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State-of-the-Art Review

Counseling in maternal–fetal medicine: SARS-CoV-2 infection in pregnancy

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a zoonotic coronavirus that crossed species to infect humans, causing coronavirus disease 2019 (COVID-19). Despite a potentially higher risk of pregnant women acquiring SARS-CoV-2 infection compared with the non-pregnant population (particularly in some ethnic minorities), no additional specific recommendations to avoid exposure are needed in pregnancy. The most common clinical symptoms and laboratory signs of SARS-CoV-2 infection in pregnancy are fever, cough, lymphopenia and elevated C-reactive protein levels. Pregnancy is associated with a higher risk of severe SARS-CoV-2 infection compared with the non-pregnant population, including pneumonia, admission to the intensive care unit and death, even after adjusting for potential risk factors for severe outcomes. The risk of miscarriage does not appear to be increased in women with SARS-CoV-2 infection. Evidence with regards to preterm birth and perinatal mortality is conflicting, but these risks are generally higher only in symptomatic, hospitalized women. The risk of vertical transmission, defined as the transmission of SARS-CoV-2 from the mother to the fetus or the newborn, is generally low. Fetal invasive procedures are considered to be generally safe in pregnant women with SARS-CoV-2 infection, although the evidence is still limited. In pregnant women with COVID-19, use of steroids should not be avoided if clinically indicated; the preferred regimen is a 2-day course of dexamethasone followed by an 8-day course of methylprednisolone. Non-steroidal anti-inflammatory drugs may be used if there are no contraindications. Hospitalized pregnant women with severe COVID-19 should undergo thromboprophylaxis throughout the duration of hospitalization and at least until discharge, preferably with low molecular weight heparin. Hospitalized women who have recovered from a period of serious or critical illness with COVID-19 should be offered a fetal growth scan about 14 days after recovery from their illness. In asymptomatic or mildly symptomatic women who have tested positive for SARS-CoV-2 infection at full term (i.e. ≥ 39 weeks of gestation), induction of labor might be reasonable. To date, there is no clear consensus on the optimal timing of delivery for critically ill women. In women with no or few symptoms, management of labor should follow routine evidence-based guidelines. Regardless of COVID-19 status, mothers and their infants should remain together and breastfeeding, skin-to-skin contact, kangaroo mother care and rooming-in throughout the day and night should be practiced, while applying necessary infection prevention and control measures. Many pregnant women have already undergone vaccination, mostly in the USA where the first reports show no significant difference in pregnancy outcomes in pregnant women receiving SARS-CoV-2 vaccination during pregnancy compared with the background risk. Vaccine-generated antibodies were present in the umbilical cord blood and breast milk samples of pregnant and lactating women who received the mRNA COVID-19 vaccine. Based on the available limited data on the safety of the COVID-19 vaccine in pregnancy, it seems reasonable to offer the option of vaccination to pregnant women after accurate counseling on the potential risk of a severe course of the disease and the unknown risk of fetal exposure to the vaccine. © *2021 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

The pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been a major public health concern since the beginning of 2020, with new cases of infection, hospitalization, admission to the

intensive care unit (ICU) and death continuing to increase on a daily basis worldwide[1,2].

In the context of SARS-CoV-2 infection, pregnancy is thought to be associated with a higher burden of maternal mortality and morbidity compared with the general population, due to the physiologic cardiovascular, respiratory and immunological adaptations of gestation[3,4]. Although numerous cohort studies and systematic reviews have evaluated the impact of SARS-CoV-2 infection on maternal and perinatal outcomes[5–11], the evidence on several aspects of the prenatal management of these pregnancies remains conflicting, including the type and frequency of fetal monitoring, potential risk associated with invasive prenatal diagnosis, timing of delivery and intrapartum monitoring.

The aim of this article is to provide an up-to-date review of the literature and to evaluate the quality of available evidence on the management of pregnancies complicated by SARS-CoV-2 infection, as summarized in Table 1.

CLINICAL QUESTIONS

What is SARS-CoV-2 infection and how can it be diagnosed?

In December 2019, a novel coronavirus termed SARS-CoV-2 (initially referred to as 2019-nCoV) was first identified in Wuhan, China, in a cluster of patients with pneumonia exposed to a seafood or wet market[1].

Coronaviruses are enveloped RNA viruses belonging to the Nidovirales order that circulate broadly among humans, other mammals and birds and cause mainly respiratory disorders[12]. Similar to the two previous zoonotic coronavirus outbreaks caused by severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-CoV-2 crossed species to infect humans, causing coronavirus disease 2019 (COVID-19).

A confirmed case of SARS-CoV-2 infection is defined as a positive result on nucleic acid amplification testing (NAAT), obtained by real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swab specimens, which is currently the gold standard for the diagnosis of SARS-CoV-2 infection. Antigen testing might also be used as an alternative to NAAT, with the advantage of faster turnaround of results at the expense of lower sensitivity[13].

Bottom line: *SARS-CoV-2 is a zoonotic coronavirus that crossed species to infect humans, causing a disease called COVID-19. The gold standard for the diagnosis of SARS-CoV-2 infection is RT-PCR assay of nasal and pharyngeal swab specimens.*

Are pregnant women more likely to get SARS-CoV-2 infection?

The contagiousness of a virus is commonly determined by its basic reproduction number (R0), which is an epidemiologic metric used to describe the transmissibility of infectious agents. R0 is affected by several biological, sociobehavioral and environmental factors that govern pathogen transmission. The potential extent of an outbreak or epidemic is often based on the magnitude of the R0 value for that event, which was estimated to be around 2 during the early SARS-CoV-2 outbreak in China. The R0 captures only the average dynamics of transmission; however, a crucial question for control is whether specific situations and settings might be driving the outbreak. A better measure of the actual risk of transmission in different settings is provided by the secondary attack rate (SAR), defined as the probability that an infection occurs among susceptible people within a specific group, which provides an estimation of how social interactions can relate to transmission risk[14–16].

Although specific studies on SAR in pregnancy are lacking, there are no consistent data showing that pregnant women are more susceptible to SARS-CoV-2 infection than the general population solely because of their pregnancy status, rather than other social or biological determinants of health (e.g. ethnicity). A recent study from Washington State found that the SARS-CoV-2 infection rate was significantly higher in pregnant patients compared with adults (both males and females) of similar age, and this difference remained after excluding pregnant patients with SARS-CoV-2 infection detected through asymptomatic screening strategies (before procedures or delivery)[17]. However, most pregnancies with SARS-CoV-2 were among women from racial and ethnic minority groups. Similarly, a report released by the USA Centers for Disease Control and Prevention (CDC) showed that, among pregnant women infected by SARS-CoV-2, 46.2% were Hispanic, 23.0% were non-Hispanic white, 22.1% were non-Hispanic black and 3.8% were non-Hispanic Asian while the respective infection rates among non-pregnant women were 38.1%, 29.4%, 25.4% and 3.2%[18]. To date, it is not clear whether this relatively higher occurrence of SARS-CoV-2 infection in Hispanic and non-Hispanic black people may be secondary to a spurious association rather than the result of a higher susceptibility of these ethnics groups to SARS-CoV-2 infection.

On this basis, there is no specific indication to avoid SARS-CoV-2 infection in pregnancy and pregnant women should follow the same recommendations as the general population for avoiding exposure to the virus.

Bottom line: *Despite a potentially higher risk of acquiring SARS-CoV-2 infection compared to the non-pregnant population (particularly in some ethnic minorities), no additional specific recommendations to avoid exposure are needed in pregnancy.*

What are the most common signs and symptoms of SARS-CoV-2 infection in pregnancy?

