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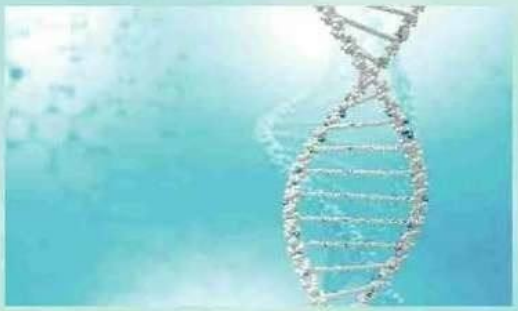

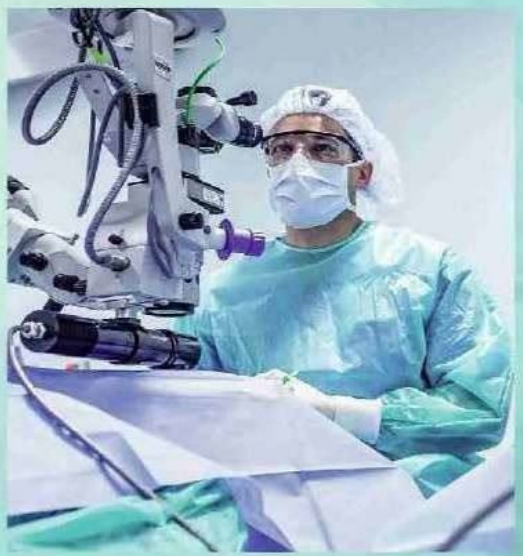

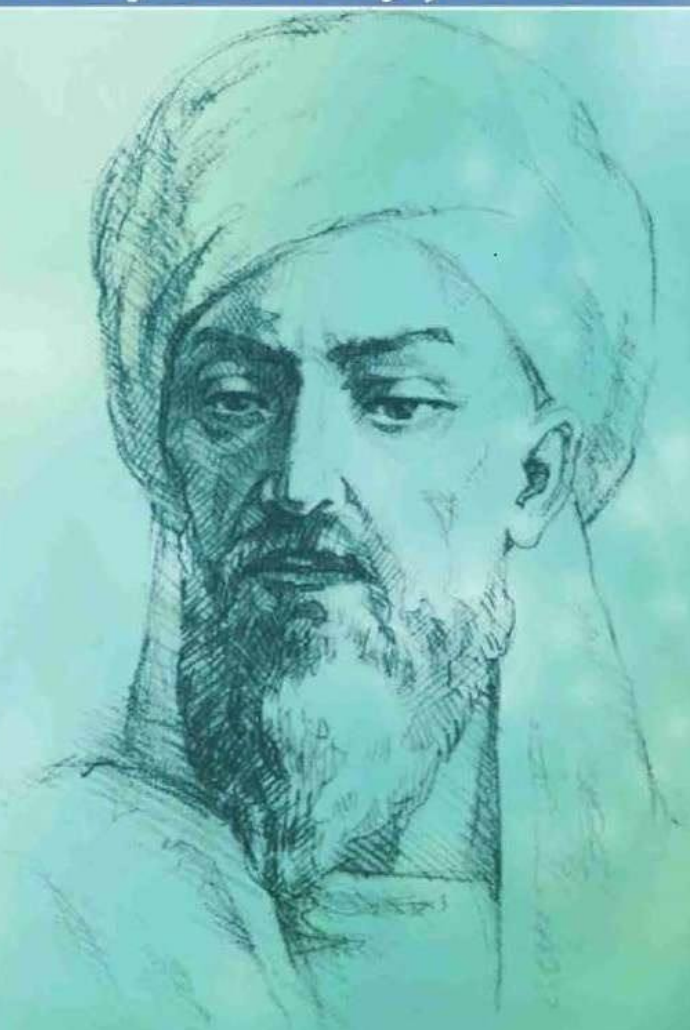

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ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

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CHANGES IN IMMUNOLOGICAL PARAMETERS IN WOMEN IN EARLY PREGNANCY WHO HAVE MISCARRIAGES WITH GENITAL INFECTIONS

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✓ ***Resume***

The work studied changes in the cellular link of immunity, as well as pro-inflammatory and anti-inflammatory interleukins, which were noted in women in the early stages of up to 12 weeks of pregnancy with a full pregnancy with genital infections, these changes were more pronounced in women who had miscarriages with genital infections. More pronounced changes in women who have miscarriages with genital infections are associated with the presence of an excessive immune response.

