

pregnancy in the first trimester. Increased concentrations of inflammatory cytokines during infection can lead to spontaneous abortions, aggravation of inflammatory immune responses in the endometrium and disruption of intercellular interactions.

Antimicrobial peptides synthesized in the cells of the immune system have antibacterial, antiviral and antifungal effects, as well as immunomodulatory activity by stimulating the synthesis of cytokines and other immune mediators. At the present time, about 200 types of AMPs have been identified and among them, defensins, cathelicidines, and endotoxin-binding proteins have been studied more in details.

Recently, extensive research has been conducted to study the role of cytokines and AMPs in amniotic fluid in determining the clinical course of pregnancy and the degree of infection of the fetus against the background of infections. These indicators have already begun to be used in clinical practice. However, there are few studies on the study of cytokines and AMPs in peripheral blood during an infectious pregnancy.

Thus, the study of the dynamics of cytokine and AMPs concentrations in pregnant women with TORCH infections depending on the stage of pregnancy may be of great scientific and practical importance.

Object of the research. Practically healthy pregnant women, pregnant women with TORCH infection and practically healthy non-pregnant women of reproductive age.

Purpose of the study: To assess the role of antimicrobial peptides, cytokines and some hormones in the pathogenesis of changes observed at different stages of pregnancy in women with TORCH infections and to study the molecular mechanisms of immune and endocrine disorders.

Objectives of the research:

1. Dynamic study of the concentration of inflammatory cytokines (IL-2, IL-6, IL-8, TNF- α , IFN- γ) in the blood of pregnant women not complicated by TORCH infections and infected with these infections;

2. Dynamic study of the concentration of anti-inflammatory

5. Compared to pregnant women not complicated by TORCH infections, the concentration of AFP increases in the first and third trimesters and the concentration of β -hCG decreases in women infected with these infections and ending their pregnancies by birth. Increase in AFP concentrations is observed against the background of unchanged β -hCG concentrations in women with miscarriages.

6. There is a negative correlation dependence between inflammatory cytokines and antimicrobial peptides in pregnant women with TORCH infections. There is a negative correlation between lactoferrin and IL-2, IL-10 and AFP, IL-8 and IL-10, endotoxin with BPI, defensin and with IL-6. There is a positive correlation between hepcidin with estradiol, BPI with defensin, AFP with IL-8 in women with TORCH ending pregnancy with miscarriage.

The scientific novelty of the study. The levels of cytokines, AMPs, and hormones in pregnant women with TORCH infections in different trimesters of pregnancy were studied in a complex and comparative manner in this research work. The role and prognostic significance of TORCH infections and hormonal balance in the pathogenesis of spontaneous abortions during pregnancy have been investigated. For the first time, a correlation between proinflammatory cytokines and antimicrobial peptides in pregnant women with TORCH infection and between cytokines, antimicrobial peptides, and hormones in pregnant women with spontaneous abortion was studied.

The practical relevance of the study. The results obtained can contribute to clarification of the role of TORCH infections in the pathogenesis of disorders observed during pregnancy, early diagnosis of abortions in pregnant women infected with these infections and arrangement of adequate treatment. The study of cytokines, AMPs, and hormonal balance in pregnant women with TORCH infections may provide more accurate understanding of the biochemical mechanisms of immune-metabolic disorders.

Approbation and application. The main provisions of the thesis work were discussed at the International Scientific Conference dedicated to the 85th anniversary of the prof. R.A.Asgarov (Baku,

2018), at the scientific-practical conference "Actual Problems of Medicine - 2018" dedicated to the 100th anniversary of the Azerbaijan Democratic Republic (Baku, 2018), at the international scientific-practical conference "Actual problems of medicine 2019" dedicated to the 100th anniversary of the Medical Faculty of Baku State University (Baku, 2019), at the conference dedicated to the 90th anniversary of the prof. D.V.Hajiyev (Baku, 2019), at the International Congress of Hematologists (Baku, 2019), at the 7th scientific-practical conference of residents of Azerbaijan Medical University (Baku, 2019), at the international conference titled "Biological markers in fundamental and clinical medicine" (Prague , 2019). The initial discussion of the thesis work was held on June 1, 2021 at a joint meeting of the staff of the Department of Biological Chemistry, Medical Microbiology and Immunology, Infectious Diseases and II Obstetrics and Gynecology of the Azerbaijan Medical University. The approbation of the thesis work was carried out on April 28, 2022 at the meeting of the Approbation Commission conducting scientific seminars of FD 2.31 Thesis Council attached to Baku State University (protocol № 2).

Application of the obtained results. The results of the dissertation are applied in the teaching process of the Department of Biological Chemistry of the Azerbaijan Medical University and in the Scientific Research Institute of Obstetrics and Gynecology of the Ministry of Health of the Republic of Azerbaijan.

Name of the organization where the dissertation was performed. Educational clinical biochemistry laboratory of the Department of Biological Chemistry of Azerbaijan Medical University.

