CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF THE COVID-19 CORONAVIRUS INFECTION IN PREGNANT WOMEN

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Introduction. The coronavirus infection caused by the SARS-CoV-2 virus remains one of the most significant global healthcare challenges [1-10]. COVID-19 has affected all aspects of modern society, from economic consequences to profound changes in healthcare systems and social structures. The relevance of studying the coronavirus infection is based on several important reasons. First, COVID-19 is characterized by its high transmission rate, leading to large outbreaks, which necessitates a detailed study of transmission methods and control measures. It should be noted that coronavirus infection affects various systems of the body, including the respiratory, cardiovascular, nervous, and immune systems. Second, the clinical manifestations of COVID-19 range from asymptomatic cases to severe forms with fatal outcomes, making it essential to thoroughly investigate both the pathogenesis and risk factors. Third, beyond the acute phase of the disease, COVID-19 can lead to serious complications, including post-COVID syndrome, also known as "long COVID-19", which requires further research to develop effective rehabilitation methods and prevent complications [7-10]. It is important to note that studying coronavirus infection in pregnant women holds particular interest [1-4]. It is well-known that changes in the circulatory, pulmonary, hormonal, and immunological systems caused by pregnancy place this group of patients at high risk of coronavirus infection [8-10]. It is evident that these physiological changes make pregnant women more vulnerable to severe courses of viral infections, including COVID-19. Research shows that pregnant women infected with coronavirus are more prone to hospitalization, the development of severe forms of the disease, the need for mechanical ventilation, and even face a higher risk of mortality compared to non-pregnant women of reproductive age [1,6, 9]. Additionally, pregnant women with COVID-19 have an increased risk of preterm birth and complications for the fetus, such as hypoxia, respiratory distress syndrome, and the need for neonatal intensive care [1-3,5,6].

Based on data from the World Health Organization (WHO) and various national research groups, pregnant women account for 5 to 10% of all hospitalizations among women of reproductive age with COVID-19 [8]. According to WHO, the mortality rate among pregnant women due to COVID-19 ranges between 1% and 3%, which is significantly higher than that of non-pregnant women of the same reproductive age [8]. National studies conducted in the USA and the UK have also shown that among pregnant women infected with the coronavirus, mortality rates are higher in groups with risk factors such as obesity, diabetes, and hypertension [6].

According to a meta-analysis conducted by Knight M., Bunch K., Vousden N., et al. in 2021, pregnant women with COVID-19 are more likely to require hospitalization in intensive care units, and the risk of mortality is increased by 22 times compared to uninfected pregnant women [6]. In this regard, the aim of this study was to determine the clinical and epidemiological aspects of the COVID-19 coronavirus infection in pregnant women.

Materials and Methods. The study involved 268 pregnant women, differing in age and gestational age, who were divided into two groups. The first group consisted of 222 pregnant women with confirmed COVID-19 coronavirus infection (PCR test for COVID-19 "positive"), while the second group, the control group (CG), included 46 uninfected women (PCR test for COVID-19 "negative"). According to the stated objective, we employed clinical, laboratory-diagnostic, and instrumental research methods. The assessment of the condition of pregnant women and parturient was conducted according to widely accepted standards of obstetric practice, based on standardized protocols for examining functional systems of the body. Special attention was given to the presence of extragenital pathology, previous gynecological diseases, as well as the reproductive

function characteristics of this group of women, gestational age, and the clinical course of the coronavirus infection.

Laboratory studies included a complete blood count, biochemical tests, coagulation profile, and urinalysis. The complete blood count comprised the determination of levels of erythrocytes, hemoglobin, hematocrit, leukocytes, lymphocytes, platelets, and monocytes, as well as erythrocyte sedimentation rate (ESR). The biochemical blood analysis included the assessment of liver enzyme levels - ALT, AST, C-reactive protein, creatinine, albumin, and lactate dehydrogenase. The coagulation profile evaluated the state of the blood coagulation system, including prothrombin time, INR, and prothrombin index.

