

CLINICAL AND EPIDEMIOLOGICAL FEATURES OF COVID-19 COURSE IN PREGNANT WOMEN

Manasova G., Golubenko M., Didenkul N., Radchenko Ya., Gladchuk I.

Odessa National Medical University, Ukraine

According to literature data, pregnant women are not included in the group of high risk of maternal morbidity and mortality associated with acute respiratory viral infection caused by SARS-CoV-2 coronavirus. They are included in the list of clinically vulnerable people with moderate risk for the purpose of prevention. However, with less vulnerability of pregnant women with COVID-19 compared to influenza caused by H1N1 ("swine flu" - pandemic 2010-2012), pregnant women, in contrast to non-pregnant women, have a higher risk of severe COVID-19 and negative perinatal outcomes, including due to mutation and the emergence of new strains of coronavirus [14].

Pregnant women with COVID-19 often need treatment in an intensive care unit, artificial ventilation of the lungs and other medical and diagnostic measures; the presence of concomitant diseases (obesity, gestational diabetes, etc.) causes the same high degree of severe disease as in non-pregnant women with these conditions. The chance of SARS-CoV-2 vertical transmission and the morbidity of the newborn is low [4, 13, 22, 25]. About 30% of pregnant women with COVID-19 require hospitalization [7].

There is an evidence that women with a severe form of COVID-19 before reaching the 37th week or in the third trimester of pregnancy are more likely to experience premature birth and fetal distress; the probability of neonatal disease is low [6, 12]. According to the authors, the low expression of angiotensin converting enzyme-2 in the mother-placenta-fetus system may be a likely reason of vertical transmission low risk.

According to the US Centers for Disease Control and Prevention (CDC), from January 22, 2020 to February 8, 2021, the number of pregnant women with SARS-CoV-2-aARD constituted 65.515 cases; 11.071 (16.9%) persons were hospitalized in in-patient departments; 76 pregnant women died. Treatment in intensive care units was carried out in 340 pregnant women (0.51% of the total number of sick pregnant women), cases of invasive ventilation - 84 (0.12%), cases of EMO - 19 (0.02%). Pregnant women of Hispanic origin, as well as black women, are more susceptible to infection with SARS-CoV-2 [5].

Despite numerous studies on COVID-19 in pregnant women, there is still not enough data to form an evidence base and draw objective conclusions regarding the course and severity of the disease, determine specific perinatal complications of COVID-19 in pregnant, assess the risks and develop tactics for managing pregnancy and childbirth. as well as prevention of vertical transmission of infection or its transmission during breastfeeding.

The aim of the work: to generalize the clinical and epidemiological features of COVID-19 course and the outcome of labor in pregnant women in the Odessa region.

Materials and methods. We analyzed 218 histories of pregnancy and childbirth of women hospitalized in "Maternity Hospital No. 2" of the Odessa City Council with a diagnosis of "Acute respiratory viral infection caused by SARS-CoV-2" from 01.03.2020 to 31.01.2021. The maternity hospital mentioned renders the 2nd level of obstetric and gynecological care, and one of its departments became a hospital base for providing medical care to pregnant women from the city of Odessa and the Odessa region sick with COVID-19. The average annual number of births is 1800-2000. Population size of the Odessa Region

amounted to 2.396.442 people, of which the residents of Odessa - 1.017.699 people (01.01.2020).

Several terms and combinations were used during the study, including COVID-19, SARS-CoV-2, PCR diagnostics, pregnancy, maternal morbidity and mortality, acute respiratory distress syndrome (ARDS), neonatal condition, fetal distress, neonatal mortality.

The selection criteria were cases of hospitalization of pregnant women with acute respiratory viral infection - SARS-CoV-2-aARD, real-time polymerase chain reaction (PCR) data with confirmation of the diagnosis of "COVID-19". Cases with suspected COVID-19 that were not confirmed by a laboratory test were not included in the study. Data on clinical manifestations, maternal and perinatal outcomes were analyzed. In addition to standard general clinical studies (general blood and urine tests, etc.), the level of C-reactive protein in the blood (quantitative method), the level of D-dimers, biochemical blood tests (bilirubin and its fractions, creatinine, urea and etc.) were determined in all pregnant women. In accordance with the patient's clinical route all pregnant women with prolonged hyperthermia, with a moderate course of COVID-19 underwent computed tomography of the chest organs. All studies were carried out after obtaining the informed consent of the patients and signed documents.

Methods of descriptive statistics, relative extensive percentage, calculation of the odds ratio, etc. were used to analyze the data obtained.

Results and discussion. For the period under analysis (01.03.2020 - 31.01.2021, 10 months), the total number of births was 8521, in "Maternity Hospital No. 2" - 1320 (15.5%). The number of hospitalized pregnant women with acute respiratory infections caused by SARS-CoV-2 constituted 16.5% (n=218) of the total number of births in the "Maternity Hospital No. 2" or 2.6% of all those who gave birth in Odessa.

It should be noted that the incidence of COVID-19 in pregnant women from August 2020 to January 2021 increased in the same way as an increase in the incidence was noted in the city and in the world [24], (Fig. 1).