Total volume and structure of the dissertation. The dissertation was published on a computer (204.100 characters), consisting of introduction (14.800 characters), literature review (54.850 characters), chapter of materials and methods (11.200 characters), results of the personal research and chapters of their discussion (72.300 + 4.950 characters), consultations (43.250 characters), results, practical recommendations (2.750 characters), and list of reference. The list of references includes 243 sources (20

Table 1

Characteristics of persons included in the research contingent by groups and age

Groups	Yaş hədləri	Say
Comparison group (without TORCH infection)	26,0±0,9 (19-37)	29
Women infected with TORCH infections and ending pregnancy by birth (I subgroup)	24,6±1,0 (18-31)	33
Women infected with TORCH infections and ending pregnancy by miscarriage (II subgroup)	26,3±0,6 (19-34)	7
Control group	25,9±1,1 (20-37)	16

Concentration of IL-2, IL-6, IL-8, IL-10, TNF- α and IFN- γ cytokines in blood serum was determined using the reagent kit of "Vector-Best" company (Russian Federation), concentration of lactoferrin, endotoxin, hepcidin, BPI and defensin using the reagent kits of Cloud-Clone Corp company (USA), AFP, β -hCG and prolactin concentration using the reagent kits of Pishtaz (Germany), estradiol and estriol concentration using the reagent kit of Nova Tech company (Germany), DHEA concentration using the reagent kit if Steroid-DHEA-sulfate company (Germany) through solid-phase "sandwich" enzyme-linked immunosorbent assay. Enzyme-linked immunosorbent assays were performed on the Stat Fax 303 Plus (USA) immune-enzyme analyzer (differential filter 450-650 nm).

RESULTS AND DISCUSSION

Concentration of cytokines, antimicrobial peptides and hormones in the blood of pregnant women not infected with TORCH infections

The normal course of pregnancy depends directly on the ratio of Th1/Th2 cytokines and Th2 immunosuppressive cytokines predominate in normal pregnancy. Cytokines produced during the initial immune response usually don't enter the bloodstream and their

effect is local. Increased levels of cytokines in the blood indicate a violation of local mechanisms of action, intensive and long-term inflammation, activation of autoimmune processes, including cells of the immune system. The carried-out researches show that the concentration of anti-inflammatory cytokines in the blood of pregnant women not infected with TORCH increases, although the concentration of inflammatory cytokines does not change significantly compared to the control group. It was observed in this group that the concentration of TNF- α increased in the first trimester and decreased in the third trimester. In the first trimester, the concentration of IL-4 and TNF- α increased 39.3% ($p=0.016$) and 69.9% ($p=0.030$), and in the third trimester, the concentration of TNF- α increased 30.5% ($p=0.026$) compared to the control group.

During pregnancy, AMPs acts as a chemical barrier to protect the fetus from intrauterine infections. The results show that the concentration of lactoferrin, endotoxin and defensin in the blood of pregnant women not infected with TORCH in the first trimester increased 75.2% ($p<0.001$); 47.2% ($p=0.026$) and 9.2% ($p=0.003$) respectively compared to the control group, while the concentration of hepcidin decreased by 10.6% ($p=0.017$). According to the bibliographic data, the concentration of LF in the amniotic fluid remains high during pregnancy. Despite that the concentration of LF in the amniotic fluid decreases at birth, it increases in the birth canal. It protects the fetus from infection by activating neutrophils.

In the third trimester, the concentration of lactoferrin and BPI increased statistically by 52.0% ($p=0.009$) and 48.8% ($p=0.008$), respectively, while the concentration of hepcidin decreased by 19.4% ($p=0.044$) compared to the control group. Although the concentration of AMPs in the third trimester decreased compared to the first trimester, it still remains high compared to the control. It protects the fetus from infection by activating neutrophils. The concentration of hepcidin decreases against the background of increasing body requirements for ferrum.

AFP, estriol, and β -hCG are used for diagnosis and monitoring purpose during pregnancy. The concentration of AFP increases 3.1 times ($p<0.001$) in the first trimester and 2.4 times ($p<0.001$) in the

third trimester. In normal pregnancy, the concentration of β -hCG in the first trimester is 37643.4 ± 2129.5 ng/ml, and in the third trimester it decreases slightly to 30791.5 ± 1493.3 ng / ml.

Unlike non-pregnant women, 90% of estrogens in the body of pregnant women are estriol. Estriol neutralizes the effects of estrone and estradiol, weakening the ability of the uterus to mature. There was a significant increase in estriol concentration - 37.9 times ($p < 0.001$) in the first trimester and 46.3 times ($p < 0.001$) in the third trimester in the blood of pregnant women not infected with TORCH infections.