To identify infections such as toxoplasmosis, herpes, cytomegalovirus, chlamydia, mycoplasmosis, and rubella, we employed the enzyme-linked immunosorbent assay (ELISA) method.

To assess the severity of the condition of pregnant women with coronavirus infection, we used the following scales: National Early Warning Score (NEWS 2) and quick Sequential Organ Failure Assessment (qSOFA). Instrumental methods of investigation included pulse oximetry, chest organ X-rays, ultrasound, pelvic Doppler ultrasound, cardiotocography (CTG), electrocardiography (ECG), echocardiography (ECHO) as indicated, and computed tomography (CT) as indicated.

Statistical analysis of the obtained data was performed using "STATISTICA-10" software, and graphical interpretation was conducted using "ORIGIN-6.1" and "Excel 2016" programs. Differences were considered statistically significant at $p<0.05$, $p<0.01$, and $p<0.001$, which corresponds to the standards of medical and biological research.

Results and Discussion. We conducted a comprehensive examination of 268 pregnant women, who were divided into two groups. Group I included 222 patients with COVID-19, while Group II consisted of 46 uninfected women (control group). Based on age, the patients were distributed as follows: 19-24 years - 61(27.5%); 25-29 years - 71(32%); 30-34 years - 58(26.1%); 35-40 years - 28(12.6%); and 41-45 years - 4(1.8%) in Group I. In Group II: 19-24 years - 16(34.8%); 25-29 years - 14(30.4%); 30-34 years - 11(23.9%); 35-40 years - 4(8.7%); 41-45 years - 0(0%); and 45 years and older - 1(2.2%). The average age of patients in Group I was 32±13 years; in Group II, it was 33.5±14.5 years, respectively (fig.1).
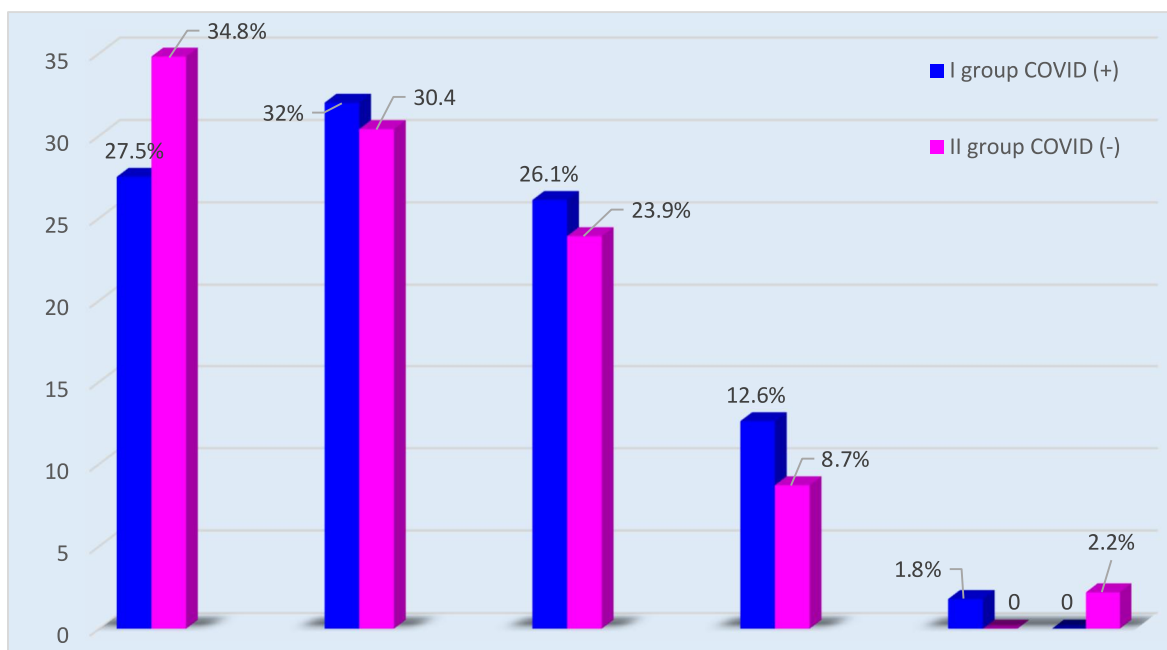