Key words: interleukins, early pregnancy, miscarriage, genital infections, cellular immunity.

ИЗМЕНЕНИЕ ИММУНОЛОГИЧЕСКИХ ПОКАЗАТЕЛЕЙ У ЖЕНЩИН НА РАННИХ СРОКАХ БЕРЕМЕННОСТИ ИМЕЮЩИХ ВЫКИДЫШИ С ГЕНИТАЛЬНЫМИ ИНФЕКЦИЯМИ

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✓ ***Резюме***

В работе изучались изменения клеточного звена иммунитета, а также провоспалительных и противовоспалительных интерлейкинов, которые отмечались у женщин в ранние сроки до 12 недель беременности, имеющих полноценную беременность с генитальными инфекциями, эти изменения в большей мере проявлялись у женщин, имеющих выкидыши с генитальными инфекциями. Более выраженные изменения у женщин, имеющих выкидыши с генитальными инфекциями, связаны с присутствием чрезмерной иммунной реакции.

Ключевые слова: интерлейкины, ранние сроки беременности, невынашивание беременности, генитальные инфекции, клеточный иммунитет.

ANAMNEZIDA HOMILA TUSHISHI KUZATILGAN VA JINSIY A'ZOLAR INFEKTSIYALARI MAVJUD AYOLLARDA HOMILADORLIKNING DASTLABKI BOSQICHLARIDA IMMUNOLOGIK PARAMETRELARNING O'ZGARISHI.

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✓ ***Rezyume***

Ishda immunitetning hujayrali aloqasidagi o'zgarishlar, shuningdek yallig'lanish oldi va yallig'lanishga qarshi interleykinlar o'rganildi, ular homiladorlikning 12 xaftaligigacha bo'lgan dastlabki bosqichlarida genital infektsiyalari mavjud to'liq homiladorlik bilan ayollarda qayd etilgan, bu o'zgarishlar anamnezida o'z-o'zidan homila tushishi bo'lgan va jinsiy a'zolar infektsiyalari mavjud ayollarda ko'proq aniqlanadi. anamnezida o'z-o'zidan homila tushishi bo'lgan va jinsiy a'zolar infektsiyalari mavjud ayollarda yaqqol o'zgarishlar immunitetning haddan tashqari reaksiyasi bilan bog'liq.

Kalit so'zlar: interleykinlar, erta homiladorlik, abort, genital infektsiyalar, hujayra immuniteti.

Relevance

Inflammation is part of the host's defense response against microbial infection. It covers the phagocytic function of macrophages and neutrophils during bacterial infection; recognition, activation and cytotoxic activity of T-cells and B-cells during viral infection; and the critical roles of these immune cells in destroying microbes. However, the concept of inflammation has been widely accepted as an immune response independent of pathogenic infection. [1].

In reproduction, many complications during pregnancy are due to inadequate inflammation. Microbial infection is an important factor in the development of complications during pregnancy; however, sometimes these complications do not reveal obvious pathogens. These data indicate that the development of complications during pregnancy can be caused by both microbial and non-microbial causes [4].

Many clinical cases of preterm birth are thought to occur without overt infection. Indeed, antibiotics are not always beneficial in the treatment of preterm labor [2].

Previous studies have reported that bacterial infection induces the production of pro-inflammatory cytokines (eg, interleukin (IL)-1β, tumor necrosis factor (TNF)-α, and IL-8), inflammatory mediators (eg, platelet activating factor, prostaglandins) [8].