As a result of the research, the concentration of prolactin in pregnant women without TORCH infections increased statistically 3.1 times ($p < 0.001$) in the first trimester and 21.3 times ($p < 0.001$) in the third trimester compared to the control group. As a result of the biological effect of prolactin, the development of the mammary glands and the lactation process are stimulated. In pregnant women, DHEA is the main substrate for estradiol synthesis in the placenta and therefore its level in the blood decreases during pregnancy. DHEA concentrations decreased 2.3 times ($p < 0.001$) in the first trimester and 41.1% ($p < 0.001$) in the third trimester compared to the control group.

Thus, in pregnant women not infected with TORCH infections, the concentration of both inflammatory and anti-inflammatory cytokines tends to increase, a statistically significant increase is determined in the concentration of lactoferrin and defensin, AFP, estriol and prolactin and a decrease in the concentration of DHEA.

Concentration of cytokines, antimicrobial peptides and hormones in the blood of women infected with TORCH infections and ending pregnancy by birth

The additional antigen load caused by TORCH infections in the fetus activates inflammatory immune mechanisms and disrupts complicated pregnancies. In pregnant women not infected with TORCH infections, the Th-2 type humoral immune response predominates over the Th-1 cell cellular immune response. This

leads to decrease in Th1/Th2 ratio in pregnant women. The concentration of IL-2 and IL-4 in the blood of women infected with TORCH and terminating pregnancy in the first trimester varies within control limits. In the first trimester, controlled to the control group, the concentration of IL-6, IL-8, TNF- α and IFN- γ increased by 2.2 times ($p=0.003$); 76.0% ($p=0.011$); 44.7% ($p=0.023$) and 41.8% ($p=0.477$), respectively. Compared to pregnant women without TORCH infections, concentration of IL-6 increased by 2.0 times ($p=0.002$); IL-8 increased by 38.7% ($p=0.050$). In the study group, the concentration of IL-10 did not change compared to pregnant women not infected with TORCH, but decreased by 38.0% ($p=0.026$) compared to the control group.

Significant changes in the concentration of cytokines in the blood of pregnant women with TORCH infections are observed in the third trimester. The results show that in pregnant women with TORCH infections, the concentration of IL-2 and IL-4 in the third trimester varies within control limits and approaches the indicators of pregnancy not infected with TORCH infections (Table 2).

The concentration of IL-6 increased statistically by 47.4% ($p=0.051$) compared to the control group and decreased by 32.1% ($p=0.012$) compared to the first trimester. This result is not significantly different from pregnant women not infected with TORCH infections.

In the third trimester, the concentrations of IL-8, TNF- α , and IFN- γ did not change significantly compared to the first trimester and pregnant women not infected with TORCH infections, but compared to the control, the concentration of TNF- α statistically increased by 35.0% ($p=0,023$). High concentrations of TNF- α indicate an increase in the cytotoxic potential of mononuclear cells in the blood and the functional activity of phagocytic monocytes.

In the third trimester, the concentration of IL-10 decreased statistically by 29.2% ($p=0.014$) compared to pregnancies not infected with TORCH infections, and by 26.8% ($p=0.024$) relative to the first trimester.

Thus, the concentration of IL-6, IL-8 and IFN- γ in the blood of pregnant women infected with TORCH infections is significantly

higher than in pregnant women not infected with TORCH. Decreased levels of inflammatory cytokines in the third trimester are important in ending pregnancy by birth. The fact that the concentration of inflammatory cytokines in the third trimester is higher compared to the control group and the anti-inflammatory cytokines do not differ from the control limits is considered as a link in the mechanism of childbirth.

Table 2
Concentration of some cytokines in the blood of women infected with TORCH infections and ending pregnancy by birth (M±m)

Indicators	Groups			
	Women infected with TORCH infections (n=33)		Women without TORCH infections (n=29)	
	I trimester	III trimester	I trimester	III trimester
Il-2, pg/ml	1,48 ± 0,16 (0,1 – 3,2)	1,64 ± 0,16 (0,3 – 4,3)	1,76 ± 0,25 (0,3 – 7,7)	1,52±0,18 (0,4-4,7)
Il-4, pg/ml	0,986 ± 0,093 (0,06 – 1,94)	1,026 ± 0,096 (0,11 – 1,99)	1,252 ± 0,190 * (0,5 – 6,2)	1,152±0,155 (0,3-4,0)
Il-6, pg/ml	4,74 ± 0,46 * ^ (0,22 – ,08)	3,22 ± 0,31 # (0,24 – ,29)	2,39 ± 0,3 (0,9 – 9,7)	2,98±0,25 (0,6-4,5)
Il-8, pg/ml	7,20 ± 0,73 * ^ (0,07 – 4,1)	5,80 ± 0,53 (1,11 – 11)	5,19 ± 0,63 (0,3 – 12,4)	5,37±0,61 (0,9-12)
Il-10, pg/ml	10,76 ± 0,88 * (0,9 – 17,7)	7,88 ± 0,78** # (0,5 – 15,3)	10,43 ± 1,09 (0,7- 20,2)	11,13±0,98 (4-20)
TNF-α, pg/ml	1,205 ± 0,12 * (0,11 – 2,38)	1,125 ± 0,109 * (0 – 2,09)	1,415 ± 0,241 * (0,04 – 6,7)	1,087±0,127 * (0,25-3,78)
IFN-γ, pg/ml	5,10 ± 0,51 (0,3 – 9,6)	4,32 ± 0,46 (0,3 – 8,5)	4,02 ± 0,46 (0,5 – 9,2)	3,87±0,40 (0,7-8,9)

