



Coronavirus Infection Effect on the Course of Pregnancy

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Annotation: Coronavirus disease is a new disease characterized by rapid progression and an increase in the number of infected and deaths since its identification in China in December 2019. This disease is caused by a new, previously unknown coronavirus SARS-CoV-2, which was first recorded in China when cases of pneumonia of unknown etiology appeared. Since then, the whole world has been exposed to a new infection. The number of infected with SARS-CoV-2 continues to grow daily. There is limited data on the 2019 coronavirus disease during pregnancy, but information on diseases associated with other highly pathogenic coronaviruses can give an idea of the consequences of this disease during pregnancy

Keywords: coronavirus, SARS-CoV-2, Middle East respiratory syndrome, severe acute respiratory syndrome, pregnancy.

The purpose of this review is to form an idea of a new coronavirus infection and, in particular, to study the possible risks and complications of pregnancy. This article analyzes the susceptibility of pregnant women to the COVID-19 virus from the point of view of anatomical, reproductive, endocrine and immune changes during pregnancy, and also examines the measures that must be followed when conducting pregnancy in an infected woman.

The outbreak of a new coronavirus disease in 2019 (COVID-19) caused by severe acute respiratory syndrome SARS-CoV-2 continues now. In this regard, there has been an increased interest in studying the role of a new coronavirus infection in the outbreak of a mass disease among the population. In many countries, the current dynamics of morbidity resembles the events that took place in China after the discovery of COVID-19. Since the history of the disease exists for a short time, there is still a small amount of data on the clinical course of SARS-CoV-2 infection, in particular, on the clinical course and possible risks of complications in infected pregnant women and newborns from infected mothers.

Coronaviruses are a family of RNA-containing viruses belonging to the suborder Nidovirales and comprising 40 species grouped into 2 suborders. Until December 2019, the coronavirus family consisted of six species pathogenic to humans, among which were the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). SARS-CoV-2 is the seventh human pathogenic species, which was added to this group in 2019 by WHO under the name "2019-nCoV", and then renamed in 2020 by the International Committee on

Taxonomy of Viruses to "SARS-CoV-2" [1]. The remaining four endemic species out of seven pathogenic to humans (HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1) also have clinical significance, causing upper respiratory tract diseases manifested by mild clinical symptoms of the common cold. These species cause approximately 10% of seasonal respiratory diseases caused by non-influenza [2]. SARS-CoV and MERS-CoV, which cause very serious symptoms and respiratory diseases associated with a high mortality rate (about 10-30%), have so far been limited to one outbreak in 2002-2003 (SARS-CoV) and 2014 (MERS-CoV) and were mainly of regional significance [4].

Coronaviruses are single-stranded RNAs, unsegmented, enveloped in viruses that cause diseases of varying severity - from the common cold to diseases with a possible fatal outcome. The term "coronavirus" comes from the Latin word corona, which means "crown" or "halo"; the name is due to the appearance of coronavirus virions viewed using electron microscopy, in which viral particles have a crown-like fringe, usually called spikes [5].

In its structure, SARS-CoV-2 contains four key proteins: nucleocapsid protein (NP), spike protein (S), small membrane protein (SM) and membrane glycoprotein (M) [6]. Angiotensin converting enzyme 2 (ACE2), located on the cells of the alveolar epithelium of types I and II, is the main receptor of SARS-CoV-2, through which the infection enters the body, causing respiratory symptoms and, ultimately, acute respiratory syndrome. Such a receptor is also found in the intestine, although in small quantities, which can cause the development of diarrhea and vomiting. Protein S is necessary for the virus to fuse with the host cell through the receptor-binding domain. This protein includes two subunits - S1 and S2; S1 determines cellular tropism, and S2 mediates the fusion of the virus with the cell membrane. After membrane fusion, viral RNA is released into the cytoplasm, and viral replication begins. Newly formed viral particles fuse with the plasma membrane through virion-containing vesicles to release the virus [6].