There are no specific COVID-19 symptoms related to pregnancy. The course of the infection has been

Table 1 Summary of evidence-based answers to questions related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnancy

Clinical question	*Up-to-date answer*	*Quality of evidence**
What is SARS-CoV-2 infection and how can it be diagnosed?	SARS-CoV-2 is a zoonotic coronavirus that crossed species to infect humans, causing a disease called COVID-19. The gold standard for the diagnosis of SARS-CoV-2 infection is RT-PCR assay of nasal and pharyngeal swab specimens.	High
Are pregnant women more likely to get SARS-CoV-2 infection?	Despite a potentially higher risk of acquiring SARS-CoV-2 infection compared to the non-pregnant population (particularly in some ethnic minorities), no additional specific recommendations to avoid exposure are needed in pregnancy.	Moderate
What are the most common signs and symptoms of SARS-CoV-2 infection in pregnancy?	Fever, cough, lymphopenia and elevated C-reactive protein levels are the most common clinical symptoms and laboratory signs of SARS-CoV-2 infection in pregnancy.	Moderate
Are pregnant women more likely to develop severe COVID-19 compared with the non-pregnant population?	Pregnancy is associated with a higher risk of severe COVID-19 compared with the non-pregnant population, including pneumonia, admission to the ICU and death, even after adjusting for potential risk factors for severe outcomes. These risks seem to be higher in hospitalized women.	Moderate
What are the fetal risks of SARS-CoV-2 infection?	The risk of miscarriage does not appear to be increased in women with SARS-CoV-2 infection. Evidence is conflicting with regards to preterm birth and perinatal death, but these risks are generally higher only in symptomatic, hospitalized women with COVID-19.	Low to moderate
What is the risk of vertical transmission of SARS-CoV-2?	The risk of vertical transmission, defined as the transmission of SARS-CoV-2 from the mother to the fetus or the newborn, is generally low, at about 3.2%.	Low to moderate
Are fetal invasive procedures safe in women with SARS-CoV-2 infection?	Based on previous evidence in pregnancies with chronic viral infections, fetal invasive procedures are considered to be generally safe in pregnant women with SARS-CoV-2 infection, although the evidence is still limited. If invasive diagnosis is required, amniocentesis is the most reasonable option. Intrauterine invasive procedures should not be delayed in case of major structural anomalies or if fetal therapeutic intervention is needed.	Very low to low
What is the optimal therapeutic strategy in symptomatic women with SARS-CoV-2 infection?	In pregnant women with COVID-19, use of steroids should not be avoided if clinically indicated; the preferred course is dexamethasone (6 mg intramuscularly every 12 h, four doses) followed by methylprednisolone (a total of 32 mg/day orally or intravenously, once a day or in divided doses) for a total of 10 days. Non-steroidal anti-inflammatory drugs may be used if there are no contraindications. Other drugs should not be considered as a first-line treatment due to the paucity of data. Oxygen supplementation should be used to maintain SpO_2 at or above 94–95%.	Low
Should pregnant women affected by SARS-CoV-2 infection receive prophylactic anticoagulation?	Asymptomatic or mildly symptomatic patients, those who do not need hospitalization for the infection and those who are hospitalized for reasons other than SARS-CoV-2 do not require anticoagulation therapy. Pregnant women hospitalized with severe COVID-19 should be offered thromboprophylaxis throughout the duration of hospitalization and at least until discharge, preferably with LMWH.	Low
What is the optimal follow-up of women after SARS-CoV-2 infection?	Women recovering from mild or moderate COVID-19 should be encouraged to attend scheduled antenatal appointments. Hospitalized women who have recovered from a period of serious or critical illness with COVID-19 should be offered a fetal growth scan about 14 days after recovery from their illness (or > 21 days from previous fetal biometry ultrasound) and subsequent antenatal care should be planned with a maternal–fetal medicine specialist before hospital discharge. Telehealth visits are a reasonable option, if feasible.	Low
What is the optimal timing of delivery of pregnancies with SARS-CoV-2 infection?	In asymptomatic or mildly symptomatic women who have tested positive for SARS-CoV-2 infection at full term (i.e. ≥ 39 weeks of gestation), induction of labor might be reasonable. To date, there is no clear consensus on the timing of delivery for critically ill women; some authors suggest earlier delivery in pregnant women with COVID-19-related pneumonia (at around 34 weeks) or those admitted to the ICU and with refractory hypoxemia (after 32 weeks) to avoid deterioration of maternal condition and fetal exposure to maternal hypoxia.	Low

Continued over.

Table 1 *Continued*

Clinical question	*Up-to-date answer*	*Quality of evidence**
What is the optimal mode of delivery of women with SARS-CoV-2 infection?	SARS-CoV-2 infection is not an indication for Cesarean delivery and the mode of delivery should not be influenced by the presence of COVID-19. If Cesarean delivery is indicated in a patient with severe or critical disease, it should be performed in a multidisciplinary setting. Operative delivery with forceps or vacuum is allowed, in the presence of obstetric indication.	Moderate
What is the optimal intrapartum care of women with SARS-CoV-2 infection?	In women with no or few symptoms, management of labor should follow routine evidence-based guidelines. Amniotomy may be utilized. Continuous electronic fetal heart rate monitoring and shortening the second stage of labor might be reasonable. COVID-19 is not a contraindication to neuraxial anesthesia.	Low to moderate
Are skin-to-skin contact, rooming-in and breastfeeding allowed for women with SARS-CoV-2?	Regardless of COVID-19 status, mothers and their infants should remain together and breastfeeding, skin-to-skin contact, kangaroo mother care and rooming-in throughout the day and night should be practiced, while applying necessary infection prevention and control measures.	Low
Can pregnant women undergo vaccination for SARS-CoV-2?	Many pregnant women have already undergone vaccination, mostly in the USA where ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet the criteria for vaccination. Initial reports from the USA show no significant difference in pregnancy outcomes in women receiving the SARS-CoV-2 vaccination during pregnancy, compared with the background risk. Vaccine-generated antibodies were present in the umbilical cord blood and breast milk samples of pregnant and lactating women who received the mRNA COVID-19 vaccine. RCOG suggests caution as safety data are lacking. Based on the available limited data on the safety of the COVID-19 vaccine in pregnancy, it seems reasonable to offer the option of vaccination to pregnant women following accurate counseling on the potential risk of a severe course of the disease and the unknown risk of fetal exposure to the vaccine.	Low

*The quality of evidence was assessed using the grading of recommendations assessment, development and evaluation (GRADE) guidelines. This system classifies the quality of evidence as one of four levels: high (further research is very unlikely to change our confidence in the estimate of effect); moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate); low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate); and very low (any estimate of effect is very uncertain)[71]. ACOG, American College of Obstetricians and Gynecologists; COVID-19, coronavirus disease 2019; ICU, intensive care unit; LMWH, low molecular weight heparin; RCOG, Royal College of Obstetricians and Gynaecologists; RT-PCR, real-time reverse transcriptase polymerase chain reaction; SpO_2, oxygen saturation.

reported to be asymptomatic in the large majority of cases, although a few case series reported lower rates of asymptomatic pregnant women[19,20]. The frequency of the presence and type of symptoms related to SARS-CoV-2 infection in pregnancy is difficult to estimate because the large majority of published studies pool together unselected and selected cohorts of women (i.e. those presenting to the hospital with clinical symptoms).

Cough and fever are present in about 40% of symptomatic pregnant women affected by SARS-CoV-2 infection, while lymphopenia (33%) and elevated C-reactive protein levels (49%) are the most common laboratory findings[20]. When compared to the non-pregnant population, the likelihood of developing fever is lower in pregnancy, which partially explains the relatively high rate of asymptomatic cases reported in some series[20].

Bottom line: *Fever, cough, lymphopenia and elevated C-reactive protein levels are the most common clinical symptoms and laboratory signs of SARS-CoV-2 infection in pregnancy.*

Are pregnant women more likely to develop severe COVID-19 compared with the non-pregnant population?

The severity of SARS-CoV-2 infection is generally graded according to symptoms, mostly based upon the degree of hypoxia, and classified into the following categories:

- Asymptomatic or presymptomatic infection, which includes individuals who tested positive for SARS-CoV-2 but are showing no symptom consistent with the disease;
- Mild illness, which includes individuals who have any of the signs and symptoms of COVID-19 but who have no dyspnea or abnormal chest imaging;
- Moderate illness, which includes individuals who show evidence of lower respiratory disease during clinical assessment or imaging but who have oxygen saturation (SpO_2) $\geq 94\%$ on room air at sea level;
- Severe illness, which includes individuals who have $SpO_2 < 94\%$ on room air at sea level, a ratio of arterial

partial pressure of oxygen to fraction of inspired oxygen < 300 mmHg, respiratory frequency > 30 breaths/min or lung infiltrates > 50%;
- Critical illness, which includes individuals who have respiratory failure, septic shock and/or multiple organ dysfunction.

These criteria are not fixed and the clinical presentation of a patient with SARS-CoV-2 infection may change over time.