Note: * - compared to the control group; ^ - compared with pregnant women without TORCH infections; # - statistical accuracy of the difference compared to the results of the first trimester

Concentrations of lactoferrin, endotoxin, hepcidin, BPI and defensin in the blood of women infected with TORCH infections and ending pregnancy by birth in the first trimester were 2.3 times (p<0.001); 63.1% (p=0.001); 37.5% (p= 0.018); 3.8 times (p<0.001)

and 2.1 times ($p < 0.001$) higher respectively compared to the control group and 31.5% ($p = 0.001$); 10.8% ($p = 0.023$); 53.8% ($p < 0.001$); 3.0 times ($p < 0.001$) and 38.8% ($p = 0.001$) higher compared to pregnant women not infected with TORCH infections. Increased endotoxin in the blood is considered a major indicator of endotoxemia.

In the third trimester, the concentration of lactoferrin increased by 32.0% ($p = 0.004$) compared to the control group, but decreased by 42.7% ($p < 0.001$) compared to the results of the first trimester. Endotoxin concentrations increased by 15.5% compared to the control group and approached the indicators of pregnant women not infected with TORCH infections. This figure is significantly 29.2% ($p < 0.001$) lower than in the first trimester.

In this group, the concentration of hepcidin varies within the control limits, it increases by 27.6% ($p = 0.009$) compared to pregnant women without TORCH infections, a statistically significant decrease of 25.2% ($p = 0.003$) is observed compared to the results of the first trimester. BPI concentrations increased 5.4 times ($p < 0.001$) compared to the control group, 3.6 times ($p < 0.001$) compared to pregnant women not infected with TORCH infections and 42.0% ($p = 0.039$) compared to the results of the first trimester. The concentration of defensin (66.3 ± 3.2 pg/ml) decreased by 44.1% ($p < 0.001$) compared to the results of the first trimester and differed little from the results of pregnant women not infected with TORCH infections (Table 3).

Thus, the concentration of AMPs in the blood of women infected with TORCH and ending pregnancy by birth increases significantly and this increase is expressed more in the concentration of BPI. Compared to the first trimester, a statistically significant decrease in AMPs concentration in the third trimester is one of the important conditions for the continuation of pregnancy.

In the first trimester, AFP concentrations increased 5.6 times ($p < 0.001$) compared to the control group and 82.1% ($p < 0.001$) compared to pregnancies not infected with TORCH infections. The concentration of β -hCG (22940.0 ± 1980.6 pg/ml) increased several times compared to the control group, but this indicator decreased significantly by 39.1% ($p < 0.001$) compared to pregnancies not

infected with TORCH infections.

Table 3
Concentration of some antimicrobial peptides in the blood of women infected with TORCH infections and ending pregnancy by birth (M±m)

Indicators	Groups			
	Women infected with TORCH infections (n=33)		Women without TORCH infections (n=29)	
	I trimestr	III trimestr	I trimestr	III trimestr
Lactoferrin, pg/ml	1,752 ± 0,090 (0,86 – 2,55) * ^	1,004 ± 0,051 (0,45 – 1,48) * #	1,332 ± 0,075 (0,51 – 1,97) *	1,156 ± 0,103 (0,25-2,3) *
Endotoxin, pg/ml	0,347 ± 0,017 (0,19 – 0,55) * ^	0,245 ± 0,011 (0,13 – 0,35) #	0,313 ± 0,035 (0,16 – 1,16) *	0,256±0,021 (0,08-0,045)
Hepsidine, pg/ml	14,28 ± 0,81 (7,8 – 22,5) * ^	10,68 ± 0,52 (3,5 – 15,9) ^ #	9,29 ± 0,28 (4,9 – 11,2) *	8,37±0,63 (1,9-14,3) *
BPI, pg/ml	1,260 ± 0,150 (0,02 – 2,54) * ^	1,788 ± 0,177 (0,18 – 3,47) * ^ #	0,422 ± 0,072 (0,04 – 1,95) *	0,495±0,043 (0,18-0,86) *
Defensin, pg/ml	118,6 ± 6,4 (60,4 – 178) * ^	66,3 ± 3,2 (33,7 – 95,7) #	85,4 ± 5,4 (33,4 - 124) *	60,8±4,7 (19,2-103,2)

Note: * - compared to the control group; ^ - compared with pregnant women without TORCH infections; # - statistical accuracy of the difference compared to the results of the first trimester

Compared to the control group, in this group, the concentration of estradiol and prolactin in the first trimester increased by 91.8% (p<0.001) and 9.7 times (p<0.001) and compared to the pregnant women without TORCH infections 67.6% (p<0.001) and 3.1 times (p<0.001). Estriol concentrations increased 6.2 times (p<0.001) compared to pregnant women not infected with TORCH and many times compared to the control group. In contrast, the concentration of

DHEA decreased by 2.8 times ($p < 0.001$) compared to the control group and by 20.0% ($p = 0.028$) compared to pregnant women not infected with TORCH infections (Figure 1).

