CRITERIA FOR PREDICTING EARLY NEONATAL ADAPTATION OF NEWBORNS IN WOMEN WHO HAD COVID-19 INFECTION DURING PREGNANCY

G.S. MANASOVA
MD, professor, Department of Obstetrics and Gynecology, Odesa National Medical University, Odesa
ORCID: 0000-0002-1600-5215

Y.O. STASIY
postgraduate student, Department of Obstetrics and Gynecology, Odesa National Medical University, obstetrician-gynecologist, CNE "Maternity hospital No. 5" of the Odessa City Council, Odesa
ORCID: 0000-0003-2623-860X

M.V. SHAPOVAL
MD, professor, Department of Obstetrics and Gynecology, Odesa National Medical University, Odesa
ORCID: 0000-0002-1087-2609

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INTRODUCTION

The coronavirus pandemic has been recognized by WHO as a public health threat and, according to numerous studies, due to the high contagiousness of the disease and the lethal risk, the health of pregnant women and their newborns is of particular concern to the medical community [1, 2].

Pregnant women are a subpopulation that experiences physiological changes over a long period of time, including changes in the chest organs and abdominal cavity. Changes in the shape of the chest and the relative position of the chest organs and abdominal cavity, the position of the diaphragm, a decrease in the total capacity of the lungs, etc. reduce resistance to hypoxia. On the other hand, physiological shortness of breath, an increase in the volume of circulating blood can lead to an increase in secretion in the respiratory tract and favor the development of infection [3, 4]. The placenta makes a significant contribution to the change in the immunological tolerance of the pregnant woman's body: the change in the innate and adaptive immune responses of the body from inflammatory to anti-inflammatory ensures protection of the fetus and passive transfer of maternal antibodies to the fetus. This protection, including during coronavirus infection, is mediated by certain hormonal, metabolic and immunological mechanisms [5, 6]. Pregnant women are most susceptible to infectious diseases in the third trimester due to increased respiratory resistance in the lungs and changes in the immune system [7].

COVID-19 infection is characterized by a wide range of clinical manifestations, and information on the disease impact on pregnant women and newborns is contradictory and constantly changing [8–10].

According to the literature (UNICEF, 2021), the overall level of vertical transmission from pregnant women to newborns is very low and there is no evidence of transmission of infection in preschools and schools [11]. Other studies have shown similar results of low levels of infection in newborns [12, 13].

In addition to the typical widespread consequences of coronavirus infection, pregnant women have a higher risk of antenatal, intrapartum and postnatal complications, including spontaneous abortion, preterm delivery, intrauterine growth retardation and vertical transmission of the disease [8, 11]. Pregnant women with COVID-19 more often (compared to non-pregnant women of reproductive age) require hospitalization in intensive care unit, mechanical ventilation, and their newborns also have a higher risk of hospitalization in intensive care unit [9, 10]. A number of authors report about association of COVID-19 with stillbirth, neonatal mortality, a high frequency of births of children with small for gestational age weight, fetal distress, but there is no direct evidence of the influence of COVID-19 on these complications [10, 14, 15]. J. Villar et al. (2021) showed that pregnant women with a history of COVID-19, have a more than 2-fold increased neonatal morbidity index compared with healthy women (odds ratio (OR) = 2.66; 95% confidence interval (CI) 1.69–4.18), perinatal morbidity and mortality (OR = 2.14; 95% CI 1.66–2.75) [10].

Due to the wide range of clinical manifestations of COVID-19 in pregnant women, including the picture of pneumonia of varying severity, the level of oxygen saturation of the blood (SpO_2) is of particular importance, which, along with pulse and respiratory rate, blood pressure, is one of the clinical criteria for assessing the patient's condition and prognosis of the disease [16–18]. The SARS-CoV-2 virus mutation and the emergence of new variants (delta, omicron, flirt) have led to an increase in its contagiousness and an increase in the incidence rate among pregnant women with all the ensuing consequences. It is noted that these patients more often require respiratory support to ensure the required level of SpO_2 [19–21].

In accordance with the recommendations of the Society for Maternal-Fetal Medicine (SMFM) and the International Federation of Gynecology and Obstetrics (FIGO), saturation in pregnant women should be maintained at ≥95% in the context of the COVID-19 pandemic, while for non-pregnant women it can be lower (SpO_2 ≥ 92%) [18, 21].

Most of the epidemiological studies of COVID-19 infection among pregnant women are based on case studies and case series devoted to the study of clinical manifestations

of the disease, the risks of transmission of infection from mother to fetus and newborn, the study of complications of pregnancy and childbirth. Few studies include pediatric populations. There are no studies aimed at preventing possible negative consequences of the disease for the fetus and newborn [11].

Objective of the study: to investigate the possibility of predicting the newborn status in women who have had COVID-19 during pregnancy based on clinical and instrumental data (saturation indicators in the pregnant woman, cardiotocography (CTG) examination of the fetus).

MATERIALS AND METHODS

Population

The participants in the prospective single-center case-control study were:

- 58 women with a confirmed diagnosis of COVID-19 during pregnancy (group A or main) and their newborns;
- 40 healthy women with a physiological course of pregnancy (group B or control) and their newborns.

