



Immunodiagnostic Prognosis of Perinatal Pathology in Women Which Complicated Births with Preeclampsia

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Abstract:

Objective. To study the role of proinflammatory cytokines in complicated labor, to develop optimal tactics of pregnancy, with simultaneous prediction of the course of birth and the postpartum period.

Subject and methods. Examined in blood serum the content of proinflammatory interleukins in 95 pregnant women, 75 of them with preeclampsia in perinatal pathology before and after induction and 20 with the physiological birth.

Results. The concentration of il-6 increased by 14.3 times, which meant the generalization of the inflammatory process. In the analyzes of 75 women with preeclampsia with antenatal fetal death, none of them had normal results, on the contrary, in 8 samples they were 8.2 times larger, amounting to 73ng/ml.

Conclusion. In general, the prognostic value of pro- inflammatory cytokines in perinatal pathologies is high and varies from 62.2% to 81% which can be recommended as one of the reliable markers for the diagnosis of perinatal pathology and as monitoring the course of the inflammatory process, which may develop in childbirth and the postpartum period, as well as to predict the outcome of the pathological condition of the fetus and mother during pregnancy.

Keywords: preeclampsia, perinatal pathology, cytokines.

Despite the achievements of modern medicine, preeclampsia in pregnant women is still one of the leading causes of maternal and perinatal mortality [2, 6,18]. The share of preeclampsia in the structure of pregnancy complications ranges from 10.1% to 20.0%, and among the causes of maternal and perinatal mortality it is 21.3% and 12.10%, respectively [4, 8,11].

The immune balance in the functional system mother-placenta-fetus is formed under the influence of factors, among which a significant role is played by the woman's health status before gestation, immune genetic differences between spouses, and local immune reactions in the mother-placenta-fetus spheres [3,9,10]. Since disruption of the fetal-maternal immune relationship during placental insufficiency is an important link in the pathogenesis, assessment of cytokine status should be an integral part of a comprehensive examination of pregnant women with complicated pregnancy and childbirth with preeclampsia, antenatal rupture of water, antenatal fetal death(AFD) [5, 7,14].

Data on the role of maternal immune system factors in the formation of complicated childbirth are diverse; therefore, the study of immune reactivity in pregnant women with placental insufficiency

has opened up new opportunities for the early diagnosis of perinatal hypoxic-ischemic damage to the placental complex and will undoubtedly contribute to the development of acceptable management tactics and prediction of further course childbirth and the postpartum period during complicated births [1, 12,13].

Purpose of the study: to study the role of pro-inflammatory cytokines during complicated labor, to develop optimal management tactics and type of induction, while simultaneously predicting the course of labor and the postpartum period in women with preeclampsia.

Materials and methods of research: In total, the content of pro-inflammatory interleukins in the blood serum was examined in 95 pregnant women, of which 75 with preeclampsia and perinatal pathologies before and after induction and 20 with the physiological course of labor. Induction was carried out according to the national protocol.

Results of the study and their discussion: It is a well-known fact that in perinatal pathology with preeclampsia, fetoplacental insufficiency occupies a special place and the main causes of which are a pronounced inflammatory reaction of the whole organism, including the uterus [1,15]. In the pathogenesis of the development of antenatal fetal death, a special place is given to inflammatory mediators, especially inflammatory ones such as IL-6 and IL-8. Of great interest are the results of the study of pro-inflammatory cytokines and the possibility of using these data to predict childbirth: timing, methods of delivery and outcome of the postpartum period in obstetric practice, which help for the subsequent development of management tactics. High values of IL-6 and IL-8 indicate the process of cervical ripening before the upcoming birth, which can also serve as a diagnostic marker [16,17].

An increase in the levels of pro-inflammatory cytokines under the influence of intrauterine IUI infection in the 2nd and 3rd trimesters of pregnancy leads to an increase in the synthesis of prostaglandin by the amniotic membranes, which contributes to the premature development of labor; based on this, we were able to predict the immediate timing of delivery.

Of the 75 women in the main group, childbirth was completed through the natural birth canal in (89%), and by caesarean section (11%) in women with uterine scars. The duration of AFD ranged from 2 to 4 days. Serum for the determination of cytokines was collected on the first day after admission to the hospital with a diagnosis of preeclampsia, AFD. The gestation periods in the two compared groups were identical. IL-6 and IL-8 are pro-inflammatory cytokines, the concentrations of which were increased.

The concentration of IL-6 increased 14.3 times, which meant the generalization of the inflammatory process. IL-6 mainly regulates the immune response, acute phase reactions and inflammation, and inhibits the synthesis of TNF- α , which was also observed in our studies. In patients with high IL-6 values, the TNF- α level decreased, approaching the normative data.