The large majority of pregnant women acquiring SARS-CoV-2 infection do not develop critical symptoms and the course of the infection is asymptomatic in approximately three-quarters of the obstetric population undergoing universal screening[20]. However, in a recent propensity score matched analysis of 5183 pregnant and 175 905 non-pregnant women with SARS-CoV-2 infection, pregnant women had a higher risk of death (odds ratio (OR), 1.84; 95% CI, 1.26–2.69), pneumonia (OR, 1.86; 95% CI, 1.60–2.16) and ICU admission (OR, 1.86; 95% CI 1.41–2.45) compared with non-pregnant patients, after adjusting for background demographic and medical factors[7]. Similarly, a recent systematic review showed that, compared with non-pregnant women of reproductive age, pregnant and recently pregnant women with suspected or confirmed COVID-19 had a higher risk of admission to the ICU (OR, 2.13; 95% CI, 1.53–2.95) and invasive ventilation (OR, 2.59; 95% CI, 2.28–2.94). Advanced maternal age, increased body mass index, chronic hypertension and pre-existing diabetes were associated with severe course of the disease in pregnancy and the presence of pre-existing maternal comorbidities was a risk factor for admission to the ICU and invasive ventilation. The occurrence of death for any cause in the overall population was 0.8% (339/41 664)[20]. These findings were confirmed by a recent report from the CDC in the USA that included over 23 000 pregnant women and over 386 000 non-pregnant women of reproductive age with symptomatic laboratory-confirmed SARS-CoV-2 infection, which showed a higher risk of admission to the ICU, need for invasive ventilation, need for extracorporeal membrane oxygenation (ECMO) and death in hospitalized pregnant women with COVID-19[21].

These findings highlight the need for a thorough follow-up of pregnant women with SARS-CoV-2 infection in order to identify those cases at higher risk of developing the most severe spectrum of the disease.

Bottom line: *Pregnancy is associated with a higher risk of severe COVID-19 compared with the non-pregnant population, including pneumonia, admission to the ICU and death, even after adjusting for potential risk factors for severe outcomes. These risks seem to be higher in hospitalized women.*

What are the fetal risks of SARS-CoV-2 infection?

From the beginning of the pandemic, several studies have investigated whether SARS-CoV-2 infection during pregnancy is associated with a higher risk of adverse perinatal outcome compared with unaffected pregnancies. To date, there is no evidence that SARS-CoV-2 infection during the first trimester of pregnancy increases the risk of early pregnancy loss[22]. Furthermore, SARS-CoV-2 infection does not affect the nuchal translucency thickness or any of the other ultrasound signs used to screen for trisomy 21 in the first trimester of pregnancy[23,24]. Finally, no specific anomaly has been reported to be associated with the infection. Although encouraging, data from early pregnancy are still limited and refer mostly to non-hospitalized and/or asymptomatic women.

The incidence of preterm birth (PTB) in pregnancies with SARS-CoV-2 infection has been reported to be higher than that in non-infected pregnancies in the majority of the studies published so far, with an incidence ranging between 15% and 20%[6,14,20]. However, the majority of the data were derived from studies including both selectively screened symptomatic patients and a smaller number of universally screened, test-positive, asymptomatic women, and most of the studies do not specify whether the reported PTB incidence includes both iatrogenic and spontaneous cases; thus, the role of SARS-CoV-2 infection in the incidence of PTB may be overestimated[4,6,20]. Indeed, reports from both European and American institutions[25–27] showed a decrease in the odds of PTB during the pandemic compared with a similar pre-pandemic period, particularly when focusing on early PTB.

The difference between hospitalized women with COVID-19 and asymptomatic test-positive women is also important when considering the association between SARS-CoV-2 infection and perinatal mortality. While some earlier studies demonstrated a significantly higher risk of perinatal death in pregnancies affected by COVID-19[28], in a recent report from 16 public health jurisdictions in the USA on pregnant patients with laboratory-confirmed SARS-CoV-2 infection, stillbirth occurred in 0.4% of cases, which is not higher than the background risk[29]. These data are supported by a recent meta-analysis which showed that the incidences of intrauterine fetal demise and neonatal death were similar between pregnancies that tested positive and those that tested negative for SARS-CoV-2 on admission for labor and delivery[30].

Bottom line: *The risk of miscarriage does not appear to be increased in women with SARS-CoV-2 infection. Evidence is conflicting with regards to PTB and perinatal death, but these risks are generally higher only in symptomatic, hospitalized women with COVID-19.*

What is the risk of vertical transmission of SARS-CoV-2?

The risk of vertical transmission, defined as the transmission of SARS-CoV-2 from the mother to the fetus or the newborn, is generally low[31]. A recent systematic review of 39 cohort studies or case series including 936 newborns from mothers affected by COVID-19 showed that the pooled proportion of

vertical transmission was 3.2%, with 27 neonates testing positive for SARS-CoV-2 infection by RT-PCR of nasopharyngeal swab specimens[32]. A subgroup analysis based on study location showed a similar rate of vertical transmission when comparing studies from China with those from outside China (2.0% vs 2.7%). Furthermore, SARS-CoV-2 RNA was found in 2.9% of neonatal cord blood samples, in 7.7% of placental samples and in 9.7% of fecal or rectal swabs, while no viral RNA was found in amniotic fluid or urine samples[32].

Bottom line: *The risk of vertical transmission, defined as the transmission of SARS-CoV-2 from the mother to the fetus or the newborn, is generally low, at about 3.2%.*

Are fetal invasive procedures safe in women with SARS-CoV-2 infection?

There are no consistent data yet indicating that pregnant women affected by SARS-CoV-2 infection undergoing invasive procedures for fetal diagnosis and therapy are at higher risk of vertical transmission or adverse fetal outcomes compared with the background risk[33,34]. The largest body of evidence on the potential effect of invasive procedures in pregnancies complicated by chronic viral infections is from past experience with the human immunodeficiency virus and hepatitis[35]. In such women, especially if they are taking antiviral therapy, the risk of vertical transmission following amniocentesis does not appear to be higher compared to that in women not undergoing invasive testing, particularly if the viral load is undetectable, although this evidence is limited by the small number of cases reported in the published literature.

In the case of a pregnant woman with SARS-CoV-2 infection requiring invasive testing for increased risk of aneuploidy based on the combined screening test, it is reasonable to postpone the procedure during the second trimester or until the patient has tested negative for SARS-CoV-2. Conversely, invasive testing should not be postponed in case of severe fetal anomaly strongly associated with aneuploidy, increased nuchal translucency thickness or positive non-invasive prenatal testing result suggesting a major chromosomal anomaly. Likewise, there should be no delay in case of acute fetal conditions requiring prompt prenatal intervention, such as twin-to-twin transfusion syndrome. In such a situation, the parents should be reassured that the risk of adverse outcome due to the fetal condition exceeds significantly that from maternal–fetal transmission of the virus. When invasive diagnosis is needed, it is preferable to opt for amniocentesis rather than chorionic villus sampling in view of the theoretical lower risk of admixture of maternal and fetal blood.

Bottom line: *Based on previous evidence in pregnancies with chronic viral infections, fetal invasive procedures are considered to be generally safe in pregnant women with SARS-CoV-2 infection, although the evidence is still limited. If invasive diagnosis is required, amniocentesis is the most reasonable option. Intrauterine invasive procedures should not be delayed in case of major structural anomalies or if fetal therapeutic intervention is needed.*

What is the optimal therapeutic strategy in symptomatic women with SARS-CoV-2 infection?

The main symptoms of COVID-19 in pregnant women are similar to those observed in non-pregnant women with COVID-19 and in the general population.

If a pregnant patient with COVID-19 requires pharmacologic intervention, medication should be selected by interdisciplinary medical personnel, taking into account the safety of the drug for the pregnant woman and the fetus. A recent review focusing on the use of steroids in the management of pregnant women with COVID-19 concluded that only pregnant patients with an appropriate indication for oxygen therapy (such as persistent SpO_2 values $< 94\%$) should be considered for such therapy[36], as the use of steroids was unsuccessful in patients who were not receiving oxygen therapy in the RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial[37]. In this scenario, the authors suggested a 10-day course of steroids when these are required for both fetal lung maturation and COVID-19, starting with a regimen of dexamethasone over 2 days (6 mg intramuscularly every 12 h for four doses) and then replacing dexamethasone with methylprednisolone (a total of 32 mg/day orally or intravenously, once a day or in divided doses) for the remaining 8 days[36].

