UDC 618.177-089.888.11]-078.33:616.69-008.8

INFLUENCE OF INFECTIOUS FACTORS ON CHANGES IN IMMUNOLOGICAL INDICATORS IN WOMEN IN THE EARLY PERIOD OF PREVENTION OF PREGNANCY

Mukhitdinova K.O., Aleinik V.A., Babich S.M., Negmatshaeva Kh.N., Ibragimova S.R., Shokirova S.M.

Andijan State Medical Institute, Andijan, Uzbekistan

✓ ***Resume***

The study studied changes in immunological parameters and protease inhibitors in women who have a full-fledged pregnancy with infections of the genitourinary system and women who have miscarriages with an infection of the genitourinary system in the early stages of up to 12 weeks of pregnancy. It was concluded that the presence of infectious factors in the absence of a significant proinflammatory immune response in early pregnancy and a sufficient corrective reaction of protease inhibitors and TGF-β1 may contribute to a favorable course of early pregnancy and the development of a full-fledged pregnancy. However, in the presence of infectious factors and the presence of an excessive pro-inflammatory immune response in early pregnancy and an insufficient corrective reaction of protease inhibitors and TGF-β1, it can contribute to an unfavorable course of early pregnancy and the development of miscarriages.

Key words: interleukins, protease inhibitors, early pregnancy, miscarriage, infections of the genitourinary system, inflammatory process.

ВЛИЯНИЕ ИНФЕКЦИОННЫХ ФАКТОРОВ НА ИЗМЕНЕНИЯ ИММУНОЛОГИЧЕСКИХ ПОКАЗАТЕЛЕЙ У ЖЕЩИН НА РАННИХ СРОКАХ НЕВЫНАШИВАНИЯ БЕРЕМЕННОСТИ

Мухитдинова К.О., Алейник В.А., Бабич С.М., Негматшаева Х.Н., Ибрагимова С.Р., Шокирова С.М.

Андижанский государственный медицинский институт, Андижан, Узбекистан

✓ ***Резюме***

В работе изучалось изменения иммунологических показателей и ингибиторов протеаз у женщин имеющие полноценную беременность с инфекций мочеполовой системы и женщин имеющие выкидыши с инфекцией мочеполовой системы на ранних сроках до 12 недель беременности. Сделано заключение, что наличие инфекционных факторов при отсутствии значительной провоспалительной иммунной реакции в ранние сроки беременности и достаточной корригирующей реакцией ингибиторов протеаз и TGF-β1 может способствовать благоприятному течению ранних сроков беременности и развитию полноценной беременности. Однако в присутствии инфекционных факторов и наличие чрезмерной провоспалительной иммунной реакции в ранние сроки беременности и недостаточной корригирующей реакции ингибиторов протеаз и TGF-β1 может способствовать неблагоприятному течению беременности в ранние сроки и развитию выкидышей.

Ключевые слова: интерлейкины, ингибиторы протеаз, ранние сроки беременности, невынашивание беременности, инфекции мочеполовой системы, воспалительный процесс

ҲОМИЛАДОРЛИКНИНГ ЭРТА ДАВРИДАГИ ТУШИШ ХАВФИДА АЁЛЛАРДА ИММУНИТЕТ ИНДИКАТОРЛАРИНИНГ ЎЗГАРИШИГА ИНФЕКЦИОН ОМИЛЛАР ТАЪСИРИ.

Мухитдинова К.О., Алейник В.А., Бабич С.М., Негмашаева Х.Н., Ибрагимова С.Р., Шокирова С.М.