Fig. 1. Distribution of patients by age

In 142(62.9%) patients in Group I, the pregnancy was maintained, while in the control group (CG), no cases of maintained pregnancy were recorded. In Group I - 57(25.7%) women delivered via cesarean section, compared to 36(78.3%) cases in Group II. Vaginal deliveries in Group I accounted for 19(8.6%) cases, while in Group II, there were 10(21.7%) cases. Figure 2 shows the distribution of patients by parity:

primiparous women constituted 46(20.7%) cases in the main Group I and 17(37.0%) in Group II, respectively. Multiparous women in Group I were 30(13.5%), while in Group II, there were 29(63.0%).

Pregnant women with COVID-19 often suffered from comorbidities and complications. For example, 146(65.8%) patients in Group I were diagnosed with anemia of I-III degree, of iron deficiency type, while in Group II - 21(45.6%) were affected (fig.3). Preeclampsia was observed in 32(14.4%) cases in Group I and in 3(6.5%) cases in Group II.
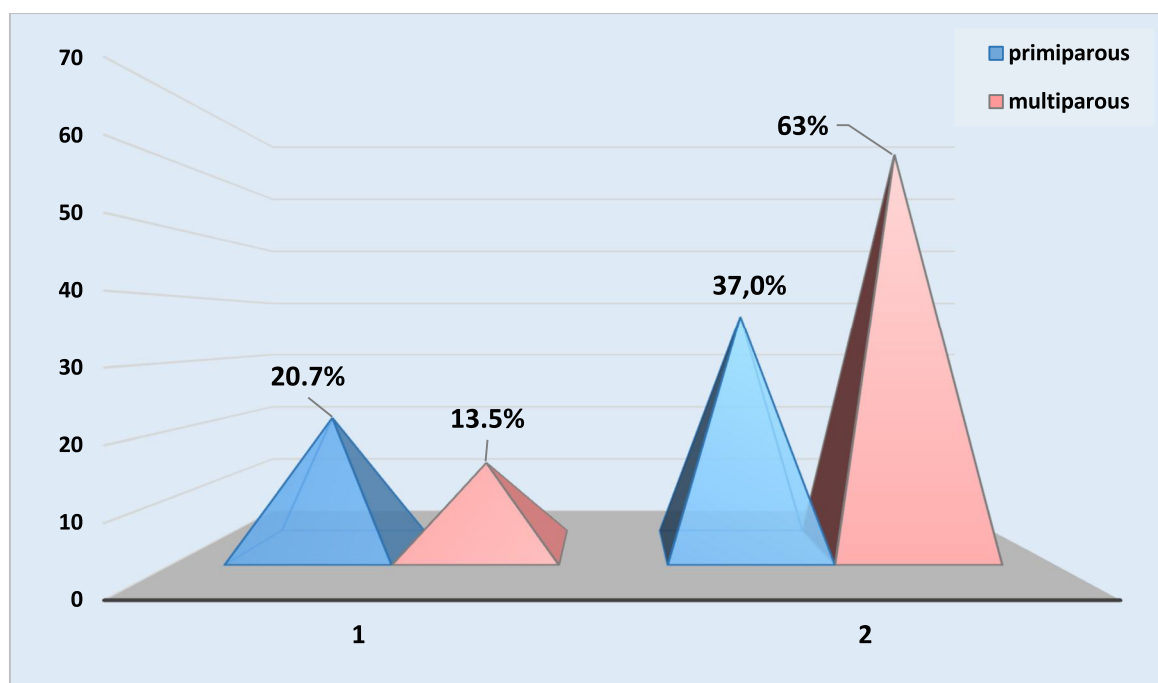