For women who are mildly or moderately symptomatic who require analgesic medication other than acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) might be used if there are no other contraindications, according to the guidance of the Society for Maternal-Fetal Medicine (SMFM) and the Society for Obstetric and Anesthesia and Perinatology Labor[38]. However, it should be borne in mind that the inhibition by NSAIDs of prostaglandin synthesis in the third trimester may be associated with premature closure of the ductus arteriosus.

Data from non-pregnant adult patients showed that tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death in hospitalized patients with COVID-19 pneumonia who were not receiving mechanical ventilation[39]. Furthermore, based on encouraging data from randomized controlled trials on the safety and effectiveness of remdesivir in patients with severe COVID-19, the US Food and Drug Administration (FDA) has approved the use of remdesivir in hospitalized children ≥ 12 years and adults with COVID-19, regardless of the disease severity[40]. However, few studies have explored the role of antiviral drugs, such as remdesivir, or other medications, such as monoclonal antibody therapy, in treating pregnant women infected by SARS-CoV-2; due to the paucity of data, these drugs should not be used broadly as a first-line treatment in the absence of specific clinical indications.

Depending on the severity of the disease, oxygen supplementation through a nasal cannula may be

provided to pregnant patients with COVID-19; however, intubation, mechanical ventilation or ECMO may also be necessary in order to maintain SpO_2 at or above 94–95%.

Bottom line: *In pregnant women with COVID-19, use of steroids should not be avoided if clinically indicated; the preferred course is dexamethasone (6 mg intramuscularly every 12 h, four doses) followed by methylprednisolone (a total of 32 mg/day orally or intravenously, once a day or in divided doses) for a total of 10 days. NSAIDs may be used if there are no contraindications. Other drugs should not be considered as a first-line treatment due to the paucity of data. Oxygen supplementation should be used to maintain SpO_2 at or above 94–95%.*

Should pregnant women affected by SARS-CoV-2 infection receive prophylactic anticoagulation?

There is ongoing evidence suggesting a higher risk of thromboembolism in pregnant compared with non-pregnant women affected by SARS-CoV-2 infection[41]. Clinical data published in the early stages of the pandemic had shown elevated D-dimer levels ($\geq$ 0.5 mg/L) in 4.2% of patients with non-severe disease and in 59.5% of patients with severe disease[42], in addition to the presence of other signs of activation of the clotting system, including mild thrombocytopenia and a moderately prolonged prothrombin time. A recent systematic review including 1063 pregnant women with a confirmed diagnosis of SARS-CoV-2 infection reported that arterial and/or venous thrombosis occurred in 0.28% and disseminated intravascular coagulation in 0.66% of cases[43].

Severe disease seems to represent a major risk factor for the occurrence of thromboembolic disorders in patients with COVID-19. In a series of 1219 pregnant women affected by SARS-CoV-2 infection, the incidence of venous thromboembolism was 6.0% in severe, 0.2% in mild to moderate and 0% in asymptomatic cases, respectively[44]. Although the pathophysiology of thromboembolism in patients with SARS-CoV-2 infection has not been completely elucidated yet, platelet hyperreactivity related to viral mediated endothelial inflammation, in addition to hypercoagulability associated with increased concentrations of coagulation factors, acquired antiphospholipid antibodies and decreased concentrations of endogenous anticoagulant proteins, seem to play a major role[45].

Since pregnancy itself carries an increased risk of thrombosis, thromboprophylaxis is an important consideration in the management of pregnant women with SARS-CoV-2 infection. The decision to commence thromboprophylaxis in these patients should take into account several factors including hospitalization, comorbidities, severity of the disease and the timing of delivery. Asymptomatic or mildly symptomatic patients, those who do not need hospitalization for the infection or those who are hospitalized for reasons other than COVID-19 do not require anticoagulation. Pregnant women hospitalized with severe COVID-19 have all three Virchow risk factors for venous thromboembolism: hypomobility, endothelial activation associated with the inflammation and the prothrombotic status that is typical of pregnancy. This subset of pregnant women should therefore undergo thromboprophylaxis throughout the duration of hospitalization and at least until discharge. Low molecular weight heparin (LMWH) at a prophylactic dose (i.e. enoxaparin 40 mg subcutaneously once a day) is the drug of choice for thromboprophylaxis in pregnant women with SARS-CoV-2 infection, unless delivery is expected within 12 h. If the woman is already on heparin for other reasons, this should not be discontinued[46].

Bottom line: *Asymptomatic or mildly symptomatic patients, those who do not need hospitalization for the infection and those who are hospitalized for reasons other than SARS-CoV-2 do not require anticoagulation therapy. Pregnant women hospitalized with severe COVID-19 should be offered thromboprophylaxis throughout the duration of hospitalization and at least until discharge, preferably with LMWH.*

What is the optimal follow-up of women after SARS-CoV-2 infection?

Even during the infection period, repeat elective ultrasound examinations should be employed prudently and only when this is expected to answer a relevant clinical question or provide a medical benefit to the patient.

To date, there are no evidence-based data to guide antenatal care following SARS-CoV-2 infection. The optimal follow-up of these women is mainly based on the gestational age at infection, maternal clinical and biochemical symptoms and signs and the presence of risk factors and/or comorbidities other than SARS-CoV-2 infection.

The Royal College of Obstetricians and Gynaecologists (RCOG) recommends that pregnant women recovering from mild or moderate COVID-19 should be encouraged to attend scheduled antenatal appointments after the period of self-isolation, and no specific additional care is required based only on their infection status[46].

For pregnant women who have recovered from a period of serious or critical illness with COVID-19 necessitating hospitalization for supportive therapy, the follow-up should be similar to that provided to pregnant women recovering from illnesses of similar severity, and the ongoing antenatal care should be planned together with a maternal–fetal specialist before hospital discharge, offering at least a fetal growth scan approximately 14 days after recovery from their illness (or > 21 days from prior fetal biometry ultrasound), unless there is a pre-existing clinical reason for an earlier scan[46,47].

It is worth noting that a recent study assessing fetal growth velocity and Doppler hemodynamic changes in pregnancies complicated by SARS-CoV-2 infection during the second half of pregnancy did not find a higher risk of fetal growth restriction due to impaired placental function or of Doppler anomalies[48].

In settings in which this is feasible, telehealth could be a reasonable choice for follow-up visits[49].

Bottom line: *Women recovering from mild or moderate COVID-19 should be encouraged to attend scheduled antenatal appointments. Hospitalized women who have recovered from a period of serious or critical illness with COVID-19 should be offered a fetal growth scan about 14 days after recovery from their illness (or > 21 days from previous fetal biometry ultrasound) and subsequent antenatal care should be planned with a maternal–fetal medicine specialist before hospital discharge. Telehealth visits are a reasonable option, if feasible.*

What is the optimal timing of delivery of pregnancies with SARS-CoV-2 infection?

SARS-CoV-2 infection in an otherwise healthy pregnancy is not an indication in itself to expedite birth. The timing of delivery should be dictated by gestational age and the presence of other maternal and fetal conditions that may represent an indication for earlier, planned delivery, regardless of SARS-CoV-2 infection[46,47,50].

In asymptomatic or mildly symptomatic women testing positive for SARS-CoV-2 infection at full term (i.e. ≥ 39 weeks' gestation), the timing of delivery should be planned balancing the possibility of worsening clinical condition with expectant management and the availability of resources for immediate delivery as well as the increased risk of exposure of healthcare personnel when delivery occurs at a time of high viremia[47]. If the likelihood of clinical deterioration is high, it might be reasonable to consider induction of labor.

Although robust data are lacking on which type of cervical ripening (mechanical *vs* pharmacological) should be preferred in women requiring induction of labor, using two methods (i.e. mechanical and misoprostol or mechanical and oxytocin) may decrease the time from induction to delivery, compared with using one agent only.

In the case of severe disease, the timing of delivery is a delicate management decision that should be individualized based mainly on maternal symptoms. To date, there is no clear consensus on the ideal timing of delivery for critically ill women with COVID-19, but the general opinion is that preterm delivery might be considered if this could putatively improve maternal condition[47].

Pregnant women with COVID-19-related pneumonia might benefit from early delivery (at around 34 weeks) in order to avoid potential deterioration of maternal condition and the subsequent fetal exposure to maternal hypoxia, as well as to facilitate respiratory support (prone position).

Finally, in women admitted to the ICU and particularly those with refractory hypoxemia, delivery after 32 weeks has been suggested if it would allow for further optimization of care[51].