The study was conducted for the period from 01.11.2021 to 31.12.2022 at the Maternity Hospital No. 2 of the Odessa City Council, which was a hospital base for the provision of obstetric and gynecological care to pregnant women with moderate COVID-19 infection who are residents of the Odessa region.

The data of the general somatic and reproductive anamnesis, demographic and anthropometric data, the course of pregnancy, perinatal outcomes for the mother and fetus/newborn, the results of conventional (general blood and urine tests) and specific laboratory tests (concentration of C-reactive protein, D-dimer, liver and kidney function, etc.) were analyzed.

The condition of the intrauterine fetus (feto- and placentometry, blood flow assessment using Doppler sonography, biophysical profile of the fetus) was assessed using ultrasound examination on the GE VOLUSON 730 EXPERT device (General Electric, USA). We used a volumetric multifrequency convex sensor RAB 4–8P and a volumetric intracavitary convex sensor RIC 5–9. Using fetal cardiac monitors "Sonicaid Team Care" (Huntleigh HEALTHCARE, LTD, UK), fetal CTG was performed with subsequent automatic decoding of the obtained curve and short-term variability (STV) was assessed using the Fisher scale.

Inclusion and exclusion criteria

Inclusion criteria for the main group: verified diagnosis of COVID-19 at the time of hospitalization for delivery or indication of inpatient treatment due to confirmed SARS-CoV-2–associated acute respiratory viral infection during pregnancy.

Exclusion criteria: the presence of severe extragenital pathology or pregnancy complications (severe preeclampsia, chronic arterial hypertension, diabetes mellitus, coagulopathy or thrombophilia), which could affect the anatomical and functional features of the placenta.

Verification of COVID-19 infection

The diagnosis was verified twice. Initially, a rapid test for coronavirus was performed, based on the detection of the SARS-CoV-2 nucleocapsid protein (antigen) by immunochromatographic analysis in smears and scrapings from the back wall of the oropharynx. Biomaterials from the back wall of the pharynx and nose (the working part of the swab) were placed in a disposable sterile test tube containing 1–1.5 ml of transport medium with a lysing viral medium (ready-made industrial production) to confirm the diagnosis. Then the biomaterial was transported to a certified laboratory in order to detect the SARS-CoV-2 virus RNA by the polymerase chain reaction in real time. Collection of material for analysis and its transportation were carried out in compliance with the requirements of regulatory documents.

The severity of the disease was classified based on the order of the Ministry of Health of Ukraine dated March 28, 2020 No. 722 "Organization of Medical Care for Patients with Coronavirus Disease (COVID-19)" as amended on January 7, 2021 No. 10 "On Approval of Medical Changes (COVID-19)" [22]. According to this standard, patients with moderate or severe disease are subject to hospitalization, i.e. patients who have a temperature above 38 °C that cannot be corrected (temporary, no more than 1–1.5 hours decrease against the background of taking antipyretic drugs with its subsequent increase), or there are signs of pneumonia and/or respiratory failure (increased respiratory rate above the physiological norm, hemoptysis, $SpO_2 \leq 93\%$, radiologically confirmed pneumonia), the presence of clinical and instrumental data of acute respiratory distress syndrome.

According to the "Patient Route" developed by the Department of Health of the Odessa City Council, pregnant women underwent an X-ray examination or computed tomography (CT) scan of the chest before hospitalization. In case of severe degree of the disease pregnant women were hospitalized at the 3rd level of medical care – the Perinatal Center of the Odessa Regional Clinical Hospital.

Ethical aspects of the study

The study was approved by the Ethics Committee of the Odessa National Medical University and was carried out in accordance with the Declaration of Helsinki after obtaining informed consent from patients. The work is part of the scientific topic of the Department of Obstetrics and Gynecology of the Odessa National Medical University "The latest therapeutic, diagnostic and preventive approaches to diseases of the female reproductive system and high-risk pregnancy", registration number No. 0117 U007494, 2022–2027.

Statistical analysis

The database was created using the software MS Excel (Google forms and Google tables) software. Calculations were made using MS Excel and the online resource Social Science Statistics [23]. By means of the Kolmogorov-Smirnov criterion it was determined that the quantitative characteristics of the variation series in this study have an abnormal distribution; therefore, nonparametric characteristics were used for statistical data processing. Calculations of average values are presented as a median and quartile deviation (Me ± Q). The methods of variation statistics, determination of the Student's t-test for unrelated populations, calculation of the Fisher exact test, nonparametric Mann-Whitney U-test were used; Kruskal-Wallis test (nonpara-

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metric alternative to one-way ANOVA test for independent variables) to determine the statistically significant difference between medians of continuous variables and their interdependence (saturation level indicators, cardiotocographic study data, Apgar scale), calculation of odds ratio (OR) and 95% confidence interval (CI). Statistically significant value was accepted at $p < 0.05$.