Fig. 2. Distribution of patients by parity

Hypertensive conditions were recorded in 57(25.7%) women with COVID-19 and in 3(6.5%) patients in the control group. Varicose veins of the lower extremities were diagnosed in 47(21.1%) patients in Group I and in 4(8.7%) women in Group II. Obesity was found in 41(21.6%) patients in the main group and in 8 women in the control group, accounting for 17.4% of cases. Pulmonary diseases, such as bronchial asthma, were noted in 4(1.8%) women with COVID-19 and in 2(4.3%) patients in Group II. Mitral insufficiency was identified in 2 patients (0.9%) in Group I and in 1(2.2%) woman in Group II. Gastrointestinal diseases (GID), particularly gastritis, cholecystitis, and a history of cholelithiasis, were noted in 12(5.4%) patients, while in the control group (CG), such cases were recorded in 7 instances, accounting for 15.2%. Urogenital system diseases (pyelonephritis, cystitis) were registered in 13(5.9%) women in the main group and in 2(4.3%) cases in Group II, respectively. Endocrine diseases (diabetes mellitus, thyroid disorders: autoimmune thyroiditis, hypothyroidism) were present in 13(5.9%) women in Group I and in 5(10.5%) patients in Group II. Thalassemia carriers were identified in 3 cases: in 2(0.9%) patients in Group I and in 1(2.2%) woman in Group II. Hepatitis B was registered in 4(1.8%) cases in the main group, while heaptitis C was noted in 3(1.4%) women.
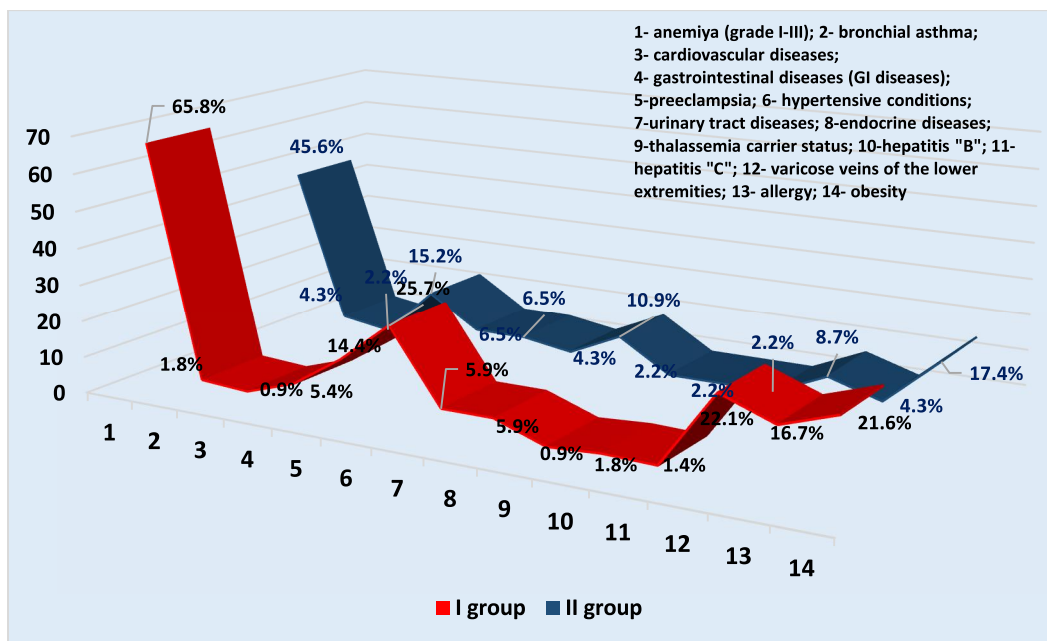
Fig. 3. Diagram of the frequency of occurrence of extragenital diseases in pregnant women