Андижон давлат тиббиёт институти, Андижон, Ўзбекистон

✓ ***Резюме***

Тадқиқот даврида урогенитал тизим инфекциялари бор ҳомиладор бўлган аёлларда ва урогенитал тизим инфекциялари бор 12 ҳафтагача хомиланинг тушиш мавжуд бўлган аёлларда иммунологик параметрлар ва протеаза ингибиторларининг ўзгаришини ўрганиб чиқилди. Ҳомиладорликнинг бошида сезиларли яллиғланишга қарши иммунитет реакцияси бўлмаганда юқумли омиллар мавжудлиги ва протеаза ингибиторлари ва TGF-β1 нинг етарли тузатувчи реакцияси эрта ҳомиладорликнинг қулай кечишига ва тўлиқ ривожланишига ёрдам бериши мумкин деган хулосага келинди. Аммо, агар юқумли омиллар мавжуд бўлиб, ҳомиладорликнинг бошида ҳаддан ташқари яллиғланишга қарши иммунитет реакцияси бўлса ва протеаза ингибиторлари ва TGF-β1 тузатувчи реакцияси етарли бўлмаса, бу эрта ҳомиладорликнинг ноқулай кечишига ва ҳомиланинг тушишига олиб келиши мумкин.

Калит сўзлар: интерлейкинлар, протеаза ингибиторлари, эрта ҳомиладорлик, ҳомила тушиш ҳавфи, урогенитал тизим инфекциялари, яллиғланиш жараёни

Relevance

Chlamydia trachomatis is one of the most commonly diagnosed sexually transmitted infections, but reports in the medical literature about the association between genital chlamydia infection and adverse obstetric outcomes are controversial. Genital chlamydial infection diagnosed during or before pregnancy does not significantly increase the risk of spontaneous premature birth [9, 4]. In other studies conducted to determine the relationship between Chlamydia tracohomatis and adverse pregnancy outcomes. There is evidence that chlamydia in pregnant women is associated with an increased likelihood of multiple adverse pregnancy outcomes [5, 6, 1].

The results of studies of the participation of M. hominis and U. urealyticum in preterm labor are also contradictory. Thus, the risk factors for vaginal infections M. hominis and U. urealyticum were studied using PCR in women who had undergone preterm labor and without preterm labor. The detection rate of M. hominis by PCR was higher than by the culture method (11.1% versus 4.0%, P = 0.010). The frequency of detection of U. urealyticum by PCR and cultivation was 16.7% and 57.1%, respectively. There was no significant difference in the prevalence of M. hominis and U. urealyticum between the groups with preterm labor and those without preterm labor [3].

In other studies, the results showed the number of copies of the U. urealyticum, M. hominis gene was higher in the recurrent spontaneous abortion group than in the normal pregnancy group of volunteers undergoing elective abortions (control group) who participated in the study. In addition, the expression level of IL-6, TNF-α, in the recurrent spontaneous abortion group was higher than that in the control group. These results support the idea that U. urealyticum and M. hominis can influence the occurrence of other bacterial infections and can stimulate recurrent spontaneous abortion and an inflammatory response [2, 7, 8].

The impact of infections on early pregnancy remains controversial, as some studies indicate an increased risk of miscarriage and others do not show an increased risk. Therefore, further research is needed to find out if certain infections actually increase the risk of miscarriage. It has been suggested that not just the presence of bacteria themselves, but differences in the host's response to the presence of genital infections, may contribute to an increased risk of preterm birth [5].

The aim of the study: to study changes in immunological parameters and protease inhibitors in women with an infection of the genitourinary system in the early stages of miscarriage.

Material and methods

In the work, 35 women were examined, who were divided into 2 groups. Group 1 included 18 women with a full pregnancy and full delivery, who had infections of the genitourinary system before pregnancy (Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis).

Group 2 included 18 women who had miscarriages at 12 weeks of pregnancy and also

had infections of the genitourinary system before pregnancy (Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis).

In the blood of women before pregnancy, at 6 and 12 weeks of pregnancy, the following parameters were determined by the ELISA method: proinflammatory - interleukin-1β (IL-1) and tumor necrosis factor-α (TNF-α), and anti-inflammatory - interleukin-10 (IL- 10) with the use of test systems of ZAO "Vector-Best" Russia, also transforming growth factor-β1 (TGF-β1) using test systems "DRG" Germany. In addition, the protease inhibitors α-1-anti-trypsin and α-2-macroglobulin were determined using test systems "Sentinel" Italy.