RESULTS

In terms of mean age no significant difference was found between the groups A and B (29.21 ± 4.3 vs 30.35 ± 3.12 years; t = 0.21, p = 0.830553). A difference was revealed between groups A and B in the number of women aged 25–39.11 years: 65.5% vs 82.5% (F = 0.0421, $p < 0.05$); at the age > 40 the difference was 3.6% vs 2.5%, respectively. Older age is a risk factor for COVID-19 incidence (OR = 4.307, 95% CI 2.38–7.78). According to parity of births (primiparous in the main and control groups were 67.24% (women) vs. 55% (22 women) (F = 0.2895, $p < 0.05$), no difference was found between the groups. In both groups, every 12th woman had a scar on the uterus after a previous cesarean section: group A – 9 patients (15.51%) and 5 patients (12.5%) in group B (F = 0.7745, $p > 0.05$).

In 41.4% of women in group IA body weight was within the normal range, in the rest women the body mass index (BMI) corresponded to pre-obesity (40.8%, 24 women) or obesity (12.8%, 7 women) (F = 0.0015, $p < 0.05$). The average BMI in patients in the main and control groups was 27.32 ± 4.48 and 22.8 ± 2.30 kg/m^2 (F = 9.79, p = 0.000023, OR = 5.667, 95% CI 2.226–14.427).

The frequency of extragenital pathology was higher in group A (81.03% (47 women) vs 45% (18 women) in group B (F = 0.0004, $p < 0.05$) due to patients with lipid metabolism disorders (43.1% vs 22.5%; U = 636, p = 0.00016, OR = 2.609, 95% CI 1.055–6.457).

The majority of pregnant women fell ill in the third trimester of pregnancy – 65.51% (38–women), in the second trimester – 25.86% (15 women), in the first trimester only 8.62% (5 women). The difference in the incidence rate depending on the gestational age was significant for each trimester (F = 148.38358, $p < 0.00001$).

50 (86.2%) pregnant women were admitted to hospital on an urgent basis, 8 (13.8%) women were referred for hospitalization by their family doctor or by self-referral. The condition of 29 (50%) women at hospitalization was assessed as satisfactory, 27 (46.6%) – as moderate, and two (3.4%) were in severe condition.

Almost half of the pregnant women (43.1%, 25 women) complained of breath shortness of varying severity. According to pulse oximetry the saturation level was 95% or more in 51 (87.9%) women, and 90–94% in 7 (12.06%) women; the average SpO_2 indicator was 97.4% (Fig. 1). It should be noted that 6 (10.3%) patients required observation and treatment in the intensive care unit, including oxygen support due to the clinical picture of respiratory distress syndrome.

According to CT scan of the chest, bilateral polysegmental pneumonia with a typical pathognomic CT picture of "ground glass" for SARS-CoV-2 associated lung damage was detected in 30 (53.4%) women (Fig. 2).

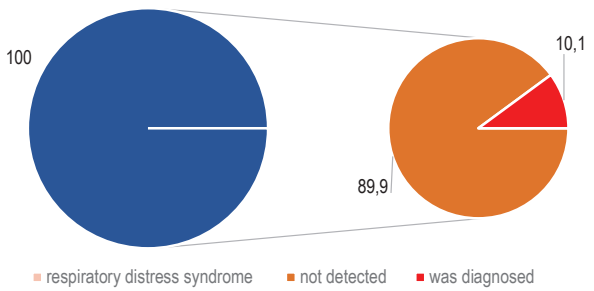

Figure 1. Frequency of respiratory distress syndrome in pregnant women with COVID-19 infection, %

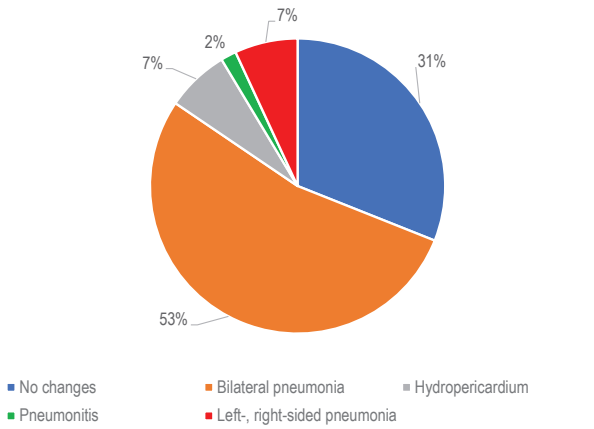

Figure 2. Results of chest CT scan in pregnant women with COVID-19, %

A picture of left- or right-sided pneumonia was detected in 4 (6.9%) women, in one (1.7%) patient was a picture of pneumonitis, in 4 (6.9%) – hydropericardium; only 31% women had no chest changes.

According to the CTG data, the following changes of the fetus condition during pregnancy (Table).