In Group II, thalassemia was noted with a frequency of 1(2.2%), as was hepatitis "B" - 1(2.2%)) and hepatitis "C" - 1(2.2%)). In Group I - 37(16.7%) women had a history of allergies, while in the control group (CG), only 2(4.3%) cases showed a tendency to allergic reactions. When characterizing the reproductive function of women during this pregnancy, it is important to note that spontaneous miscarriages were reported in 4(1.8%) patients in Group I, whereas in the CG, there were only 2 cases, accounting for 4.3%. In our opinion, the frequency of spontaneous miscarriages is associated with increased risk factors or medical indications in patients of this category. In Group I, antepartum fetal death was registered in 7 cases, which constituted 3.2%. In the CG, only one case of antepartum fetal death was noted, which corresponded to 4.3%. Non-developing pregnancies occurred in both groups, but somewhat more frequently in Group I - 19(8.6%) cases compared to 3(6.5%) cases in Group II, which may be related to differences in conditions or risk factors. In vitro fertilization (IVF) was performed in 5(2.3%) women in Group I and in one patient (2.2%) in Group II.

Among the clinical manifestations in pregnant women with COVID-19, the most common were: bilateral pneumonia (69.4%) (confirmed by RH studies), elevated temperature (≥ 37.5°C - 84.7%), pallor of the skin (71.6%), cough (71.6%), hyperemia of the pharynx, sore throat (52.7%), general weakness and lethargy (52.7%), shortness of breath (42.8%), difficulty in nasal breathing (48.6%), loss of appetite (46.4%), and rapid fatigue (41.4%), highlighting the necessity for careful monitoring of these patients' conditions.

A particularly interesting finding was the detection of leukopenia or leukocytosis in the blood of women in Group I. As is well known, qualitative and quantitative changes in peripheral blood leukocytes can serve as secondary symptoms in various forms of infectious and non-infectious pathology of internal organs. Additionally, pregnant patients with a positive PCR test for COVID-19 exhibited lymphopenia, lymphocytosis, thrombocytosis, increased levels of C-reactive protein, ALT, AST, creatinine, albumin, ferritin, and prothrombin index (indicating hypercoagulation), lactate dehydrogenase (indicating tissue damage), and D-dimer (indicating activation of thrombus formation and fibrinolysis), which can be regarded as warnings of worsening conditions. It is known that C-reactive protein is a plasma protein that belongs to the group of acute phase proteins and is one of the most informative indicators of the inflammatory process in the body.

It should be noted that anemia and hypertensive disorders are the most common extragenital diseases among pregnant women infected with COVID-19. It is also important to highlight that varicose veins of the lower extremities, obesity, and allergic reactions were more frequently observed in patients with coronavirus infection compared to the control group. It is crucial to emphasize that varicose veins in the lower extremities indicate a significant burden on the

vascular system in this population of women. Allergic diseases, in turn, point to the particularities of the immune system in these patients.

Thus, coronavirus infection may influence pregnancy outcomes by increasing the risk of complications, which is a significant issue in modern society. The data obtained during this study demonstrate that COVID-19 infection during pregnancy is regarded as a serious and severe disease, highlighting the need for careful monitoring and management of complications in pregnant women with coronavirus infection. However, the impact of the infection on pregnancy outcomes, such as preterm birth, fetal abnormalities, and perinatal mortality, still requires further investigation and confirmation.

XULASƏ

Hamilə qadınlarda COVID-19 koronavirus infeksiyasının klınik və epidemioloji xüsusiyyətləri

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Açar sözlər: koronavirus infeksiyası, hamiləlik, hamilələrdə COVID-19, virus infeksiyası

Biz 268 hamilə qadının kompleks şəklində müayinəsini aparmışıq və iki kliniki qrupa ayırmışıq. Birinci qrupa COVID-19 koronavirus infeksiyası təsdiq edilmiş 222 hamilə qadın daxil olmuşdur (COVID-19 PCR testi "müsbət" olan). İkinci nəzarət qrupu (NQ) olaraq 46 infeksiyaya yoluxmamış qadınlar daxil edilmişdir (COVID-19 PCR testi "mənfi" olan). Araşdırmalar göstərdi ki, COVID-19 infeksiyası ilə yoluxmuş hamilə qadınlar arasında ən çox rast gəlinən ektragenital xəstəliklər aşağıdakılardır: anemiya, preeklampsiya, hipertenziya, aşağı ətrafların varikoz genişlənməsi, piylənmə və allergik reaksiyalar. COVID-19-a yoluxmuş hamilə qadınlarda ən çox rast gəlinən kliniki əlamətlər bunlar idi: iki tərəfli pnevmoniya (69,4%), hərarətin artması (≥ 37,5°C - 84,7%), dəri örtüklərinin solğunluğu (71,6%), öskürək (71,6%), boğazın hiperemiyası və boğaz ağrısı (52,7%), ümumi zəiflik və halsızlıq (52,7%), nəfəs darlığı (42,8%), burun tənəffüsünün çətinləşməsi (48,6%), iştahın itməsi (46,4%), sürətli yorğunluq (41,4%). Bu nəticələr hamilə qadınların vəziyyətinə diqqətli monitorinq aparılmasının vacibliyini vurğulayır.