The production of IL-1 in the decidua can promote the production of prostaglandins in the decidua and amnion and is an important factor inducing labor during intrauterine infection [6]. In addition, IL-1 can cause contractions of the myometrium, leading to preterm labor [7]. TNF-α, produced by the decidua in response to bacterial infection, can also promote the production of prostaglandins by the decidua, amnion, and myometrium [5]. Thus, bacterial infection is an important finding for initiating precocious cervix, labor, and rupture of membranes.

The impact of infections on early pregnancy remains controversial, as some studies indicate an increased risk of miscarriage while others do not show an increased risk. Therefore, further research is needed to find out whether certain infections actually increase the risk of miscarriage. It has been suggested that not just the presence of the bacteria themselves, but differences in host response to the presence of genital infections may contribute to an increased risk of preterm birth [3].

The purpose of the study: to study the change in immunological parameters in the presence and absence of genital infections in women in early pregnancy.

Material and methods

In the work, 88 women were examined, which were divided into 2 groups. Group 1 included 32 women who had a full pregnancy and full birth, who had no genital infections before pregnancy. Group 2 included 28 women who had a full pregnancy and full birth, who had genital infections before pregnancy (Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis). Group 3 included 27 women who had a history of miscarriages up to 12 weeks of gestation, an excessive pro-inflammatory immune response, who had genital infections before pregnancy (Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis).

In the blood of women before pregnancy, after 6 and 12 weeks, the following indicators were determined by ELISA: pro-inflammatory - interleukin-1β (IL-1) and tumor necrosis factor-α (TNF-α), and anti-inflammatory - interleukin-10 (IL-10) using the test systems of CJSC Vector-Best. In addition, an immunogram was studied, and in a scraping from the cervix before pregnancy, indicators of chlamydia (DNA of Chlamydia trachomatis), mycoplasmosis (DNA of Mycoplasma hominis) and ureoplasmosis (DNA of Ureaplasma urealyticum) were determined by PCR using test systems CJSC "Vector-Best" Russia.

Results and its discussion

From the results of the study of pro-inflammatory and anti-inflammatory interleukins, it was determined that in the blood of women of the 1st group, at the 6th week of pregnancy, the results of pro-inflammatory interleukin TNF-α were significantly higher than those before pregnancy. At the same time, in women, these results at the 12th week of pregnancy were not significantly greater than at the 6th week of pregnancy and were significantly more significant than similar results before pregnancy (Table 1).

In the study of the results of TNF-α in women of group 2 at 6 weeks of pregnancy, this figure was significantly higher than similar data before pregnancy. At the same time, the results at 12 weeks of pregnancy were not significantly more than at 6 weeks of pregnancy and significantly more significant than similar data before pregnancy. At the same time, in women of group 2, the results of TNF-α, before pregnancy there were significantly more similar data in women without infections.

In women of the 3rd group, the TNF-α index before pregnancy is significantly and significantly, more than 2.0 times, was higher than in women of the 1st group. At the 6th week of pregnancy, women of the same group of TNF-α also significantly and significantly, more than 3.1 times, had more similar results than women in group 1, and also significantly and significantly, 1.9 times, higher than the results before pregnancy.

Table 1.

Changes in immunological parameters in women in early pregnancy

INTERLEUKINS				
Investigational Indicators	**Group**	**Before pregnancy**	**6 weeks gestation**	**12 weeks gestation**
TNF-a pg/ml	1	6,2±0,8	9,7±1,2*	11,9±1,5 *
	2	9.6±1.1^{o}	12,7±1,4*	15,2±1,6 *
	3	19.5±2.2^{o}	38.8±4.3*^{o}	48.1±5.1 *^{o}
IL-1β pg/ml	1	3,7±0,4	7,2 ± 0,9*	10,1±1,2*
	2	6.5±0.8 ^{o}	10,3 ± 1,2*	13,2±1,4*
	3	14.9±1.7 ^{o}	26.5 ± 3.1*^{o}	33.6±3.7*^{o}
IL-10 pg/ml	1	9,3±1,2	7,4±0,8	5,9±0,7*
	2	8,5±1,0	6,3±0,7	4,6±0,5*
	3	4.2±0.6 ^{o}	2.7±0.4*^{o}	2,1±0,3*^{o}

Note: 1- women who have a full pregnancy without genital infections; 2 - women who have a full pregnancy with genital infections; 3 - women who have miscarriages with genital infections.