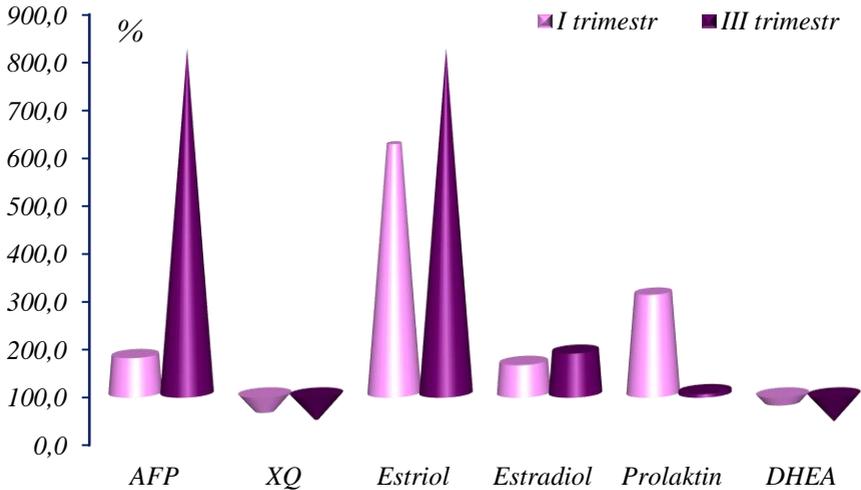


Figure 1. Concentration of some hormones in the blood of women infected with TORCH infections and ending pregnancy by birth (compare group - 100%)

In the third trimester, the concentration of AFP increased by 20.0 times ($p < 0.001$) compared to the control group and average rate was 69.1 ± 2.9 pg/ml. This indicator was 8.2 times ($p < 0.001$) higher than in pregnant women not infected with TORCH and 3.6 times higher ($p < 0.001$) than in the first trimester. The concentration of β -hCG increased several times compared to the control group and average rate was 13301.3 ± 1458.6 pg/ml. Compared to pregnancies not infected with TORCH infections, this indicator was 2.3 times ($p < 0.001$), and 42.0% ($p < 0.001$) higher compared to the results of the first trimester.

In the third trimester, compared to the control group, the concentration of estradiol increased 2.5 times ($p < 0.001$), 91.6% ($p < 0.001$) compared to pregnant women not infected with TORCH infections and 29.4% ($p = 0.022$) compared to the results of the first

trimester. In this group, estriol concentrations increased several times compared to the control group, 60.2% ($p < 0.001$) compared to the first trimester, and 8.2 times ($p < 0.001$) compared with the results of pregnancies not infected with TORCH infections.

The concentration of prolactin increased by 2.1 times ($p < 0.001$) compared to the results of the first trimester, approaching the rates of pregnant women not infected with TORCH infections. The concentration of DHEA increased 35.2% ($p < 0.001$) compared to the results of the first trimester, 4.4 times ($p < 0.001$) compared to the control group and 2.6 times ($p < 0.001$) compared to the results of pregnant women not infected with TORCH.

The concentration of prolactin increased by 2.1 times ($p < 0.001$) compared to the results of the first trimester and approached the rates of pregnant women not infected with TORCH infections. The concentration of DHEA decreased 35.2% ($p < 0.001$) compared to the results of the first trimester, 4.4 times ($p < 0.001$) compared to the control group, and 2.6 times ($p < 0.001$) compared to the results of pregnant women not infected with TORCH.

Thus, the concentration of AFP in the blood of women infected with TORCH and ending pregnancy by birth increased compared to the rate of pregnant women not infected with TORCH, while the concentration of β -hCG decreased. In this group, the concentrations of estradiol, estriol and prolactin in the first and third trimesters increased significantly compared to the results of the first trimester, while the concentration of DHEA decreased.

Concentration of cytokines, antimicrobial peptides and hormones in the blood of women infected with TORCH infections and ending pregnancy with miscarriage

Change in the Th1/Th2 ratio in the direction of Th1 during pregnancy is one of the main reasons of miscarriages. Th1 has a direct cytotoxic effect on the cells of the embryo, activating the coagulation system, leading to the formation of intravascular thrombi, circulatory disorders and destruction of the fetus. As mentioned above, spontaneous abortions were reported in 7 pregnant

women with TORCH infections. Examination of the cytokine profile reveals serious disorders in their blood.

