CHARACTERISTICS OF THE CLINICAL COURSE OF COVID-19 INFECTION IN PREGNANT WOMEN

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ABSTRACT

Different manifestations of symptoms and complications of coronavirus infection in pregnant women depend on the gestational period of pregnancy, women's age, concomitant diseases and several other factors. Studying the clinical condition of COVID-19 in pregnant women will help to prevent side effects of the disease and develop preventive measures. The purpose of the study: to study the clinical features of the coronavirus in pregnant women. Conclusion: COVID-19 presents with stronger symptoms in pregnant women compared to women in other contingents, and the risk of transitioning to severe forms of the disease is relatively high in pregnant women. Conclusion: The development of complications of viral infection in pregnant women infected with the coronavirus is more frequent than in healthy women, and the analysis of the clinical course of COVID-19 in pregnant women provides an opportunity to take measures to prevent risks depending on the trimesters of pregnancy.

Key words: Coronavirus, tachypnea, pneumonia, anemia, saturation, alkalosis, artificial ventilation.

INTRODUCTION

Relevance. Pregnancy is a physiological state with changes in various systems of a woman's body. This process is an auxiliary factor for the outbreak of respiratory infections and increases the risk of transitioning to severe forms of the disease [1].

Also, the role of interleukins (IL) in the outbreak of COVID-19 and the development of severe forms is presented in many literatures [2,3,4,5,6,7]. As there are changes in all organs and systems during pregnancy, physiological changes also occur in cytokines and immune cells [8]. The immunological state in pregnancy is characterized by a weakened immune response to protect the genetically foreign fetus, but at the same time, an immune response that maintains immunity against other pathogenic infections is also necessary. Humoral immunity, also known as antibody-mediated immunity, occurs during this period and is most effective against extracellular pathogens. Present antigens stimulate pathogen-specific B lymphocytes and enhance their immune response[9].

Fetal development during pregnancy is associated with respiratory and immunological adaptations. Total body oxygen demand is approximately 20% higher compared to nonpregnant subjects, with minute ventilation significantly increased, leading to compensated respiratory alkalosis [10]. An important pattern of immunological adaptations in pregnancy is the decline of adaptive immune function, which is particularly prominent in the third trimester [11].

Today, there is no clear evidence about the state of pregnancy and the effect of viral infection on the fetus due to the lack of experiments conducted on pregnant women infected with the coronavirus. Nor has it been proven that pregnant women have different clinical symptoms or a higher risk of serious complications than women in other contingents. Also, there is no evidence of transmission of Covid-19 from mother to child, considering that the virus indicator is negative in samples taken from vaginal secretions, amniotic fluid, umbilical cord blood, and breast milk.

Changes in hormone levels during pregnancy, reduction in lung volume and weight of the uterus, and changes in the immune system can lead to rapidly deteriorating clinical conditions in women infected with COVID-19, causing great harm to both the mother and the fetus. Alternatively, the above physiological conditions during pregnancy may increase women's vulnerability to severe infection and hypoxia [11, 12].

Therefore, it is necessary to study the course of the virus infection in pregnant women according to the trimesters, the effect of the coronavirus on the pregnancy process and at the same time on the condition of the fetus.

The purpose of the study. To study the specific features of the course of COVID-19 infection in pregnant women.

Material and methods. In the study, we used the data obtained during the examination, the medical history data, and the data obtained directly and by phone from the patient's relatives to assess the dynamics of the condition of women. 120 pregnant women aged 18 to 41 who tested positive for COVID-19 were included in the study. Among them, 40 (36.4%) pregnant women aged 18-25 years, 54 (49.1%) women aged 25-35 years were recorded at the highest level. Only 14.5% (16 people) were aged between 35 and 41 (Table 1).

Table 1

Characteristics of pregnant women by age and duration of pregnancy

Age	1-trimester		2-trimester		3-trimester		Total	
	N=24	%	N=38	%	N=58	%	N	%
18-25 years old	8	33.4	13	34.2	20	34.5	41	34.2
25-35 years old	11	45.8	21	55.3	31	53.4	63	52.5
Over 35 years old	5	20.8	4	10.5	7	12.1	16	13.3
Total	24	100	38	100	58	100	120	100

In the study, the number of women infected with COVID-19 in the 3rd trimester is higher than those infected at other times of pregnancy. In the age analysis, taking into account that the best reproductive age is 20-35 years old, the number of pregnant women over 35 infected with coronavirus was relatively low, 13.3%.

