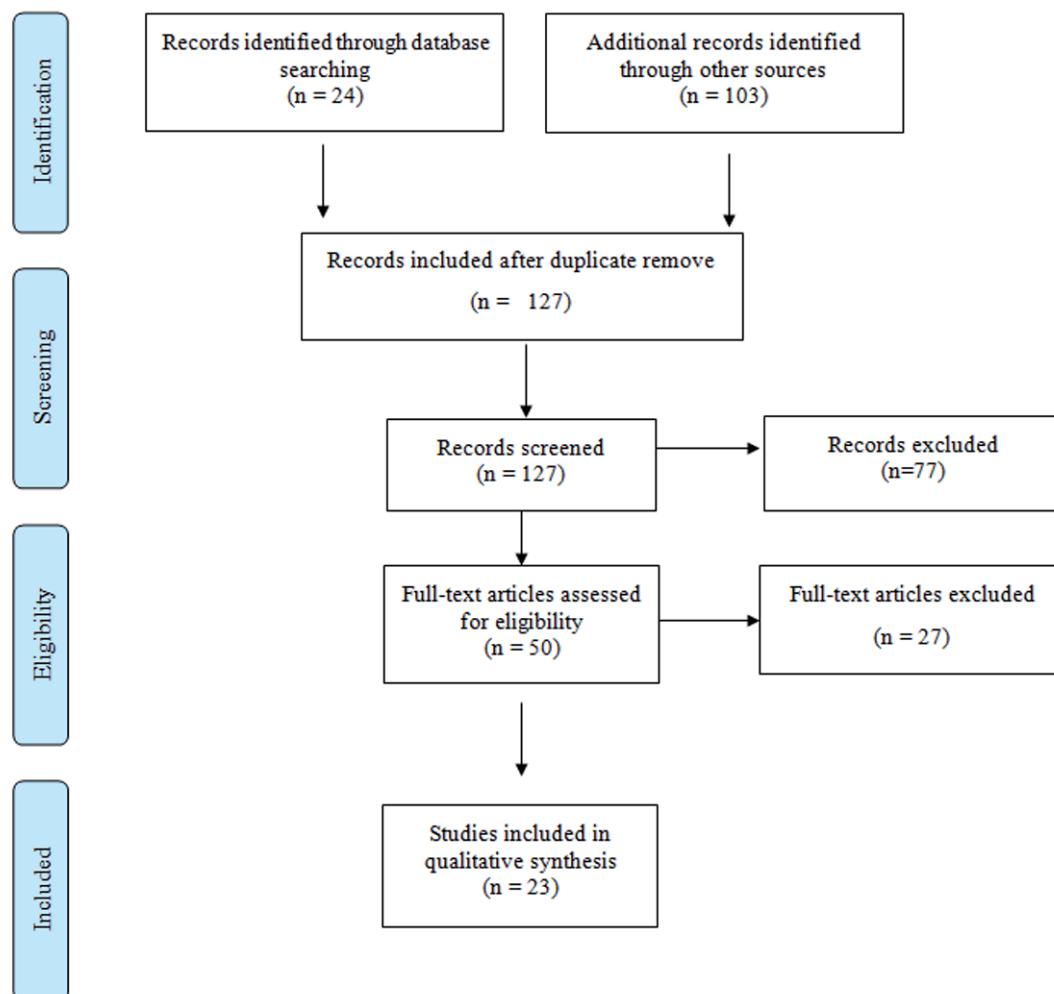


Fig. 1. Methods of study selection



ths/cesarean section although it has been shown an elevation in alcoholic beverages consumption during the COVID pandemic (63–65). Increased stress (45.7%), elevated alcohol availability (34.4%), and boredom (30.1%) were the main reasons for augmented alcohol assumption during a pandemic (64) nevertheless the well-known toxic effect of alcohol abuse (66–77). COVID-19 and alcohol abuse during pregnancy have both been highlighted as new challenges for healthcare professionals in the next decade (14,78).

The limitations of our study were the paucity of pertinent articles found on the present topic, especially because most of the studies are not centered on the mode of delivery and neonatal outcomes. Very few studies talk about stillbirths.

## Conclusions

Although there is no diriment evidence about the vertical transmission of SARS-Cov-2, positivity to COVID-19 is not an indication for elective cesarean section. Although some authors highlighted an increase in fetal deaths in pregnant women affected with COVID-19, no histological findings proved the relationship between the infection and those deaths. Some authors suggested a possible role of COVID in causing placental damage and disrupting maternal-fetal perfusion. Most clinicians chose to perform a cesarean section in women positive to COVID-19 due to obstetrical indications or severe deterioration of maternal conditions.

Pieces of evidence do not prove the preventive role of cesarean section in reducing fetal deaths in pregnancies complicated with COVID-19.

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