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## Current State of Knowledge About SARS-CoV-2 and COVID-19 Disease in Pregnant Women

Authors' Contribution:  
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Funds Collection G

ABDEF 1 **Mariusz Gujski**  
BDEF 2 **Ewa Humeniuk**  
ACDEF 3 **Iwona Bojar**

1 Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland  
2 Department of Pathology and Rehabilitation of Speech, Medical University of Lublin, Lublin, Poland  
3 Department of Women's Health, Institute of Rural Health in Lublin, Lublin, Poland





**Corresponding Author:** Mariusz Gujski, e-mail: [mariusz.gujski@wum.edu.pl](mailto:mariusz.gujski@wum.edu.pl)  
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During any epidemic of infectious diseases, pregnant women constitute an extremely sensitive group due to altered physiology and immune functions, and thus altered susceptibility to infection. With regard to the management of pregnant COVID-19 patients, in addition to the treatment of the infection itself, which is not that different from generally accepted principles, it is interesting to consider which obstetric procedures should be used to minimize the adverse effects on mother and child. Questions arise concerning the continuation of pregnancy, how to terminate the pregnancy, the possibility of virus transmission through the placenta, isolation of the newborn after birth, and breastfeeding.

The aim of this study was to review the current state of knowledge about SARS-CoV-2 infection and COVID-19 disease in pregnant women. Because the epidemic began in China, most of the available literature comes from studies conducted there. The studies used to prepare this review article are the first non-randomized studies containing small groups of examined women. They do not provide clear indications, but show that in an epidemic situation, special care should be taken in pregnancy management, making decisions about termination of pregnancy, and handling of the newborn baby to minimize the risk of subsequent health consequences. Further analysis is needed on the incidence of COVID-19 among pregnant women and its consequences. This will allow us to develop recommendations on how to deal with patients in the future in case of repeated epidemic emergencies.

**MeSH Keywords:** **COVID-19 • Parturition • Pregnancy • Pregnancy Complications, Infectious • Pregnancy Outcome • SARS Virus**

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The first global problem with viral infections belonging to the Coronavirinae subfamily in the Coronaviridae family in the current century appeared in 2002, and it was SARS-CoV [1]. Another epidemic with a significant mortality rate was MERS-CoV [2]. At present, the entire world is struggling with the SARS-CoV-2 infection pandemic. It has been observed that some types of coronavirus (CoV) that are dangerous to human health and life appear periodically and unpredictably and spread rapidly. SARS-CoV-2 infection and COVID-19 disease were first identified in Wuhan, Hubei province, China at the end of 2019. This virus has spread rapidly throughout the world. At the beginning of March, the epicenter moved to Europe. In mid-March 2020, the WHO declared a pandemic [3]. At present, the SARS-CoV-2 epidemic affects virtually the entire world.

The aim of this study was to review the current state of knowledge about SARS-CoV-2 infection and COVID-19 disease in pregnant women. Since the beginning of the epidemic was in China, the majority of available literature comes from studies conducted in that area.

Immunological studies have led to a partial understanding of the body's response to viral infections and the immune response to viruses. The immune response inhibits virus replication, promotes virus removal, induces tissue repair, and triggers an extended adaptive immune response against viruses.

Similar mechanisms of immune response occur during SARS-CoV-2 infection, causing pulmonary and systemic inflammatory responses [4]. The viral inflammatory response plays a key role in cases of lung damage caused by SARS-CoV-2. In an Australian study, elevated levels of antibody-secreting cells (ASC), T follicular helper cells (TFH), activated CD4+ and T CD8+ T lymphocytes, and IgM and IgG antibodies that bind the coronavirus SARS-CoV-2 causing COVID-19 were observed, and immunological changes persisted for at least 7 days after full resolution of symptoms [5].