It should be noted that during the development of atypical pneumonia, ACE2 is also used as a receptor for cell entry, however, the receptor binding capacity of pneumonia with SARS-CoV-2 is 10-20 times higher than that of atypical pneumonia, and the number of cases of such pneumonia exceeded the number of infections with atypical pneumonia during the outbreak in China in 2002-2003, which indicates higher transmission rates [6]. In addition, men tend to have higher levels of ACE2 than women, and Asians show higher levels of ACE2 expression in alveolar cells than Caucasians and African Americans, which suggests that Asian men are most susceptible to this infection.

Transmission of SARS-CoV-2 is mainly carried out by airborne droplets from person to person during coughing or sneezing, as well as in close contact with an infected person or objects on which these drops could settle [7]. After contact with an infected COVID-19 that spreads the virus, the average incubation period of the disease is about 5 days, varying from 1 to 14 days. Clinically, SARS-CoV-2 infection can occur both asymptotically and with the development of severe respiratory failure. In most cases, the clinical picture is similar to that of Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). The most common symptoms are fever, cough, and a feeling of congestion in the chest. Confirmation of the presence of infection requires laboratory diagnostics in order to detect SARS-CoV-2 RNA by PCR [9, 10].

Immunosuppression and other physiological changes during pregnancy cause high susceptibility to respiratory pathogens and severe pneumonia in pregnant women, which can lead to hospitalization in intensive care units and artificial lung ventilation. Hormone levels and immune competence show significant fluctuations throughout pregnancy. Pregnancy in the first trimester is more at risk due to adaptive changes in response to fetal antigens, however, with the gradual regulation of the immune and endocrine systems of the mother, the processes stabilize in the later stages of pregnancy. The initial stages of pregnancy are crucial in the development of fetal organs, and the immune system is especially sensitive at this stage, which significantly affects the course of the infectious process.

Experience with previous respiratory virus epidemics may offer some insights regarding the susceptibility of COVID-19 and the frequency of complications during pregnancy. Approximately 50% of pregnant women suffering from SARS needed intensive care, and about 33% needed artificial lung ventilation. The mortality rate of pregnant women during the SARS epidemic reached 25%. Taking into account the MERS epidemic, which has led to a much larger number of confirmed cases and deaths, it can be argued that MERS in its course progresses much faster to the development of respiratory failure and leads to higher mortality rates than SARS-CoV. However, there was no evidence of vertical transmission from mother to fetus. Based on this evidence, there is no doubt that SARS-CoV and MERS-CoV infections are associated with high rates of complications among pregnant women.

Despite the fact that the COVID-19 epidemic continues, data on the course of the disease in pregnant women are limited. Recent reports indicate that the clinical characteristics of the course of the disease detected in pregnant women with confirmed SARS-CoV-2 infection are similar to those in non-pregnant women with COVID-19 pneumonia. Also, so far, no evidence of vertical transmission of SARS-CoV-2 at the end of pregnancy has been obtained.

Currently, there are two retrospective studies of pregnancies complicated by confirmed SARS-CoV-2 infection. In each case, the development of pneumonia was noted, with the help of CT, typical infiltrates were detected in both studies. Laboratory tests showed a decrease in the level of leukocytes and lymphocytes, moderate thrombocytopenia and increased liver function tests. Most pregnant women have mild or moderate symptoms of the disease.

Currently, there is a small amount of data on the possible risk of vertical transmission of infection from mother to fetus. The risk of transmission of SARS-CoV-2 was considered in a study recently published in *The Lancet*, devoted to the study of the incidence of Wuhan residents. To do this, immediately after delivery, samples of amniotic fluid, umbilical cord blood and throat swabs were taken from newborns, the results of the study were negative. Milk samples taken during this study immediately after the first appearance of milk in the postpartum period were also unremarkable. In one of the case studies, the placentas of three pregnant women with confirmed SARS-CoV-2 infection were examined. None of the newborns were diagnosed with the infection. Histopathological correlates for infection in placentas were not found [10]. Thus, now, based on the very low number of published cases of pregnancy in women with confirmed COVID-19, as well as based on the experience gained during the SARS-CoV epidemic, it is not possible to talk about intrauterine transmission of SARS-CoV-2 infection.

