

Updates on COVID-19 Infection During Pregnancy

Chen Wang^{1,2}, Dun-Jin Chen³, Hui-Xia Yang^{1,2,*}

The 2019 coronavirus disease (COVID-19) is a public health emergency in China this winter. Since it was first reported in Wuhan in December 2019, it has been quickly spreading across Hubei Province and the whole country, and even other parts of the world. As of February 23, 2020, the total number of confirmed cases in mainland China has reached 77 150,¹ the Chinese government and people are making an all-out effort to fight the virus. Due to the limited knowledge of this new virus, in addition to fighting on the clinical frontline, health providers also strive to intensify studies on COVID-19, so as to provide scientific support and powerful “weapons” for the epidemic prevention and control.

Huang *et al.*² first reported a cohort of 41 patients with laboratory-confirmed COVID-19 infection, and pointed out that clinical manifestations of patients with COVID-19 infection include fever, dry cough, myalgia, fatigue, headache, sputum production, diarrhea, normal or decreased leukocyte counts, and lymphopenia. And they had representative chest computed tomography (CT) images showed bilateral ground glass opacity and subsegmental areas of consolidation. After Huang’s study, several other studies with larger sample sizes have been published subsequently and showed similar results.^{3,4} Based on these studies and clinical experience, the National Health Commission of the People’s Republic of China makes a constant update of the “New coronavirus pneumonia prevention and control program” and the latest is the sixth edition.⁵ The diagnostic criteria for suspected and confirmed patients with COVID-19 infection based on epidemic history, clinical manifestations, laboratory examination, chest CT, and 2019 novel coronavirus (2019-nCoV) test using quantitative reverse transcription-polymerase chain reaction (qRT-PCR) on

specimens from the respiratory tract. Confirmed cases must have positive results of 2019-nCoV qRT-PCR tests. However, in the fifth edition of the program, the National Health Commission once recommended that, in Hubei province where is the worst-hit areas in China, suspected patients with typical findings of chest CT images could be clinical confirmed of COVID-19 to isolate and monitor patients who may have false-negative results from 2019-nCoV qRT-PCR tests. Thus, in our opinion, in addition to using nucleic acid tests as the “gold standard” for the diagnosis of COVID-19 infection, a complete relevant examinations including laboratory examination and chest CT, and a comprehensive evaluation of a patient’s medical history, epidemiological exposure, and symptoms are also of great importance, especially in Hubei Province.

Pregnancy as a special physiological stage is considered at increased risk of severe infections. For example, severe acute respiratory syndrome coronavirus (SARS-CoV)⁶ and Middle East respiratory syndrome coronavirus (MERS-CoV)⁷, which are two notable strains of the coronavirus family, are both known to be responsible for severe complications during pregnancy, such as application of endotracheal intubation, admission to the intensive care unit, renal failure, and death. So does the situation for the 1918 Spanish influenza⁸ and the H1N1 2009 influenza virus⁹. However, a study in *The Lancet* by Chen *et al.*¹⁰ reported that the clinical characteristics of COVID-19 infected pregnant women were similar to those of non-pregnant adult patients with COVID-19 infection, and seemed to be less serious than that caused by SARS-CoV, which has up to 85% sequence similarity with 2019-nCoV. Even though only nine pregnant patients were recruited in Chen’s study and all enrolled patients were in the third trimester, notably, such results from this study were consistent with what we have learned from other clinical cases during pregnancy with COVID-19 infection in several hospitals of Wuhan. As far as we know, only one COVID-19 infected pregnant patient was admitted to the intensive care unit. Her symptoms of COVID-19 infection appeared on the second day after vaginal delivery, and then she was confirmed to have COVID-19 infection.