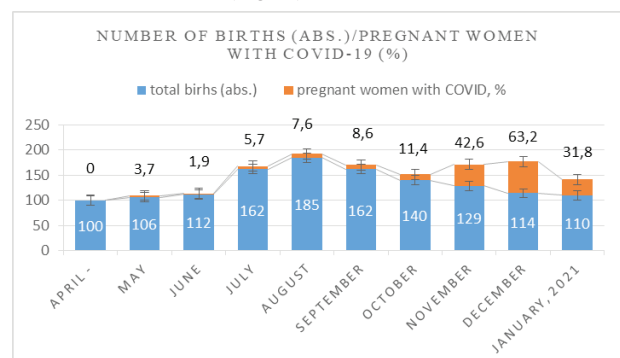


Fig. 1. The incidence of acute respiratory disease in pregnant women caused by the SARS-CoV-2 coronavirus infection in the Odessa region

Since August, the morbidity rate has increased and the proportion of pregnant women with COVID-19 has doubled in August and amounted to 7.6%, in September - 8.6%. In October 2020 it thrice and constituted 11.4%; in November-December 2020

it was 42.6% - 63.1% of all pregnant women who gave birth in this institution were admitted with this diagnosis. In January 2021, the number of infected persons decreased to 31.8% from the number of births.

The average age of women was 29.08 ± 6.5 years old, (Me \pm σ , min=16, max=49); the majority of pregnant women - 61.9% (n=135) aged 26 - 39 years old, 32.6% (n=71) aged 19-25 years old, 3 women were from 16 to 18 years old (1.38%) and 9 women were over 40 years old (4.1%), (Fig. 2).

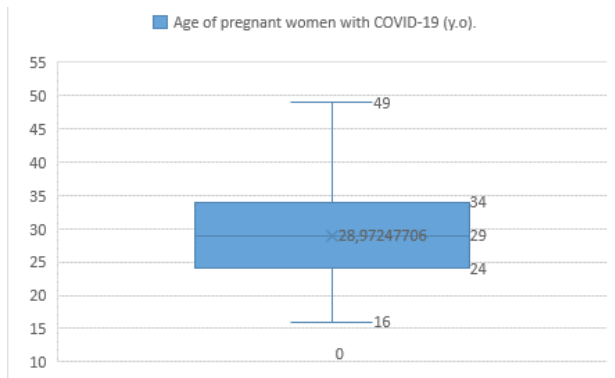


Fig. 2. Age (y.o.) of pregnant women with COVID-19 who were admitted to the hospital

The proportion of city dwellers (n=142) among pregnant women with SARS-CoV-2-associated acute respiratory infections (SARS-CoV-2 aARD) was almost twice higher than that among villagers (65.2% vs 34.8%), but still not less than one third of the patients (n=76) were residents of rural areas.

Most of the women fell ill in the 3rd trimester of pregnancy - 67.4% (n=147), in the 2nd trimester there were 25.7% of sick persons (n=56) and in the 1st trimester there were 6.9% (n=15).

When assessing the body mass index (BMI), it was found that 40.8% (n=89) of pregnant women had pre-obesity with a BMI of 24 kg/m², a normal weight had 41.2% (n=90; BMI=25-30 kg/m²), the diagnosis "obesity" had 12.8% (n=28; BMI=30-35 kg/m²), "severe obesity" had 5.05% (n=11; BMI=35-40 kg/m²) (OR=2.25; 95% CI 1.98-3.96; P < 0,05), (Fig. 3).

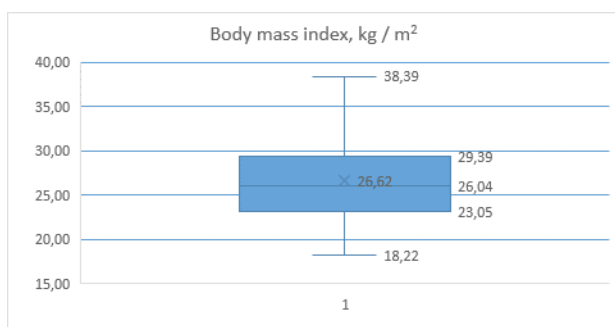


Fig. 3. Body mass index (kg/m²) of pregnant women with COVID-19 who were admitted to the hospital

At birth parity, 50% of patients were primiparous and 50% were multiparous. 36.7% (n=80) of women had various extragenital pathologies. Chronic kidney disease (pyelonephritis, urolithiasis) was the most frequent, it was met in 13.3% (n=29) of the pregnant women, chronic venous insufficiency had 3.2% (n=7), disease of cardio-vascular system and thyroid gland had by 4.1% (n=9), GIT pathology was diagnosed in 3.7% (n=8), 3 cases (1.4%) each accounted for diabetes mellitus, hepatitis C and pulmonary tuberculosis.

The course of pregnancy in the participants under study was accompanied by a number of complications. Anemia was diagnosed in 28.9% (n=63), the threat of miscarriage at various stages of pregnancy was in 11.9% (n=26), early gestosis were found in 5.05% (n=11), gestational pyelonephritis had 3.2% (n=7). 19 women (8.7%) indicated spotting at various stages of pregnancy, the cause of which was probably pathological low placentation (according to ultrasound scanning data). In 3 patients (1.4%) there was placental abruption, in 15 - fetal distress (6.9%). In addition, 63 (28.9%) women indicated an acute respiratory viral infection that had been transferred during this pregnancy, but was not associated with SARS-CoV-2.

With recovery, 201 women (92.2%) were discharged, 17 patients (7.8%) due to the need of treatment in an intensive care unit were transferred to a multidisciplinary hospital of the 3rd level of medical care.

Of the 218 women with SARS-CoV-2 aORZ who were admitted to the maternity hospital, 111 (50.9%) ended their pregnancy in this institution. 96 women (86.5% of 111) gave birth on time, 11 women (9.9%) gave birth before term, 3 women (2.7%) had a spontaneous late abortion at 13 - 17 weeks, another 1 (0.9%) had small cesarean section due to total placental abruption. 62 women (55.8%) gave birth through the vaginal birth canal, 33 women (29.7%) gave birth by caesarean section (OR= 1.61 95% CI 0.85-3.06; P > 0,05 - in comparison with the frequency of caesarean section in Ukraine in 2019); during labor 7 women (6.3%) underwent vacuum extraction of the fetus, in 14 (12.6%) labor was accompanied by induction of labor with oxytocin (OR=2.67 95% CI 0.81-8.81; P > 0,05).

