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COVID-19: History, Taxonomy, Etiopathogenesis, Course And Pregnancy Outcomes (Literary Review)

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Abstract This article is a review of the literature on the History, taxonomy, etiopathogenesis of Covid-19, the course and outcomes of pregnancy with it.

Keywords Covid-19, Course and outcomes of pregnancy

1. Introduction

Humankind has experienced massive outbreaks of various infectious diseases, including acute viral respiratory diseases. Although there have been three outbreaks of coronavirus infections in the last two decades, but there has not been such a global spread as COVID-19. Consequently, WHO declared coronavirus disease (COVID-19) on March 11, 2020, the causative agent of which is SARS-CoV-2, as a pandemic [Opening remarks by WHO Director-General at a media briefing on COVID-19 - March 11, 2020. 11-march-2020; Sinchikhin S.P., Stepanyan L.V., Mamiev O.B.2020].

As of March 16, 2023, a total of 682,102,022 people worldwide have been infected, 655,045,761 have recovered, 6,815,731 have died, and 20,240,530 people are ill.

On March 15, 2020, quarantine requirements were declared in Uzbekistan due to the detection of the first case of SARS-CoV-2 infection. Since then, the detected cases amounted to 251,430, recovered only 241,486, died 1637, total sick as of 16.03.2023 8307, infected with SARS-CoV-2 - 183 people [Statistics and news of coronavirus "Covid-19" in Uzbekistan for today https://horosho-tam.ru/uzbekistan/coronavirus].

It is known that infectious diseases during pregnancy have a negative impact on the course and outcome of pregnancy. To date, sufficient information on COVID-19 has been accumulated. However, it is still controversial whether a pregnant woman becomes susceptible to COVID-19 infection, what is the course and outcomes. In this regard, we conducted a study of the literature data as changed over the past 5 years the ideas about the disease, pathogenesis and the impact on the course and outcomes of pregnancy.

The primary purpose of a literary review is to increase the theoretical knowledge of obstetricians-gynecologists, general practitioners, masters and clinical residents of the new coronavirus infection, based on the data of foreign and domestic sources.

In the 20th century, coronaviruses were an urgent veterinary problem. However, coronaviruses (CoV) have become a plague of the XXI century and for mankind, as already at the beginning of the new century in 2002 there was the first outbreak of SARS (severe acute respiratory syndrome), where the causative agent was SARS-CoV, when the mortality rate among pregnant women reached up to 25%. The second outbreak was observed in 2012-MERS (Middle East respiratory syndrome), the causative agent of which was MERS-CoV, when mortality among pregnant women reached up to 37% [43].

The third outbreak of novel coronavirus infection (NCVI) has occurred in the administrative center of Wuhan in China's Hubei province, where according to the census at the end of 2018 the population approached 12 million, thus threatening the spread of a new unknown infection to all mankind. The new coronavirus was originally named 2019-nCoV (Novel coronavirus). However, due to the peculiarities of the genome structure of the new 2019-nCoV coronavirus, the International Committee on Taxonomy of Viruses (ICTV) renamed it as SARS-CoV-2 (Severe acute respiratory syndrome 2). [38], and the disease it causes was named COVID-19 (abbreviation for Corona Virus Disease 2019) Clinical features of the course of COVID-19 in children of different age groups. 2020 [17]. The first was the SARS virus that caused the outbreak of SARS in 2002, in connection with which the new pathogen was designated by the figure SARS-CoV-2 [COVID-19 in pregnant women in the light of current data, Sinchikhin S.P., Stepanyan L.V., Mamiev O.B.].

There are 4 variants of coronaviruses (CoVs) α-ccoronavirus, β-coronavirus, γ-coronavirus, and delta-coronavirusα. Meanwhile, Shchelkanov cites the data

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that "the taxonomic structure of Coronaviridae underwent a serious revision in August 2018, on the one hand due to the introduction of the concept of subgenus and on the other hand due to the description of a new coronavirus called lethovirus" [11].

In mammals, including humans, mainly alpha and beta coronaviruses cause disease. The six coronavirus species that cause infection in the human respiratory tract (human coronavirus, HCoV) are the best known. Coronaviruses that are particularly dangerous to humans are included in two β-coronavirus subgenera: Sarbecovirus (SARS-CoV and SARS-CoV-2) and Merbecovirus (MERS-CoV) [11]. The remaining four (HCoV-NL63, HCoV-229E, HCoV-OC43 and HKU1) cause mild upper respiratory tract disease in immunocompetent adults and severe in children. Gamma and Δ-coronaviruses are causative agents of disease in birds. [20].