The concentration of IL-2 and IL-4 in this group tends to decrease by 34.2% and 11.2% compared to pregnant women ending pregnancy by birth and 44.9% and 30.0% compared to pregnant women without TORCH infections (Figure 2).

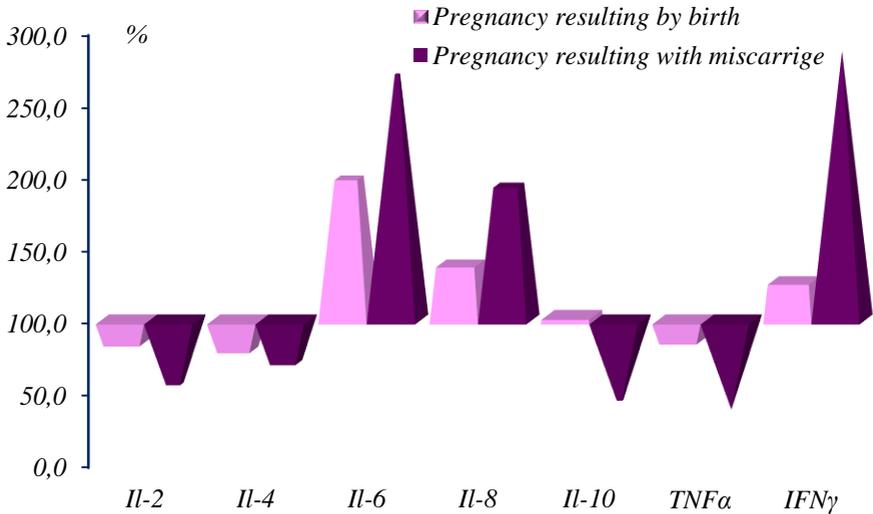


Figure 2. Concentration of cytokines in the blood of women infected with TORCH infections and ending pregnancy with miscarriage (compare group - 100%).

The concentration of IL-6, IL-8, and IFN-γ increased 3.0 times ($p=0.002$); 2.4 times ($p=0.005$); and 3.2 times ($p=0.006$) respectively compared to the control group; 2.7 times ($p<0.001$); 92.9% ($p=0.012$); 2.7 times ($p=0.048$) and 2.9 times ($p=0.005$) compared to pregnant women not infected with TORCH infections; 36,3%; 39,1%; 2,3 times ($p=0,029$) and 2,2 times ($p=0,044$) compared to pregnant women ending pregnancy by birth. The concentration of IL-10 decreased by 41.6% compared to the control group, 2.4 times ($p=0.006$) compared to the group without miscarriages and 2.3 times ($p=0.010$) compared to pregnant women without TORCH infections.

Thus, the secretion of Th1-type embryotoxic cytokines in miscarriages is accelerated and the immune and inflammatory response to trophoblasts is complicated. The concentration of IL-6, IL-8 and IFN- γ in the blood of women infected with TORCH and having miscarriage increases significantly compared to the corresponding indicators of pregnant women not infected with TORCH, while the concentration of IL-10 and TNF- α decreases.

Concentrations of lactoferrin, endotoxin, hepcidin, BPI and defensin increased 2.7 times ($p < 0.001$); 4.5 times ($p = 0.001$); 2.4 times ($p < 0.001$); 5.2 times ($p = 0.002$) and 4.1 times ($p < 0.001$) respectively compared to the control group, 54.7% ($p = 0.009$); 3.0 times ($p = 0.001$); 2.6 times ($p = 0.001$); 4.1 times ($p = 0.002$) and 2.8 times ($p = 0.003$) compared to pregnant women not infected with TORCH infections; 17.7 %, 2.7 times ($p = 0.003$); 71.3% ($p = 0.007$); 36.7% and 2.0 times ($p = 0.044$) compared women whose pregnancies resulted in childbirth (Figure 3).

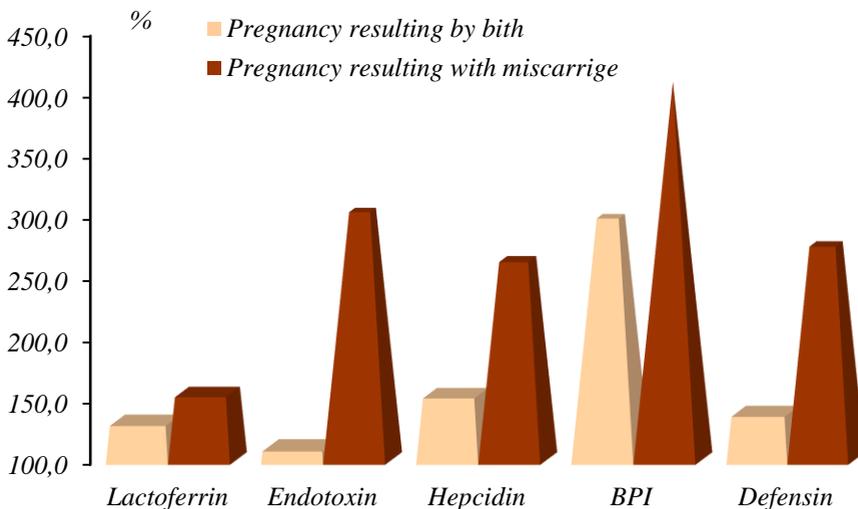


Figure 3. Concentration of some antimicrobial peptides in the blood of women infected with TORCH infections and ending pregnancy with miscarriage (compare group - 100%).