The average body weight of newborns was 3100 ± 577 g (min=810 g, max=4400 g); their average height was 50.4 ± 2.91 cm. The average Apgar score was 6 - 8 points, min - 2 - 4 points. 9 (8.1%) of 107 newborns needed surfactant administration, 1 newborn with extremely low body weight needed mechanical ventilation and was subsequently transferred to the second stage of nursing. In one case, there was antenatal fetal death (0.9% of all women with COVID-19 who completed pregnancy).

The state of the overwhelming majority of women (50.6% or 110 people) at the admission to the in-patient department was satisfactory, in 46.3% (n=101) it was of moderate severity and in 3.2% (n=7) it was regarded as "heavy" (Fig. 4)

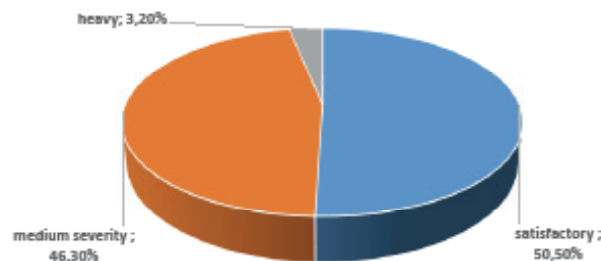


Fig. 4. Condition of COVID-19 pregnant women upon admission to the in-patient department

According to pulseoximetry data, the average index of peripheral blood oxygen saturation (SpO₂) was 97.4%, the min index - 91% was determined in 7 women (3.2%). In general, according to the saturation level in 22 women (10.09%), the disease was characterized by a moderate course with mild respiratory failure (RF) (with a SpO₂=90-94%), the rest 86.7% (n=189) had no RF (Fig. 5).

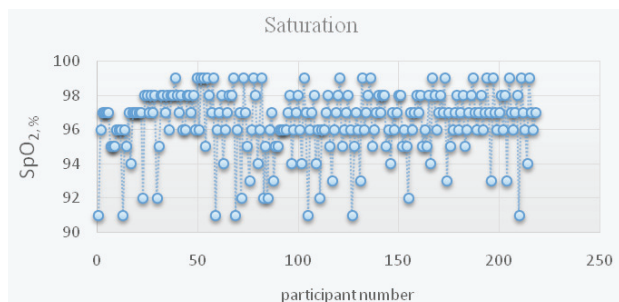


Fig. 5. Indicator of blood oxygen saturation (saturation,%) in pregnant women with COVID-19 upon admission to the hospital

When analyzing the body temperature reaction, we established that 63 women (28.8%) of 218 pregnant admitted with SARS-CoV-2 aARD, had temperature values in the range of 36.4 - 37.0 °C, in 62 women (28.4%) it was 37.1 - 38.0 °C, 91 women (41.7%) had severe hyperthermia from 38.1 to 38.9 °C, in 2 patients (0.9%) the temperature rose to 39.4 °C.

In accordance with the patient's clinical route all pregnant women with prolonged hyperthermia, with a moderate course of COVID-19 underwent computed tomography of the chest organs, which resulted in the following data (Fig. 6.)

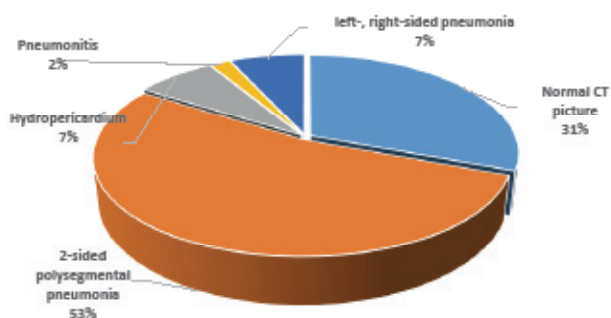


Fig. 6. Results of computed tomography of the chest organs of pregnant women with COVID-19 upon admission to the hospital

1/3 of pregnant women (n=67; 30.7%) had no chest pathology; more than half of the women (n=116; 53.2%) had a typical for SARS-CoV-2 associated bilateral polysegmental pneumonia with varying degrees of lung tissue damage (pattern of "frosted glass"). In addition, 15 women (6.9%) were diagnosed with left or right-sided pneumonia, 16 (7.3%) had a pattern of hydropericardium, and 4 patients (1.9%) had a pattern of pneumonitis. Every tenth patient had mild respiratory failure, the rest of 89.9% of women had no signs of respiratory distress syndrome (RDS).

According to laboratory diagnostics, an increase in the level of C-reactive protein in the blood by 2-4 times was revealed in 125 women (57.3%): the average value was 6.7±4.8 mg/L with a minimum content of 6.0 mg/L, and maximum of 24.5 mg/L. This was determined in every fifth patient (43 women or 19.7%).

Indicators of the procoagulation and anticoagulation potential of blood samples taken for test upon women's admission to the hospital before the start of therapy showed, in general, the absence of critical changes in the hemostasis system (fibrinogen - 5.6±0.9 g/l; INR - 1.04±0.06, PTI - 89.9±12.4%). Nevertheless, it should be noted a significant increase in the level of D-dimers in the blood of 158 (72.4%) pregnant women with COVID-19: 1096±587 ng/ml (max - 5030 ng/ml, min - 335 ng/ml).