The clinical condition of pregnant women infected with COVID-19 was analyzed in accordance with the standards in the field of obstetrics. From them, family, allergic, related diseases and obstetric anamnesis were collected and monitored.

All women underwent standard clinical, laboratory and instrumental examinations. The results have been determined.

The control group consisted of 105 conditionally healthy women.

Results. According to the results of the study, the characteristics of women according to the presence of comorbidities in pregnant women infected with COVID-19 are presented in Table 2. In this case, women (presence of hypertensive conditions during pregnancy, anemia, diabetes, chronic urinary tract infection SSY, obesity, varicose disease were taken into account).

Table 2

Characteristics of women in the study according to the presence of additional diseases

Additional diseases	1-trimester n=24		2-trimester n=38		3-trimester n=58		Control group n=105	
	N	%	N	%	N	%	N	%
Hypertensive conditions	1	4,2	1	2.6	4	6.9	0	0
Anemia	21	87.5	32	84.2	50	86.2	50	47,6*
SSI	6	25	12	31.6	24	41.4	5	4,7*
Excess weight	4	17	5	13.2	10	17.2	4	3,8*

Note:*-reliability of data between groups (p<0.05)

Most of the analyzed women had anemic conditions. In women in the main group, low levels of hemoglobin were detected in 85.8% of cases on average, and in 47.6% of cases in the control group. In the analysis of hypertensive cases, the increase in blood pressure in women was mainly disturbed in the 3rd trimester and was detected in 4 women. In the observations, it was found that urinary tract infection was more common in the group of women in the 3rd trimester and made up 41.4%, in the 2nd trimester it was detected in 31.6% of women, and in the 1st trimester in 25% of women. Varicose veins affected 5 women (13.2%) in the 2nd trimester, 2 pregnant women (8.3%) in the 1st trimester, and 13.8% of women in the 3rd trimester. Overweight (estimated by BMI) in pregnant women, taking into account the estimated weight of the fetus, the estimated weight of the placenta and fetal fluid according to the term, was determined in a total of 19 women in the main group, and 1 of them developed metabolic syndrome. The highest proportion of obesity was observed in pregnant women in the 3rd trimester (17.2%).

In patients, coronavirus infection manifests itself with various symptoms depending on a number of physiological, social and individual conditions. The following table lists the symptoms caused by the coronavirus disease in women at different stages of pregnancy.

As can be seen from the above data, the exacerbation of symptoms of the disease in pregnant women was determined in different indicators in different trimesters. From the results of observation, it can be seen that mild symptoms of viral infection in the 1st trimester of pregnancy were complete and dyspeptic conditions were slightly higher compared to pregnant women in other trimesters. Of these, body temperature increase was observed in 79.2% (19) cases, taste and smell disturbances in 75% cases, dyspeptic disorders (nausea, vomiting) in 29.2%

(7) cases. 41.7% (10 people) complained of shortness of breath, 66.7% (16 people) of shortness of breath. Those whose saturation (SpO$_2$) was below 94 did not exceed 3 (12.5%).

Table 3

Symptoms and characteristics of the disease in pregnan.t women infected with COVID-19

№	Symptoms	1-trimester n=24		2-trimester n=38		3-trimester n=58		Total n=120	
		№	%	№	%	№	%	№	%
1	Increase in body temperature	19	79,2	35	92,1	51	88,0	105	87.5
2	Cough	21	87,5	37	97,4	56	96.5	114	95
3	Complete violation of the sense of smell	18	75,0	28	73,7	30	51.7	76	63.3
4	Increased feeling of fatigue	21	87,5	36	94,7	57	98.3	114	95
5	Changes in the digestive system (vomiting, nausea, loss of appetite)	7	29,2	5	13,2	8	13,8	20	16,7
6	Shortness of breath	10	41,7	23	60.5	54	93.1	87	72.5
7	Tachypnoea	16	66,7	29	76.3	56	96.5	101	84.2
8	Saturation<94	3	12,5	2	5.2	8	13.8	13	10.8
9	Diarrhea	2	4,2	3	7,9	3	5,1	8	6,7

38 women in the 2nd trimester were mainly bothered by cough, shortness of breath and fatigue. Among them, 92.1% (35 people) had an increase in body temperature, 97.4% (37 people) had a cough, 94.7% (36 people) had severe fatigue, weakness, 76.3% (29 people) had shortness of breath, and 60.5% (23 73.7% (28 women) complained of dyspeptic disorders, while 73.7% (28 women) complained of dyspeptic disorders. Diarrhea was observed in 7.9% of women (3). Among them, the number of women who needed artificial ventilation and SpO$_2$ >94 was 2 (5.2%).