Thus, according to the nature of the basal rhythm and the CTG curve, there is a reliable difference between the groups (χ^2 = 14.9055, p = 0.00058): the undulating type of curve, i.e. with optimal indicators of the number of accelerations, heart rate (HR) responses to fetal movements, etc. (the most typical for the normal state of the intrauterine fetus) was most often in the control group (87.5% vs 50%). The saltatory curve with HR fluctuations ≥ 25 beats was in the main group (32.7% vs 10%), as well as the monotonous one (17.24% vs 2.5%). A statistically significant difference was found between the integral index of fetal HR variability for one-minute time intervals of 3.75 seconds (short-term variability (STV)) – the index was significantly higher in the control group (8.39 ± 2.03 ms vs 7.78 ± 2.56 ms; U = 687, p = 0.00022). The assessment of number of fetal movements based on CTG data showed that were significantly more women with reduced fetal activity in Group A (12.31% vs 2.86%; F = 0.0287, $p < 0.05$). The average basal HR did not differ significantly between the groups and was 146.02 ± 25.36 vs 154.6 ± 11.95 bpm (U = 926.5, $p > 0.05$). 46 and 38 women in groups A and B gave birth on time and 9 and 2 women in groups A and B gave birth before term (15.51% vs 5%); spontaneous termination of pregnancy at 12–21.6 weeks was noted in 2 cases only in group A (3.44%; relative risk (RR) = 4.14, OR = 4.957, 95% CI 1.044–25.526). One pregnant woman in the

Table. Comparative results of cardiotocographic examination of pregnant women

Indicators	Reference indicators	Main group with COVID-19, n = 58	Control group, n = 40	Statistical indicators
Type of CTG	Undulating, n (%)	29 (50%)	35 (87.5%)	$\chi^2 = 14.9055$, $p = 0.00058$
	Saltatory, n (%)	19 (32.7%)	4 (10%)	
	Monotonous, n (%)	10 (17.24%)	1 (2.5%)	
The basal heart rate beats per minute	Average indicator, M ± SD	146.02 ± 25.36	154.6 ± 11.95	U = 926.5, p > 0.05
	< 120, n (%)	5 (8.62%)	1 (2.5%)	$\chi^2 = 5.6086$, $p = 0.06055$, $p > 0.05$
	120–160, n (%)	35 (60.34%)	33 (82.50%)	
	> 160, n (%)	18 (31.03%)	6 (15.00%)	
Short-term variability, ms	M ± SD	7.78 ± 2.56	8.39 ± 2.03	U = 687, p = 0.00022

main group underwent a minor cesarean section due to premature placental abruption and bleeding. Caesarean section was performed in 20 and 5 pregnant women in the main and control groups (34.48% vs 12.5%), *per vias naturalis* – 47 and 35 women (81.03% vs 87.5%; F = 0.0181, p < 0.05, OR = 3.684, 95% CI 1.248–10.873). A total of 54 live births were performed in the main group; late abortions with fetal weight up to 500 g were performed in three women. There were no perinatal losses in the control group; it was 1 case of stillbirth in the main group.

Anthropometric characteristics of newborns showed a significant difference in weight (3067.93 ± 620.21 vs 3617.25 ± 354.58 g; t = 5.81, F = 27.76675, p <0.00001) and height (50.4 ± 2.91 and 54.25 ± 2.08 sm; t = 6.92, F = 40.36303, p < 0.00001) between the main and control groups.

Assessment on the Apgar scale in the first minute of life showed a statistically significant difference between the main and control groups (M ± SD: 6.48 ± 2.39 vs 8.05 ± 0.54 points; $\chi^2 = 21.933$, p < 0.001) (Fig. 3). Only 8 (20%) newborns in the control group were assessed at 7 points in the first minute, the remaining 80% received a score of 8 or more points, while 28 children in the main group were assessed at 7 points or less (51.85%, F = 0.00246, p < 0.05, OR = 4.308, 95% CI 1.681–11.037).

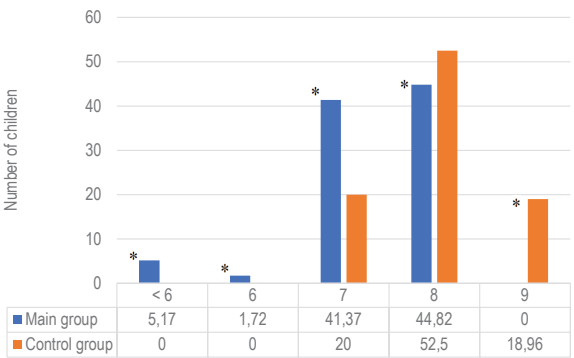

Figure 3. Apgar score in points in the main and control group, %
* p < 0.001.

Every tenth newborn (6 children, 10.34%) required intensive care, three (5.17%) required surfactant administration, one (1.72%) – mechanical ventilation followed by CPAP therapy. Regression analysis revealed that the indicator of early neonatal adaptation of the newborn on the Apgar scale in the first minute of life in women with a history of coronavirus infection is determined by the level of blood oxygen saturation of the pregnant woman (Fig. 4), and can be calculated using the formula:

Y = 0.89X – 79.19,

where Y is the Apgar scale indicator, X is the saturation indicator in the pregnant woman.