When study the level of hepatic enzymes (bilirubin and its fractions, ALT and AST), it was found that in 206 (94.4%) women the total bilirubin content was in the limits of norm (12.7±11.4 µmol/l), an increase was found only in 12 pregnant women (5.5%) with a maximum content of 35.9 µmol/l. The average concentrations of ALT (28.06±15.08 U/L) and AST (35.4±14.9 U/L) in most women (n=163; 74.8%) did not exceed normal values, the rest 25.2% (n =55) had an increased by 2-3 times (max - 193 U/l) level of these enzymes. There were no pathological changes in creatinine levels indicating impaired renal function or possible myositis (73.9±6.1 µmol/L).

The data obtained on the analysis of COVID-19 incidents in pregnant women in the Odessa region allow us to identify the following clinical and epidemiological features. In April 2020, no pregnant women with COVID-19 were hospitalized. From May to July 2020, the number of cases did not exceed 3.7% among all those who gave birth in this institution. Since August the morbidity rate has increased and the number of pregnant women with COVID-19 in December 2020 amounted to 63.1% of all births. In January 2021, the number of cases decreased by half. In general, the situation with the incidence of coronavirus infection caused by SARS-CoV-2 in the Odessa region reflects the global trend in the prevalence of COVID-19.

There is a 2-fold prevalence of pregnant urban dwellers compared to the rural ones (65.2% vs 34.8%).

According to the literature, COVID-19 pandemic is, on the one hand, an additional argument in favor of de-urbanization and limitation of large and largest urban agglomerations growth and the development of rural areas, on the other hand, the risk of a more severe course of SARS-CoV-2 aARD in the countryside is higher. According to the US Centers for Disease Control and Prevention (CDC), the incidence of COVID-19 per 100.000 persons in rural areas exceeds the number of cases in urban and suburban areas, and this figure continues to increase [8]. On average, more elderly and retired people live in these areas than in cities and suburbs, they are at a significantly higher risk of contracting the virus, and they have less access to highly qualified medical care.

The health departments of the Odessa Regional State Administration and the Odessa City Council organize medical care for pregnant women who fell ill with SARS-CoV-2 aARD, namely, hospitalization of all without exception to one of the city maternity hospitals was aimed at the timely prevention of severe forms of the disease and ensured the availability of specialized medical care.

The greater number of COVID-19 cases in the 3rd trimester of pregnancy (6.9%- 1st; 25.7%-2nd; 67.4%-3rd trimester) can apparently be explained by physiological changes in the body of pregnant women, namely a significant increase in the load on the respiratory organs due to body weight increase, change of the chest shape, high standing of the diaphragm against the background of increased metabolic processes and increased demand for oxygen. Restriction of the respiratory excursion of the diaphragm and a decrease in the amplitude of oscillations of the chest are accompanied by a decrease in the vital capacity of the lungs [3]. In addition, by the end of pregnancy, there is a decrease of the abdominal wall in the muscle tone, relaxation of the ligamentous apparatus of the ribs. When studying the function of external respiration (FER) in pregnant women, a progressive decrease in the reserve expiratory volume and, to a lesser extent, a decrease in the residual lung volume was found. As a result of the changes described, functional residual lung capacity by the end of pregnancy decreases by approximately 20% [2].

All these changes are most characteristic for the 3rd trimester of pregnancy, which causes a high frequency of lesions of the pulmonary-respiratory system in acute respiratory infections.

Obesity is a well-known risk factor for severe COVID-19 disease: according to some reports, overweight can triple the risk of hospitalization due to COVID-19 infection [16, 17]. Possible reasons that increase the risk of severe COVID-19 course in obese people include the general increase in subcutaneous adipose tissue, the volume of ectopic fat in the visceral, perivascular, epicardial and other areas. Systemic endothelial dysfunction and activation of pro-inflammatory, prothrombotic and vasoconstrictive potential of the endothelium, in particular, the peptide hormone ACE inhibitors, insulin resistance, hypertension, decrease in immunity and other concomitant obesity components exacerbate the risk of COVID-19 severe complications [19].

Another negative side of overweight is the behavioral characteristics of the population in connection with quarantine measures, which are associated with limited physical activity, frequent snacks, overeating, lack of motivation and other factors characteristic of “lockdown” [15]. Our data indicate the presence of overweight in 2/3 or 58.8% of pregnant women, which is a definite confirmation of the pathogenetic significance of obesity in the severity of COVID-19.

As to the frequency of extragenital diseases (36.7%), the group under study did not differ in any way from the general population, however, these women, in addition to SARS-CoV-2 aARD, against the background of the “objectively existing discrepancy between the interests of the mother and the fetus” during pregnancy, had higher risk of obstetric and perinatal complications [1].

The “favorable” outcome of the disease is evidenced by the number of patients discharged with recovery - 92.2%, which is consistent with the literature data [4, 7, 13, 14]. The remaining 7.8% of pregnant women who were transferred to the intensive care unit of a multidisciplinary medical establishment (level 3) were also discharged with recovery, there were no maternal deaths.

As for the outcome of pregnancy, we obtained data about an increase in the frequency of preterm births and pregnancy losses in the early and late stages of women with COVID-19. There were only 86.5% full-termed pregnancies. We are talking about a possible increase in the premature births in this cohort of pregnant women in comparison with the city average index, which is 3.6% - 4.2%; the risk of pregnancy loss in the group of pregnant women who have had COVID-19 is 4 times higher than in those who did not get sick (OR=4.23 95%CI 1.35 - 13.25; P<0.05). As for the frequency of intrauterine growth retardation syndrome and cesarean sections, we have not received convincing data in favor of these indicators increase.

