

## Pregnancy and COVID-19

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### Abstract

The COVID-19 virus also affects pregnant women. While the vast majority of infected patients have few symptoms, about 10% of them may have a pneumonia that is important to diagnose and treat. Initial data from the literature suggest management similar to that of the general population. There is a greater risk of premature delivery requiring the administration of corticosteroids for fetal lung maturation in the event of imminent delivery. The route of delivery should be guided by obstetric history even though a large proportion of caesarean sections are included in the published series. Loco-regional anaesthesia is allowed. To date, only a few cases of mother-fetal transmission have been described, rather related to per or postpartum transmission. The rate of perinatal morbidity and mortality is very low. Only one maternal death has been described. Breastfeeding is allowed with protective measures (hand disinfection, mask for the delivery). In conclusion, all the current studies suggest that pregnant women infected with COVID-19 and their newborn babies have a good prognosis of evolution, but it will be necessary to wait for large multicentric and well-documented series to confirm these data.

**Keywords:** Pregnancy; COVID-19; Respiratory distress; Influenza; Mechanical ventilation

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**Citation:** Moussaoui KE, Baidada A,  
Kharbach A (2021) Pregnancy and  
COVID-19. J Women's Health Reprod Med  
Vol. 5 No. 3: 11.

**Received:** February 03, 2021; **Accepted:** February 18, 2021; **Published:** February 25, 2021

### Introduction

A new strain of coronavirus called SARS (Severe Acute Respiratory Syndrome)-CoV-2 or COVID-19 was isolated from humans in late 2019 in China. She is currently responsible for a pandemic recognized by WHO as a public health emergency. If 75% are not very symptomatic (flu-like syndrome, myalgia, headache, cough, nasal congestion), the remaining 25% may present with moderate to severe respiratory distress having taken hospital care and sometimes respiratory assistance. Incubation is on average 5 days [1-13] and contagiousness is greater than that of seasonal influenza. The population particularly at risk of complications concerns elderly, immune compromised patients or those who carry co-morbid factors such as obesity, cardiovascular disease, diabetes or cancer [14,1]. The pregnant woman could theoretically be part of these risk groups by immunosuppression induced by pregnancy as well as other physiological changes such as elevation of the diaphragm, increased oxygen consumption, edema. Respiratory mucous membranes which make it more vulnerable to hypoxia [2].

### COVID-19 and Pregnancy: What We Know from the Chinese Experience

Several publications have described the clinical course of pregnant women infected with COVID-19; Chen et al. reported 9 cases of pregnant patients who presented with lung disease in the 3rd trimester linked to COVID-19. All of them gave birth by caesarean section either for deterioration of the general

condition or because of acute fetal distress. No maternal deaths have been observed. Analysis of amniotic fluid, cord blood, throat smear and breast milk were negative, suggesting the absence of maternal-fetal transmission of the virus [3]. Liu et al. described a series of 13 pregnant patients between 22 and 36 weeks of which 77% presented with pyrexia and 3% were dyspneic. Their clinical course allowed 23% to return home and the remaining 77% gave birth by caesarean section either for fetal distress or following a premature rupture of the water bag with failure of the trial of labor. Almost half of them (46%) gave birth prematurely between 32 and 36 weeks. There is one case of fetal death in utero. Only one patient presented with severe respiratory distress requiring the initiation of ECMO (Extra Corporeal Membrane Oxygenation) [4].

Chen et al. studied the placentas of 3 pregnant women infected with COVID-19 and who had an emergency caesarean section. Histological analysis showed the presence of fibrin deposits but no lesions suggestive of villitis or chorioamnionitis. Both placentas and new borns have tested negative for the presence of viral RNA suggesting the absence of vertical transmission of COVID-19 [5]. A meta-analysis published by Schwartz on a series of 38 infected Chinese pregnant women shows that COVID-19 causes morbidity and mortality in pregnant women that is less than those of other coronaviruses such as SARS or MERS (Middle East Respiratory Syndrome). No cases of severe pneumonia or maternal mortality have been reported. However, there is an increased incidence of delivery haemorrhage. There was one neonatal death in a child

born prematurely and died on day 9 in a context of multi-systemic decompensation. Liu et al. reported a series of 15 pregnant women in the third trimester with COVID-19 Pneumonia: The main clinical complaints were fever (86%) and cough (60%). In biology, lymphopenia was present in 80% of cases. All patients received a low-dose chest CT scan (between 0.01 and 0.66 mGy) with a lead abdominal apron that showed images of frosted glass opacities, with peripheral distribution that appear to be pathognomonic for COVID pneumonia. All patients were put on oxygen and none used mechanical ventilation. They did not receive antiviral treatment or hydroxy-chloroquine but only an antibiotic carrier to avoid bacterial super infection.

The latest meta-analysis published by Zaigham and Andersson analysed 108 pregnancies with proven COVID-19 infection, the majority of which were in the Chinese population. In 80% of cases, the infection occurred in the third trimester, with 68% having fever, 34% coughing, 59% lymphocytopenia and 70% elevated CRP. A caesarean section was performed in 91% of cases. With regard to fetal and neonatal morbidity, there was 1 case of fetal death in utero, 1 neonatal death at 34 weeks [8]. In this meta-analysis, it is noted that there were two new-borns tested positive for COVID-19 (PCR) and carrying IgM antibodies to COVID, suggesting a possible infection in utero [9]. In the USA, a first series of 43 cases of infected pregnant women reported a rate of 67.4% of symptomatic patients (86% moderate, 9.3% severe and only 4.7% critical) Among the 32.6% of asymptomatic patients detected by universal testing, 70% later presented symptoms [10]. Finally, a first case of maternal-fetal mortality linked to COVID-19 was reported by Karami et al. in Iran in a young 27-year-old patient in the third trimester with severe pneumonia leading to intubation and lethal multi-systemic decompensation [11].

