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INDICATORS OF ADAPTIVE IMMUNITY IN PREGNANT WOMEN WITH COVID-19

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ABSTRACT

Summary: COVID-19 can have negative consequences for pregnant women and their newborns. According to statistics, pregnant women, people over the age of 60 and patients with severe somatic diseases (bronchopulmonary, cardiovascular, autoimmune) were the most sensitive to this virus. **The aim of the study:** was to study the cellular and humoral parameters of the immune system in women with COVID-19 who were in the third trimester of pregnancy. **Material and research methods:** We examined 67 pregnant women at 32-37 weeks of gestation who were in Maternity Complex No. 3 in Tashkent with a confirmed diagnosis of COVID-19, which made up 2 groups depending on the severity of COVID-19: 39 women were with moderate and 28 - severe severity. All examined women underwent clinical, laboratory and immunological examination. Immunological examination included determination of the level of cells with the CD3, CD4, CD8, CD16 phenotype in peripheral blood and the level of IgA, IgG, IgM in blood serum by ELISA. **Results:** It was found that in women with coronavirus infection, depending on the severity, there is an imbalance in the studied parameters of cellular and humoral immunity. **Conclusion.** In pregnant women with a gestational age of more than 32 weeks, coronavirus infection has a damaging effect on immune system parameters, depending on the severity of the disease. The more severe the disease, the stronger the changes in the state of the immune system are observed.

KEYWORDS: COVID-19, pregnant women, cellular and humoral immunity.

INTRODUCTION

COVID-19 can have negative consequences for pregnant women and their newborns.[1-5] According to statistics, pregnant women, people over the age of 60 and patients with severe somatic diseases (bronchopulmonary, cardiovascular, autoimmune) were the most sensitive to this virus.[3-4] The few publications on the impact of COVID-19 on the gestational period, fetus and newborn note that pregnant women are less tolerant to respiratory pathogens and therefore suggest that they are more susceptible to COVID-19 as well.[5] However, in the leading countries of the world, a number of protocols have been developed for the management and treatment of pregnant women with COVID-19.[5,6,7]

High susceptibility to respiratory infections and severe pneumonia in pregnant women is associated with immunosuppression and other physiological changes during pregnancy, in such cases, pregnant women require hospitalization in intensive care units and mechanical ventilation.[7]

In most cases, pneumonia develops during infection in the third trimester - during the period of maximum change in cell-mediated immunity, while there is a rapid development of respiratory failure and secondary bacterial complications.[6,7] Among the most common complications of COVID-19 are acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC) syndrome, renal failure, secondary bacterial pneumonia, and sepsis.[8]

According to D.I. Sheveleva (2020) infection with COVID-19 is more susceptible to primiparous in the 1st (61.6%) and 3rd (70.6%) trimester of pregnancy and multiparous in the 2nd (62.5%) trimester of gestation with a burdened obstetric and gynecological history (58.3%) and concomitant pathology (41.5%).

The aim of the study was to study the cellular and humoral parameters of the immune system in women with COVID-19 who were in the third trimester of pregnancy.

MATERIAL AND RESEARCH METHODS. For the period from 03/17/2021 to 11/07/2021, 1913 patients with obstetric and gynecological pathology were treated in the Maternity Complex No. 3. Of these, there were a total of 2256 pregnant women at various gestational ages. Of these, 1890 pregnant women were with a confirmed SARS-COV-2 viral infection, which were isolated and were in the red zone, 366 pregnant women

were treated with various obstetric and somatic pathologies, as they were in contact with patients with COVID-19. In order to study the clinical and immunological features of the course of the gestational process, 67 women infected with this viral infection were taken under observation, which made up 2 groups depending on the severity: group 1, 35 women with a moderate degree of coronavirus infection and group 2 22 women with severe COVID-19.

Immunological studies were carried out by quantitative study of the number of lymphocytes with the phenotype CD3, CD4, CD8, CD20 in peripheral blood using monoclonal antibodies of the LT series (LLC "Sorbent" Moscow, Russia), determining the level of IgG, IgA, IgM in blood serum by ELISA using test systems of LLC "Vector Best" (RF), according to the attached instructions. The control group consisted of 20 women with physiological pregnancy.

The study materials were subjected to statistical processing using the Student's t-test using the standard Windows 2000 statistical software package.