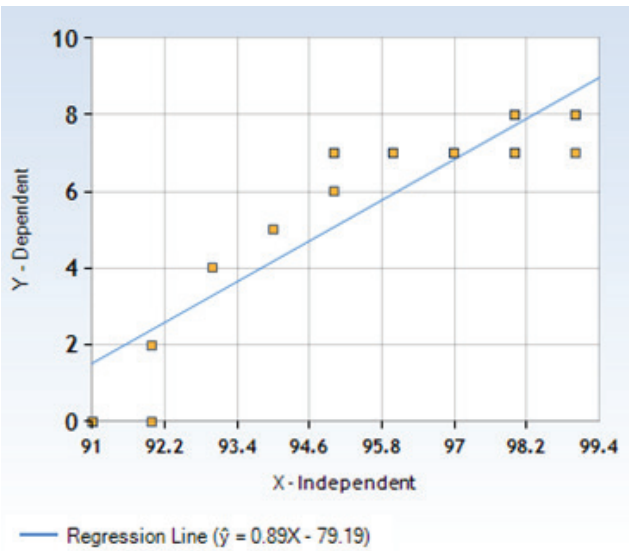

Figure 4. Association between the blood saturation in a pregnant woman and a newborn's Apgar score at the first minute

A study of the relationship between the saturation level in pregnant women with COVID-19, fetus CTG data and the Apgar score in the first minute of life using multiple linear regression modeling showed the possibility of predicting the condition of newborns using the following formula:

Y = 0.89 X1 + 0.028 X2 – 79.53,

where Y is the Apgar score, X1 is the saturation level in the pregnant woman, X2 is the STV score according to CTG data.

High light

Based on an assessment of the level of hypoxemia in a pregnant woman with COVID-19, CTG data of the fetus, it is possible to predict the condition of the newborn - namely to predict the course of the early neonatal adaptation period from the first minutes after birth.

Studies that allow predicting the condition of a newborn from a mother with a history of COVID-19 are routine clinical

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and instrumental examination methods that are safe, effective and accurate, without economic burden.

DISCUSSION

Special attention is paid to the maternal and child healthcare system, indicators of maternal, perinatal and infant morbidity and mortality in the context of any pandemic. Acute respiratory viral infection associated with the SARS-CoV-2 coronavirus is no exception [1, 2].

The results of numerous studies about the course of COVID-19 in pregnant women, pregnancy complications and perinatal outcomes, and the possibility of vertical transmission of the disease are contradictory. There is information about a higher post-COVID-19 risk of ante-, intra- and postnatal complications, a higher frequency of the need for hospitalization of pregnant women and subsequently their newborns in intensive care units, mechanical ventilation [8–10]. According to other authors, pregnant women do not belong to the high-risk group for SARS-CoV-2 infection and the disease can be asymptomatic [9, 24].

The variety of clinical manifestations of COVID-19 infection, development of multiple organ failure syndrome significantly increases the likelihood of involvement of the uteroplacental complex in the inflammatory process. Numerous studies of coronavirus infection in recent years are devoted to the issues of the course of pregnancy, vertical transmission of the disease, and direct infection of the placenta. However, there are not enough works devoted to changes in the functional state of the placenta and predicting perinatal outcomes. Therefore, the aim of our study was to investigate the relationship between the condition of the pregnant woman (saturation as hypoxemia level) directly during COVID-19 disease, CTG indicators for assessing the fetus status and assessment of newborns on the Apgar scale in the first minute of neonatal adaptation.

The main group (A) included 58 pregnant women with a verified diagnosis of COVID-19 during pregnancy, regardless of the gestational age, and the control group (B) included 40 healthy women with a physiological course of pregnancy. Women with severe forms of chronic hypertension, diabetes mellitus, etc., which could affect the course of both pregnancy and coronavirus infection, were excluded from the study. The distribution of women by age showed that in the main group there were more women aged 25–39.11 years (in groups A and B respectively 65.5% vs 82.5%; $F = 0.0421$, $p < 0.05$; and over 40 years old –3.6% vs 2.5%). That is, older age, as in the population, is a risk factor for COVID-19 (OR = 4.307, 95% CI 2.38–7.78), which coincides with the literature data.

The risk of severe COVID-19 increases with age and pregnant women are no exception: this risk increases by 1.5–2 times for them (OR = 1.82; 95% CI 1.27–2.63) [10].

Analysis of the anthropometric characteristics of patients with a history of coronavirus infection showed that only 41.4% (24 women) had normal body weight, the remaining 58.6% had a violation of lipid metabolism with an average BMI in groups A and B respectively 27.32 ± 4.48 and 22.8 ± 2.30 kg/m^2, ($F = 19.77899$, $p = 0.000023$; OR = 5.667, 95% CI 2.226–14.427). BMI in women in the main group was a reliable risk factor for COVID-19 more than 5 times compared to the control group. Obesity, according to some data, is a well-known risk factor for severe COVID-19 disease and can increase this risk threefold [25, 26]. Possible mechanisms explaining this fact are a systemic inflammatory process with a corresponding increase in the production of proinflammatory cytokines (interleukin (IL) type 6, tumor necrosis factor α (TNFα), etc.) and chemokines, which is inherent in impaired lipid metabolism. This can also be supplemented by oxidative stress, insulin resistance, endothelial dysfunction and other mechanisms. Pregnant women diagnosed with COVID-19 are more likely to have hypertensive complications (OR = 1.46; 95% CI 1.05–2.02), preeclampsia (OR = 1.76; 95% CI 1.27–2.43), infections requiring antibiotic therapy (OR = 3.38; 95% CI 1.63–7.01), and they also have a higher risk of admission to the intensive care unit (OR = 5.04; 95% CI 3.13–8.10): they are 6 times more likely to be referred for treatment to a higher level of medical care (OR = 6.07; 95% CI 1.23–30.01).