Result and discussion

In women of group 1, the TNF-α index at 6 weeks of gestation was 1.3 times significantly higher than the similar result before pregnancy. In the same group, TNF-α at 12 weeks of gestation was not significantly higher than at 6 weeks and reliably 1.6 times higher than the same indicator before pregnancy (table).

In women of the 2nd group, the TNF-α index before pregnancy was significantly and reliably more than 2.0 times higher than in women of the 1st group. At the 6th week of pregnancy, women in the same TNF-α group also significantly and reliably more than 3.1 times more than similar results for women in group 1, and also significantly and reliably 1.9 times higher than the results before pregnancy. At the 12th week of pregnancy, women in group 2 of TNF-α were also significantly more than 3.2 times more than similar results of women in group 1, and also reliably 2.5 times higher than indicators before pregnancy in the same group. (table).

As a result of the conducted studies of IL-1β, it was revealed that the changes in this indicator are similar to those of TNF-α. In women of the 1st group, the IL-1β index at 6 weeks of gestation was significantly higher than the similar result before pregnancy. In the same group, this indicator at 12 weeks of gestation was not significantly higher than at 6 weeks and significantly higher than the same indicator before pregnancy (table). In women of group 2, the IL-1β index before pregnancy was significantly and reliably higher than in women of group 1. At the 6th week of pregnancy in women of the same group, IL-1β is also significantly and reliably more than similar results for women in group 1, as well as significantly and reliably higher than the results before pregnancy. At the 12th week of pregnancy, women in group 2 also had significantly more similar results for women in group 1, and also significantly higher than indicators before pregnancy in the same group (table).

Table.

Changes in the parameters of pro-inflammatory (TNF-α, IL-1β), anti-inflammatory (IL-10) interleukins, TGF-β1 and protease inhibitors in the blood of women in the surveyed groups

Investigated indicators	Group	Before pregnancy	6 weeks pregnant	12 weeks pregnant
IL-TNF pg / ml	1	9,6±1,1	12,7±1,4*	15,2±1,6 *
	2	19,5±2,2º	38,8±4,3* º	48,1±5,1 * º
IL-1β pg / ml	1	6,5±0,8	10,3 ± 1,2*	13,2±1,4*
	2	14,9±1,7 º	26,5 ± 3,1* º	33,6±3,7* º
IL-10 pg / ml	1	8,5±1,0	6,3±0,7	4,5±0,5*
	2	4,2±0,6 º	2,7±0,4* º	2,1±0,3* º
TGF-β1 ng / ml	1	51,2 ± 6,3	72,9 ± 7,4*	79,6±9,1*
	2	21,3 ± 1,9 º	14,5 ± 1,7*º	11,4±1,5* º
α -1-anti-trypsin mg / dl	1	168±17,2	216±20,3	245±23,1*
	2	71±8,0º	49±5,2* º	38±4,1* º
α -2 -macro-globulin mg / dl	1	293±31,4	311±32,5	324±34,6
	2	231±25,3	210±22,9 º	196±21,4 º

Note: 1- women who have a full-fledged pregnancy with infections of the genitourinary system; 2 - women who have miscarriages with an infection of the genitourinary system.

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

º - reliably different values to the indicators of group 1

In the same studies, the result of IL-10 in the blood of women of group 1 at 6 weeks of gestation was insignificantly lower than similar data before pregnancy. In women of the same group at 12 weeks, IL-10 was insignificantly less than in women after 6 weeks of pregnancy and significantly lower than similar results before pregnancy. At the same time, IL-10 in women of group 2 before pregnancy was significantly 2.0 times lower than those of women in group 1 and significantly 1.6 times less than results by 6 and another 2.0 times less at 12 weeks of pregnancy in relation to indicators before pregnancy of the same group. Also, IL-10 in women of group 2, after pregnancy at 6 weeks by 2.3 times and at 12 weeks by 2.1 times was significantly lower than similar results of group 1 (table).

