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COMPARATIVE OUTCOMES OF PREGNANCY AND CHILD IN WOMEN WITH A HISTORY OF ANTIPHOLIPID SYNDROME DURING THE PANDEMIC PERIOD.

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Abstract: The spectrum of antiphospholipid antibodies was studied in patients with antiphospholipid syndrome during a pandemic30 patients and 19 pregnant women with coronavirus infection treated in Bukhara and Kagan maternity hospitals.
Keywords: coronavirus infection, antiphospholipid syndrome, pregnancy

Relevance: Currently, during the pandemic, the study of the problem of thrombophilic complications during pregnancy remains one of the main, promising tasks of modern obstetrics [2, 3, 5]. Recent studies have revealed a clear relationship between the development of autoimmune processes and reproductive disorders in the form of recurrent miscarriage, primary and secondary infertility, premature birth, and autoreaction to phospholipids [10, 12].The complexeffect of interrelated damaging factors (coronavirus infection, the presence of antiphospholipid antibodies, bad habits, nervous strain, disruption of the regimen and sleep) lead to a shift in homeostasis during pregnancy. In this case, an imbalance occurs in the immune system, and against the background of a failure, antibodies are produced to the body's own tissues [3, 4, 6].

During pregnancy, hereditary and acquired coagulation disorders (infections, inflammation, obesity, dehydration, etc.) are also risk factors. The postpartum period poses an even higher risk [8, 10, 11], and during this period it increases 15-35 times compared to age-matched non-pregnant women [10, 12]. The daily risk of pregnancy-related VTE is highest during the first 3-6 weeks. after childbirth [3]. Thereafter, it declines rapidly, although a small residual risk may persist for up to 12 weeks. after childbirth [13]. In the structure of the causes of maternal death, although not a primary place, is obstetric embolism [12]. Maternal mortality is 0.1 per 100,000 births in vaginal delivery and 10 times higher (1-1.6 per 100,000) after caesarean section [2]. Venous thrombosis and embolism are among the uncontrollable causes of maternal mortality, in addition, venous thrombosis of the main veins leads to thrombosis of the placental vessels, thereby leading to a deterioration in the uteroplacental circulation and the intrauterine state of the fetus [6], which creates a real threat to life and health not only mother, but also the fetus.

To better understand the problem of thrombophilic conditions, it is necessary to remember what hemostasis is and how it "works". The hemostasis system is a biological system that ensures the preservation of the liquid state of the blood, on the one hand, and the prevention and stop of bleeding, on the other hand, by maintaining the structural integrity of the walls of blood vessels and sufficiently rapid thrombosis of the latter in case of damage [3, 4, 13].

In the process of stopping bleeding, both mechanisms are interrelated [2]. Platelet thrombus stops bleeding only in microvessels with low blood pressure. In larger vessels, platelet thrombus is not able to provide reliable hemostasis, and here the leading role belongs to coagulation hemostasis [11, 12].

In recent years, more and more attention has been paid to the study of the role of

thrombophilic conditions both in the development of obstetric complications and thromboembolic complications.The analysis of many studies made it possible to single out thrombophilias as an independent group of causes of miscarriage [10]. According to different authors, the role of thrombophilia in the structure of causes of fetal loss syndrome is 40-75% [1-4, 6, 7].Antiphospholipid syndrome remains the most common form of acquired thrombophilia.(AFS).With the beginning of the rapid development of clinical hemostasiology and immunology in the 80-90s. In the 20th century, a number of genetic forms of thrombophilia were discovered one after another, including the FV Leiden mutation, the G20210A prothrombin mutation, polymorphisms of the genes that control the fibrinolysis system: PAI-1, 4G / 5G, polymorphisms of tissue plasminogen activator t-PA I/D, fibrinogen-455 A/G, factor XII, etc. [3, 4, 13].Due to thrombophilia, up to 55% of reproductive losses occur. The term "thrombophilia" was first introduced in 1965 to describe a tendency to venous thrombosis in a Norwegian family with antithrombin III (AT III) deficiency. Later, this term was widely introduced into clinical practice and began to combine many disorders accompanied by an increased predisposition to thrombosis, including both hereditary and acquired forms [10, 11, 14].