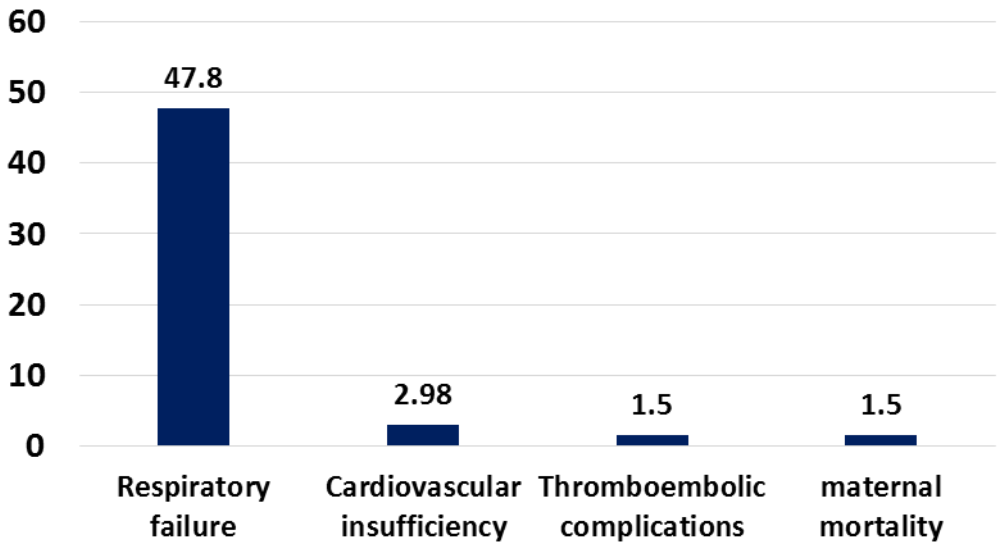
RESULTS AND ITS DISCUSSION

An analysis of anamnestic data showed that coronavirus infection, when it enters the body of pregnant women, primarily causes damage to both the upper and lower respiratory tract. So, among the observed 3.4% of pregnant women, it led to damage to the upper respiratory tract, 49% of pregnant women were diagnosed with bilateral viral pneumonia. The main indications for hospitalization of pregnant women with confirmed coronavirus infection were various obstetric pathologies. Thus, the most frequent obstetric complication was oligohydramnios in terms of gestation above 30 weeks (21.3%). Also, often pregnant women were hospitalized with a diagnosis of premature detachment of a normally located placenta of mild and severe degree (1.3%), polyhydramnios (0.9%) and antenatal fetal death (0.5%). Such a formidable complication of the gestational period as preeclampsia was diagnosed in 5 pregnant women. Of these, 4 had mild preeclampsia and 1 pregnant woman was diagnosed with severe preeclampsia, which was an indication for early termination of pregnancy.

It should be noted that for pregnant women with coronavirus infection, the frequency of concomitant somatic pathology was characteristic.

Most often, pregnant women with iron deficiency anemia (68.6%) were infected with COVID-19, among which the vast majority were women with chronic anemia that developed before the onset of this pregnancy (64%). Also, pregnant women with chronic respiratory diseases, obesity (7.5%) and urinary tract infection (2.98%) were more likely to become infected with SARS-COV-2 viral infection.

The clinical history showed that the course of COVID-19 in pregnant women is especially difficult in the third trimester of pregnancy (Pic.1).