Thus, the concentration of AMPs in the blood of women infected with TORCH and having a miscarriage was significantly higher than that of women infected with TORCH and ending pregnancy by birth. This increase is observed more in the increase in the concentration of endotoxin and defensin.

During spontaneous abortions, the hormonal balance between mother and placenta-fetus is disturbed. The concentration of AFP increased 12.6 times compared to the control ($p < 0.001$), 4.1 times compared to the results of pregnancies not infected with TORCH infections ($p < 0.001$) and 2.3 times ($p < 0.001$) compared to the results of pregnant women infected with TORCH infections and ending pregnancy by birth (Figure 4).

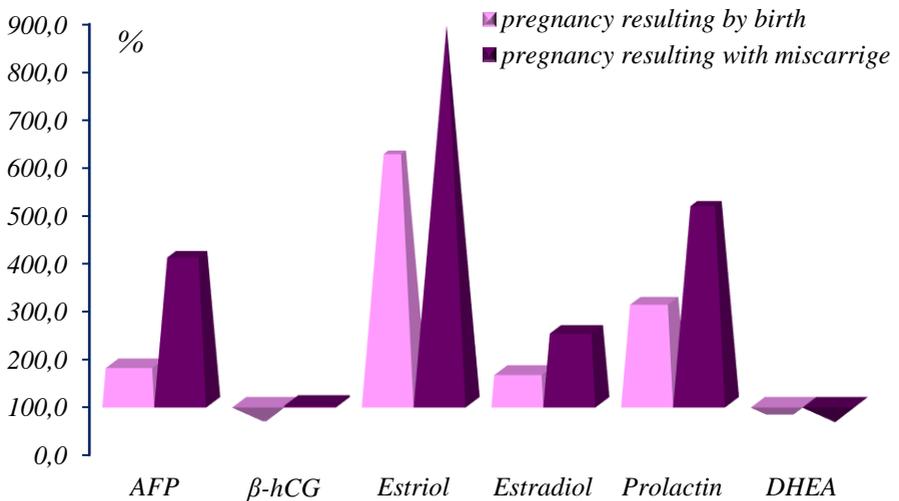


Figure 4. Concentration of some hormones in the blood of women infected with TORCH infections and ending pregnancy with miscarriage (compare group - 100%)

The concentration of β -hCG increases several times compared to the control group and varies within the limits of the corresponding values of pregnant women not infected with TORCH. Compared to women infected with TORCH infections and ending pregnancy by

birth, its concentration increased by 70.1% ($p=0.001$).

In the study group, the concentration of estradiol was 2.9 times higher than in the control group and 2.5 times higher than in pregnant women not infected with TORCH infections and 51.3% ($p=0.017$) higher than in women not having miscarriages and ending their pregnancies by birth.

Estradiol and prolactin concentrations increased several times and 16.0 times ($p<0.001$) compared to the control group, 8.9 times ($p<0.001$) and 5.2 times ($p<0.001$) compared to pregnant women without TORCH infections and 42.5% ($p=0.011$) and 64.5% ($p=0.019$) compared to pregnant women who had no miscarriage. The concentration of DHEA is reduced by 27.6% compared to the group without miscarriages. In general, the concentration of DHEA in this group decreased statistically significantly by 3.9 times ($p<0.001$) compared to the control group and by 42.1% ($p=0.001$) compared to pregnant women not infected with TORCH.

Thus, in the first trimester, the concentration of AFP, β -hCG, estradiol, estradiol, and prolactin in the blood of women with TORCH infections and miscarriages increased statistically significantly compared with the corresponding results of women who ended their pregnancies by birth, while the concentration of DHEA decreased.

The correlative relationships between cytokines, AMPs and hormones in pregnant women with TORCH infections

The study found a correlation between cytokines, AMPs and the endocrine system in pregnant women with TORCH infections. As a result of Spearman's correlation analysis, a correlation was observed between the indicators of pregnant women involved in the study. Thus, a negative correlation between IL-2 and IL-4 ($p=-0.373$; $p=0.032$) was found in the blood of 33 women infected with TORCH and whose pregnancy ended by childbirth. In addition, a positive correlation was found between IL-8 and IL-4 ($p=0.447$; $p=0.009$) and IL-2 ($p=0.589$; $p<0.001$). The results show that a decrease in IL-2 leads to an acceleration of the synthesis of IL-4 and IL-8 in the blood. There is a positive correlation between IL-6 and IL-10

($p=0.386$; $p=0.026$) and a negative correlation between IFN- γ ($p=-0.438$; $p=0.011$). This suggests that IL-6 has a stimulating effect on IL-10 synthesis and IFN- γ has a suppressive effect.