In the vast majority of cases, the immune system of people infected with SARS-CoV-2 coronavirus can cope with the infection, and patients recover without the need for experimental antiviral treatment. In the context of being at risk of further CoV infections with high mortality rates, pregnant women seem to be in a special situation. Pregnancy is a period of far-reaching physiological adaptation of a woman's body to ensure proper development of the fetus. The immune system is particularly subject to changes, as on one hand it must be ready to combat infections and, on the other hand, it must tolerate antigenically foreign fertilized egg cells. According to current knowledge, this is caused by immune mechanisms associated with functional regulation of the elements of specific and non-specific maternal immunity and by immunoregulation of placenta and fetal origin. The most important immunological

mechanisms ensuring the correct development of pregnancy include weak trophoblast antigenicity, the immunoregulatory role of cytokines (e.g., predominance of Th2 over Th1 immune response), the immunoregulatory effect of progesterone, the immunoregulatory role of blocking antibodies, and immunoregulation at the temporal level [6].

Changes in the immunology of a pregnant woman's body are discussed in relation to further emerging infection risks. The reaction of a pregnant woman's body to an infectious agent may be slightly different. During the SARS and MERS epidemics, heavier courses of infections and higher mortality rates were observed among pregnant women than among non-pregnant ones [7]. Therefore, it cannot be ruled out that in the current SARS-CoV-2 pandemic, there will be a more severe course of this infection among pregnant women compared to non-pregnant ones. On the contrary, Dashraath et al. assumed that changes in the hormonal environment during pregnancy that affect the immune response to viral pathogens, together with the physiological predominance of Th2, may promote the expression of the anti-inflammatory effect of cytokines (e.g., IL-4 and IL-10), and, together with other unidentified mechanisms of immune adaptation, may affect the immune response associated with SARS-CoV-2. This may result in lower intensity of COVID-19 symptoms in pregnant women compared to non-pregnant women [8].

Current epidemic data indicate that COVID-19 more often affects men than women, but there is still too little data on pregnant women to be certain of the prognosis in this group. In the current situation, when most countries are fighting the SARS-CoV-2 epidemic, even incomplete data can be useful for planning the protection of infected pregnant women.

With regard to the management of pregnant COVID-19 patients, in addition to the treatment of the infection itself, which is not that different from generally accepted principles, it is interesting to consider what obstetric procedures should be applied to minimize the adverse effects on mother and child. Questions arise concerning the continuation of pregnancy, how to terminate the pregnancy, the possibility of virus transmission through the placenta, isolation of the newborn after birth, and breastfeeding. In the face of current life-saving measures, few wonder about the subsequent psychological effects of mothers and their children.

There are few studies on the incidence of COVID-19 in pregnant women. In a study by Chen et al. [9], 9 women were diagnosed with COVID-19 during the third trimester of pregnancy. Although none of the women have previously had concomitant diseases such as diabetes, cardiovascular diseases, or hypertension, single cases of infection have resulted in pregnancy hypertension and pre-eclampsia. The clinical

symptoms of COVID-19 were similar to those in other adults: fever (7/9), cough (4/9), muscle pain (3/9), sore throat (2/9), malaise (2/9), gastrointestinal symptoms (1/9), and dyspnea (1/9). Laboratory tests showed elevated CRP (6/9), lymphopenia (5/9), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) (3/9). CT scans of the thorax were abnormal in 8 of 9 women. In all women, the pregnancy was terminated by cesarean section, 4 women gave birth prematurely, but none before 36 weeks of pregnancy [9].

The condition of newborns assessed on the Apgar scale was 8–9 after 1 minute and 9–10 after 5 minutes. The presence of SARS-CoV-2 was assessed in 6 out of 9 cases in amniotic fluid, breast milk, umbilical cord blood culture, and newborn throat swab culture. All tests were negative [9].

In a study by Zhu [10] in 9 pregnant women (8 single pregnancies, 1 twin pregnancy) with confirmed COVID-19 infection, the clinical symptoms developed in 4 cases before delivery, in 2 cases on the day of delivery, in the remaining ones after childbirth (7 cesarean sections, 2 natural deliveries). Most of the first symptoms were fever and cough, and 1 patient developed diarrhea. Six women gave birth prematurely and 4 delivered on time. Although none of the newborns were confirmed to be infected, 6 had dyspnea, 2 had fever, 2 had thrombocytopenia with associated normal liver function, 1 had increased heart rate, 1 had vomiting, and 1 had pneumothorax. One of the newborns died [10].