The high burden of complications owing to prematurity in preterm deliveries before 32 weeks' gestation is a relative contraindication to expeditious delivery, unless this is strictly required by maternal and/or obstetric complications.

Bottom line: *In asymptomatic or mildly symptomatic women who have tested positive for SARS-CoV-2 infection at full term (i.e. ≥ 39 weeks of gestation), induction of labor might be reasonable. To date, there is no clear consensus on the timing of delivery for critically ill women; some authors suggest earlier delivery in pregnant women with COVID-19-related pneumonia (at around 34 weeks) or those admitted to the ICU and with refractory hypoxemia (after 32 weeks) to avoid deterioration of maternal condition and fetal exposure to maternal hypoxia.*

What is the optimal mode of delivery of women with SARS-CoV-2 infection?

SARS-CoV-2 infection is not an indication for Cesarean delivery (CD) and therefore the mode of delivery should not be influenced by the presence of COVID-19, unless a critical maternal condition requires urgent intervention for birth[46,50,52].

In a systematic review of 49 studies reporting on the mode of delivery and infant infection status of 655 women and 666 neonates, 2.7% of babies born vaginally compared with 5.3% of those born by CD tested positive for SARS-CoV-2, thus reaffirming the evidence that CD does not reduce the already low risk for intrapartum vertical transmission[53]. Data on perinatal transmission available to date do not preclude the use of forceps or vacuum when indicated[38].

Although some authors have described successful induction of labor in intubated women and patients on ECMO support, the majority of patients with severe or critical disease undergo CD in a multidisciplinary setting involving at least maternal–fetal medicine specialists, neonatologists and intensivists[54,55].

Bottom line: *SARS-CoV-2 infection is not an indication for CD and the mode of delivery should not be influenced by the presence of COVID-19. If CD is indicated in a patient with severe or critical disease, it should be performed in a multidisciplinary setting. Operative delivery with forceps or vacuum is allowed, in the presence of obstetric indication.*

What is the optimal intrapartum care of women with SARS-CoV-2 infection?

In women with no or few COVID-19 symptoms, management of labor should follow routine, evidence-based guidelines for both the first and second stage of labor[56,57]. SMFM suggests that amniotomy may still be utilized for labor management if clinically indicated, given the reassuring (but limited) data on vertical transmission, since SARS-CoV-2 has rarely been detected in vaginal secretions or amniotic fluid[38].

Since fetal heart rate changes have been described in pregnancies with SARS-CoV-2 infection[58], it is reasonable to consider such pregnancies as 'high risk' and offer continuous electronic fetal heart rate monitoring, in accordance with the guidelines of the American

College of Obstetricians and Gynecologists (ACOG) and the National Institute for Health and Care Excellence (NICE)[59,60].

Shortening the second stage of labor, which might be intuitively achieved by immediate pushing in the second stage[61], has been suggested in order to reduce the risk of respiratory secretion exposure to the accompanying partner and medical personnel[62]. However, active pushing with deep breathing and maternal expulsive efforts may still increase partner and personnel exposure to the patient's respiratory secretions[62]. Thus, there is currently no clear indication on whether to suggest immediate or delayed pushing in the second stage of labor in pregnant women affected by COVID-19.

Finally, COVID-19 is not a contraindication to neuraxial anesthesia. Early epidural analgesia for labor should be considered to mitigate the risks associated with general anesthesia and to reduce cardiopulmonary stress[38].

Bottom line: *In women with no or few symptoms, management of labor should follow routine evidence-based guidelines. Amniotomy may be utilized. Continuous electronic fetal heart rate monitoring and shortening the second stage of labor might be reasonable. COVID-19 is not a contraindication to neuraxial anesthesia.*

Are skin-to-skin contact, rooming-in and breastfeeding allowed for women with SARS-CoV-2?

Skin-to-skin contact (when the naked infant is placed on the mother's bare chest immediately after delivery) and rooming-in (allowing mothers and infants to remain together 24 h a day) policies are usually encouraged to create a baby-friendly environment in the healthcare setting and mostly to increase breastfeeding rates and duration[63]. At the beginning of pandemic, many centers did not allow these practices or the presence of a birth partner during labor.

To date, data show no difference in the risk of infection of the neonate whether it is cared for in a separate room or remains in the mother's room when the mother has suspected or confirmed SARS-CoV-2 infection and, therefore, ACOG recommends rooming-in combined with safety measures to minimize the risk of transmission, such as wearing a mask and practicing hand hygiene before any contact with the newborn[64].

SARS-CoV-2 infection is not a contraindication to breastfeeding. As evidence from observational studies has shown that breastfeeding is associated with short- and long-term health benefits both for the mother and the child, breastfeeding should be encouraged for mothers with COVID-19, taking all possible precautions to avoid transmission of the virus to the infant, including hand hygiene and wearing a mask or cloth face covering, if possible, while breastfeeding[64].

In a recent update on newborn care, the World Health Organization has recommended that, regardless of COVID-19 status, mothers and their infants should remain together and breastfeeding, skin-to-skin contact, including kangaroo mother care, and rooming-in throughout the day and night should be practiced, while applying necessary infection prevention and control measures[65].

Bottom line: *Regardless of COVID-19 status, mothers and their infants should remain together and breastfeeding, skin-to-skin contact, kangaroo mother care and rooming-in throughout the day and night should be practiced, while applying necessary infection prevention and control measures.*

Can pregnant women undergo vaccination for SARS-CoV-2?

The subject of whether vaccination to prevent SARS-CoV-2 infection should be considered for use in pregnancy is currently a 'hot topic'. Pregnant women are often underrepresented in clinical research and excluded from trials solely due to their pregnancy status, and as such they were excluded from the trials for vaccination against SARS-CoV-2.

Three SARS-CoV-2 vaccines have been currently approved by both the US FDA and the European Medicines Agency: the Pfizer-BioNtech mRNA vaccine, the Moderna mRNA-1273 vaccine and the Janssen Pharmaceutica Ad26.COV2.S vaccine.

In their recent Practice Advisory, ACOG recommended that SARS-CoV-2 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on the Advisory Committee on Immunization Practices (ACIP)-recommended priority groups[66], and therefore several pregnant women have already undergone vaccination in the USA.

Conversely, in the UK, based on the recommendations of the Joint Committee on Vaccination and Immunisation (JCVI), RCOG does not advocate the routine use of SARS-CoV-2 vaccines during pregnancy in the absence of safety data, although the available data do not indicate any safety concern or harm to pregnancy. However, the JCVI advises that vaccination should be considered for pregnant women defined as being clinically extremely vulnerable as well as those who are frontline health or social care workers[67].

At the time of writing, about 20 000 pregnant women in the USA had received the Pfizer-BioNTech vaccine with no severe acute signs reported. Based on this evidence, the International Federation of Gynecology and Obstetrics (FIGO) recently declared that there are no risks – actual or theoretical – that would outweigh the potential benefits of vaccination for pregnant women, thus supporting COVID-19 vaccination of pregnant and breastfeeding women[68]. Moreover, in March 2021 the CDC released the first reassuring data from the V-safe COVID-19 vaccine pregnancy registry, which showed no significant difference in pregnancy outcomes, such as miscarriage, perinatal mortality or congenital anomalies, in pregnant women who received the vaccination compared with the background risk[69]. Finally, very recent (preprint) data show that vaccine-generated antibodies were present in the umbilical cord blood and breast milk

samples of pregnant and lactating women who received the mRNA COVID-19 vaccine[70].

Thus, despite the limited data on the safety of the COVID-19 vaccine in pregnancy, it seems reasonable to offer the option of vaccination to pregnant women after appropriate counseling on the potential risk of a severe course of the disease and the unknown risk of fetal exposure to the vaccine.