Laborator araşdırmalara əsasən, PCR testi COVID-19 "pozitiv" çıxan hamilə xəstələrin periferik qanında aşkar olunmuşdur: leykopeniya və ya

РЕЗЮМЕ

Клинические и эпидемиологические аспекты коронавирусной инфекции COVID-19 у беременных женщин

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Ключевые слова: оронавирусная инфекция, беременность, COVID-19 у беременных, вирусная инфекция

Нами проведено комплексное обследование 268 беременных женщин, которые были разделены на две группы. Первую группу составили 222 беременных женщин с подтвержденной коронавирусной инфекцией COVID-19 (ПЦР-тест на COVID-19 "позитив"), во вторую контрольную группу (КГ) были включены 46 неинфицированных женщин, (ПЦР-тест на COVID-19 "негатив"). Проведенные исследования показали, что у беременных женщин, инфицированных COVID-19, наиболее распространенными экстрагенитальными заболеваниями являются: анемия, преэклампсия, гипертензивные состояния, варикозное расширение вен нижних конечностей, ожирение и аллергические реакции.

Среди клинических проявлений у беременных женщин с COVID-19 наиболее распространенными были: двухсторонняя пневмония (69,4%), повышение температуры (≥ 37,5°C - 84,7%), бледность кожных покровов (71,6%), кашель (71,6%), гиперемия зева, боли в горле (52,7%), общая слабость, вялость (52,7%), одышка (42,8%), затруднение носового дыхания (48,6%), потеря аппетита (46,4%), быстрая утомляемость (41,4%), что подчеркивает необходимость тщательного мониторинга за состоянием этих пациенток.

leykositoz, limfopeniya və ya limfositoz, trombositoz, C-reaktiv zülalın artması, ALT, AST artması, kreatinin, albumin, ferritin, protrombin indeksinin yüksəlməsi, laktatdehidrogenaza və D-dimerin artması.

Beləliklə, hamiləlik dövründə COVID-19 koronavirusuna yoluxma ciddi və ağır bir xəstəlik kimi qiymətləndirilir, bu da hamilə qadınlarda koronavirus infeksiyası zamanı fəsadların diqqətli monitorinqini və idarə edilməsini vacib edir. Bununla belə, infeksiyanın hamiləliyin nəticələrinə, o cümlədən vaxtından əvvəl doğuş, dölün anomaliyaları və perinatal ölümə təsiri hələ də əlavə araşdırmalar və təsdiq tələb edir.

Согласно лабораторным исследованиям у беременных пациенток с положительным ПЦР-тестом на COVID-19 в периферической крови выявлены: *лейкопения или лейкоцитоз, лимфопения или лимфоцитоз, тромбоцитоз, повышение С-реактивного белка, АЛТ, АСТ, креатинина, альбумина, ферритина, повышение протромбинового индекса, лактатдегидрогеназы, D-димера.*

Таким образом, инфицирование коронавирусом COVID-19 во время беременности расценивается как серьезное, тяжелое заболевание, что подчеркивает необходимость тщательного мониторинга и управления осложнениями у беременных женщин при коронавирусной инфекции. Однако, *влияние инфекции на исходы беременности, такие как преждевременные роды, аномалии плода и перинатальную смертность, всё ещё требуют дальнейшего исследования и подтверждения.*

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