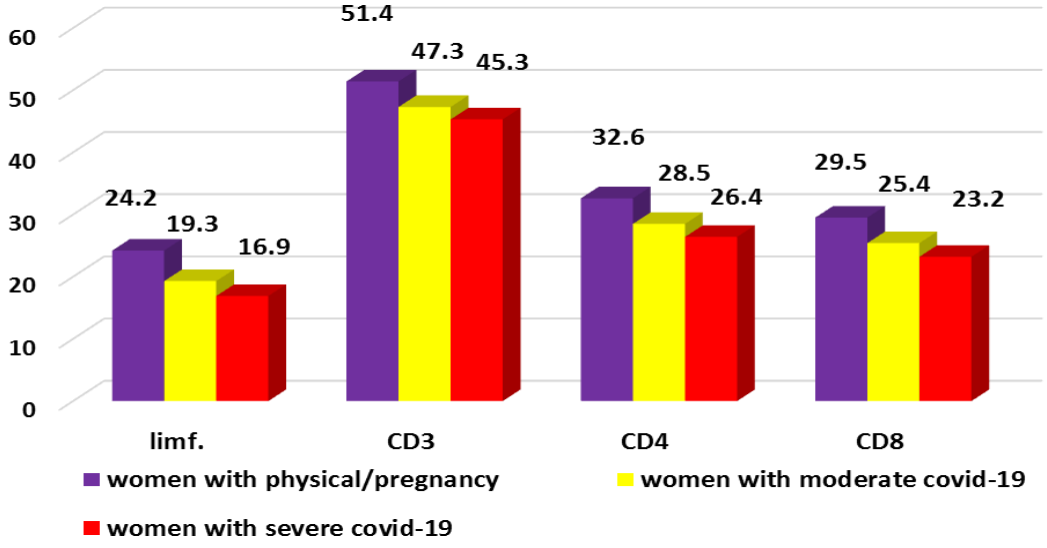


Pic. 1. Pregnant women with COVID-19.

Despite the fact that pregnant women were under continuous supervision of both gynecologists and resuscitators, they were periodically consulted by virologists from the Research Institute of Virology of the Ministry of Health of the Republic of Uzbekistan, almost half of the infected pregnant women had symptoms of respiratory failure (48.7%), such as shortness of breath, increased respiratory rate above 22 per minute, decrease in saturation (SpO2 below 95%), elevated body temperature (38˚-39˚), which lasted for 3-4 days.

We noted that the SARS-COV-2 virus leads to severe disorders of the coagulation link of hemostasis. Despite the use of both antiplatelet agents and injectable anticoagulants, 7 (10.4%) pregnant women in the third trimester of pregnancy developed thrombophilic complications.

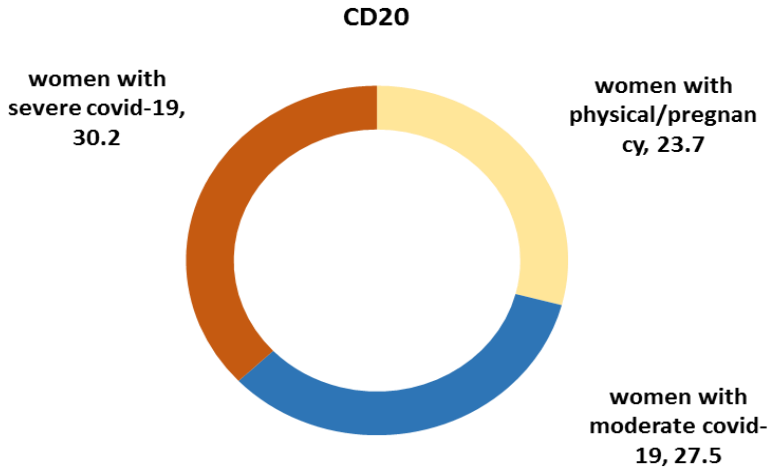
Conducted immunological studies have shown that pregnant women with coronavirus infection are characterized by suppression of cellular immunity (Table 2). As can be seen from the data in Pic.2, suppression of the immune system is manifested by general lymphopenia, (P<0.01). Analysis of relative values showed a significant decrease in the level of CD3 cells (P<0.01), as well as a decrease in the relative number of T-helpers (CD4+) (P<0.05) and T-suppressors (P<0.01).



Pic. 2. Indicators of the cellular link of immunity in the examined women, %.

Persistent insufficiency of T-cell immunity contributes to the long-term persistence of viruses and poses a threat of the process becoming chronic.[2] The consequence of the disturbed balance between the infectious agent and the body's defense mechanisms may be the suppression or activation of immune responses. A change in the immune status leads, in turn, to the activation of the infection. It is assumed that prolonged asymptomatic infection triggers immunity to microbial epitopes that are also present in humans (Neuer A., 1999). The last stages of pregnancy are in a threatened position, because the fetoplacental system is under severe pressure due to the large release of serotonin caused by the stimulation of the infectious process, as well as the direct toxic effect of the virus on the mother's immune apparatus.[6]

When studying the content of the total pool of B-lymphocytes, it was found that their relative number significantly increased (p<0.05), and the maximum value was recorded in women with severe coronavirus infection (P<0.05), (Pic.3).

