

Effects of Coronavirus and Pneumonia on Pregnancy and Fetal Status

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Abstract: One of the most common complications in pregnant women infected with COVID-19 is the development of pneumonia. Taking into account that the supply of oxygen to the fetus directly depends on the level of oxygen in the mother's blood, respiratory failure often caused by the pathology of the respiratory system leads to hypoxia of the fetus. Also, the effect of the virus on the fetus is different and can often cause the development of pathological conditions. And since the treatment is carried out by prescribing antibiotics, the effectiveness of the therapy can be achieved at the cost of harming the health of the unborn child. Therefore, as a solution to this problem, it is necessary to thoroughly study the complications of new coronavirus infection in pregnancy, develop preventive and rehabilitation measures.

Key points: COVID-19, SARS-CoV-2, viral pneumonia, premature birth, asphyxia, severe preeclampsia.

Enter. When the symptoms of the disease are evident in pregnant women infected with COVID-19, in particular, when the severe and critical form of the disease is detected, the risk of adverse pregnancy outcomes is high [1]. Pregnant women with mild or asymptomatic coronavirus had the same outcomes as those without a diagnosis of COVID-19, except for an increased risk of preeclampsia [2].

A study of cases of pregnant women with known or suspected SARS-CoV-2 infection in 12 countries worldwide showed an all-outcome early neonatal mortality rate of 0.2 to 0.3 percent, compared with national pre-pandemic rates not higher than the indicators [3]. Given the relatively recent onset of the pandemic, data on long-term outcomes are very limited [4].

It is known that after 20 weeks of pregnancy, the risk of maternal infection increases, and after 26 weeks of pregnancy, maternal infection increases the risk of a composite of adverse neonatal outcomes [5]. Also, the number of preterm births, the number of operative deliveries, and the increase in perinatal mortality in pregnant women infected with COVID-19 are related to the condition of the mother and the fetus due to the hypoxemia of the women [6].

COVID-19 infection is a potential risk factor for pregnancy, as impaired immune function and angiotensin-converting enzyme 2 (ACE2) receptor expression in trophoblastic tissue make pregnant women less resistant to disease [7].

Since the pandemic is a stress factor for pregnant women, it can have a negative effect on the condition of both the mother and the child [8]. During their research, Chinese scientists concluded that coronavirus infection is likely to cause premature birth and distress syndrome in the fetus [9].

There is anecdotal evidence that the level of vulnerability to COVID-19 in pregnant women depends on the trimesters of pregnancy. There is no significant evidence of effects in the first and second trimesters, but infection-induced elevated body temperature may harm the fetus [10]. The third trimester is the most dangerous period. Viral infection can lead to premature rupture of the fetal bladder, premature birth and undetermined condition of the fetus [11].

One of the important associations of coronavirus infection is hospitalization in the neonatal intensive care unit (birth asphyxia) and perinatal death [12]. Women with comorbidities such as hypertension, diabetes, and obesity have a higher risk of developing severe complications [13]. In addition, according to the results of many studies in the world, the risk of death in infected women was 22 times higher than in pregnant women who were not infected with COVID-19 [13].

SARS-CoV-2 cellular entry depends on the ACE 2 receptor and the serine protease TMPRSS2, which are minimally co-expressed in the placenta [14]. SARS-CoV-2 infection in the fetus is rare, but a postnatal analysis of infected patients showed inflammatory changes in the placenta, including thrombotic and vascular abnormalities [15].

As the primary target of COVID-19 is the respiratory system, respiratory distress is a common symptom in pregnant women [16]. Because of the normal physiological adaptation during pregnancy, the work of the respiratory system, which is working with tension, increases even more [17]. In addition, according to recent data, SARS-CoV-2 virus can cause rare complications such as multisystem inflammatory syndrome in pregnant women [18].

According to the data confirmed by the Swedish laboratory, the rate of need for intensive care, the risk of abortions and premature birth are higher in pregnant and postpartum women infected with SARS-CoV-2 than in other contingents [19].

During pregnancy, SARS-CoV-2 infections cause serious respiratory disorders, including pneumonia-like acute respiratory distress syndrome, disseminated microembolism, and blood coagulation disorders, causing non-obstetrical deaths of pregnant women [20].