Bottom line: *Many pregnant women have already undergone vaccination, mostly in the USA where ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet the criteria for vaccination. Initial reports from the USA show no significant difference in pregnancy outcomes in women receiving the SARS-CoV-2 vaccination during pregnancy, compared with the background risk. Vaccine-generated antibodies were present in the umbilical cord blood and breast milk samples of pregnant and lactating women who received the mRNA COVID-19 vaccine. RCOG suggests caution as safety data are lacking. Based on the available limited data on the safety of the COVID-19 vaccine in pregnancy, it seems reasonable to offer the option of vaccination to pregnant women following accurate counseling on the potential risk of a severe course of the disease and the unknown risk of fetal exposure to the vaccine.*

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REFERENCES

1. Perlman S. Another Decade, Another Coronavirus. *N Engl J Med* 2020; **382**: 760–776.
2. https://covid19.who.int/ [Accessed on January 5, 2021].
3. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, Vecchiet J, Nappi L, Scambia G, Berghella V, D'Antonio F. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM* 2020; **2**: 100107.
4. The WAPM (World Association of Perinatal Medicine) Working Group on COVID-19. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection. *Ultrasound Obstet Gynecol* 2021; **57**: 232–241.
5. Di Mascio D, Sen C, Saccone G, Galindo A, Grünebaum A, Yoshimatsu J, Stanojevic M, Kurjak A, Chervenak F, Rodríguez Suárez MJ, Gambacorti-Passerini ZM, Baz MLAA, *et al*. Risk factors associated with adverse fetal outcomes in pregnancies affected by Coronavirus disease 2019 (COVID-19): a secondary analysis of the WAPM study on COVID-19. *J Perinat Med* 2020; **48**: 950–958.
6. Huntley BJF, Huntley ES, Di Mascio D, Chen T, Berghella V, Chauhan SP. Rates of maternal and perinatal mortality and vertical transmission in pregnancies complicated by severe acute respiratory syndrome coronavirus 2 (SARS-Co-V-2) infection: a systematic review. *Obstet Gynecol* 2020; **136**: 303–312.
7. Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, Torres-Torres J, Espino Y Sosa S, Sandoval-Mandujano K, Castro-Bernabe DA, Medina-Jimenez V, Monarrez-Martin JC, Figueras F, Poon LC. Pregnant women with SARS-CoV-2 infection are at higher risk of death and pneumonia: propensity score matched analysis of a nationwide prospective cohort (COV19Mx). *Ultrasound Obstet Gynecol* 2021; **57**: 224–231.
8. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol* 2020; **56**: 15–27.
9. Gracia PV, Caballero LC, Sánchez J, Espinosa J, Campana S, Quintero A, Luo C, Ng J. Pregnancies recovered from SARS-CoV-2 infection in second or third trimester: obstetric evolution. *Ultrasound Obstet Gynecol* 2020; **56**: 777–778.
10. Cheng SO, Khan S, Alsafi Z. Maternal death in pregnancy due to COVID-19. *Ultrasound Obstet Gynecol* 2020; **56**: 122.
11. Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, Penfield CA, Roman AS, DeBolt CA, Stone JL, Bianco A, Kern-Goldberger AR, Hirshberg A, Srinivas SK, Jayakumaran JS, Brandt JS, Anastasio H, Birsner M, O'Brien DS, Sedev HM, Dolin CD, Schnettler WT, Suhag A, Ahluwalia S, Navathe RS, Khalifeh A, Anderson K, Berghella V. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. *Am J Obstet Gynecol MFM* 2020; **2**: 100134.
12. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020; **382**: 727–733.
13. Cheng MP, Papenburg J, Desjardins M, Kanjilal S, Quach C, Libman M, Dittrich S, Yansouni CP. Diagnostic Testing for Severe Acute Respiratory Syndrome-Related Coronavirus 2: A Narrative Review. *Ann Intern Med* 2020; **172**: 726–734.
14. Ryan GA, Purandare NC, McAuliffe FM, Hod M, Purandare CN. Clinical update on COVID-19 in pregnancy: A review article. *J Obstet Gynaecol Res* 2020; **46**: 1235–1245.
15. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* 2020; **382**: 1199–1207.
16. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro Surveill* 2020; **25**: 2000058.
17. Lokken EM, Taylor GG, Huebner EM, Vanderhoeven J, Hendrickson S, Coler B, Sheng JS, Walker CL, McCartney SA, Kretzer NM, Resnick R, Kachikis A, Barnhart N, Schulte V, Bergam B, K K, Albright C, Larios V, Kelley L, Larios V, Emhoff S, Rah J, Retzlaff K, Thomas C, Paek BW, Hsu RJ, Erickson A, Chang A, Mitchell T, Hwang JK, Gourley R, Erickson S, Delaney S, Kline CR, Archabald K, Blain M, Lacourse SM, Adams Waldorf KM. Higher severe acute respiratory syndrome coronavirus 2 infection rate in pregnant patients. *Am J Obstet Gynecol* 2021: S0002-9378(21)00098-3.
18. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, Nahabedian J, Anderson K, Gilboa SM. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**: 769–775.
19. Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Matern Fetal Neonatal Med* 2020; **30**: 1–4.
20. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, Debenham L, Llavall AC, Dixit A, Zhou D, Balaji R, Lee SI, Qiu X, Yuan M, Coomar D, van Wely M, van Leeuwen E, Kostova E, Kunst H, Khalil A, Tiberi S, Brizuela V, Broutet N, Kara E, Kim CR, Thorson A, Oladapo OT, Mofenson L, Zamora J, Thangaratinam S; for PregCOV-19 Living Systematic Review Consortium. 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.
21. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, Woodworth KR, Nahabedian JF 3rd, Azziz-Baumgartner E, Gilboa SM, Meaney-Delman D; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**: 1641–1647.
22. Cosma S, Carosso AR, Cusato J, Borella F, Carosso M, Bovetti M, Filippini C, D'Avolio A, Ghisetti V, Di Perri G, Benedetto C. Coronavirus disease 2019 and first-trimester spontaneous abortion: a case-control study of 225 pregnant patients. *Am J Obstet Gynecol* 2020; **8**: S0002-9378(20)31177-7.
23. la Cour Freiesleben N, Egerup P, Vauvert Römmelmayer Hviid K, Rosenbek Severinsen E, Kolte AM, Westergaard D, Fich Olsen L, Prætorius L, Zedeler A, Hellerung Christiansen AM, Reinhardt Nielsen J, Bang D, Berntsen S, Ollé-López J, Ingham A, Bello-Rodríguez J, Marie Storm D, Ethelberg-Findsen J, Hoffmann ER, Wilken-Jensen C, Stener Jørgensen F, Westh H, Løvendahl Jørgensen H, Nielsen HS. SARS-CoV-2 in first trimester pregnancy: a cohort study. *Hum Reprod* 2021: **36**: 40–47.
24. Rotshenker-Olshinka K, Volodarsky-Perel A, Steiner N, Rubenfeld E, H Dahan M. COVID-19 pandemic effect on early pregnancy: are miscarriage rates altered, in asymptomatic women? *Arch Gynecol Obstet* 2021; **303**: 839–845.
25. Hedermann G, Hedley PL, Bækvad-Hansen M, Hjalgrim H, Rostgaard K, Poorisrisak P, Breindahl M, Melbye M, Hougaard DM, Christiansen M, Lausten-Thomsen U. Danish premature birth rates during the COVID-19 lockdown. *Arch Dis Child Fetal Neonatal Ed* 2021; **106**: 93–95.
26. Philip RK, Purtill H, Reidy E, Daly M, Imcha M, McGrath D, O'Connell NH, Dunne CP. Unprecedented reduction in births of very low birthweight (VLBW) and extremely low birthweight (ELBW) infants during the COVID-19 lockdown in Ireland: a 'natural experiment' allowing analysis of data from the prior two decades. *BMJ Glob Health* 2020; **5**: e003075.
27. 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.
28. Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the Incidence of Stillbirth and Preterm Delivery During the COVID-19 Pandemic. *JAMA* 2020; **324**: 705–706.
29. Woodworth KR, Olsen EO, Neelam V, Lewis EL, Galang RR, Oduyebo T, Aveni K, Yazdy MM, Harvey E, Longcore ND, Barton J, Fussman C, Siebman S, Lush M, Patrick PH, Halai UA, Valencia-Prado M, Orkis L, Sowunmi S, Schlosser L, Khuwaja S, Read JS, Hall AJ, Meaney-Delman D, Ellington SR, Gilboa SM, Tong VT; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team; COVID-19 Pregnancy and Infant Linked Outcomes Team (PILOT). Birth and Infant Outcomes Following Laboratory-Confirmed SARS-CoV-2 Infection in