It is known that the level of C-reactive protein (CRP), which is one of the early markers of the inflammatory process, usually does not increase significantly during viral respiratory infection. According to the literature, severely ill patients with COVID-19 showed a significant increase in CRP values. Presumptive reasons for stimulating CRP production are overproduction and activation of proinflammatory cytokines, which can cause damage to the vascular endothelium, lung tissue, and other components of the systemic inflammatory response syndrome (SIRS) [23, 26]. There is evidence that CRP levels are directly correlated with the severity, prevalence of inflammatory infiltration and prognosis in pneumonia, as well as the progression of COVID-19 [27]. The CRP level indicators in COVID-19 pregnant women under examination are consistent with the literature data and indicate the presence of moderate SIRS.

There is a sufficient literature database, according to which COVID-19 develops a hypercoagulable state associated with endothelial dysfunction and corresponding changes in laboratory parameters, of which the level of D-dimer can be used as a marker of a negative prognosis of the disease [21]. It is assumed that SARS-CoV-2 virus has the ability to invade directly into endothelial cells, which is accompanied by endothelial damage, vasculitis and endothelial exocytosis and/or endotheliitis, which play a major role in the pathogenesis of ARDS and multiple organ failure [10,11,20].

According to our data, the level of D-dimer was increased in 75.8% of pregnant women with COVID-19. Considering that physiological pregnancy is a “procoagulant” state with a significant scatter of D-dimer values, it is likely that high concentrations of this fibrin degradation product in the presence of SARS-CoV-2 associated ARD during gestation should be used, along with clinical and other laboratory data, as only an auxiliary non-specific marker of the severity of the disease.

According to most works, biochemical studies of liver and kidney function in patients with COVID-19 do not carry any specific information, but, nevertheless, may reflect the presence of multiple organ dysfunction or indicate decompensation in patients with chronic diseases. The changes revealed in the biochemical analysis of blood can affect the tactics of choosing drug therapy and have a certain prognostic value. In critically ill patients, the level of blood aminotransferases is elevated, although clinically significant liver damage is rare [18, 28]. According to our data, a transient increase in the level of liver enzymes (ALT and AST) without clinical manifestations was detected in a quarter of pregnant women, bilirubin was increased only in 5.5% of the patients. Probably, there are no sufficient grounds to talk about liver damage of toxic or other genesis. There were no pathological changes in creatinine levels indicative of impaired renal function or severe myositis.

Conclusions: In the Odessa region, during the pandemic, there is an increase in the incidence of COVID-19 among pregnant women, as well as in the population as a whole. The highest morbidity rate is observed in the age group 26-39 y.o. Fat metabolism disorder is a significant risk factor for COVID-19 morbidity, (OR=2.25 95% CI 1.98-3.96; P < 0.05). Pregnant women with COVID-9 significantly more often have early and late spontaneous pregnancy losses (OR=4.23 95% CI 1.35 - 13.25; P < 0.05) and this is accompanied by an increase of the cost of nursing of low birth weight newborns (mechanical ventilation, surfactant, etc.).

The results obtained reflect the situation in a specific administrative region during the pandemic period (1 linear maternity hospital), but the number of patients (218) is insufficient to form the evidence base. To obtain reliable data on the impact of COVID-19 on pregnant women and intrauterine patients, including under conditions of constant mutation of the etiological factor, it is necessary to conduct further multicenter studies and enter the data obtained into specially designed registries with subsequent analysis of the results.

REFERENCES

1. Medved VI. Extragenital pathology of pregnant women: maternal and perinatal problems. // *ZhinochiyLikar*. 2010; 4: 5-10. <https://z-l.com.ua/upload/journals/30/4-2010site1.pdf>.
2. Mozheiko LF, Tsareva NV, Tsareva SN. Features of the course of pregnancy and indicators of respiratory function in