Moreover, Chen’s results¹⁰ also indicated that COVID-19 infection in the third trimester were less likely to be associated with neonatal complications and adverse outcomes. These might be due to the facts that all of the nine recruited patients did not have severe complications, and they were all in the third trimester, the duration between their COVID-19 infection onset and cesarean section was short. And most importantly, no evidence for intrauterine infection caused by vertical transmission has been found so far although its detailed mechanism remains not clear.¹⁰

¹ Department of Obstetrics and Gynecology, Peking University First Hospital, Beijing 100034, China; ² Beijing Key Laboratory of Maternal Fetal Medicine of Gestational Diabetes Mellitus, Beijing 100034, China; ³ Key Laboratory for Major Obstetric Diseases of Guangdong Province, Department of Gynaecology and Obstetrics, Third Affiliated Hospital of Guangzhou Medical University, Guangdong 510150, China.

* Corresponding author: Prof. Hui-Xia Yang, Department of Obstetrics and Gynecology, Peking University First Hospital; Beijing Key Laboratory of Maternal Fetal Medicine of Gestational Diabetes Mellitus, Beijing 100034, China. E-mail: yanghuixia@bjmu.edu.cn

Copyright © 2020 The Chinese Medical Association, published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Maternal-Fetal Medicine (2020) 2:2

Received: 23 February 2020

<http://dx.doi.org/10.1097/FM9.000000000000049>

For obstetricians, when a new virus appears, their major concern is whether the virus can cause mother-to-baby transmission. Even though, previous studies have already shown no evidence of perinatal SARS infection, which has a similar pathogenic potential as COVID-19, among infants born to mothers who developed SARS infection during pregnancy.^{6,11} What about COVID-19? In Chen's study, they first collected samples of amniotic fluid, cord blood and neonatal throat swabs at birth, and found no evidence of 2019-nCoV existence in all of the above samples, suggesting that there were no intrauterine fetal infections due to the COVID-19 infection.¹⁰ Nevertheless, all of the samples were collected in the third trimester, so we were unable to ascertain the possibility of intrauterine vertical transmission during the first or second trimester. As we know, the effect of virus on fetal outcomes can vary from time to time during pregnancy. For example, as the most well-known virus that has different effects on the fetus during different gestational weeks, the rubella virus was reported could affect up to 90 percent of fetus with congenital infection before 12 weeks. At 13–14 gestational weeks, this incidence was 50%, and by the end of the second trimester, it was 25%.¹²

In addition to intrauterine vertical transmission, which is the major way of fetal and neonatal infection caused by mother-to-baby transmission, other ways of some fetal and neonatal infections include intrapartum and contact transmission. In Chen's study, they also collected breast milk samples from patients with COVID-19 infection after their first lactation and found that the breast milk samples appeared to be free from 2019-nCoV.¹⁰ However, Chen and colleagues did not collect placental specimens for the 2019-nCoV testing. But one recent study has proved that the expression and distribution of the angiotensin-converting enzyme 2 that was identified as the surface receptor of sensitive cells for 2019-nCoV was very low in maternal-fetal interface,¹³ which supported Chen's study and explained the possible reason for "no intrauterine vertical transmission". Besides, the youngest patient infected with 2019-nCoV till now was reported to be at 36 hours after birth; however, from the limited clinical details of the news, there was no direct evidence to support the intrauterine vertical transmission, and the approximately 30 hours after birth can not exclude the possibility of contact transmission.¹⁰ Thus, based on the limited evidence during the limited period, more observational studies and follow-up studies of pregnant women with COVID-19 infection, as well as neonates should be conducted to further evaluate their safety and health.

The work done by Zhao *et al.* shared another case of pregnant woman with COVID-19 infection, hopefully, the characteristics and treatment and clinical outcomes of this patient can increase our experience in diagnosis and management of pregnancy with COVID-19 infection. Additionally, Zhao *et al.* has summarized the contents of the fifth edition of "New coronavirus pneumonia prevention and control program" proposed by the National Health Commission of the People's Republic of China¹⁴, thus to help more clinicians, medical practitioners, and health care providers obtain the knowledge of clinical management of COVID-19 infected pregnant women.