To date, there are no studies on severe COVID-19 and obstetric complications during the first trimester of pregnancy, so there is not enough information to judge the potential impact of infection on the course of pregnancy in the initial stages. As for other coronaviruses, the epidemics of SARS and MERS did not reveal a correlation with the frequency of malformations. In addition, data from the current epidemic should be considered for the management of COVID-19 infections during pregnancy, since the clinical course of this disease and the response to treatment are determined to differ from previous outbreaks of other types of coronaviruses. Further research is needed to understand the pathogenesis and epidemiology of SARS-CoV-2 during pregnancy, including aspects such as the time of infection of the mother, gestational age, the influence of comorbid factors and the frequency of adverse outcomes; however, preliminary observations of pregnant women infected make it possible to make an optimistic prognosis regarding the clinical course.

It is important to take into account that the COVID-19 pandemic has caused psychological stress and anxiety among the general population, including pregnant women. A number of issues of concern were raised regarding potential infection during pregnancy, including the presence of family members in quarantine near pregnant women; potential infection of 8LYA8-OU-2 during a visit to a doctor; the

potential need for early delivery by caesarean section; the constant use of disinfectants containing alcohol, which can have toxic effects; the development of potential postpartum complications, for example, during breastfeeding or newborn care [21]. Therefore, it is necessary to comply with infection control measures and conduct diagnostic testing in all pregnant women with suspected COVID-19.

Currently, when conducting pregnancy in infected women, it is advisable to observe the following measures:

- with a mild severity of the disease for up to 12 weeks, prolongation of pregnancy is possible, since there is no evidence of a negative effect of SARS-CoV-2 on the fetus;
- in severe and moderate course of the disease for up to 12 weeks, it is possible to terminate pregnancy after the destruction of the infectious agent; if a woman is against termination, it is necessary to conduct a study of chorionic villi to assess the presence or absence of chromosomal abnormalities in the fetus [10];
- treatment that is considered appropriate for non-pregnant patients should also be used in case of infection of pregnant women, provided there are no clear contraindications for available therapy;
- in case of suspicion of infection in pregnant women, it is necessary to take isolation measures at an early stage of the development of the disease and conduct diagnostic studies to confirm or refute the disease;
- it is necessary to monitor the condition of the fetus; in order to exclude placental insufficiency with the development of intrauterine growth retardation, regular CTG studies with fetal size measurement, as well as dopplerometry and amniotic fluid examination should be carried out.

As for the method of delivery of infected pregnant women, currently, due to the small number of cases, no recommendations can be given. At the moment, it is considered unlikely that infection of a child can occur during passage through the birth canal, which means that the choice of the method and time of delivery should be strictly individual, based on the clinical condition of the woman and fetus, as well as the gestation period.

Based on the most recent epidemiological data on COVID-19 and the course of pregnancy against the background of infection, there is no evidence indicating an increased risk to the mother or fetus. Most likely, the course of the disease after infection in pregnant women does not differ from that of other people. In addition, recent data indicate the absence of any association of vertical transmission of infection from mother to fetus; there is also no data on the occurrence of fetal malformations associated with this infection. It is obvious that the management of pregnant patients should be individualized, based on obstetric indications and the condition of the mother and fetus. It is important to take into account that the current COVID-19 pandemic causes psychological stress and anxiety in pregnant women, which can have an adverse effect on the course of pregnancy and lead to complications. In addition, in order to prevent infection, it is important to follow the recommendations on social isolation and quarantine issued by health authorities in order to avoid further spread of COVID-19.

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