- women with abdominal obesity. // UO BDMU. 2015; 3: 91-95. <https://www.bsmu.by/medicaljournal/c5bfcea1641c11164bed6836e61484b>.
3. Frolov AA, Botasheva TL, Kaushanskaya LV, Avrutskaya VV, Denisenko IA, Astvatsaturyan EI, Alexandrova EM. Functional features of the external respiration system in pregnant women in the prenatal period and in childbirth, depending on the stereoisomerism of the female body // Modern problems of science and education. 2015; 4. URL: <http://www.science-education.ru/ru/article/view?id=20705>.
4. Adhikari EH, Moreno W, Zofkie AC, MacDonald L, McIntire DD, Collins RRJ, Spong CY. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. // JAMA Netw Open. 2020;3(11):e2029256. doi: 10.1001/jamanetworkopen.2020.29256. <https://covid.cdc.gov/covid-data-tracker>.
5. Covid.cdc.gov [Internet]. Centers for Disease Control and Prevention (CDC). Available from: <https://covid.cdc.gov/covid-data-tracker>.
6. Diriba K, Awulachew E, Getu E. The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis. // Eur J Med Res. 2020;25(1):39. doi: 10.1186/s40001-020-00439-w.
7. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-June 7, 2020. // MMWR Morb Mortal Wkly Rep. 2020;69(25):769-775. doi: 10.15585/mmwr.mm6925a1.
8. Idsociety.org [Internet]. COVID-19 Policy Brief: Disparities Among Rural Communities in the United States Version: December 22, 2020. Available from: https://www.idsociety.org/globalassets/idsa/public-health/covid-19/covid19-health-disparities-in-rural-communities_leadership-review_final_ab_clean.pdf.
9. Knight M, Bunch K, Vousden N, Morris E, Simpson N, Gale C, et al. UK obstetric surveillance system SARS-CoV-2 infection in pregnancy collaborative group. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. // BMJ. 2020;369:1-7. doi: 10.1136/bmj.m2107.
10. Libby P, Lüscher T. COVID-19 is, in the end, an endothelial disease. // Eur Heart J 2020; 41:30-38. doi: 10.1093/eurheartj/ehaa623.
11. Lowenstein CJ, Solomon SD. Severe COVID-19 Is a Microvascular Disease. // Circulation. 2020;142(17):1609-1611. doi:10.1161/CIRCULATIONAHA.120.050354.
12. Maleki DP, Kolahdooz F, Sadoughi F, Moazzami B, Chaichian S, Asemi Z. COVID-19 and pregnancy: a review of current knowledge. // Infez Med. 2020;28(1):46-51. PMID: 32532938.
13. Matar R, Alrahmani L, Monzer N, Debiante LG, Berbari E, Fares J et al. Clinical presentation and outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. // Clin Infect Dis. 2021 Feb 1;72(3):521-533. doi: 10.1093/cid/ciaa828.
14. Rcoq.org.uk [Internet]. Coronavirus (COVID-19) infection and pregnancy – guidance for healthcare professionals: Version 13 (cited 19 Feb 2021). Available from: <https://www.rcog.org.uk/coronavirus-pregnancy>.
15. Robinson E, Boyland E, Chisholm A, Harrold J, Maloney NG, Marty L et al. Obesity, eating behavior and physical activity during COVID-19 lockdown: A study of UK adults. // Appetite. 2021;156:104853. doi: 10.1016/j.appet.2020.104853.
16. Sanchis-Gomar F, Lavie CJ, Mehra MR, Henry BM, Lipi G. Obesity and outcomes in COVID-19: when an epidemic and pandemic collide. // Mayo Clin Proc. 2020;95(7):1445-1453. doi: 10.1016/j.mayocp.2020.05.006.
17. Sattar N, McInnes IB, McMurray JJV. Obesity is a risk factor for severe COVID-19 infection: multiple potential mechanisms. // Circulation. 2020;142(1):4-6.
18. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. // Lancet Infect Dis. 2020;20:425-434. [http://dx.doi.org/10.1016/S1473-3099\(20\)30086-4](http://dx.doi.org/10.1016/S1473-3099(20)30086-4)
19. Tartof SY, Qian L, Hong V, Wei R, Nadjafi RF, Fischer H et al. Obesity and Mortality Among Patients Diagnosed With COVID-19: Results From an Integrated Health Care Organization // An of Intern Med. 2020;173(10):773-781 <https://doi.org/10.7326/M20-3742>.
20. Thomas P, Alexander PE, Ahmed U, Elderhorst E, El-Khechen H, Mammen MJ et al. Vertical transmission risk of SARS-CoV-2 infection in the third trimester: a systematic scoping review. // J Matern Fetal Neonatal Med. 2020;1:1-8. doi: 10.1080/14767058.2020.1786055.
21. Uptodate.com [Internet]. Coronavirus disease 2019 (COVID-19): Hypercoagulability; c2021 (cited Feb 10, 2021). Available from: <https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-hypercoagulability>.
22. Vasileva D, Badawi A. C-reactive protein as a biomarker of severe H1N1 influenza. // Inflamm Res. 2019;68(1):39-46. doi: 10.1007/s00011-018-1188-x.
23. Vivanti AJ, Vauloup-Fellous C, Prevot S, Zupan V, Suffee C, Do Cao J et al. Transplacental transmission of SARS-CoV-2 infection. Nat Commun. 2020 Jul 14;11(1):3572. doi: 10.1038/s41467-020-17436-6.
24. Worldometers.info [Internet]. COVID-19. Coronavirus Pandemic. Available from: <https://www.worldometers.info/coronavirus>.
25. Wu W, Shi D, Fang D, Guo F, Guo J, Huang F et al. A new perspective on C-reactive protein in H7N9 infections. // International Journal of Infectious Diseases. 2016;44:31-36. DOI: 10.1016/j.ijid.2016.01.009.
26. Young BE, Ong SWX, Kalimuddin S. et al. Singapore 2019 Novel Coronavirus Outbreak Research Team. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. // JAMA. 2020;323(15):1488-1494. doi: 10.1001/jama.2020.3204.
27. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. // Acta Obstet Gynecol Scand. 2020;99(7):823-829. doi: 10.1111/aogs.13867.

SUMMARY

CLINICAL AND EPIDEMIOLOGICAL FEATURES OF COVID-19 COURSE IN PREGNANT WOMEN

Manasova G., Golubenko M., Didenkul N., Radchenko Ya., Gladchuk I.

Odessa National Medical University, Ukraine

Numerous studies have been devoted to the problem of the incidence of COVID-19 in pregnant women, but there is no suf-

ficient evidence base to formulate specific recommendations for the management of pregnancy, prevention of perinatal complications and possible vertical transmission of the disease.

The objective - to summarize clinical and epidemiological features of COVID-19 course and outcomes of labor in pregnant women in the Odessa region (Ukraine).

218 case histories of pregnancy and childbirth of women hospitalized to the specialized hospital base "Maternity hospital No. 2" of the Odessa City Council (Ukraine) with diagnosis of COVID-19, have been analyzed. The diagnosis was verified by the PCR. The study was conducted from 01.03.2020 to 31.01.2021.

The incidence of COVID-19 in pregnant women from April 2020 to January 2021 increased from 3.7% to 63.1% of the total number of births. Among the patients the city dwellers predominated (65.2%), women were more likely to get sick in the 3rd trimester (67.4%). 58.8% of women were overweight. 53.2% of the patients under observation were diagnosed with 2-sided polysegmental pneumonia; hyperthermia was noted in 71.2% of pregnant. The incidence of ARDS was noted in 10.1% of cases. An increase in the level of D-dimers was revealed in 72.4% of cases, and in 57.3% - in the level of CRP. All pregnant women recovered, 7.8% needed therapy in the intensive care unit. 86.5% of women gave birth on time, 9.9% of women had premature labour; 3.6% had an abortive outcome. The caesarean section rate constituted 29.7% (OR= 1.61 95% 0.85 3.06; P>0,05).