At the same time, the TGF-β1 indicator in the blood of women of group 1 at 6 weeks of gestation was reliably 1.4 times higher than similar data before pregnancy. In the same group, in women at 12 weeks gestation, TGF-β1 was not significantly higher than in women at 6 weeks of gestation and reliably 1.6 times higher than the same indicators before pregnancy. In women of group 2, the opposite direction of the TGF-β1 indicator before pregnancy was significantly and reliably 2.4 times lower than in women of group 1. In the same group in women at the 6th week of pregnancy, TGF-β1 was significantly and reliably more than 5 times less than the similar results of women in group 1, and also 1.5 times lower than the indicators before pregnancy in the same group. At the 12th week of pregnancy in women of group 2, TGF-β1 was also significantly and reliably more than 6 times less than similar data for women in group 1, and also 1.9 times significantly lower than the indicators before pregnancy in the same group (table).

At the same time, the indicators of α -1-anti-trypsin in women of group 1 at 6 weeks of gestation were not significantly higher compared with the same data before pregnancy. In women of the same group at 12 weeks, the α -1-anti-trypsin index was not significantly higher than in women at 6 weeks of gestation, and also reliably 1.5 times more than similar data before pregnancy. In women of the 2nd group, the opposite direction of the results, the index of α -1-anti-trypsin before pregnancy was significantly 2.4 times lower in relation to the results of women of the 1st group. Also, in women of group 2 at 6 weeks of gestation, the result of α -1-anti-trypsin was significantly and reliably 4.8 times less than similar data for women in group 1 and reliably 1.4 times less than the same data before pregnancy in the same group. In addition, in women of the 2nd group at the 12th week of pregnancy, α -1-anti-trypsin was also significantly more than 6 times lower than those of women in the 1st group and significantly 1.9 times less than the data before pregnancy in the same group (table).

The results of the study of α-2 -macro-globulin showed that women in group 1 showed a slight increase in this indicator at 6 weeks of gestation and even more at 12 weeks. In women of group 2, the opposite dynamics of changes in α-2 -macro-globulin was also noted, which manifested itself in an insignificant decrease in the results at 6 weeks and an even greater decrease at 12 weeks of gestation in relation to the same results before pregnancy of the same group. At the same time, in women of group 2, α -2 -macro-globulin was 1.5 times at week 6 and 1.7 times significantly lower at week 12 than in women of group 1 (table).

From the data obtained, it can be seen that the level of TNF-α, IL-1β in the blood, both in women of group 1 and group 2, was significantly higher at 6 weeks of gestation and even more at 12 weeks of gestation compared with the same indicators before pregnancy. At the same time, the indicators of TNF-α, IL-1β in women of group 2 were significantly and reliably higher than in women of group 1. At the same time, the level of IL-10 in the blood, both in women of group 1 and group 2, had the opposite direction. It decreased in relation to the indicators before pregnancy, not significantly at 6 weeks and significantly at 12 weeks in women of group 1, and also significantly at 6 weeks and at 12 weeks in women of group 2. In addition, it was found that all indicators of IL-10 in women of group 2 before pregnancy, at 6 and 12 weeks of pregnancy were significantly and reliably lower than similar results in women of group 1. It was also found that TGF-β1 in the blood of women in

group 1 significantly increased at 6 weeks and even more at 12 weeks of gestation, compared with similar indicators before pregnancy. At the same time, in women of group 2, TGF-β1 also had the opposite direction and significantly decreased at 6 and 12 weeks of pregnancy in relation to the results before pregnancy. At the same time, in women of the same group, the TGF-β1 values at 6 and 12 weeks of gestation were significantly lower than the same results in group 1. In the study of protease inhibitors, a greater change in α -1-anti-trypsin was noted in women of group 2. This was manifested in a significant decrease in this indicator before pregnancy, as well as at 6 and 12 weeks of pregnancy in relation to similar results for women in group 1. Also in a significant decrease in α -1-anti-trypsin at 6 and 12 weeks of pregnancy in relation to similar results before pregnancy. Changes in α-2-macro-globulin were noted to a lesser extent. This was manifested in an insignificant increase in this indicator in women of group 1, at 6 weeks and even more at 12 weeks of gestation, compared with the results before pregnancy. Nevertheless, in women of group 2 at 6 and 12 weeks of pregnancy, a significant decrease in α-2-macro-globulin was observed, compared with the results in relation to similar data of group 1.