Women in their 3rd trimester had a slightly more severe infection with COVID-19 than women in other trimesters, because the physiological changes of pregnancy are at a higher risk of contributing to the exacerbation of symptoms. In 88% (51) of women in the last trimester of 58 pregnancies, an increase in body temperature was detected during the anamnesis collection. Among them, 96.5% (56 people) had diarrhea, 51.7% (30 people) had a sense of taste and smell, 98.3% (57 people) had shortness of breath, 96.5% had shortness of breath. Only 13.8%

(8) of these pregnant women complained of dyspeptic disorders, 5.1% (3) of diarrhea. 13.8% (8) of pregnant women with SpO2>94 on artificial ventilation.

So, in all pregnant women, the increase in body temperature is 87.5%, cough is 95%, full sense of smell is 63.3%, fatigue is 95%, dyspeptic conditions are 16.7%, shortness of breath is 72.5%, shortness of breath is 84.2%. Among these 120 pregnant women, the number of those with SpO2<94 was 13 (10.8%).

When analyzing the severity of the disease in pregnant women, 50 of the pregnant women had a relatively mild form of coronavirus infection, acute respiratory viral infection, and X-ray examination did not reveal any focal changes or signs of pneumonia. None of them had long-term fever, cough, or shortness of breath. Symptoms were manifested by subfebrile fever, impaired sense of smell, severe fatigue, sore throat, and sometimes cough. The duration of disease symptoms was 7-10 days. None of them had an increase in body temperature for more than 2-3 days. In 70 pregnant women, the disease passed in moderate and severe forms, severe symptomatic signs and pathological foci typical of pneumonia were detected in the X-ray examination.

The severity of COVID-19 varies depending on the trimester of pregnancy. The characteristics of pregnant women according to the results of the observations are presented in Table 4.

Table 4

Characteristics of patients according to the severity of the coronavirus disease

Levels of severity of COVID-19	1-trimester		2-trimester		3-trimester		Total	
	N	%	N	%	N	%	N	%
Light grade	12	50	15	39.5	13	22.4	40	33.3
Moderate severity	11	45.8	18	47.4	35	60.3	64	53.4
Severe level	1	4.2	4	10.5	8	13.8	13	10.8
Critical situation	0	0	1	2.6	2	3.5	3	2.5
Total	24	100	38	100	58	100	120	100

According to our observations, as the duration of pregnancy increased, the severity of COVID-19 increased, and severe and critical forms of the coronavirus were found mainly in pregnant women in the 2nd and 3rd trimesters. Mild levels of COVID-19 were observed in 50% of cases in the 1st trimester, in 39.5% of women in the 2nd trimester, and in 22.4% of cases in the 3rd trimester. In general, the occurrence of the disease in a medium-severe form was observed more often in pregnant women (53.4% in total). Of these, 2.5% of patients had a critical form of COVID-19, and these women needed intensive treatment. One of them died biologically: in the intensive care unit, in the intensive care unit, despite the

resuscitation measures, he died due to the main disease (COVID-19), cardiorespiratory failure.

The amount of IgG in the women's blood was checked, and the results are given below. This indicator in the blood of pregnant women was analyzed depending on the severity of the viral infection.
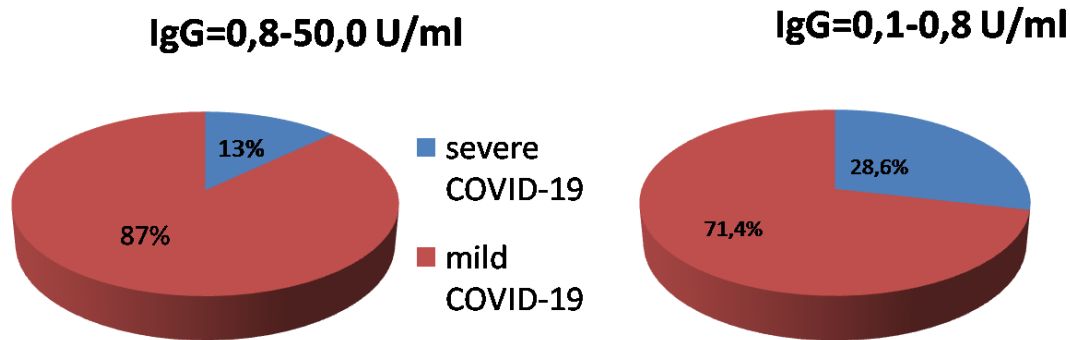