**- significantly different values to the indicators before pregnancy.*

^{o} - significantly different values to the indicators of group 1.

At the 12th week of pregnancy in women of group 3, TNF-α also significantly, more than 3.2 times, had more similar results in women of group 1, and also significantly, 2.5 times, higher than before pregnancy in women of the same group (Table 1).

A similar direction of change in IL-1β parameters was noted in women of groups 1,2, and 3(Table1).

At the same time, in the blood of women of the 1st group, at the 6th week of pregnancy, the results of anti-inflammatory interleukins IL-10 were not significantly less than those before pregnancy. At the same time, this indicator in women at the 12th week of pregnancy was not significantly lower than at the 6th week of pregnancy and significantly less than similar results before pregnancy. IL-10 levels in women of the 2nd group after 6 weeks of pregnancy were also not significantly lower than similar results before pregnancy. These results at 12 weeks of gestation were also not significantly lower than at 6 weeks of gestation and significantly less than similar results before pregnancy. At the same time, the IL-10 index in women of the 2nd group before pregnancy was not significantly lower than similar data of the 1st group. At the same time, IL-10 in women of group 3 before pregnancy was significantly, 2.2 times, lower than those of women in group 1 and significantly, 2.0 times, less than women of group 2.

Table 2.

Changes in cellular immunity in women in early pregnancy

Immunogram						
Indicators	**Norm**		**Group**	**Before Pregnancy**	**6 weeks gestation**	**12 weeks gestation**
Leukocytes	V 1 µl	4000-10000	1	5200±463	4700±418	5450±457
			2	5600±519	5950±536	6200±558
			3	4900±457	5200±496	5800±549
Lymphocytes	%	20-40	1	35±3,1	31±2,6	28±2,4
			2	31±2,5	23±1.8 º	19±1,6*º
			3	24±2.2 º	19±1.5 º	16±1,2*º
	V 1 µl	800-4000	1	1820±159	1457±127	1526±139
			2	1736±148	1369±113 º	1178±94*º
			3	1176±112 º	988±86 º	928±81*ˢ
B-lymphocytes (CD20)	%	10-36	1	32±2,9	27±2,4	25±2,3
			2	27±2,3	21±1,6*	17±1,4*o
			3	23±2.1 º	18±1,3*o	15±1.2*s
	V 1 µl	162-700	1	582±53	393±34*	381±33*
			2	468±38	287±23*s	200±15*s
			3	271±24 º	178±15*s	139±12*º
T lymphocytes (CD3)	%	48-80	1	56±5,1	49±4,3	44±3,7
			2	48±4,5	43±3,9	39±3,5
			3	41±3.6 º	33±3.1 º	29±2,6*º
	V 1 µl	800-2400	1	1019±95	713±64*	623±52*
			2	833±74	588±55*	459±38*
			3	482±43	326±28*ˢ	269±23*ˢ
Helper T-cells (CD4)	%	24-42	1	25±2,1	23±1,7	20±1,5
			2	22±1,6	21±1,4	19±1,3
			3	20±1,7	17±1.5 º	15±1,2*º
T-suppressors (CD8)	%	14-29	1	15±1,2	17±1,3	18±1,6
			2	16±1,4	18±1,5	20±1,7
			3	18±1,5	21±1,9	24±2.1º
CD4/ CD8		1,2-2,0	1	1,7±0,13	1,4±0,11	1,1±0,09*
			2	1,4±0,11	1,2± 0,08	1,0±0,07*
			3	1.3±0.10 º	1.1± 0.07 º	0,8±0,06*º
Natural killers-CD16	%	4-27	1	9,0±0,6	11±0,9	13±1,1*
			2	10,0±0,7	12,0±0,8	14,0±1,2*
			3	12.0±0.9 º	15.0±1.3 º	17,0±1,5*º
CD25 activated lymphocytes	%	7-18	1	11±0,8	13±1,0	15±1,3*
			2	12±0,9	14±1,1	17±1,4*
			3	14±1,2	17±1.5 º	20±1,7*ˢ
CD95 (apoptosis marker)	%	34-46	1	15±1,2	12±0,9	10±0,7*
			2	13±1,1	10±0,7*	9±0,6*
			3	12±1,0	9±0,6*º	7±0.5* about