It should be kept in mind that viral pneumonia has a higher risk of infection and serious complications in pregnant women than bacterial pneumonia [21]. In fact, physiological etiologies in pregnancy include: changes in cell-mediated immunity and changes in lung function increase the risk of developing pneumonia [22]. Some historical evidence indicates that pneumonia has a negative effect on the state of pregnancy, especially at the end of pregnancy [23]. It has been found that pneumonia in pregnant women can cause several complications: premature rupture of the membranes, intrauterine death of the fetus, restriction of fetal growth and premature birth [24, 23].

Complications of respiratory system infection in pregnant women with severe forms of COVID-19 lead to an increase in the number of transfers of the mother to artificial lung ventilation. Deterioration of the mother's respiratory condition, intubation and mechanical ventilation cause an increase in the number of premature births and caesarean sections. Studies of the period during which pregnant women were admitted to the hospital revealed that 72.7% of them had a cesarean section and 68.2% had a preterm birth (a third of preterm births occurred before 34 weeks of pregnancy) [25].

According to data from the Centers for Disease Control and Prevention as of June 2020, 31.5% of pregnant women and 5.8% of non-pregnant women were hospitalized with COVID-19 in 2019. During pregnancy, the high rate of this indicator is caused by severe and serious complications in pregnancy [26].

Pneumonia is a common lung infection that causes acute respiratory distress, especially in pregnancy, and requires hospitalization in 0.5–1.5 per 1000 pregnant women in the United States [27, 28]. Pneumonia is the most common non-obstetrical cause of maternal death in the United States [29, 30]. A number of physiological and immunological changes during pregnancy are the cause of more severe complications of pneumonia and death [28, 31].

Also, Romanyuk et al observed that pneumonia is associated with a significant increase in the incidence of early placental abruption, COPD, cesarean delivery, asphyxia, and severe preeclampsia in pregnant women [32].

Shariatzadeh, Marrie et al. (2006) recognized that pneumonia in pregnancy does not have any harmful effect on the condition of the fetus [28]. Therefore, as the relationship between pneumonia and pregnancy outcomes remains unclear, further local studies are required.

At the same time, the previous research results of some scientists did not show significant differences in premature delivery and low birth weight babies in pregnant women with pneumonia compared to other women [33]. These opposite findings were described in a relatively small group (10-15) of samples. Therefore, the available results indicate that pneumonia during pregnancy is understudied, which suggests that the research findings are not robust [34].

Early detection and timely treatment of severe pneumonia are important for normal pregnancy [35]. Gestational age has proven to be an important risk factor for pneumonia [35]. Other studies have shown that pregnant women are more susceptible to vaccine-preventable diseases than non-pregnant women [36]. Anemia for pneumonia, a woman's age, asthma, harmful habits (smoking), the use of corticosteroids and tocolytic agents before delivery create an additional risk group for pregnant women [37].

According to data from several scientific studies, anxiety, depression, and stress during pregnancy can increase vulnerability to infectious diseases [38], and additionally lead to complications [39], an increase in the number of premature pregnancies [40]. In addition to the above, it is important to study the condition of pregnant women and the fetus, which allows for more in-depth development of infection prevention programs.

Summary. The literature on the course of COVID-19 depending on the trimesters of pregnancy and the effect on the fetus is scarce and the data are insufficient.

Thus, evidence-based risk assessment, in-depth study of the pathogenetic mechanisms of COVID-19 may lead to the identification of individualized preventive methods and new effective treatment directions. Therefore, it is appropriate to study the effect of viral infection in different trimesters of pregnancy. Studies comparing the clinical and perinatal characteristics of pregnant women with COVID-19 according to their gestational age and evaluating medical data are needed.