Zhang et al. [11] performed a retrospective analysis comparing the results of pregnant women infected with SARS-CoV-2 with pneumonia (n=16) and 45 without pneumonia. Only 1 of the patients with pneumonia had severe condition. The methods of delivery in both groups were cesarean sections, and the weeks of pregnancy were (38.7±1.4) weeks and (37.9±1.6) weeks, with no significant differences being found. There was also no difference in intraoperative blood loss and neonatal weight loss. None of the newborns had been infected. There were no differences in the condition of newborns [11].

Liu et al. [12] described the clinical course and results of 13 pregnant women with COVID-19. Cesarean section was performed in 5 patients (38%). There was a single case of stillbirth. Premature delivery with various indications occurred in 6 women (46%). One woman had multi-organ failure and was mechanically ventilated [12].

Wang et al. [13] described a 28-year-old pregnant woman (30<sup>th</sup> week) who reported to the hospital with a week-long fever. A throat swab test for SARS-CoV-2 was negative. After 2 days, a CT scan of the thorax showed pneumonia. Repeated testing for SARS-CoV-2 was positive. The patient was transferred to the intensive care unit, where she was placed in isolation.

On the third day of hospitalization, the fetus' movements decreased; therefore, a cesarean section was performed. The newborn (1.83 kg) received 9 and 10 points on the Apgar scale after 1 and 5 minutes, respectively. Samples were taken from the placenta, amniotic fluid, umbilical cord blood, swab cultures from the infant's gastric juice, and throat – all results for SARS-CoV-2 were negative. Seven and 9 days after delivery, the smears from the throat of the mother and infant were negative [13].

Fan et al. [14] described 2 cases of pregnant women (both physicians) with COVID-19 in the third trimester. Fever (37.3–37.5°C) was found in a 34-year-old woman in the 37<sup>th</sup> week of the second pregnancy, without significant diseases. After 2 days, the fever dropped, but returned 2 days later, along with a rash on her stomach, which spread quickly throughout the entire body. SARS-CoV-2 was confirmed 6 days after the beginning of the fever. Pneumonia was confirmed on day 8. A cesarean section was performed on day 10. The baby weighed 3400 g, received 9 and 10 points on the Apgar scale 1 and 5 minutes after birth, respectively. The baby was separated from its mother immediately. On day 3 of life, the child developed fever and abdominal bloating with lymphopenia (16.87%). On day 4, an X-ray of the thorax demonstrated pneumonia, with good response to drugs. The results of SARS-CoV-2 tests were negative. The treatment of the mother was completed after 1 month [14].

The second analyzed case was a 29-year-old woman, in the 36<sup>th</sup> week of her first pregnancy, with no past health problems. The symptoms started with a fever (37.6–38.5°C), nasal mucosa congestion, and sore throat. The patient was admitted to the hospital after 2 days. The nasopharyngeal swab was positive for SARS-CoV-2. Pneumonia was diagnosed 5 days after the first symptoms appeared. Due to the persistent fever, a cesarean section was performed after another 2 days. The weight of the newborn was 2890 grams and the results on the Apgar scale were 9 and 10 after 1 and 5 minutes, respectively. Although SARS-CoV-2 has not been detected, the newborn developed mild pneumonia and lymphopenia (10.5%), with good response to treatment. The treatment of the mother was completed after 26 days [14].