Note: 1- women who have a full pregnancy without genital infections; 2 - women who have a full pregnancy with genital infections; 3 - women who have miscarriages with genital infections.

**- significantly different values to the indicators before pregnancy.*

º - significantly different values to the indicators of group 1.

Also, the results of group 3 at week 6 are 1.6 times and at week 12 of pregnancy 2.0 times less in relation to the indicators before pregnancy. In addition, IL-10 in women of the 3rd group, at the 6th week of pregnancy was 2.7 times less in relation to the same indicator in the 1st group and 2.3 times lower in relation to the similar result of the 2nd group, and at the 12th week of pregnancy it was less in 2.8 times in relation to group 1 and 2.2 times in relation to group 2 (Table 1).

When studying the cellular link of immunity (Table 2), there was no significant difference in the content of leukocytes in the blood of women in group 1 and women in group 2. There was also no significant difference in both groups in women at 6 and 12 weeks of pregnancy relative to women before pregnancy. At

the same time, there was not a significant decrease in the relative content of lymphocytes in % in women of the 1st group by 6 and even more at 12 weeks of pregnancy in relation to the results before pregnancy. A similar, but more significant direction of the decrease in the content of lymphocytes in % was observed in women of the 2nd group, with a significant difference in women of the 12th week of pregnancy in relation to women before pregnancy. When studying the absolute content of lymphocytes in 1 μl, there was an insignificant decrease in this indicator in women of group 1 and a significant decrease in group 2 at 6 and 12 weeks of pregnancy compared with women in group 1. In the 2nd group of pregnancy, at the 6th and 12th week of pregnancy in relation to the same indicators of women in the 1st group. Also, in women of the 3rd group, in relation to women before pregnancy, there was a significant decrease in the content of lymphocytes in 1 μl at the 12th week of pregnancy (Table 2).

In women of the 3rd group, a significant decrease in lymphocytes was revealed, both in relative and absolute terms, until a significant decrease in the content of lymphocytes in relative and absolute terms was observed at the 12th week of pregnancy in relation to women before pregnancy (Table 2).

According to the results of the study of B-lymphocytes, a significant decrease in this indicator in relative and absolute values was revealed at the 6th and 12th weeks of pregnancy in women of groups 1, 2, and 3 in relation to the results before pregnancy. Also, a significant decrease in B-lymphocytes in relative and absolute terms before pregnancy, at 6 and 12 weeks of pregnancy in women of the 3rd group, less pronounced in the 2nd group in relation to the similar results of the 1st group (Table 2). The direction of the change in T-lymphocytes was similar to that of B-lymphocytes, but less pronounced with a significant decrease in the relative indices of T-lymphocytes only at the 12th week of pregnancy in women of the 3rd group in relation to the same result before pregnancy in the same group. There was also a significant decrease in T-lymphocytes in women of the 3rd group before pregnancy, at 6 and 12 weeks of pregnancy in relation to the results of similar indicators in women of the 1st group. The change in T-lymphocytes in absolute terms was manifested in a significant decrease at 6 and 12 weeks of pregnancy in women of groups 1, 2, and 3 in relation to the results before pregnancy. Also in a significant decrease in this indicator at 6 and 12 weeks of pregnancy in women of the 3rd group in relation to the same indicators of women of the 1st group (Table 2).