## Proposed Care for Pregnant Women Infected with COVID-19

Several consensus articles on the management of pregnant women with a suspected or confirmed diagnosis of COVID-19 have been published [12,13,15].

### Prevention

Importance of classic eviction strategies (hand washing, wearing a mask). Since the beginning of April, there has been a recommendation to screen all pregnant women admitted to the delivery room following a New York study. Published in the NEJM showing that if 2% are symptomatic and test positive, there are 13.5% of parturients who are asymptomatic carriers [16].

### Management

In case of suspected infection, if the symptomatology is mild and the patient is not beyond the 24-week term of fetal viability, rest at home and management with the attending physician. If the patient has more severe symptoms (fever, cough, respiratory discomfort) or presents comorbid factors, she should be seen in a COVID screening unit and tested by nasopharyngeal swab (screening for COVID-19 viral RNA and Influenza by RT PCR).

In case of suspicion or confirmation of infection, provide for isolation (if possible in a negative pressure room), reception by

staff equipped according to recommended standards (FFP2 mask, hat, safety glasses, gown, on shoes).

Monitoring of clinical parameters (temperature, pulmonary auscultation, respiratory frequency, O<sub>2</sub> saturation) and biological parameters (CRP, haemogram, hepatic enzymology, CK, coagulation tests). Placing an entry route according to severity and if hospitalisation-oxygen therapy if SpO<sub>2</sub> is less than 95% [17].

### Treatment

Depending on the degree of severity, the various authors propose the use of the same treatments as for other patients. The antiviral drugs of choice during pregnancy are Lopinavir/Ritonavir (200 mg/50 mg per capsule) even if they are not approved by the FDA [13]. Indeed, the risk of teratogenicity of these antivirals is very low [18]. Hydroxy-chloroquine is authorised during pregnancy [15]. Antibacterial treatment is also recommended to avoid bacterial super infection, e.g. with IV ceftriaxone, ampicillin or azithromycin (0.5 mg/d) PO for 5 days [13-15,18]. Corticosteroid use remains a subject of discussion: Methylprednisolone (1-2 mg/kg/day) has been administered for 3-5 days in cases of severe persistent hypoxemia. If there is a risk of premature delivery, fetal lung maturation with beta or dexamethasone according to standard obstetric protocols should be administered, but in cases of severe or critical impairment, this can be discussed with internists [18,15].

### Monitoring of the fetus

It should be considered from the time of viability, given the potential risks of fetal distress related to infection and pyrexia. In symptomatic patients and of course, depending on their degree of severity, cardiotocograms are recommended and should be repeated as well as ultrasound monitoring of fetal growth, amniotic fluid index and fetal Dopplers. Invasive examinations such as amniocentesis are not indicated [12,15].

### The decision to give birth

This should not be taken before term except in the event of deterioration in maternal health or fetal distress. There appears to be no benefit in recommending a caesarean section unless the pneumonia is severe and uncontrolled. In the Chinese studies, they were mostly carried out because of a deterioration in fetal cardiac monitoring [12,15]. In the case of vaginal delivery, it should be borne in mind that if the amniotic fluid is sterile, the virus may be present in the maternal faeces. The timing of delivery should be chosen if there are associated obstetric complications (placenta previa, pre-eclampsia) or if the patient's clinical situation remains unstable and not improved by treatment [19].

### The delivery

It should ideally take place in a room with negative pressure. Staff should be limited to what is strictly necessary and should be equipped with appropriate protective clothing. The route of delivery is related to obstetric conditions, but the risk of caesarean section must be anticipated to enable the teams to take adequate protective measures in case of emergency [19]. It appears that postpartum haemorrhage is more frequent, as is the case with other infections. In the case of COVID-19 viremia, there

are changes in haemostasis parameters which can mimic a HELLP syndrome with thrombocytopenia and hepatic cytolysis. A greater than physiological increase in D-dimers, a drop in fibrinogen, an alteration in PTT and accelerated fibrinolysis can also be observed in cases with a severe prognosis. The thrombotic risk is also greater in patients infected with COVID-19, so care should be taken to ensure proper hydration, use support stockings and administer Low Molecular Weight Heparin (LMWH) when bed rest. In the event of caesarean section, it is recommended that thromboprophylaxis be maintained for 6 weeks postpartum [20]. The use of prostaglandins as an utero tonic should be discussed with internists in view of their broncho constrictor effect in cases of severe pneumonia.

### Fetal complications

To date, no studies have reported cases of fetal malformation or miscarriage associated with COVID-19, but caution should be exercised due to the lack of information on the evolution of infected pregnancies in the first and second trimesters, and one case of in utero mortality in a context of severe maternal respiratory distress and ECMO [4]. There is an increased incidence of premature deliveries, some of which are spontaneous as a result of infection and pyrexia, but others are elective as a result of fetal distress or deterioration in maternal status [3-6]. Given that the pandemic occurred only 4 months ago, there is also a lack of information on the long-term consequences of the inflammation produced after the acute phase of infection on the fetus and placenta. For this reason, there is a need for closer ultrasound follow-up in patients infected during pregnancy, even if they were moderately infected, and for long-term studies of the fate of the children.

### Neonatal complications

The risk of maternal-fetal vertical transmission appears to be very low and even non-existent in the small series published to date [3,4,6,7] but the whole paragraph will be discussed in another article in this special issue.

### Conclusion

Pregnant women are by definition at greater risk of developing a lung infection mainly due to physiological changes in lung function. All the studies based on small series and meta-analyses show that pregnant women infected with COVID-19 and their new-borns have a rather good prognosis both in terms of morbidity and mortality.

### Conflict of Interest

None.

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