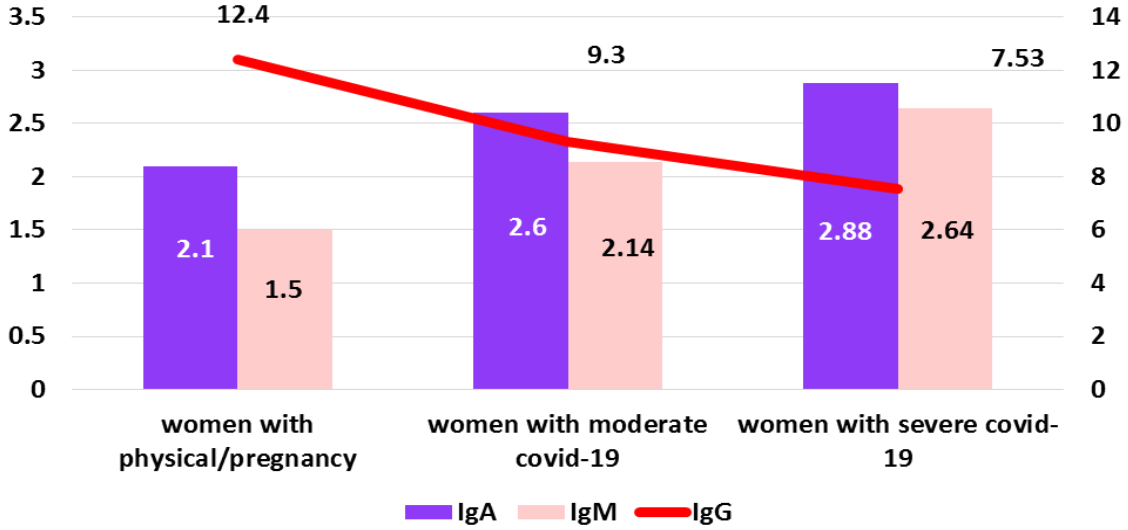


Pic 3: The level of B-lymphocytes in the examined women,%.

It is known that immunoglobulins perform an important function of mediators in the cascade development of the immune response and can partially determine the effectiveness of the final, effector reactions of cellular immunity in inactivation and elimination of bacterial and viral antigens.[7]

From the data in Pic.4, it can be seen that women with coronavirus have class G dysimmunoglobulinemia, while IgA and IgM levels were significantly elevated (P<0.05), and these changes are deeper in severe coronavirus infection.

Elevated levels of IgA and IgM, according to a number of authors, are associated with the synthesis of incomplete immunoglobulins by B-lymphocytes.[4,5] As you know, the IgG molecule consists of 3 fragments: 2 identical fragments associated with antigens (Fab), and 1 crystallizing fragment (Fc). With the help of the active site, the Fab fragment binds to the determinant group of the antigen. The intensity of this interaction is determined by the affinity of the antibodies. On this basis, they can be high or low affinity. The latter inefficiently bind to the antigen and, therefore, they are ineffective in its elimination from the body.[5] The existence of an unutilized antigen-antibody complex, in which the virus remains in a virulent state, maintains the infection of the organism for a long time.[2,3]



Pic 4: The level of immunoglobulins in the examined women,g/l.

There is concern that the coronavirus infection, affecting the mother's body, can penetrate the fetoplacental barrier into the body of the developing fetus, causing the same changes in immune-protective processes as in the mother. It is known that the transplacental transfer of maternal immunoglobulins to the fetus is an important factor in its protection during the gestational period. Against the background of coronavirus infection, significant disturbances occur in the metabolism of the fetoplacental barrier. First of all, the synthesis of the leading placental hormones – estriol, estradiol, dehydroepiandrosterone and progesterone[1,3], is sharply suppressed, which helps to reduce the level of T-suppressors to 7-5.3% in the 3rd trimester of pregnancy.[5,6]

Thus, during physiological pregnancy, the inclusion of fetoprotective mechanisms is observed that activate the immune system in the direction of the Th2-type immune response and, probably, have a modulating effect on the Th1-dependent immune response. With coronavirus infection in pregnant women, this inclusion is not observed, which leads to a breakdown in tolerance and the occurrence of a number of pregnancy complications.

CONCLUSION

In pregnant women with a gestational age of more than 32 weeks, coronavirus infection has a damaging effect on immune system parameters, depending on the severity of the disease. The more severe the disease, the stronger the changes in the state of the immune system are observed.

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