However, the sixth edition of "New coronavirus pneumonia prevention and control program" has just issued,⁵ which emphasizes that a confirmed case requires a positive result on 2019-nCoV qRT-PCR test, and lesions showed on the chest CT image progressed to >50% in 24–48 hours should be classified as severe COVID-19 infection, and severe COVID-19 infection has a possibility to lead to multiple organ failure.

All in all, pregnant women are susceptible to virus infection. Though there is currently no evidence of pregnant women with COVID-19 infection are more likely to develop severe pneumonia, nor intrauterine vertical transmission in women who develop COVID-19 pneumonia in late pregnancy. The existing data is still insufficient. Thus, in case the viral infection would probably result in more adverse maternal and neonatal outcomes among pregnant women with COVID-19 infection, we would like to emphasize that pregnant women and newborns are the focus group for the prevention and control of COVID-19 infection.

Funding

None.

Conflicts of Interest

None.

References

- [1] National Health Commission of the People's Republic of China. The latest data of COVID-19 in China by February 23rd. Available at: <http://www.nhc.gov.cn/xcs/yqtb/202002/945bd98a9d884aeeb54d76afa02ca813.shtml>.
- [2] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506. doi:10.1016/S0140-6736(20)30183-5.
- [3] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus infected pneumonia in Wuhan, China. *JAMA* 2020. doi:10.1001/jama.2020.1585.
- [4] Weijie Guan, Zhengyi Ni, Yu Hu, et al. Clinical characteristics of 2019 novel coronavirus infection in China. *medRxiv* 2020. doi:10.1101/2020.02.06.20020974.
- [5] National Health Commission of the People's Republic of China. New Coronavirus Pneumonia Prevention and Control Program (6th ed.) (In Chinese). 2020. Available at: <http://www.nhc.gov.cn/yzygj/s7652m/202002/54e1ad5c2aac45c19eb541799bf637e9.shtml>.
- [6] Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol* 2004;191(1):292–297. doi:10.1016/j.ajog.2003.11.019.
- [7] Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East respiratory syndrome coronavirus (MERS-CoV) infection during pregnancy: report of two cases & review of the literature. *J Microbiol Immunol Infect* 2019;52(3):501–503. doi:10.1016/j.jmii.2018.04.005.
- [8] Gottfredsson M. The Spanish flu in Iceland 1918. *Lessons in medicine and history. Laeknabladid* 2008;94(11):737–745.
- [9] Jamieson DJ, Honein MA, Rasmussen SA, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet* 2009;374(9688):451–458. doi:10.1016/S0140-6736(09)61304-0.
- [10] 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. doi:10.1016/s0140-6736(20)30360-3.
- [11] Shek CC, Ng PC, Fung GP, et al. Infants born to mothers with severe acute respiratory syndrome. *Pediatrics* 2003;112(4):e254. doi:10.1542/peds.112.4.e254.

- [12] Bouthry E, Picone O, Hamdi G, et al. Rubella and pregnancy: diagnosis, management and outcomes. *Prenat Diagn* 2014;34(13):1246–1253. doi:10.1002/pd.4467.
- [13] Zheng QL, Duan T, Jin LP. Single-cell RNA Expression Profiling of ACE2 and AXL in the Human Maternal–Fetal Interface. *Reprod Dev Med* 2020. Available at: <http://www.repdevmed.org/preprintarticle.asp?id=278679>.
- [14] National Health Commission of the People’s Republic of China. New Coronavirus Pneumonia Prevention and Control Program (5th ed.) (In Chinese). 2020. Available at: <http://www.nhc.gov.cn/yzygj/s7653p/202002/d4b895337e19445f8d728fcdf1e3e13a/files/ab6bec7f93e64e7f998d802991203cd6.pdf>.

Edited By Yang Pan