Literature

1. Khan DSA, Hamid LR, Ali A, et al. Differences in pregnancy and perinatal outcomes among symptomatic versus asymptomatic COVID-19-infected pregnant women: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2021;21(1):801. Published 2021 Dec 1. doi:10.1186/s12884-021-04250-1.
2. Villar J, Ariff S, Gunier RB, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study [published correction appears in *JAMA Pediatr*. 2022 Jan 1;176(1):104]. *JAMA Pediatr*. 2021;175(8):817-826. doi:10.1001/jamapediatrics.2021.1050
3. Mullins E, Hudak ML, Banerjee J, et al. Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. *Ultrasound Obstet Gynecol*. 2021;57(4):573-581. doi:10.1002/uog.23619
4. Edlow AG, Castro VM, Shook LL, Kaimal AJ, Perlis RH. Neurodevelopmental Outcomes at 1 Year in Infants of Mothers Who Tested Positive for SARS-CoV-2 During Pregnancy. *JAMA*

- Netw Open. 2022;5(6):e2215787. Published 2022 Jun 1. doi:10.1001/jamanetworkopen.2022.15787
5. Badr DA, Picone O, Bevilacqua E, et al. Severe Acute Respiratory Syndrome Coronavirus 2 and Pregnancy Outcomes According to Gestational Age at Time of Infection. *Emerg Infect Dis.* 2021;27(10):2535-2543. doi:10.3201/eid2710.211394
 6. АдамянЛ.В., ВечоркоВ.И., ФилипповО.С., КонышеваО.В., ХарченкоЭ.И., ФаттаховаД.Н.//Новаякоронавируснаяинфекция (COVID-19). Исходы родов у женщин с COVID-19 и без COVID-19 в период пандемии (данные акушерского отделения ГБУЗ «ГКБ №15 ДЗМ»)//Проблемы репродукции. 2021;27(3-2): 15-22.
 7. Phoswa WN, Khaliq OP. Is pregnancy a risk factor of COVID-19?. *Eur J Obstet Gynecol Reprod Biol.* 2020;252:605-609. doi:10.1016/j.ejogrb.2020.06.058
 8. Кажигаликызы Р., Ахметова Ж.К., Донбаева З.Б., Билибаева Г.Ж., Хайбуллаева Г.Ф., Имашева Б.И. Беременность и перинатальные исходы у женщин с коронавирусной инфекцией (COVID-19) // Наука о жизни и здоровье, 2020. № 4. С. 94-100
 9. 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. doi:10.21037/tp.2020.02.06
 10. Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Matern Fetal Neonatal Med.* 2022;35(8):1619-1622. doi:10.1080/14767058.2020.1759541
 11. Rajewska A, Mikołajek-Bedner W, Lebdowicz-Knul J, Sokołowska M, Kwiatkowski S, Torbé A. COVID-19 and pregnancy - where are we now? A review. *J Perinat Med.* 2020;48(5):428-434. doi:10.1515/jpm-2020-0132
 12. Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J ObstetGynecol MFM.* 2020;2(2):100-107. doi:10.1016/j.ajogmf.2020.100107
 13. Scheler CA, Discacciati MG, Vale DB, Lajos GJ, Surita F, Teixeira JC. Mortality in pregnancy and the postpartum period in women with severe acute respiratory distress syndrome related to COVID-19 in Brazil, 2020. *Int J Gynaecol Obstet.* 2021;155(3):475-482. doi:10.1002/ijgo.13804
 14. Hecht JL, Quade B, Deshpande V, et al. SARS-CoV-2 can infect the placenta and is not associated with specific placental histopathology: a series of 19 placentas from COVID-19-positive mothers. *Mod Pathol.* 2020;33(11):2092-2103. doi:10.1038/s41379-020-0639-4
 15. Prochaska E, Jang M, Burd I. COVID-19 in pregnancy: Placental and neonatal involvement. *Am J Reprod Immunol.* 2020;84(5):e13306. doi:10.1111/aji.13306
 16. Zambrano LD, Ellington S, Strid P, et al. 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(44):1641-1647. Published 2020 Nov 6. doi:10.15585/mmwr.mm6944e3
 17. LoMauro A, Aliverti A. Respiratory physiology of pregnancy: Physiology masterclass. *Breathe (Sheff).* 2015;11(4):297-301. doi:10.1183/20734735.008615
 18. Gulersen M, Staszewski C, Grayver E, et al. Coronavirus Disease 2019 (COVID-19)-Related Multisystem Inflammatory Syndrome in a Pregnant Woman. *Obstet Gynecol.* 2021;137(3):418-422. doi:10.1097/AOG.0000000000004256
 19. Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. *ActaObstetGynecol Scand.* 2020;99(7):819-822.doi: 10.1111/aogs.13901

