Features of the Course of COVID-19 in Pregnant Women in the Third Trimester of Pregnancy

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ABSTRACT
Novel coronavirus infection with severe acute respiratory syndrome (SARS-CoV-2; also known as 2019-nCoV) caused severe damage worldwide. The disease caused by coronavirus-2 severe acute respiratory syndrome is highly contagious. COVID-19 is a global health emergency that can cause serious health problems during pregnancy. Pregnant women are highly prone to contracting this infection due to altered physiological and immunological functions.

Keywords: COVID-19, pregnancy, SARS-CoV-2, coronavirus infection, fetus, placenta, newborns, pandemic, symptoms, vertical transmission.

Relevance
The current coronavirus-2 (SARS-CoV-2) severe acute respiratory syndrome pandemic continues to spread rapidly. The global pandemic, having infected more than 138 million people, has affected a significant number of pregnant women around the world. Alarmingly rising mortality rates require early identification and protection of this vulnerable population group. Although favorable maternal and perinatal outcomes are reported in most cases, the scientific evidence for the management of this vulnerable population remains unclear [1]. There is little evidence to demonstrate pharmacological treatments and maternal and perinatal outcomes during the COVID-19 pandemic.

Most COVID-19 patients have mild symptoms of an upper respiratory tract infection, but sometimes they could progress to severe illness, even to respiratory failure in some people [2, 3]. Unlike the general population, pregnant women constituted a special group with a significantly higher risk of viral pneumonia as a unique “immunological” condition and changes in lung function during pregnancy [4, 5, 6], and intrauterine infection is one of the most serious complications of viral pneumonia. diseases during pregnancy.

To protect the fetus from various pathogens that can be infected during pregnancy, the placenta plays an important role as a natural barrier [7]. Recently, several cases of SARS-COV-2 invasion into the placenta in pregnant women in the second and third trimesters have been clearly confirmed [8, 9, 10], suggesting that transplacental transmission may occur. In addition, pathology criteria for the diagnosis of intrauterine transplacental infection have been published [5, 6], but the number of cases targeted for such studies is still limited, and the specific mechanism of SARS-COV-2 invasion into the placenta in women in late pregnancy is still not completely clear. Thus, to study the above issue, further studies of the structure of the placenta and study of the role of the placenta in the mechanism of vertical transmission of the COVID-19 virus in pregnant women are needed.

Purpose. To study the clinical characteristics and pathological changes in the placenta in pregnant women who underwent COVID-19 in the third trimester of pregnancy and to assess the possibility of vertical transmission.

Materials and research methods. В этом исследовании мы собрали ткани плаценты у 28 беременных женщин с COVID-19 в третьем триместре. Мы стремились проанализировать клинические характеристики беременных женщин, инфицированных SARS-CoV-2, и их новорожденных. В нашем исследовании мы попытались установить соответствующие клинико-патологические связи, оценить возможность внутриутробной вертикальной передачи и обеспечить основу для оптимального ведения таких беременных женщин.

Research results. During the study period, a total of 28 pregnant women were hospitalized in the maternity complexes of the city of Samarkand. The age of patients ranges from 25 to 36 years. The gestational age at admission ranged from 33 weeks to 40 weeks. 14 patients who underwent COVID-19 had mild symptoms.
None of the 28 patients had symptoms of high fever (body temperature > 39 °C). Only one patient had a fever (temperature 38.5 °C) for 3 days before delivery, but there was no fever after delivery. 3 patients had a cough. Reverse transcription polymerase chain reaction showed a positive reaction for SARS-CoV-2 ribonucleic acid in swabs from the nasopharynx of all patients in the third trimester. The main complications in all 28 patients were anemia (96.4%), hypertension and low amniotic fluid (28.6%), thrombocytopenia (10.7%), pyelonephritis and hypothyroidism (39.3%).

Laboratory examination showed that some patients with COVID-19 had a slightly elevated C-reactive protein (2/8, > 5.0 mg / l). In addition, none had leukopenia and lymphopenia, and all patients had normal concentrations of alanine aminotransaminase (AMT) and aspartate aminotransferase (AMF).