The authors of a large multinational study that included 706 pregnant women diagnosed with COVID-19 and 1,424 pregnant women without a COVID-19, concluded that the presence of any symptoms of COVID-19 is associated with increased morbidity and mortality [10]. Maternal and neonatal morbidity and mortality were highest in women with clinical features of systemic involvement (fever and dyspnea, especially their prolongation for 1–4 days). This observation should influence clinical care and directions of the COVID-19 management strategy in pregnant women [10].

According to our data, every 10th (10.3%) pregnant woman with coronavirus infection required treatment in the intensive care unit; almost half (46.6%) had a moderate condition upon admission. The SpO_2 level In 12.06% of pregnant women was 90–94% and they required respiratory support, which, according to the Society for Maternal-Fetal Medicine (2020), J. Eid et al. (2022), is critical for the pregnant woman and the fetus [17, 18].

The systemic inflammatory process was confirmed by the results of chest CT scan: 69% of pregnant women had bilateral polysegmental or unilateral lung damage, pneumonitis and hyperpericardium. The most common (53.4%) was the CT picture of "ground glass" typical for SARS-CoV-2 associated lung damage.

The high frequency of inflammatory lesions of the chest organs can be explained by the following:

- Firstly, the clinical picture of COVID-19 is very individual and depends on the direct effect of the virus on cells and the body's immune response. Cytokine storm is accompanied by the involvement of lung tissue in a systemic process with subsequent hypoxemia, hypercoagulation and hypoxic vasoconstriction in the main target organ.
- Secondly, hypoxemia of varying degrees, hypoperfusion / ischemia of organs is accompanied by a decrease in the adaptive and compensatory capabilities (increased heart rate and oxygen consumption, decreased lung capacity and an increased risk of thromboembolic complications) of the pregnant woman's body, including under conditions of labor stress, stress on the overall energy balance and the risk of intranatal complications.
- Thirdly, the relative position of the chest organs in pregnant women, the tropism of coronavirus to lung

tissue, an increase in the volume of circulating blood during pregnancy with a subsequent increase in the respiratory tract secretion can favor the development of infection. These changes affect maternal morbidity, placental function with subsequent risk to the fetus and newborn [3, 27].

In our opinion, the identified frequency of hypoxemia in pregnant women with COVID-19 not only indicates a high risk of a severe form of the disease and may affect perinatal outcomes; it is probably necessary to focus on the timeliness of seeking medical care at the outpatient stage and provide more thorough antenatal care.

The results of the CTG assessment of the fetus status in the women we examined showed the presence of reliable differences in the nature of the basal rhythm of the HR curve ($\chi^2 = 14.9055$; $p = 0.00058$) and STV of the HR between groups A and B (8.39 ± 2.03 vs 7.78 ± 2.56 ms; U = 687, $p = 0.00022$). Probably, these data can be regarded as a direct reflection of hypoxemia in pregnant women with COVID-19, which was subsequently confirmed by perinatal outcomes.

Every fifth (20.7%) woman in the main group either had a miscarriage in the 1st or 2nd trimester or gave birth prematurely. At the same time, the impact of COVID-19 infection on the frequency of preterm births seems obvious (20.68% vs. 5%, F = 0.039, $p < 0.05$, RR = 4.14, OR = 4.96, 95% CI 1.044–23.526). The consequences of hypoxemia in this group of pregnant women are evidenced by the frequency of fetal distress during childbirth (7.4% vs. 0%, F = 0.13367, $p > 0.05$) and anthropometric indicators of newborns, which were significantly ($p < 0.00001$) lower compared to the control group. The indicators of the early neonatal adaptation period in the main group reflected the relationship between COVID-19 infection and the newborns status: the frequency of assessment on the Apgar scale of 7 points or less in the main and control groups respectively was 51.85% vs 20% (F = 0.00246, $p < 0.05$, OR = 4.308 95% CI 1.681–11.037). There was no assessment less than 7 points in the control group. Newborns with a violation of the adaptation period (10.34%) were observed in the intensive care unit, 5.17% of patients required respiratory support.

The obtained results are consistent with the data of S.S. Foo et al. (2021), O.M. Man et al. (2024), who note a high risk of respiratory disorders even in full-term newborns from mothers with COVID-19, and explain this by an imbalance in the cytokine profile of the pregnant woman (interferon-lambda (IFN-λ), IL-1β / IL-18 / caspase-1 (CASP1), etc.) [28, 29]. Negative perinatal outcomes were also reported by J. Villar et al. (2021), who showed that perinatal morbidity and mortality are more than 2 times higher in pregnant women with COVID-19 than in healthy women [10]. However, there is also information about the absence of differences in the newborns status between in the compared groups [30].