The new SARS-CoV-2 coronavirus is a natural focal virus and its natural source is bats. The intermediate host between bats and humans is still debated, but evidence suggests that it is pangolins *(Pholidota)*, a peculiar insectivorous mammal found in Central and Southern Africa and South Asia.

SARS-CoV- RNA-containing virus, 90-140 nm in size, rounded in shape [24] has a lipid envelope that originates from the membranes of the endoplasmic reticulum of the host cell. Three structural transmembrane protein structures are embedded in the lipid envelope: trimers of glycosylated protein S forming characteristic club-shaped peplomers (9-12 nm), which gave their name to the family Coronaviridae, as well as pentamers of protein E in small amounts and the most abundant glycosylated protein M in the virion [11].

SARS-CoV-2 penetrates into the target cell after the formation of the S1-RBD×PD-ACE2 complex, i.e., after interaction of the receptor-binding domain of the first subunit of the spike glycoprotein of the virus (S1- RBD - receptor binding in S1 subunit) with the peptidase domain (PD - peptidase domain) of the cell receptor - angiotensin-converting enzyme type 2 (ACE2 - angiotensin-converting enzyme 2) [27]. Moreover, the S1 and S2 subunits of the spike protein are bound covalently before penetrating the target cell surface and then cleaved by cellular transmembrane serine protease type 2. [28]. After cleavage of the S1-RBD×PD-ACE2 complex, a hydrophobic fusion peptide (S2- FP - fusion peptide in S2 subunit) previously located within the second subunit of the S-protein is released, which induces fusion of the viral and cell membrane [30], and the nucleocapsid penetrates the cell cytoplasm. Until May 2021.

During the last 5 years, three waves of COVID-19 epidemic process were observed and each wave was characterized by new strains of SARS-CoV-2, which were named according to the geographical place of their appearance: "English", "Indian", "Brazilian", etc. [45]. However, in May 2021, the World Health Organization decided to designate the strains of the virus by letters of the Greek alphabet, emphasizing that "offensive designations for any ethnic, cultural, national, social and professional group should always be avoided in the designation of diseases and viruses" [Zhang YP. [Zhang YP. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Chin J Epidemiol].

To date, the spread of SARS-CoV-2 coronavirus is thought to be mainly by airborne transmission [4]. After infection of the upper respiratory tract, SARS-CoV-2 virus is able to penetrate into organs and tissues (lower respiratory tract and digestive tract) [20], where surface receptors - ACE2 and CD147, and serine protease (TMPRSS2) are expressed. A study conducted by Ruochen Zang et al (2020) showed that not only TMPRSS2 but also another serine protease - TMPRSS4 - is expressed in intestinal epithelium, co-expression of the two proteases allows the virus to infect cells with maximum efficiency, and inactivation of TMPRSS4 had a stronger effect on reducing the level of virus replication than the absence of TMPRSS2 [32].

ACE2 and CD147 receptors have also been found in cells of heart, adrenal, bladder, brain, and other organ tissues. The virus nucleocapsid protein has been detected in the cytoplasm of epithelial cells of salivary glands, stomach, duodenum and rectum, urinary tract, lacrimal fluid, semen, and vaginal secretions.

The changes that occur throughout a woman's body during pregnancy, including in the respiratory and immune systems, increase her susceptibility to severe infection and hypoxic distress. In addition, the observed increase in ACE2 expression during pregnancy in uterine and placental cells increases a pregnant woman's vulnerability to COVID-19 [15].

During physiological pregnancy there is a decrease in T cells to create a favorable condition for embryo implantation, growth and maturation of the placenta [22]. It was alarming that SARS-CoV-2 affects the respiratory and cardiovascular organs, i.e. those organs that experience an additional load at the end of the gestational period [51]. Meanwhile, data regarding the greater susceptibility of pregnant women to Covid-19 coronavirus infection are contradictory. Some data are presented about a more severe course of COVID-19 in pregnant women compared to the general population [33]. Thus, according to American researchers, in the USA, pregnant women with COVID-19 are 2 times more likely to require intensive care than non-pregnant women of similar age [24].

According to W. Guan et al. pregnant women are similarly susceptible to infection and to the development of severe pneumonia as the general population [36]. A joint World Health Organization mission (citation: Melekhina E.V. et al.) "consisting of 25 national and international experts visited the affected regions of China between February 16 and 24, 2020 and examined 147 pregnant women (64 confirmed, 82 suspected and 1 asymptomatic COVID-19). Among these women, 8% had severe disease and 1% had critical disease. The experts concluded that pregnant women are not at higher risk of developing severe disease because of COVID-19."