A negative correlation was found between IL-2 and prolactin ($p=-0.389$; $p=0.025$), and a positive correlation ($p=0.355$; $p=0.045$) between IFN- γ and prolactin. This dependence suggests that an increase in IFN- γ during infectious pregnancy accelerates prolactin synthesis. In contrast, increased prolactin may suppress IL-2 synthesis. A positive correlation was also observed between estradiol and BPI ($p=0.356$; $p=0.042$) in this group.

The negative correlation between IL-10 and IL-6 ($p=-0,571$) and IL-8 ($p =-0,821$; $p=0.023$) in the blood of pregnant women with TORCH infections and accompanied by miscarriage is one of the evidences of weakening the synthesis and expression of cytokines and exacerbation of inflammation at the background of increase in inflammatory cytokines. According to the results of the study, a negative correlation was observed between lactoferrin and IL-2 ($p=-0.786$; $p=0.036$) and positive correlation between IL-6 ($p=0.643$). An increase in the concentration of IL-6 and a decrease in IL-2 in pregnant women increase the risk of miscarriage. Negative correlation is observed between endotoxin and IL-6 ($p=-0.786$; $p=0.036$). Thus, an increase in the concentration of endotoxin in pregnant women leads to a decrease in the synthesis of IL-6. Moreover, a negative correlation is observed between endotoxin and BPI ($p=-0.788$; $p=0.036$) and defensin ($p=-0.821$; $p=0.023$), hepcidin and estradiol ($p=-0.893$; $p=0.007$) and positive correlation between BPI and defensin ($p=0.929$; $p=0.003$) and prolactin ($p=0.786$; $p=0.035$). A positive correlation between TNF- α and estradiol ($p=0.821$; $p=0.023$), IFN- γ and estradiol ($p=0.788$; $p=0.036$) indicates a direct relationship between the synthesis of inflammatory cytokines and hormones.

According to the results of the correlation analysis, AMPs induces the synthesis of inflammatory cytokines, which can lead to miscarriages exacerbating inflammation.

The results of the research show that changes in the concentration of cytokines and AMPs in pregnant women with

TORCH infections, as well as endocrine disorders, indicate the development of inflammatory processes in the body of a pregnant woman, as well as the possibility of miscarriages. Thus, in pregnant women with TORCH infections, the concentration of inflammatory cytokines, AMPs, prolactin and estriol increases significantly, while the concentration of IL-10 and DHEA decreases. These disorders of the immune and hormonal systems are observed more in pregnant women ending pregnancies by miscarriages.

CONCLUSION

1. Compared to women not infected with TORCH, the concentration of IL-6, IL-8 and IFN- γ in the blood of women infected with TORCH and ending pregnancy increased 2 times ($p=0.002$); 38.7% ($p=0.050$) and 27.0% respectively in the first trimester and in the blood of pregnant women infected with TORCH and ending pregnancy by increased by 2.7 times ($p<0.001$); 92.9% ($p=0.012$) and 2.9 times ($p=0.005$) respectively, while the TNF- α concentration decreases statistically significantly by 2.7 times ($p=0.048$) [6, 8].

2. Compared to women not infected with TORCH, the concentration of IL-10 in the blood of women infected with TORCH and ending pregnancy decreased by 29.2% ($p=0.014$) in the third trimester and in the blood of pregnant women with TORCH infections and ending pregnancy by miscarriage - 2.3 times ($p=0.010$) [8].

3. Compared to pregnant women not infected with TORCH, the concentration of lactoferrin, endotoxin, hepcidin, BPI and defensin in the blood of pregnant women infected with TORCH and resulting in miscarriage increased 54.7% ($p=0.009$); 3.0 times ($p=0.001$); 2.6 times ($p<0.001$); 4.1 times ($p=0.002$) and 2.8 times ($p=0.003$) respectively [7].

4. Compared to pregnant women not infected with TORCH, estriol in the blood of pregnant women infected with TORCH and resulting in miscarriage increased 8.9 times ($p<0.001$); estradiol increased 2.5 times ($p<0.001$) and prolactin 5.2 times ($p<0.001$),

The defense will be held on “ ____ ” _____ 2022, at _____
at the meeting of the Dissertation council FD 2.31 at Baku State
University

Address: AZ 1073/1, Baku, Academician Zahid Khalilov str.33,
BSU, main building, IV floor, 445th auditorium.

Dissertation is accessible at the library of Baku State University.

Electronic versions of the dissertation and its abstract are available
on the official website of the Baku State University
(<http://elibrary.bsu.edu.az>).

Abstract was sent to the required addresses “ ____ ”
_____ 2022.

Signed for printing: 20.05.2022

Paper format: 60x84 ¹/₁₆

Volume: 35.749 characters

Number of hard copies: 30