The change in T-helpers was found in a significant decrease at the 12th week of pregnancy in group 3 in relation to similar data before pregnancy in this group and a significant decrease at 6 and 12 weeks of pregnancy in group 3 in relation to similar results in group 1 (Table 2). In the study of T-suppressors, a slight increase in this indicator at 6 and 12 weeks of pregnancy in groups 1, 2, and 3 was revealed in comparison with the results before pregnancy and with a significant increase at 12 weeks of pregnancy in women of the 3rd group of T-suppressors in relation to similar the results of group 1. The transformation of the CD4 / CD8 ratio was manifested in all groups in a decrease in groups 6 and 12, but significant at the 12th week of pregnancy in relation to before pregnancy. Also in a significant decrease in this indicator before pregnancy, at 6 and 12 weeks of pregnancy in group 3 in relation to similar results for women in group 1. The results of the study of natural killers and active lymphocytes (Table 2) had the same direction of changes, which was expressed in an increase in these indicators at 6 and 12 weeks of pregnancy, with a significant increase at 12 weeks compared to before pregnancy. With this, a significant increase at 6 and 12 weeks of pregnancy in group 3 in relation to the results of group 1. The results of the study of apoptosis markers showed, in relation to the results before pregnancy, a significant decrease in this indicator by 12 weeks in women of the 1st group, by 6 and 12 weeks in women of the 2nd and 3rd groups in relation to before pregnancy. Also, a significant decrease at 6 and 12 weeks of pregnancy in women of the 3rd group in relation to similar results of the 1st group (Table 2).

From the presented results, it can be seen that the level of pro-inflammatory interleukins TNF-α, IL-1β in the blood of women with a full pregnancy with genital infections at 6 and 12 weeks of pregnancy was not significantly higher, and in women with miscarriages with genital infections they were significantly higher than in women with a full pregnancy. pregnancy without genital infections. The significant increase in pro-inflammatory interleukins in women who have miscarried with genital infections is apparently due to the presence of an excessive immune response. At the same time, the results of anti-inflammatory interleukin IL-10 in the blood had the opposite direction of changes in women with a full pregnancy with genital infections at 6 and 12 weeks of pregnancy, not significantly, and in women with miscarriages with genital infections, they were significantly less than in women with a full pregnancy without genital infections. A significant decrease in anti-inflammatory interleukins in women who have miscarriages with genital infections is also apparently associated with the presence of an excessive immune response.

In the study of the cellular link of immunity, no significant changes in the content of leukocytes were observed. At the same time, there was a significant decrease in the relative and absolute content of lymphocytes at 6 and 12 weeks of pregnancy in women with a full pregnancy with genital infections and

more pronounced in women with miscarriages with genital infections than in women with a full pregnancy without genital infections. A significant decrease in lymphocytes in women who have miscarriages with genital infections is also associated with the presence of an excessive immune response. A similar direction of changes was observed in the study of B-lymphocytes, but less pronounced in relative terms. These changes in B-lymphocytes and T-lymphocytes also had the opposite direction of modifications in relation to the pro-inflammatory interleukins TNF-α and IL-1β and the same direction in relation to the anti-inflammatory interleukins IL-10.

A significant decrease in T-helpers and an increase in T-suppressors in women who have miscarriages with genital infections relative to women who have a full pregnancy without genital infections is apparently also associated with the presence of an excessive immune response. For the same reason and with a similar focus, there is a decrease in the CD4/CD8 ratio. Obviously, at 6 and 12 weeks of gestation, a significant increase in natural killers and activated lymphocytes, as well as a decrease in the apoptosis marker in women who have miscarriages with genital infections compared with women who have a full pregnancy without genital infections, is probably also associated with the presence of an excessive immune response. Thus, in women who have miscarriages with genital infections in relation to women who have a full pregnancy without genital infections, pronounced changes in the cellular link of immunity, pro-inflammatory and anti-inflammatory interleukins are associated with the presence of an excessive immune response.

Conclusions

Changes in the cellular link of immunity, as well as pro-inflammatory and anti-inflammatory interleukins, were noted in women in the early stages up to 12 weeks of pregnancy, who had a full pregnancy with genital infections, which were more pronounced in women who had miscarriages with genital infections. These more pronounced changes in women who have miscarriages with genital infections are associated with the presence of an excessive immune response.

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