Although the overall risk of severe disease and death in

pregnant women is low, pregnant women with a new COVID-19 coronavirus infection may develop critical conditions with a fairly stable course of the disease [44]. It should be noted that pregnant women with comorbid status (fat metabolism disorders, gestational diabetes mellitus, etc.) have a higher risk of developing severe COVID-19 than non-pregnant women with the same diseases [1]. The group with the highest risk of developing severe COVID-19 is made up of pregnant women with somatic diseases: chronic lung diseases, including bronchial asthma of moderate and severe severity; cardiovascular diseases, arterial hypertension; diabetes mellitus; immunosuppression, including against the background of cancer treatment; obesity (BMI>40); chronic kidney disease, liver disease, APS [temporary river of Russia].

Literature analysis showed that with each new wave of the epidemic process SARS-CoV-2 was more aggressive and characterized by higher virulence, short incubation period [16]. Taking into account the specificity of SARS-CoV-2 aggression in subsequent waves of the epidemic process, we analyzed the dynamics of the course of COV-2 in pregnant women in each wave. The aggravation of COVID-19 in pregnant women with each new wave of the epidemic process is noteworthy. Thus. According to the data of G.B. Malgina, in the dynamics of the epidemic process, women with higher parity were exposed to infection. In the first "wave" 56.45% were ill, in the second - 70.29%, in the third - 78.22% of repeat births, which can be explained by the possibility of infection of family members from children. There is an increasing incidence of mild to severe NKVI: 1/186 (0.5%) patients in the first "wave", 9/412 (2.2%) women in the second and 18/225 (8%) pregnant women in the third "wave". There is an increase in the risk of hospitalization of pregnant women with moderately severe form in the second and third "waves" of the epidemic process (OR = 3.9; 95% CI 1.7-8.8; $p<0.05$) [G.B. Malgina].

It is encouraging that no cases of intrauterine transmission of SARS-CoV-2 from pregnant women with Covid-19 to their fetuses have been confirmed. At the same time, there are data on the effect of Covid-19 on the course and outcomes of pregnancy. Thus, iron deficiency anemia - 44.2%, preeclampsia - 38.2%, threat of preterm labor - 35.3% prevailed in the structure of pregnancy complications. Preterm labor occurred in 36.8% of cases [8].

The impact of coronavirus infection on the formation of fetal stunting syndrome and placental dysfunction has been determined in scientific studies [13].

In the first and second trimesters of pregnancy after COVID-19 infection, spontaneous miscarriages, prenatal rupture of fetal membranes, premature labor, exacerbation of chronic somatic pathology (diseases of the cardiovascular system, respiratory organs, autoimmune processes, endocrine pathology), and postpartum hemorrhage have been observed [35].

Menzhinskaya I.V. et al (2023) studied the levels of autoantibodies to ACE2 in infertile patients who had undergone COVID-19 and in fertile women in infertile patients, regardless of COVID-19 history, determined a higher prevalence and levels of antibodies to ACE2 than in fertile women. and concluded that: "ACE2 antibodies are associated with primary and secondary infertility and may be involved in the pathophysiology of infertility".

The leading cause of mortality in COVID-19 patients is hypercoagulability, thrombosis and respiratory failure due to pulmonary microvascular thrombosis [46]. In this regard, SARS-CoV-2 infection during pregnancy may be an additional trigger for severe thrombotic complications [48], as physiologic hypercoagulability is observed during pregnancy. SARS-CoV-2 promotes endothelitis in various organs and tissues, leading to endothelial damage [46] and, in turn, thrombotic microangiopathy [50]. An important etiologic factor leading to thrombotic microangiopathy is the deficiency of metalloproteinase ADAMTS-13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13). ADAMTS-13 belongs to the family of peptidase proteins whose biological function is to cleave von Willebrand factor (vWF) multimers [7].

In scientific studies, great interest has appeared in the role of the relationship between ADAMTS-13 and vWF in the evaluation of acute conditions caused by SOVID-19. Thus, a prospective randomized case-control study with 135 pregnant women conducted by Gashimova N.R. et al. showed an imbalance of the ADAMTS-13/vWF axis in pregnant women after COVID-19 and the authors confirm the hypothesis that persistent endotheliopathy and hemostasis dysfunction persist after COVID-19 during pregnancy [7].

2. Conclusions

Thus, the analysis of data from the literature has shown that the outbreak of a new coronavirus infection, spreading throughout the world, has led to a state of emergency. Thanks to all possible measures taken by the world community in the fight against the new coronavirus infection, stabilization of the situation around the world has been achieved. The data presented in the review indicate that COVID-19 has a milder course in pregnant women compared to the general population. At the same time, with each new wave of outbreaks, the risk of a more severe course of COVID-19 during pregnancy increases.

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