Pregnancy - SET-NET, 16 Jurisdictions, March 29-October 14, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**: 1635–1640.
30. Huntley BJF, Mulder IA, Di Mascio D, Vintzileos WS, Vintzileos AM, Berghella V, Chauhan SP. 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**: 585–596.
31. Wang C, Zhou YH, Yang HX, Poon LC. Intrauterine vertical transmission of SARS-CoV-2: what we know so far. *Ultrasound Obstet Gynecol* 2020; **55**: 724–725.
32. Kotlyar AM, Grechukhina O, Chen A, Popkhadze S, Grimshaw A, Tal O, Taylor HS, Tal R. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2021; **224**: 35–53.e3.
33. Salomon LJ, Sotiriadis A, Wulff CB, Odibo A, Akolekar R. Risk of miscarriage following amniocentesis or chorionic villus sampling: systematic review of literature and updated meta-analysis. *Ultrasound Obstet Gynecol* 2019; **54**: 442–451.
34. Di Mascio D, Khalil A, Rizzo G, Buca D, Liberati M, Martellucci CA, Flacco ME, Manzoli L, D'Antonio F. Risk of fetal loss following amniocentesis or chorionic villus sampling in twin pregnancy: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2020; **56**: 647–655.
35. Wilson RD. Guideline No. 409: Intrauterine Fetal Diagnostic Testing in Women with Chronic Viral Infections. *J Obstet Gynaecol Can* 2020; **42**: 1555–1562.e1.
36. Saad AF, Chappell L, Saade GR, Pacheco LD. Corticosteroids in the Management of Pregnant Patients With Coronavirus Disease (COVID-19). *Obstet Gynecol* 2020; **136**: 823–826.
37. RECOVERY Collaborative Group; Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie JK, Haynes R, Landray MJ. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med* 2021: **384**: 693–704.
38. Society for Maternal-Fetal Medicine and Society for Obstetric and Anesthesia and Perinatology. Labor and Delivery COVID-19 Considerations. Available at: https://s3.amazonaws.com/cdn.smfm.org/media/2542/SMFM-SOAP_COVID_LD_Considerations_-_revision_10-9-20_(final).pdf [Accessed on January 4, 2021].
39. Salama C, Han J, Yau L, Reiss WG, Kramer B, Neidhart JD, Criner GJ, Kaplan-Lewis E, Baden R, Pandit L, Cameron ML, Garcia-Diaz J, Chávez V, Mekebeb-Reuter M, Lima de Menezes F, Shah R, González-Lara MF, Assman B, Freedman J, Mohan SV. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. *N Engl J Med* 2021; **384**: 20–30.
40. Rubin D, Chan-Tack K, Farley J, Sherwat A. FDA Approval of Remdesivir - A Step in the Right Direction. *N Engl J Med* 2020; **383**: 2598–2600.
41. Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia: a random association? *Eur Heart J* 2020; **41**: 1858.
42. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; **382**: 1708–1720.
43. Servante J, Swallow G, Thornton JG, Myers B, Munireddy S, Malinowski AK, Othman M, Li W, O'Donoghue K, Walker KF. Haemostatic and thrombo-embolic complications in pregnant women with COVID-19: a systematic review and critical analysis. *BMC Pregnancy Childbirth* 2021; **21**: 108.
44. Metz TD, Clifton RG, Hughes BL, Sandoval G, Saade GR, Grobman WA, Manuck TA, Miodovnik M, Sowles A, Clark K, Gyamfi-Bannerman C, Mendez-Figueroa H, Sehdev HM, Rouse DJ, Tita ATN, Bailit J, Costantine MM, Simhan HN, Macones GA; Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network. Disease Severity and Perinatal Outcomes of Pregnant Patients With Coronavirus Disease 2019 (COVID-19). *Obstet Gynecol* 2021; **137**: 571–580.
45. Piazza G, Morrow DA. Diagnosis, Management, and Pathophysiology of Arterial and Venous Thrombosis in COVID-19. *JAMA* 2020; **324**: 2548–2549.
46. The Royal College of Obstetricians and Gynaecologists, The Royal College of Midwives. Coronavirus (COVID-19) Infection in Pregnancy. Available at: https://www.rcog.org.uk/coronavirus-pregnancy [Accessed on January 4, 2021].
47. Society for Maternal-Fetal Medicine. Coronavirus (COVID-19) and Pregnancy: What Maternal-Fetal Medicine Subspecialists Need to Know. Available at: https://s3.amazonaws.com/cdn.smfm.org/media/2589/COVID19-What_MFMs_need_to_know_revision_11-23-20_final.pdf [Accessed on January 4, 2021].
48. Rizzo G, Mappa I, Maqina P, Bitsadze V, Khizroeva J, Makatsarya A, D'Antonio F. Effect of SARS-CoV-2 infection during the second half of pregnancy on fetal growth and hemodynamics: a prospective study. *Acta Obstet Gynecol Scand* 2021. DOI: 10.1111/aogs.14130.
49. Boelig RC, Saccone G, Bellussi F, Berghella V. MFM guidance for COVID-19. *Am J Obstet Gynecol MFM* 2020; **2**: 100106.
50. Benski C, Di Filippo D, Taraschi G, Reich MR. Guidelines for Pregnancy Management During the COVID-19 Pandemic: A Public Health Conundrum. *Int J Environ Res Public Health* 2020; **17**: 8277.
51. Halscott T, Vaught J and the SMFM COVID-19 Task Force. Management Considerations for Pregnant Patients With COVID-19. Available at: https://s3.amazonaws.com/cdn.smfm.org/media/2734/SMFM_COVID_Management_of_COVID_pos_preg_patients_2-2-21_(final).pdf [Accessed on March 27, 2021].
52. Boelig RC, Manuck T, Oliver EA, Di Mascio D, Saccone G, Bellussi F, Berghella V. Labor and delivery guidance for COVID-19. *Am J Obstet Gynecol MFM* 2020; **2**: 100110.
53. Walker KF, O'Donoghue K, Grace N, Dorling J, Comeau JL, Li W, Thornton JG. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. *BJOG* 2020; **127**: 1324–1336.
54. Liu C, Sun W, Wang C, Liu F, Zhou M. Delivery during extracorporeal membrane oxygenation (ECMO) support of pregnant woman with severe respiratory distress syndrome caused by influenza: a case report and review of the literature. *J Matern Fetal Neonatal Med* 2019; **32**: 2570.
55. Slayton-Milam S, Sheffels S, Chan D, Alkinj B. Induction of Labor in an Intubated Patient With Coronavirus Disease 2019 (COVID-19). *Obstet Gynecol* 2020; **136**: 962.
56. Berghella V, Baxter JK, Chauhan SP. Evidence-based labor and delivery management. *Am J Obstet Gynecol* 2008; **199**: 445–454.
57. Alhafez L, Berghella V. Evidence-based labor management: first stage of labor (part 3). *Am J Obstet Gynecol MFM* 2020; **2**: 100185.
58. Gracia-Perez-Bonfils A, Martinez-Perez O, Llurba E, Chandraharan E. Fetal heart rate changes on the cardiotocograph trace secondary to maternal COVID-19 infection. *Eur J Obstet Gynecol Reprod Biol* 2020; **252**: 286–293.
59. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 106: Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol* 2009; **114**: 192. Reaffirmed 2019.
60. Intrapartum care for healthy women and babies. NICE guideline published December 2014. https://www.nice.org.uk/guidance/cg190/chapter/1-Recommendations#monitoring-during-labour [Accessed on January 5, 2021].
61. Di Mascio D, Saccone G, Bellussi F, Al-Kouatly HB, Brunelli R, Benedetti Panici P, Liberati M, D'Antonio F, Berghella V. Delayed versus immediate pushing in the second stage of labor in women with neuraxial analgesia: a systematic review and meta-analysis of randomized controlled trials. *Am J Obstet Gynecol* 2020; **223**: 189–203.
62. Stephens AJ, Barton JR, Bentum NA, Blackwell SC, Sibai BM. General Guidelines in the Management of an Obstetrical Patient on the Labor and Delivery Unit during the COVID-19 Pandemic. *Am J Perinatol* 2020; **37**: 829–836.
63. World Health Organization. Global Strategy for Infant and Young Child Feeding (2003). www.who.int/nutrition/publications/infantfeeding/en/index.html [Accessed on January 4, 2021].
64. American College of Obstetricians and Gynecologists. Practice advisory: Novel Coronavirus 2019 (COVID-19). Available at: https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019 [Accessed on January 4, 2021].
65. World Health Organization. What we know about breastfeeding and newborn care in the context of COVID-19. Geneve, 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/risk-comms-updates/update-38 [Accessed on January 4, 2021].
66. American College of Obstetricians and Gynecologists. Practice advisory: Vaccinating pregnant and lactating patients against COVID-19. Available at: https://www.acog.org/en/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-Pregnant-and-Lactating-Patients-Against-COVID-19 [Accessed on January 4, 2021].
67. The Royal College of Obstetricians and Gynaecologists (RCOG). Updated advice on COVID-19 vaccination in pregnancy and women who are breastfeeding. Available at: https://www.rcog.org.uk/en/news/updated-advice-on-covid-19-vaccination-in-pregnancy-and-women-who-are-breastfeeding/ [Accessed on January 4, 2021].
68. The International Federation of Gynecology and Obstetrics (FIGO). COVID-19 Vaccination for Pregnant and Breastfeeding Women. Available at: https://www.figo.org/covid-19-vaccination-pregnant-and-breastfeeding-women [Accessed on March 11, 2021].
69. CDC National Center for Immunization & Respiratory Diseases. COVID 19 vaccine safety update. Advisory Committee on Immunization Practices (ACIP) March 1, 2021 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf [Accessed on March 27, 2021].
70. Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, Baez AM, Shook LL, Cvrk D, James K, De Guzman RM, Brigida S, Diouf K, Goldfarb I, Bebell LM, Yonker LM, Fasano A, Rabi SA, Elovitz MA, Alter G, Edlow AG. COVID-19 vaccine response in pregnant and lactating women: a cohort study. *medRxiv* [Preprint] 2021. DOI: 10.1101/2021.03.07.21253094.
71. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336**: 924–926.