A retrospective study [15] described 7 women aged 29–34 years, with gestational age from 37 to 41 weeks. Clinical symptoms included fever (86%), as well as cough, dyspnea, and diarrhea (14%). All patients had normal leukocyte count and elevated C-reactive protein level. Bilateral pneumonia was present in 86% and 14% had unilateral pneumonia. In 71%, neutrophil counts were higher than normal, and lymphocyte counts were lower than normal. In total, 29% had various degrees of liver function abnormalities, low platelet count, and D-dimer level above normal. Antiviral treatment including oseltamivir (75 mg every 12 hours, orally), ganciclovir (0.25 g every 12 hours, intravenously) and interferon (40 µg daily, spray inhalation), and

arbidol tablets (200 mg 3 times per day, orally) was administered. All patients received treatment with antibiotics (cephalosporin, quinolones and macrolides). Methylprednisolone was also used after cesarean section in 71%. All women had a cesarean section within 3 days of COVID-19 clinical symptom onset. The birth weights of newborns and the Apgar scores were normal. Three newborns were tested for SARS-CoV-2, with 1 being infected – it had minor symptoms of dyspnea, and an X-ray of the thorax showed mild pneumonia. The authors emphasized that although they administered antiviral treatment, no data concerning their safety and efficacy in COVID-19 treatment in general and in pregnant women have been published so far [15].

The largest described group of pregnant women (43) with confirmed SARS-CoV-2 was presented by Breslin et al. [16]. These patients were hospitalized in 2 hospitals in New York from March 13 to 27, 2020. Fourteen women (32.6%) did not have any viral symptoms associated with COVID-19 at the time when SARS-CoV-2 infection was detected. Among them, 10 (71.4%) developed symptoms or signs of COVID-19 infection during or early after delivery. In 29 patients (67.4%) who had symptomatic COVID-19 infection, 3 women required hospitalization and antiviral treatment, and 1 woman received oxygen treatment after delivery due to her deteriorating condition. This study did not confirm SARS-CoV-2 cases in newborns. In summary, the authors stated that 37 (86%) women had a benign form of COVID-19, 4 (9.3%) had serious disease, and 2 (4.7%) developed critical disease [16].

Studies published so far on pregnant women infected with SARS-CoV-2 and suffering from COVID-19 do not allow clear conclusions on the clinical course or the condition of the mother and the newborn [17]. At present, there is also no evidence that SARS-CoV-2 is subject to intrauterine or transplacental transmission to the fetus [18].

There are no conclusive data indicating fetal organ damage during maternal virulence [19].

The suspicions that the course of SARS-CoV-2 infection and COVID-19 disease may be more severe in pregnant women compared to non-pregnant women were not confirmed. Breslin et al. found that the percentages of pregnant women with mild, severe, and critical COVID-19 were similar to those in the general population [16]. This does not confirm previous observations that changes in the immune system in pregnancy

predispose to a more severe infection course, as was the case during the SARS and MERS epidemics. This is encouraging data that requires confirmation by studies in larger groups. However, some experts suggest that if pregnant women have been diagnosed with COVID-19, the newborn should be isolated and assessed for possible negative effects [20].

There are ongoing efforts with experts trying to develop rules for dealing with infected people in every country affected by the COVID-19 pandemic. This is also the case for infected pregnant women. The cases of pregnant women described by Chen et al. are an example of extreme caution exercised by Chinese doctors when managing pregnant women during the epidemic [21].

At the beginning of February 2020, a multidisciplinary teleconference with Chinese doctors and researchers was held, and strategies for the medical management of COVID-19 infection during pregnancy were discussed. The 10 most important recommendations were presented, which are being discussed and supplemented on an ongoing basis. These recommendations concern the isolation, treatment, and monitoring of infections in pregnant women. On the other hand, with still inadequate data, the optimal time of labor and the safety of vaginal delivery or cesarean section should be individualized based on obstetric indications and the condition of the mother and fetus [22].

In the future, the analysis of the COVID-19 disease among pregnant women will allow us to develop recommendations on management of patients in case of repeated epidemic risk situations.