Our study of the relationship between the saturation level of a pregnant woman with COVID-19 at hospitalization, and the CTG indicators of the fetus, revealed the possibility of predicting the newborn status at birth. Thus, the assessment on the Apgar scale in the first minute of life is determined by the level of oxygen saturation of the blood of a pregnant woman with a history of COVID-19 and can be mathematically calculated using the formula Y = 0.89X – 79.19 or, taking into account additional CTG data during pregnancy, using the formula Y = 0.89 X1 + 0.028 X2 – 79.53. We did not find similar data in the published literature.

Given the conflicting data on the relationship between the history of coronavirus infection during pregnancy and the newborn status, as well as the data of our study, the impact of COVID-19 infection on the condition of children cannot be denied. This may be due to both the mother status and possible intrauterine infection, which requires further research. We believe that regardless of the condition at birth, such children need long-term clinical observation in order to prevent possible risks.

A probable explanation for the difference in anthropometric indicators and the newborns status between the study groups may be the following. Firstly, the main group included moderate cases of COVID-19 with systemic inflammatory response syndrome and hypoxemic state. Secondly, most women had a comorbid status (impaired lipid metabolism, etc.), which can be an independent cause of placental dysfunction. Thirdly, the risks of developing multiple organ pathological changes typical of coronavirus can be critical due to a violation of the barrier function of the placenta, which is also involved in the systemic inflammatory process. These reasons together could have caused a difference in anthropometric parameters and the newborns status, but the sample size is insufficient to form convincing evidence, further research is required. Nevertheless, management strategies for pregnant women with symptomatic and asymptomatic COVID-19 cannot be the same: the group of newborns from mothers with a symptomatic course is at risk and requires special attention in the neonatal period and in the long term.

Limitations

The main limitation of this study is the small sample size. Further studies are needed to obtain a representative data set that will help draw any conclusions about the impact of SARS-CoV-2 infection on pregnant women and newborns, and to identify new possibilities for predicting perinatal outcomes for both mother and newborn. Further studies should include larger populations and, probably, it is necessary to study the possibilities of predicting perinatal outcomes depending on the gestational age at which COVID-19 infection occurred.

CONCLUSIONS

COVID-19 infection continues to be a pressing problem in modern medical science due to its high contagiousness, ongoing mutation of the virus, and long-term consequences of diseases, including among the population of pregnant women.

The course of the disease in pregnant women is characterized by various clinical features due to physiological changes; inflammatory lesions of the chest organs occur in more than half of women in this population. Clinicians should pay special attention to assessing the blood oxygen saturation index in a pregnant woman with COVID-19 infection and antenatal CTG assessment of the fetus: there is a direct association between these indicators and early neonatal adaptation of the newborn.

Pregnant women with a history of COVID-19 require special attention from medical personnel, careful individual antenatal, intra- and postnatal care to obtain a positive pregnancy experience. Newborns from women who have had COVID-19 infection during pregnancy are recommended to be classified as a risk group with a disrupted adaptation period and possible long-term consequences.

Conflict of Interest
The authors declare no conflict of interest.

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КРИТЕРІЇ ПРОГНОЗУВАННЯ РАННЬОЇ НЕОНАТАЛЬНОЇ АДАПТАЦІЇ НОВОНАРОДЖЕНИХ У ЖІНОК, ЯКІ ПЕРЕХВОРІЛИ ПІД ЧАС ВАГІТНОСТІ НА COVID-19

Г.С. Манасова, д. мед. н., професорка кафедри акушерства та гінекології, ОНМЕдУ, м. Одеса

Я.О. Стасій, аспірантка кафедри акушерства та гінекології, ОНМедУ, лікар акушер-гінеколог КНП «Пологовий будинок № 5» Одеської міської ради, м. Одеса

М.В. Шаповал, д. мед. н., професор кафедри акушерства та гінекології, ОНМедУ, м. Одеса

Мета дослідження: вивчити можливість прогнозування ранньої неонатальної адаптації новонароджених на підставі клініко-інструментальних даних оцінки стану вагітної з інфекцією COVID-19 та внутрішньоутробного плода.

Матеріали та методи. До дослідження було залучено 58 вагітних із діагнозом COVID-19 (група А) та 40 жінок із фізіологічним перебігом вагітності (група В), а також їхні новонароджені діти. Крім аналізу результатів стандартних обстежень, перинатальних наслідків для матері та плода / новонародженого, вивчався взаємозв'язок між рівнем сатурації (SpO_2) у вагітної, показником short-term варіабельності (STV) серцевого ритму плода за даними кардіотокографії та оцінкою новонародженого за шкалою Апгар.

Результати. Рівень SpO_2 становив 95% і більше у 87,9% інфікованих вагітних, а у 12,06% – 90–94% (критичний для вагітних). Інтенсивної терапії та респіраторної підтримки потребували 10,3% вагітних, у 69% жінок виявлено запальні зміни органів грудної клітки (пневмонія та ін.) Кардіотокографія показала значну різницю за типом базального серцевого ритму між групами ($\chi^2 = 14{,}9055$, $p = 0{,}00058$) та STV ($7{,}78 \pm 2{,}56$ проти $8{,}39 \pm 2{,}03$ мс) відповідно між групами А та В ($U = 687$, $p = 0{,}00022$).