Target. To study the spectrum of antiphospholipid antibodies in patients with antiphospholipid syndrome during the COVID-19 pandemic

Research methods.30 patients were examined with antiphospholipid syndrome and 19 pregnant women who underwent coronavirus infection treated in Bukhara and Kagan maternity hospitals. The control group consisted of 15 women with a physiological course of pregnancy who applied to the Bukhara city maternity complex.When assessing the hemostasis system, activated partial thromboplastin time (APTT), prothrombin time (PT), prothrombin index (PTI), fibrinogen concentration, antithrombin III activity (AT III), and platelet count were determined.in addition to hematological, biochemical studies, Doppler uteroplacental circulation was studied to identify disorders in the circulatory system. Doppler studies of pregnant women were carried out in the Bukhara Regional Screeningcenter and private clinic Faizmed doctor Rakhmatova D.

Results. All 30 examined patients who were diagnosed with COVID-19 infection and ahistory of antiphospholipid syndrome were in the third trimester of pregnancy.In 16 patients, the main symptom was fever without significant leukopenia and lymphopenia, and 14 patients had antiphospholipid syndrome.As of September 25, 2020, none of the 19 women had progressed to a serious illness and died (all patients were cured and discharged). Histopathological analysis of the placenta showed that 13.5% had chorionic hemangioma and 14.5% had multifocal infarction; in all cases, different degrees of fibrin deposition were observed in the interstitium of the villi or around it under a microscope, and local syncytial nodules also increased; chorioamnionitis was not found.

Table No. 1

Clinical and laboratory data of pregnant women with APS and COVID-19 in a comparative aspect with healthy patients

indicator	*1st group, n=30*	*2nd group, n=19*	*Control group, n=15*
Hb, g/l	*84.2±1.3****	*83.2±1.3****	*99.4±4.3*
Erythrocytes, 1012/l	*3.8±0.2***	*4.2±0.2*	*4.8±0.3*
Ht, %	*32.2±1.0*	*33±1.0*	*34.9±1.1*
Leukocytes, 109/l	*11.8±0.4**	*18.7±0.4**	*5.7±0.5*
Platelets, 109/l	*168.3±11.5****	*196.3±11.5*	*210.2±6.0*
COE, mm/h	*22.6±1.1****	*27.3±1.1**	*19.5±0.6*

Note: *- differences relative to the data of the control group are significant (* - P<0.05; ** - P<0.01; *** - P<0.001)

In our total cohort of pregnant women infected with COVID-19, 8 of 19 patients (32.6%) initially had no symptoms associated with COVID-19. Two of these women were initially admitted for induction of labor for obstetric indications. Both developed symptoms mimicking obstetric complications but were ultimately diagnosed with COVID-19 as part of a wide differential as previously described by this group.

A study of laboratory data in the dynamics of pregnancy in patients with APS and COVID-19 showed that the levels of hemoglobin concentration and the number of erythrocytes were significantly higher and are compensatory-acceptable. All examined patients had anemia: Hb - 84.2±1.3% with reduced Hb values by 7.7%. A tendency to thrombocytopenia, an increase in ESR by 33.1%, and leukocytosis were noted (Table 2).

*Considering the high importance*COVID-19 and antiphospholipid syndrome*as the occurrence of a risk factor for TEC, in these women the blood coagulation system was studied, with the presence of D-dimers, ferritin (Table 3).*

Table №3

Clinical and laboratory data of pregnant women with APS and COVID-19 in a comparative aspect with healthy patients

indicator	*1st group, n=30*	*2nd group, n=19*	*Control group, n=15*
Prothrombin index (PTI), %	96.2±1.1*	66.2±0.2*	121±3.2
Fibrinogen, g/l	4.0±0.6***	5.3±0.3***	3.5±0.5
Antithrombin III, mg/l	74.1±1.2**	59.9±1.2*	95.6±1.7
APTT	32.1±1.1**	30.7±2.3**	40.3±1.5
D-dimer ng/ml	*970.2±6.0**	*3096.3±11.5**	*168.3±11.5*
Ferritin ng/ml	*122.6±1.1**	*327.3±1.1**	*29.5±0.6*