The prevalence of COVID-19 among pregnant women in the Odessa region is characterized by a common situation for a pandemic. Violation of fat metabolism in pregnant women is a significant risk factor for the incidence of COVID-19 (OR 2.25 95% CI 1.98-3.96; P<0.05). COVID-19 is a risk factor for increased pre-term births and early pregnancy losses (OR=4.23 95% CI 1.35 - 13.25; P < 0.05). Further multicenter studies are needed to obtain reliable data on the impact of COVID-19 on pregnant women and intrauterine patients.

Keywords: COVID-19, pregnancy, childbirth.

РЕЗЮМЕ

КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ТЕЧЕНИЯ COVID-19 У БЕРЕМЕННЫХ

Манасова Г.С., Голубенко М.Ю., Диденкул Н.В., Радченко Я.А., Гладчук И.З.

Одесский национальный медицинский университет, Украина

Проблеме COVID-19 у беременных посвящены многочисленные исследования, однако достаточной доказательной базы для формирования конкретных рекомендаций по ведению беременности, профилактике перинатальных осложнений и возможной вертикальной трансмиссии заболевания по сей день не разработано.

Цель исследования - обобщение клинико-эпидемиологических особенностей течения COVID-19 и исхода родов у беременных Одесского региона.

Проведен анализ 218 историй беременности и родов женщин, госпитализированных в Коммунальное неприбыльное предприятие «Родильный дом №2» Одесского городского совета с диагнозом COVID-19, верифицированным ПЦР-методом, за период с 01.03.2020 по 31.01.2021 гг.

Частота заболеваемости COVID-19 у беременных в пери-

од с апреля 2020 г. по январь 2021 г. увеличилась с 3,7% до 63,1% от общего количества родивших. Большинство больных проживали в городе (142; 65,2%), чаще болели женщины в 3 триместре беременности (147; 67,4%). У 128 (58,8%) женщин отмечалась избыточная масса тела. У 116 (53,2%) диагностирована 2-сторонняя полисегментарная пневмония, у 155 (71,2%) - гипертермия. Частота острого респираторного дистресс-синдрома составила 22 (10,1%). У 158 (72,4%) выявлено повышение уровня Д-димеров, у 125 (57,3%) - уровня С-реактивного белка. Выздоровели все беременные, 17 (7,8%) нуждались в терапии в условиях отделения реанимации и интенсивной терапии. Доносили беременность 188 (86,5%), родили до срока 22 (9,9%) женщины; у 8 (3,6%) отмечался abortивный исход. Частота кесарева сечения составила 65 (29,7%), OR=1.61 95% 0.85 3.06; P>0,05.

Распространенность заболевания COVID-19 среди беременных Одесского региона характеризуется общей для пандемии картиной. Нарушение жирового обмена у беременных является достоверным фактором риска заболеваемости COVID-19 (ОШ= 2,25 95% ДИ 1,98-3,96; P<0,05). COVID-19 является фактором риска увеличения частоты родов до срока и потерь беременности на ранних сроках (OR=4,23 95% CI 1,35 - 13,25; P<0,05). Для получения достоверных данных о влиянии COVID-19 на беременных и внутриутробных пациентов необходимо проведение дальнейших многоцентровых исследований.

რეზიუმე

COVID-19-ის მიმდინარეობის კლინიკურ-ეპიდემიოლოგიური თავისებურებები ორსულეებში

გ.მანასოვა, მ.გოლუბენკო, ნ.დიდენკული, ი.რადჩენკო, ი.გლადჩუკი

ოდესის ეროვნული სამედიცინო უნივერსიტეტი, უკრაინა

COVID-19-ის მომდინარეობას ორსულეებში ეძღვნება საკმაოდ ბევრი კვლევა, მიუხედავად ამისა, საკმარისი მტკიცებულებითი ბაზა ორსულობის მართვის, პერინატალურ გართულებათა და დაავადების ვერტიკალური ტრანსმისიის პრევენციისათვის სადღეისოდ შემუშავებული არ არის.

კვლევის მიზანს წარმოადგენდა ორსულეებში COVID-19-ის მიმდინარეობის და მშობიარობის გამოსავლის კლინიკურ-ეპიდემიოლოგიური თავისებურებების განზოგადება ოდესის რეგიონში.

ჩატარებულია ოდესის "№2 სამშობიარო სასტუმრო" ჰოსპიტალიზებული 218 ქალის ორსულობის და მშობიარობის ისტორია. COVID-19-ის დიაგნოზი ვერიფიცირებული იყო პჯრ-მეთოდით 01.03.2020-დან 31.01.2021-მდე პერიოდში.

COVID-19-ით ავადობის სიხშირე ორსულეებში 2020 წლის აპრილიდან 2021 წლის იანვრამდე პერიოდში გაიზარდა 3,7%-დან 63,1%-მდე. დაავადებულთა შორის მეტია ქალაქის მოსახლეთა რაოდენობა (142, 65,2%), ქალები მეტად ავადდებოდნენ მესამე ტრიმესტრში (147, 67,4%). 128 (58,8%) ქალს აღენიშნებოდა სხეულის ჭარბი მასა. 116 (53,2%) პაციენტში დიაგნოსტირდა პოლისეგმენტური პნევმონია, 155-ში (71,2%) - პიპერტურმია. მწვავე რესპირაციული დისტრეს-სინდრომის სიხშირემ შეადგინა 22 (10,1%). 158-ში (72,4%) გამოვ-

ლინდა D-დიმერის დონის მომატება, ხოლო 125-ში (57,3%) - C-რეაქტიული ცილის მანვენების. გამო-
ჯანმრთელდა ყველა ორსული; 17 (7,8%) ესაჭიროე-
ბოდა მკურნალობა რენიმაციული და ინტენსიური
თერაპიის განყოფილების პირობებში. ორსულობა
ბოლომდე მიიყვანა 188 (86,%) ვადაზე ადრე იმშო-
ბიარა 22 (9,9%) ქალმა; 8 (3,6%) ქალს განუვითარდა
აბორტული გამოსავალი. საკეისრო კვეთის სისშირემ
შეადგინა 65 (29,7%), OR=1.61 95% 0.85 3.06; P>0,05.