Conclusions

Thus, the presence of infectious factors in the absence of a significant pro-inflammatory immune response in early pregnancy and a sufficient corrective reaction of protease inhibitors and TGF-β1 may contribute to a favorable course of early pregnancy and the development of a full-fledged pregnancy. However, in the presence of infectious factors and the presence of an excessive pro-inflammatory immune response in early pregnancy and an insufficient corrective reaction of protease inhibitors and TGF-β1, it can contribute to an unfavorable course of early pregnancy and the development of miscarriages. **These results are consistent with the suggestion that it is not just the presence of bacteria themselves, but differences in the host's response to the presence of genital infections that may contribute to an increased risk of preterm birth [5]**

LIST OF REFERENCES:

1. Baud, D., Goy, G., Jaton, K., Osterheld, M. C., Blumer, S., Borel, N., ... & Greub, G. Role of Chlamydia trachomatis in miscarriage //Emerging infectious diseases. – 2011. – T. 17. – №. 9. – C. 1630-1635.
2. Cao, C. J., Wang, Y. F., Fang, D. M., & Hu, Y. Relation between mycoplasma infection and recurrent spontaneous abortion //Eur Rev Med Pharmacol Sci. – 2018. – T. 22. – №. 8. – C. 2207-11.
3. Choi, S. J., Park, S. D., Jang, I. H., Uh, Y., & Lee, A. he prevalence of vaginal microorganisms in pregnant women with preterm labor and preterm birth //Annals of laboratory medicine. – 2012. – T. 32. – №. 3. – C. 194-200.
4. Farhadifar, F., Khodabandehloo, M., Ramazanzadeh, R., Rouhi, S., Ahmadi, A., Ghaderi, E., ... & Rezzaii, M. Survey on association between Mycoplasma hominis endocervical infection and spontaneous abortion using Polymerase Chain Reaction //International Journal of Reproductive BioMedicine. – 2016. – T. 14. – №. 3. – C. 181-186.
5. Giakoumelou, S., Wheelhouse, N., Cuschieri, K., Entrican, G., Howie, S. E., & Horne, A. W. The role of infection in miscarriage //Human reproduction update. – 2016. – T. 22. – №. 1. – C. 116-133.
6. Hoenderboom, B. M., van Bergen, J. E., Dukers-Muijrers, N. H., Götz, H. M., Hoebe, C. J., de Vries, H. J., ... & van Benthem, B. H. Pregnancies and time to pregnancy in women with and without a previous Chlamydia trachomatis infection //Sexually transmitted diseases. – 2020. – T. 47. – №. 11. – C. 739-747.
7. Kletzel, H. H., Rotem, R., Barg, M., Michaeli, J., & Reichman, O. Ureaplasma urealyticum: the role as a pathogen in women's health, a systematic review //Current infectious disease reports. – 2018. – T. 20. – №. 9. – C. 1-12.
8. Ma, C., Du, J., Dou, Y., Chen, R., Li, Y., Zhao, L., ... & Zhang, K. The Associations of Genital Mycoplasmas with Female Infertility and Adverse Pregnancy Outcomes: a Systematic Review and Meta-analysis //Reproductive Sciences. – 2021. – C. 1-19.
9. Reekie, J., Roberts, C., Preen, D., Hocking, J. S., Donovan, B., Ward, J., ... & Wand, H. Chlamydia trachomatis and the risk of spontaneous preterm birth, babies who are born small for gestational age, and stillbirth: a population-based cohort study //The Lancet Infectious Diseases. – 2018. – T. 18. – №. 4. – C. 452-460.

Entered 09.07.2021