20. Berkowitz K, LaSala A. Risk factors associated with the increasing prevalence of pneumonia during pregnancy. *Am J Obstet Gynecol.* 1990;163(3):981-985. doi:10.1016/0002-9378(90)91109-p
21. Ahmed M. Maged El-Goly. Covid-19 Infection and Pregnancy. UK. Academic Press (24 July 2021);1-38
22. Jamieson DJ, Theiler RN, Rasmussen SA. Emerging infections and pregnancy. *Emerg Infect Dis.* 2006;12(11):1638-1643. doi:10.3201/eid1211.060152
23. Noha S. Soliman, Yosra M. Hassan, Adel M. Nada. Epidemiology, virology, and history of Covid-19 infeksi. Ahmed M. Maged El-Goly. Covid-19 Infection and Pregnancy. UK. 2021: 12-b
24. Benedetti, T. J., Valle, R., & Ledger, W. J. (1982). Antepartum pneumonia in pregnancy. *American journal of obstetrics and gynecology*, 144(4), 413–417. [https://doi.org/10.1016/0002-9378\(82\)90246-0](https://doi.org/10.1016/0002-9378(82)90246-0)
25. DeBolt CA, Bianco A, Limaye MA, et al. Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls. *Am J Obstet Gynecol.* 2021;224(5):510.e1-510.e12. doi:10.1016/j.ajog.2020.11.022
26. Andrikopoulou M, Madden N, Wen T, et al. Symptoms and Critical Illness Among Obstetric Patients With Coronavirus Disease 2019 (COVID-19) Infection. *Obstet Gynecol.* 2020;136(2):291-299. doi:10.1097/AOG.0000000000003996.
27. Yost NP, Bloom SL, Richey SD, Ramin SM, Cunningham FG. An appraisal of treatment guidelines for antepartum community-acquired pneumonia. *Am J Obstet Gynecol.* 2000;183(1):131-135. doi:10.1067/mob.2000.105743
28. Shariatzadeh MR, Marrie TJ. Pneumonia during pregnancy. *Am J Med.* 2006;119(10):872-876. doi:10.1016/j.amjmed.2006.01.014
29. Ramsey, P S, and K D Ramin. "Pneumonia in pregnancy." *Obstetrics and gynecology clinics of North America* vol. 28,3 (2001): 553-569. doi:10.1016/s0889-8545(05)70217-5.
30. Romanyuk V, Raichel L, Sergienko R, Sheiner E. Pneumonia during pregnancy: radiological characteristics, predisposing factors and pregnancy outcomes. *J Matern Fetal Neonatal Med.* 2011;24(1):113-117. doi:10.3109/14767051003678275.
31. Kaunitz A.M., Hughes J.M., Grimes D.A., Smith J.C., Rochat R.W., Kafrisen M.E. Causes of maternal mortality in the United States. *Obstet Gynecol.* 1985;65:605–612.
32. Chen YH, Keller J, Wang IT, Lin CC, Lin HC. Pneumonia and pregnancy outcomes: a nationwide population-based study. *Am J Obstet Gynecol.* 2012;207(4):288.e1-288.e2887. doi:10.1016/j.ajog.2012.08.023.
33. Graves CR. Pneumonia in pregnancy. *Clin Obstet Gynecol.* 2010;53:329–336.
34. Alisa K., Linda O. E., Janet A. E. The history of maternal immunization. Elke E.L., Marta C.N., Christine E.J. *Maternal Immunization.* India. Elsevier Inc. 2020 ;4-b
35. Rotmensch S, Vishne TH, Celentano C, Dan M, Ben-Rafael Z. Maternal infectious morbidity following multiple courses of betamethasone. *J Infect.* 1999;39(1):49-54. doi:10.1016/s0163-4453(99)90102-0.
36. Christian LM, Franco A, Iams JD, Sheridan J, Glaser R. Depressive symptoms predict exaggerated inflammatory responses to an in vivo immune challenge among pregnant women. *Brain Behav Immun.* 2010;24(1):49-53. doi:10.1016/j.bbi.2009.05.055
37. Staneva A, Bogossian F, Pritchard M, Wittkowski A. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: A systematic review. *Women Birth.* 2015;28(3):179-193. doi:10.1016/j.wombi.2015.02.003