COVID-19-ის გავრცელებას ორსულებში ოდესის

რეგიონში აქვს პანდემიისათვის დამახასიათებელი
სურათი. ცხიმოვანი ცვლის დარღვევა ორსულებში
COVID-19-ით ავადობის სარწმუნო რისკ-ფაქტორია.
COVID-19 წარმოადგენს რისკის ფაქტორს ვადამდე-
ლი მშობიარობისა და ადრეულ ვადაზე ორსულობის
შეწყვეტისათვის (OR=4,23 95% CI 1.35 - 13.25; P<0,05).
ორსულებსა და პრენატალურ პაციენტებზე COVID-
19-ის გავლენის შესახებ სარწმუნო მონაცემების
მიღებისათვის აუცილებელია მულტიცენტრული
კვლევების გაგრძელება ამ მიმართულებით.

MODERN CLASSIFICATION OF POSTERIOR CIRCULATION STROKE: CLINICAL DECISION MAKING AND DIAGNOSIS (REVIEW)

¹Prokopiv M., ²Fartushna O.

¹O. Bogomolets National Medical University, Kyiv; ²Ukrainian Military Medical Academy, Kyiv, Ukraine

Posterior circulation strokes (PCS) account for approximately 20-25% of ischemic strokes [1-4]. These strokes are less represented in the scientific literature, are more difficult to diagnose, have a more severe clinical course and have higher mortality compared to anterior circulation strokes [5-12]. Terminological definitions and classification of PCS have been discussed and changed over the years. That is why we consider it necessary to focus the attention of physicians on the modern classification of PCS.

We aimed to provide a narrative review of the modern classification of posterior circulation stroke.

Material and methods. This article is the part of the research topic named "To determine the features of the course and consequences of stroke in patients of different age groups, taking into account genetic and infectious factors and comorbid pathology" for 2018-2021 with the state registration number - 0118U003695.

A comprehensive electronic literature search on Scopus, Web of Science, MEDLINE, ScieLo, PubMed, The Cochrane Library, EMBASE, Global Health, CyberLeninka, RINC databases, and databases of government scientific libraries of Ukraine, European Union, United Kingdom, and the USA for the period 1991–2021. It was performed to identify scientific publications that discussed the modern classification of PCS. The applicable articles are cited and referenced. No limit is placed on publication time or the language of the article. All relevant articles were identified and screened by two authors (MP and OF), and disagreements were resolved by consensus. The results are summarized narratively.

Results and discussion. PCS is classically defined as an infarction within the vertebrobasilar arterial system (VBS). The posterior circulation is supplied by the bilateral vertebral (VA) and basilar arteries (BA). VBS serves as a critical arterial supply to the cervical spinal cord brainstem, cerebellum, thalamus, and occipital lobes [13]. VAs arise from the right and left subclavian arteries and travel cranially through the transverse foramina of the cervical vertebrae [14].

First studied in the XIX century, PCS remains poorly understood compared to anterior stroke. Terminological definitions and classification of PCS have been discussed and changed over the years [15]. Neuroimaging techniques have revolutionized

an understanding of clinical aspects, causes, mechanisms, treatment programs, and consequences of PCS [16].

Anatomic Classification

According to the modern classification, PCS are divided into three intracranial anatomical areas [17, 18] (Fig. 1):

- *proximal* territory, covering the medulla oblongata and the posterior lower part of the cerebellum, which are supplied with blood by intracranial VA, the largest branch of the VA - posterior inferior cerebellar artery (PICA), and numerous branches of the paramedian arteries that branch from them;

- *middle* territory of the posterior circulation that includes the pons Varolii, the anterior-lower part of the cerebellum, which is supplied with blood by BA, one of the lateral branches of the BA - anterior inferior cerebellar artery (AICA), deep perforated, and paramedian arteries;

- *distal* territory of the posterior circulation covers the mid-brain, upper part of the cerebellum, thalamus, occipital lobe, and the area of the posterior temporal lobes of the cerebral hemispheres that are vascularized by the rostral part of the BA, its branches - superior cerebellar artery (SCA), AICA, deep perforated arteries, and posterior villous artery.

This classification takes into account the presence of vascular syndromes of the posterior circulation and brainstem in the case of damage only to the deep arteries, not superficial. In addition, this classification accounts for the previously mentioned features of the distribution of intra-stem branches of arteries, as well as arteries of the posterior circulation of the cerebellum and thalamic vascular areas.

According to the modern classification, strokes in the mentioned above *proximal*, *middle*, and *distal* areas are divided into *medial*, *lateral*, *dorsal*, *combinations of medial and lateral strokes*, and *classic thalamic stroke (anterior, paramedian, lower lateral, and posterior)* [13,19-24]. Clinical and neuroimaging allows accurately verifying the topography of the brainstem, cerebellar, thalamic stroke, and the corresponding arterial area involved in the pathological process in the case of PCS. Infarcts of certain parts of the brainstem, cerebellum, or thalamus are identified as isolated.