## Conclusions

During any epidemic of infectious diseases, pregnant women constitute an extremely sensitive group due to altered physiology and immune functions, and thus altered susceptibility to infection. In an epidemic situation, special care should be taken in pregnancy management and in making decisions on termination of pregnancy and handling of the newborn baby in order to minimize the risk of subsequent health consequences. Further analysis is needed of the incidence of COVID-19 among pregnant women and its consequences. This will allow us to develop recommendations on management of patients in case of repeated epidemic emergencies.

## References:

1. Hörmansdorfer S, Campe H, Sing A: SARS – pandemie und emerging disease. *J Verbr Lebensm*, 2008; 3: 417–20
2. Wernery U, Lau S, Woo P: Middle East respiratory syndrome (MERS) coronavirus and dromedaries. *Vet J*, 2017; 220: 75–79
3. Cucinotta D, Vanelli M: WHO Declares COVID-19 a pandemic. *Acta Biomed*, 2020; 91(1): 157–60
4. Li G, Fan Y, Lai Y et al: Coronavirus infections and immune responses. *J Med Virol*, 2020; 92(4): 424–32
5. Thevarajan I, Nguyen THO, Koutsakos M et al: Breadth of concomitant immune responses prior to patient recovery: A case report of non-severe COVID-19. *Nat Med*, 2020; 26(4): 453–55
6. Malinowski A, Wilczyński JR: Immunologiczne mechanizmy utrzymania ciąży. *Gin Prakt*, 2003; 11(4): 47–56 [in Polish]
7. Mullins E, Evans D, Viner RM et al: Coronavirus in pregnancy and delivery: Rapid review. *Ultrasound Obstet Gynecol*, 2020; 55(5): 586–92
8. Dashraath P, Wong LJJ, Lim MXK et al: Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *Am J Obstet Gynecol*, 2020 [Epub ahead of print]
9. Chen H, Guo J, Wang C et al: Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *Lancet*, 2020; 395(10226): 809–15
10. Zhu H, Wang L, Fang C et al: Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*, 2020; 9(1): 51–60
11. Zhang L, Jiang Y, Wei M et al: [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province.] *Zhonghua Fu Chan Ke Za Zhi*, 2020 [in Chinese] [Epub ahead of print]
12. Liu Y, Chen H, Tang K et al: Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect*, 2020 [Epub ahead of print]
13. Wang X, Zhou Z, Zhang J et al: A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. *Clin Infect Dis*, 2020 [Epub ahead of print]
14. Fan C, Lei D, Fang C et al: Perinatal transmission of COVID-19 associated SARS-CoV-2: Should we worry? *Clin Infect Dis*, 2020 [Epub ahead of print]
15. Yu N, Li W, Kang Q et al: Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: A retrospective, single-centre, descriptive study. *Lancet Infect Dis*, 2020; 20(5): 559–64
16. Breslin N, Baptiste C, Gyamfi-Bannerman C et al: COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM*, 2020 [Epub ahead of print]
17. Sahu KK, Lal A, Mishra AK: COVID-2019 and pregnancy: A plea for transparent reporting of all cases. *Acta Obstet Gynecol Scand*, 2020 [Epub ahead of print]
18. Schwartz DA: An analysis of 38 pregnant women with COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: Maternal coronavirus infections and pregnancy outcomes. *Arch Pathol Lab Med*, 2020 [Epub ahead of print]
19. Luo Y, Yin K: Management of pregnant women infected with COVID-19. *Lancet Infect Dis*, 2020; 20(5): 513–14
20. Working Group for the Prevention and Control of Neonatal 2019-nCoV Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics. [Perinatal and neonatal management plan for prevention and control of 2019 novel coronavirus infection (1<sup>st</sup> Edition)]. *Zhongguo Dang Dai Er Ke Za Zhi*, 2020; 22(2): 87–90 [in Chinese]
21. Chen Y, Li Z, Zhang YY et al: Maternal health care management during the outbreak of coronavirus disease 2019 (COVID-19). *J Med Virol*, 2020 [Epub ahead of print]
22. Chen D, Yang H, Cao Y et al: Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection. *Int J Gynaecol Obstet*, 2020; 149(2): 130–36