19 (68.9%) patients were delivered by caesarean section, and 9 (32.1%) patients were delivered naturally. Apgar scores for all newborns were 7 or 8 at 1 minute and 8-9 at 5 minutes at birth and were tested for SARS-CoV-2 pharyngeal swab nucleic acid, all of which were negative for SARS-CoV-2 infection. All mothers were discharged home asymptomatically and there was no clinical or serologic evidence indicating vertical transmission of SARS-CoV-2.

**Pathological examination of placenta samples.** In all cases, the placenta was intact. Overall, in 28 cases, intact placental tissues were spongy and dark red, outwardly completely normal. Microscopic examination of the placental disc revealed edema of the villous stroma and moderate acute intervillitis only in 2 cases, the inflammatory infiltration was focal and consisted of several neutrophils and scanty histiocytes. 4 cases showed chronic plasma cell deciduitis, which was a symptom of chronic inflammation. In addition, 3 cases showed infiltration of maternal inflammatory cells into subchorionic fibrin, but there were no signs of acute willitis. As for the ascending intrauterine infection, the study of the placenta membrane showed that only in 2 cases there was an infiltration of neutrophils (more than 30 neutrophils in a high-power field) in the tissues of the fetal membrane with fibrin deposits. However, neutrophil infiltration was limited to fibrin under the chorionic plate or decidual layer of the fetal membrane, suggesting acute chorioamnionitis, maternal inflammatory response, stage 1 (acute choriitis). First of all, although various inflammatory reactions were detected in the placenta of pregnant women with SARS-CoV-2 infection, there are no typical changes, such as massive infiltration of mononuclear cells into the intervillous spaces and necrosis of trophoblasts, which were considered as a risk factor for transplacental transmission of SARS-CoV-2 [10]. On the other hand, maternal vascular malperfusion was present in all 28 cases. Signs included central placental infarction (3/28), peripheral placental infarction (3/28), distal villous hypoplasia (4/28), increased syncytial nodes (28/28). Nominal decidual arteriopathy was noted in all cases. No pathologies were found in the umbilical arteries and branches of the umbilical vein.

**Discussion of research results.** This study retrospectively analyzed the clinical characteristics of 28 cases of pregnant women with COVID-19 in the third trimester. Limited data showed that the clinical manifestations of pregnant women infected with SARS-CoV-2 were largely similar to those in the infected general population, and there were no serious adverse mother-to-child outcomes. In this study, we simultaneously performed microscopic observations and immunohistochemical tests to determine if the number of inflammatory cells and placental macrophages of the fetus increased in the placenta of pregnant women undergoing COVID-19. No specific inflammatory pathological changes suggesting invasion of the placenta by SARS-CoV-2 were observed during microscopic examination. Detection of SARS-CoV-2 ribonucleic acid in placental tissues and detection of neonatal pharyngeal swabs using reverse transcription polymerase chain reaction were negative in all cases. This study did not show any definite evidence pointing to vertical mother-to-fetus transmission of the virus in pregnant women with COVID-19 late in pregnancy, and provided important clues to further understanding the clinical characteristics, pregnancy outcomes, and the assessment of intruterine transmission of SARS-CoV-2 in late pregnancy.

This research still has some limitations. First of all, all the cases collected in this study were mild patients, and it was still unknown whether patients with severe infections would develop intrauterine infection during pregnancy, which is a direction for further research in later studies. Second, a recent report suggested that a positive SARS-CoV-2 infection in women in the second trimester of pregnancy could lead to miscarriage, and there was evidence of SARS-CoV-2 infection in the placenta [10]. Therefore, it is necessary to collect additional cases, including women with COVID-19 at different stages of pregnancy, especially in the first and second trimester, in order to study the impact on the safety of the mother and fetus.

Thus, we found no evidence of vertical transmission in the third trimester placenta of pregnant women with COVID-19, observing histological changes and nucleic acid test, we also analyzed whether the number of
inflammatory cells and macrophage cells increased by immunohistochemistry. Although the sample size of this study was limited given the important adverse effects of this ongoing global health emergency, our findings were very useful in understanding the clinical characteristics of COVID-19 infection in late pregnant women and whether it has potential for vertical transmission. This was important and provided some basis for the best clinical management of women in late pregnancy.

**List of used literature:**