Показник шкали Апгар у групах А та В був $6{,}48 \pm 2{,}39$ та $8{,}05 \pm 0{,}54$ бала відповідно ($\chi^2 = 21{,}933$, $df = 4$). У групі В 20% новонароджених на першій хвилині отримали оцінку 7 балів, 80% – 8 балів і більше; у групі А 7 балів і менше отримали 51,85% новонароджених ($F = 0{,}00246$, $p < 0{,}05$, ВШ 4,308, 95% довірчий інтервал 1,681–11,037). 10,34% новонароджених потребували інтенсивної терапії, 5,17% – введення сурфактанта, 1,72% – штучної вентиляції легень. Регресійний аналіз засвідчив, що показник шкали Апгар на першій хвилині життя в новонароджених у групі А залежить від рівня SpO_2 вагітної ($Y = 0{,}89X1 - 79{,}19$), а також від STV ($Y = 0{,}89X1 + 0{,}028X2 - 79{,}53$), де Y – оцінка за шкалою Апгар, X1 – показник SpO_2 у вагітної, X2 – показник STV.

Висновки. У вагітних із COVID-19 особливої уваги потребує оцінка ступеня гіпоксемії самої жінки та кардіотокографічна оцінка стану плода: між цими показниками та оцінкою новонародженого за шкалою Апгар є прямий зв'язок, який дає змогу прогнозувати перебіг періоду ранньої неонатальної адаптації. Цих новонароджених рекомендується відносити до групи ризику з порушенням періоду адаптації та можливими довгостроковими наслідками.

Ключові слова: вагітність і COVID-19, гіпоксемія, сатурація, кардіотокографія, прогнозування стану новонародженого, шкала Апгар.

CRITERIA FOR PREDICTING EARLY NEONATAL ADAPTATION OF NEWBORNS IN WOMEN WHO HAD COVID-19 INFECTION DURING PREGNANCY

G.S. Manasova, MD, professor, Department of Obstetrics and Gynecology, Odesa National Medical University, Odesa

Y.O. Stasiy, postgraduate student, Department of Obstetrics and Gynecology, Odesa National Medical University, obstetrician-gynecologist, CNE "Maternity hospital No. 5" of the Odessa City Council, Odesa

M.V. Shapoval, MD, professor, Department of Obstetrics and Gynecology, Odesa National Medical University, Odesa

Objective of the study: to investigate the possibility of predicting the early neonatal adaptation of newborns based on clinical and instrumental data that assesses the status of pregnant woman with COVID-19 infection and the fetus.

Materials and methods. The participants of the study were 58 pregnant women with a diagnosis of COVID-19 (group A) and 40 women with a physiological course of pregnancy (group B), as well as their newborns. In addition to the analysis of standard examinations results, perinatal consequences for the mother and the fetus/newborn, the association between the saturation level (SpO_2) in the pregnant woman, the short-term heart rate variability (STV) according to cardiotocography data of the fetus and the assessment of the newborn according to the Apgar scale was studied.

Results. The SpO_2 level was 95% or more in 87.9% of infected pregnant women, in 12.06% it was 90–94% (critical for pregnant women). 10.3% of pregnant women needed intensive therapy and respiratory support, 69% of women had inflammatory changes in the chest organs (pneumonia, etc.). Cardiotocography showed a significant difference in the type of basal heart rate between the groups ($\chi^2 = 14.9055$, $p = 0{,}00058$) and STV (7.78 ± 2.56 vs 8.39 ± 2.03 ms) in groups A and B, respectively ($U = 687$, $p = 0.00022$).

The Apgar scale index in groups A and B was 6.48 ± 2.39 and 8.05 ± 0.54 points, respectively ($\chi^2 = 21.933$, $df = 4$). 20% of newborns in group B had 7 points in the first minute, 80% had 8 points or more. 51.85% of newborns in group A had scored 7 points or less ($F = 0.00246$, $p < 0.05$, odds ratio 4.308, 95% CI 1.681 – 11.037). 10.34% of newborns required intensive care, 5.17% – administration of surfactant, 1.72% – artificial lung ventilation. Regression analysis showed that the Apgar scale indicator at the first minute of life in newborns in group A depends on the SpO_2 level of the pregnant woman ($Y = 0.89X1 - 79.19$), as well as on the STV ($Y = 0.89X1 + 0.028X2 - 79.53$), where Y is the score on the Apgar scale, X1 is the SpO_2 in a pregnant woman, X2 is the STV.

Conclusions. Assessment of the hypoxemia degree in pregnant women with COVID-19 infection and the cardiotocographic assessment of the fetus state require special attention: there is a direct association between these indicators and the assessment of the newborn according to the Apgar scale, which allows predicting the course of the period of early neonatal adaptation. It is recommended that these newborns be classified as a risk group with a violation of the adaptation period and possible long-term consequences.

Keywords: pregnancy and COVID-19, hypoxemia, saturation, cardiotocography, prediction of the newborn status, Apgar scale.