IgG=0,8-50,0 U/ml
- 13% severe COVID-19
- 87% mild COVID-19

IgG=0,1-0,8 U/ml
- 28,6%
- 71,4%

Figure 1. Data on the blood test of IgG in pregnant women infected with COVID-19

It is known that one of the most reliable diagnostic methods for COVID-19 is the IFA (immunoenzyme analysis) blood test, the concentration of IgG is important, and its indicator is: 0-0.8 U / ml = negative response to the virus no counter-reply; At 0.81-1.0 U/ml = weak positive response, at 1.1-50.0 U/ml = positive response and antiviral effect is effective in 50% of cases, at >50.0 U/ml = very high virus neutralizing activity. In our study, when this laboratory result was analyzed according to the ratio of positive and negative amounts (the limit is 0.8 U/ml), it can be seen that the amount of IgG in the blood of patients with a more severe form of COVID-19 compared to patients with a mild form of the disease was relatively higher. That is, 87% of women with IgG>0.8 U/ml (positive) had more severe COVID-19. 71.4% of pregnant women with IgG<0.8 U/ml (negative) results were treated with a mild form of the disease at the same time (the highest determined level of IgG in the examined women was 24.3 U/ml). It can be seen that the amount of IgG was determined in different indicators at different severity levels of the disease.

Discussion. Among pregnant women infected with COVID-19, we analyzed the pregnancy trimester of the mother, the presence of additional diseases, and the age of the mother in the classification according to the severity of the disease. Clinical manifestations of COVID-19 vary across nations, populations, sexes, and races. According to the results of our observations in the contingent of pregnant women of the Uzbek population, the state of pregnancy increases the risk of

aggravation of the coronavirus disease and the occurrence of more severe clinical manifestations and even maternal death. At the same time, in the 3rd trimester of pregnancy, the clinical course of COVID-19 is more severe than in the 1st-2nd trimesters, and the rate of severe complications is high.

Of course, it was found that the outbreak of this viral infection depends not only on the physiological processes during pregnancy, but also on the age of the examined women, additional diseases and the level of IgG in the blood. All women were tested for SARS-CoV-2. In 44 of them, IgM and IgG levels were analyzed by enzyme immunoassay (IFA). Considering that the patients were in the hospital with obvious symptoms, it was natural that the amount of IgM increased in them, that is, the result was positive. The main focus was on the difference in the amount of IgG in women during the almost simultaneous outbreak of the coronavirus disease. According to the results, 87% of women with IgG=0.1-0.8 U/ml have more severe forms of the disease, and on the contrary, 71.4% of women with IgG=0.8-50 U/ml have a mild viral infection.

When the literature was reviewed, our results were similar to the findings of Stephen Lapinski's (2012) research. He conducted research on pregnant women and non-pregnant patients and found that pregnant women are more prone to develop acute respiratory distress syndrome (ARDS) due to increased blood pressure, hypoalbuminemia and immunological factors. ra state of pregnancy and the birth process lead to the development of ORDS with the appearance of inflammatory-like changes [13]. According to scientists from the University of Texas Yost N and others, the risk of pneumonia in pregnant women is the lowest in the first trimester. [14].

The results of our study do not match the data of Breslin N (2020) and Zunyou Wu (2020). Because when the clinical course of COVID-19 was analyzed in these two studies, viral infection was observed in 86% mild and 9% severe or critical (5%) cases in pregnant women, which is similar to the distribution of the clinical course observed in the non-pregnant population, in which: mild (81%), severe (14%) and critical (5%) [15, 16]. Also, Yi-Hua Chen found that about 93.6 percent of pregnant women infected with coronavirus developed pneumonia in the first trimester, and these women have a higher risk of developing pathological conditions and negative consequences in pregnancy compared to other women [17].

Summary. The conclusions of our observations showed that the physiological conditions during pregnancy, the age of women and especially the duration of pregnancy are optimal conditions for the outbreak of the coronavirus disease. The 3rd trimester of pregnancy is the most dangerous period that increases

the risk of complications and serious conditions. The presence of additional diseases during pregnancy and the indicator of IgG in the analysis of IFA are important in the identification of clinical forms of COVID-19.

Thus, the results of our research allow to determine the risk group for the origin of pneumonia and the development of severe forms of the disease in pregnant women infected with COVID-19, which helps to improve the quality of early prediction of the severity of the disease. Prevention of the outbreak of viral infection is important for the prevention of the deterioration of the mother's life and the condition of the fetus, the occurrence of various serious complications.

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