Note: *- differences relative to the data of the control group are significant (* - P<0.05; ** - P<0.01; *** - P<0.001)

When studying the hemostatic system, some deviations were revealed: in pregnant women withCOVID-19more pronounced disorders of the coagulation link of hemostasis were observed compared with the control group. Despite the mild course of the disease, changes in the hemostasis system were significantly higher (P<0.01). The increase in fibrinogen is of clinical importance. The level of D-dimer is significantly increased in severe cases, which is a potential risk factor and the basis for a poor prognosis. In patients receiving anticoagulant therapy, it is necessary to monitor the level of APTT, D-dimer, VSC. The question of stopping anticoagulant therapy should be decided on the basis of coagulogram and D-dimer indicators.

COVID-19 and antiphospholipid syndrome is a serious threat during pregnancy, which may well be the cause of various perinatal complications up to antenatal mortality. Based on the current clinical and laboratory studies of morbidity, it should be expected that it is the asymptomatic course that the change in the hemostasis system is significantly higher, and thus the number of pregnant women seeking medical help is reduced. Our results suggest that COVID-19 is often asymptomatic and should be considered in all pregnant women in high-prevalence areas.

Significantly significant changes in BMD in pregnant women with APS and COVID-19 in comparison with the data of the control group were noted in the umbilical artery - an increase in IR 0.72ë0.02; in the uterine artery - an increase in LMS up to 2.26ë0.02 and IR up to 0.61ë0.02; in the middle cerebral artery - a decrease in the data of IR, PI and LMS. Such changes in the uterine artery and umbilical artery indicate an increase in resistance in the peripheral sections, in the middle cerebral artery there was a decrease in all indicators (Table 2).

Table 3

Doppler indicators of utero-placental-fetal hemodynamics in women of the examined groups (M±m)

Investigated parameters	*CDO*	*IP*	*PI*
1 group, n = 30			
Uterine arteries	*2.26±0.02****	*0.61±0.02****	*0.93±0.05****
Umbilical cord artery	*3.21±0.02****	*0.72±0.02****	*0.84±0.08**
Middle cerebral artery	*2.82±0.02****	*0.91±0.02****	*1.89±0.02****
group 2, n = 19			
Uterine arteries	*2.06±0.05****	*0.48±0.01*	*0.81±0.05****
Umbilical cord artery	*3.84±0.05****	*0.63±0.01****	*0.76±0.05*
Middle cerebral artery	*1.69±0.05****	*0.96±0.03****	*1.99±0.02****
Control group n = 15			
Uterine arteries	*1.89±0.05*	*0.39±0.05*	*0.56±0.02*
Umbilical cord artery	*2.65±0.05*	*1.11±0.02*	*065±0.05*
Middle cerebral artery	*4.65±0.02*	*0.74±0.01*	*1.39±0.02*

Note: * - differences relative to the data of the control group are significant (* - P<0.05; ** - P<0.01; *** - P<0.001)

When studying the peculiarities of blood circulation in the mother-placenta-fetus system in pregnant women with APS and COVID-19, MPPC disorders were detected in 30 (68.2%) cases. Blood flow disorders in the uterine arteries were detected in 12 (27.2%) patients, fetal blood flow - in 8 (18.2%), combined disorders were observed in 7 (16%) cases.It also has adirect relationship between the severity of COVID-19 and impaired blood flow in the MPC. In pregnant women with a mild degree of COVID-19, disturbances in the placental-fetal blood flow (PPC) are not detected; in the presence of moderate and severe COVID-19, significant changes in the PUC are detected.

Conclusions.

1.In pregnant women who have undergone a new coronavirus infection COVID-19 and with antiphospholipid syndrome, hypercoagulation was noted, as well as impaired uteroplacental-fetal blood flow.

2.Pregnant women who have had COVID-19 and women withantiphospholipid syndromeit is necessary to refer to the risk group for the development of PN and to carry out timely prevention of PN.

3.Correction of disorders in the hemostasis system in pregnant women with thrombophilia andCOVID-19during the period of placental formation until the completion of trophoblast invasion, it is necessary not only to prolong pregnancy, but also to prevent long-term complications of pregnancy (severe forms of preeclampsia, placental insufficiency, fetal growth restriction syndrome).

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