Ultrasound Obstet Gynecol 2021; **57**: 687–697
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Asesoramiento en medicina materno-fetal: Infección por SARS-CoV-2 en el embarazo

RESUMEN

El coronavirus del síndrome respiratorio agudo grave 2 (SRAS-CoV-2) es un coronavirus zoonótico que ha contagiado a otras especies e infectado a los seres humanos, causando la enfermedad de coronavirus 2019 (COVID-19). A pesar del riesgo potencialmente mayor de que las mujeres embarazadas adquieran la infección por el SRAS-CoV-2 en comparación con la población no embarazada (en particular en algunas minorías étnicas), no se necesitan recomendaciones específicas adicionales para evitar la exposición durante el embarazo. Los síntomas clínicos y los indicios de laboratorio más comunes de la infección por SRAS-CoV-2 en el embarazo son fiebre, tos, linfopenia y niveles elevados de proteína C reactiva. El embarazo se asocia a un mayor riesgo de infección grave por SRAS-CoV-2 en comparación con la población no embarazada, que incluye neumonía, ingreso en la unidad de cuidados intensivos y la muerte, incluso después de ajustar con respecto a los posibles factores de riesgo de resultados graves. El riesgo de aborto no parece ser mayor en las mujeres con infección por SRAS-CoV-2. La evidencia relativa al parto prematuro y a la mortalidad perinatal es contradictoria, pero estos riesgos suelen ser mayores sólo en las mujeres sintomáticas y hospitalizadas. El riesgo de transmisión vertical, definido como la transmisión del SRAS-CoV-2 de la madre al feto, o al recién nacido, es generalmente bajo. Las intervenciones traumáticas fetales se consideran generalmente seguras en las mujeres embarazadas con infección por el SRAS-CoV-2, aunque la evidencia es aún limitada. En las mujeres embarazadas con COVID-19, no debe evitarse el uso de esteroides si está indicado clínicamente; el régimen preferido es un tratamiento de 2 días de dexametasona seguido de un tratamiento de 8 días de metilprednisolona. Si no hay contraindicaciones, se pueden utilizar antiinflamatorios no esteroideos. Las mujeres embarazadas hospitalizadas con COVID-19 grave deben someterse a tromboprofilaxis durante toda la hospitalización y al menos hasta el alta, preferiblemente con heparina de bajo peso molecular. A las mujeres hospitalizadas que se han recuperado de un período de enfermedad grave o crítica con COVID-19 se les debe ofrecer una exploración del crecimiento fetal unos 14 días después de haberse recuperado de su enfermedad. En las mujeres asintomáticas o ligeramente sintomáticas que han dado positivo en la prueba de infección por SRAS-CoV-2 a término (es decir, ≥ 39semanas de gestación), la inducción del parto podría ser aconsejable. Hasta la fecha, no existe un consenso claro sobre el momento óptimo para el parto de las mujeres en estado crítico. En las mujeres asintomáticas o con pocos síntomas, la atención durante el parto debe seguir las pautas rutinarias basadas en la evidencia. Independientemente del estatus de COVID-19, las madres y sus bebés deben permanecer juntos y se debe practicar la lactancia materna, el contacto piel con piel, el cuidado madre canguro y mantener la cuna al lado día y noche, al tiempo que se aplican las medidas necesarias de prevención y control de infecciones. Muchas mujeres embarazadas ya han sido vacunadas, sobre todo en los Estados Unidos, donde los primeros informes no muestran diferencias significativas en los resultados del embarazo en las mujeres embarazadas que se vacunan contra el SRAS-CoV-2 durante el embarazo, en comparación con el riesgo de base. Se encontraron anticuerpos generados por la vacuna en las muestras de sangre del cordón umbilical y de leche materna de las mujeres embarazadas y lactantes que recibieron la vacuna de ARNm para COVID-19. A partir de los limitados datos disponibles sobre la seguridad de la vacuna para COVID-19 en el embarazo, parece razonable ofrecer la opción de la vacunación a las mujeres embarazadas después de un asesoramiento preciso sobre el riesgo potencial de una evolución grave de la enfermedad y el riesgo desconocido de exposición del feto a la vacuna.

母婴医学咨询：怀孕期间的 SARS-CoV-2 感染

摘要

冠状病毒 2 严重急性呼吸系统综合征（SARS-CoV-2）是一种人畜共患的冠状病毒，其跨物种感染人类，导致 2019 年冠状病毒疾病爆发（COVID-19）。尽管与未怀孕的人群（尤其是在某些少数族裔人群中）相比，孕妇感染 SARS-CoV-2 的风险可能更高，但怀孕期间无需额外的具体建议避免接触感染源。孕妇 SARS-CoV-2 感染最常见的临床症状和实验室表征是发烧，咳嗽，淋巴细胞减少和 C 反应蛋白水平升高。与非妊娠人群（包括肺炎，重症监护病房入院和死亡）相比，妊娠与严重的 SARS-CoV-2 感染风险较高相关，即使在调整了严重后果的潜在危险因素后也是如此。患有 SARS-CoV-2 感染的女性流产的风险似乎没有增加。关于早产和围产期死亡率的证据相互矛盾，但这些风险通常仅在有症状，住院的妇女中更高。垂直传播（定义为 SARS-CoV-2 从母亲向胎儿或新生儿传播）的风险通常较低。尽管证据仍然有限，但认为胎儿入侵性检查对患有 SARS-CoV-2 感染的孕妇通常是安全的。患有 COVID-19 的孕妇，如果符合临床适应症，使用类固醇则不应当被避免。优选的方案是地塞米松 2 天疗程，随后使用甲基泼尼松龙 8 天疗程。如果没有禁忌症，可以使用非甾体类抗炎药。住院的严重 COVID-19 孕妇应在整个住院期间进行血栓预防治疗至少持续至出院前，最好使用低分子量肝素。从严重或重症 COVID-19 疾病中康复的住院孕妇，应在疾病康复后约 14 天接受胎儿生长扫描。<14>在足月（即</ 14>≥<263>妊娠 39 周）SARS-CoV-2 感染呈阳性的无症状或轻度症状的女性中，引产是较合理的。</ 263>迄今为止，对于重症孕妇的最佳分娩时间尚无明确共识。对于没有症状或症状很少的孕妇，分娩治疗应遵循常规的循证指南。不论 COVID-19 状况如何，母亲和婴儿都应保持在一起及母乳喂养，并应用皮肤接触，袋鼠妈妈护理法则及全天候产房内护理方案，同时采取必要的感染防控措施。许多孕妇已经进行了疫苗接种，大部分在美国的第一份报告显示，与背景风险相比，怀孕期间接受 SARS-CoV-2 疫苗接种的孕妇的妊娠预后没有显着差异。接受 mRNA COVID-19 疫苗的孕妇和哺乳期妇女的脐带血和母乳样品中均存在疫苗产生的抗体。根据现有的关于 COVID-19 疫苗在妊娠中安全性的有限数据，在对严重病程的潜在风险和未知的胎儿病毒接触风险进行了准确的咨询之后，为孕妇提供疫苗接种选择似乎是合理的。