The concentration of IL-8 was also high, where the average concentration was 60.8 ± 7.9 pg/ml, exceeding 1.8 times the control group, amounting to 35.6 ± 10.2 pg/ml. Local action of IL-8 results in increased infiltration of activated macrophages, which may contribute to placental dysfunction.

In general, patients with decompensated chronic renal failure, which was complicated by preeclampsia and perinatal pathology, are characterized by the presence of pronounced systemic disorders of the immune status in the form of increased serum levels of IL-6, IL-8.

According to the indicators of pro-inflammatory interleukins, it became possible to timely intervene in the process of childbirth, despite some theories, with the simultaneous emergence of the prospect of reducing the incidence of bleeding and septic complications in the postpartum period. It should also be noted that our results will serve as a prognostic criterion for the outcome of the disease.

According to literature data [10,13], an increase in the levels of IL-6 and IL-8 predicts an extremely serious condition of the patient or even her impending death in case of delayed intervention. Such results were observed in 10 (13.3%) of 75 patients, where the final diagnosis was AFD with a limitation period of intrauterine death of up to 5 days with bacteremia. Referring to a set of

diagnostic markers, we were able to make timely decisions in favor of emergency induction of labor, after maximum stabilization of hemostasis.

In the pathogenesis of the development of preeclampsia and antenatal fetal death, a special place is given to inflammatory mediators, especially proinflammatory ones such as IL-6 and IL-8. Of great interest are the results of the study of pro-inflammatory cytokines and the possibility of using these data to predict childbirth: timing, methods of delivery and outcome of the postpartum period in obstetric practice, which help for the subsequent development of management tactics.

Also, studying the parameters of pro-inflammatory cytokines IL-6, IL-8 in the blood serum of patients, as a possible test for assessing the state of immunity, establishing the degree of maturity of the cervix and the generic dominant and predicting a possible infectious risk, as well as their relationship with each other.

Pro-inflammatory cytokines ensure the mobilization of the inflammatory response: IL-6, IL-8, having pronounced pleiotropic effectiveness and their main effect has a large role in the development and course of the generic dominant with subsequent reactions of the whole organism.

In a pathomorphological study of biopsy samples from women with preeclampsia in AFD, signs of a chronic inflammatory process were revealed, with a simultaneous increase in the concentration of interleukins in the serum indicating the presence of a pronounced and prolonged inflammatory reaction, which echoes where, with severe inflammatory processes in pregnant women, there were high values of such interleukins as IL-6 and IL -8, belong to pro-inflammatory cytokines, the concentrations of which were increased. The concentration of IL-6 increased 14.3 times, which meant the generalization of the inflammatory process. In tests taken from 75 women with preeclampsia during AFD, none of the results were normal; on the contrary, in 8 samples they were 8.2 times higher, amounting to 73 pg/ml.

IL-6 mainly regulates the immune response, acute phase reactions and inflammation, and inhibits the synthesis of TNF- α , which was also observed in our studies. In women with high IL-6 values, the TNF- α level decreased, approaching the normative data. 16 out of 45 samples had such results.

Table 1. Comparative data on serum levels of cytokines in women with preeclampsia with antenatal fetal death

Studied Cytokines	Serum cytokine concentration (pg/ml)		
	Control group, n=20	Before induction n=75	After induction n=45
IL-6	8,9 \pm 3,1	73,7 \pm 17,4	11,6 \pm 5,2
IL-8	35,6 \pm 10,2	60,8 \pm 7,9	39,6 \pm 11,9

Note: *- significance of differences (P<0.05)

The main functions of IL-6 are the regulation of the processes of maturation of antibody-forming cells and the production of serum immunoglobulins. The concentration of IL-6 was on average 73.7 \pm 17.4 pg/ml in patients with AFD**, almost 9 times higher than in healthy pregnant women (8.9 \pm 3.1 pg/ml *).

In those samples where the levels of IL-6 were high, in comparison with the control (there were 32 patients with preeclampsia with AFD), the clinical period of antenatal death coincided with the period of limitation of more than 2 weeks and was characterized by profound changes in the fetoplacental complex, which was confirmed by morphological data studies of the placenta and biopsy samples after childbirth.

According to the literature, IL-6, along with other cytokines, promotes successful implantation and is capable of being secreted by the trophoblast. By activating the suppressor component of lymphocytes, IL-6 can hinder the implementation of effector reactions of the mother's immune system in relation to the fetus. On the other hand, IL-6 activates coagulation reactions and can lead to the formation of placental insufficiency. This means that not only chronic IUI can contribute to the

development of a decompensated form of FPN, but high values of pro-inflammatory cytokines complicate blood coagulation parameters, resulting in AFD with the layering of preeclampsia.

The concentration of IL-8 was also high, where the average concentration was 60.8 ± 7.9 pg/ml, exceeding 1.8 times the control group, amounting to 35.6 ± 10.2 pg/ml.

Interleukin 8 (IL-8) is one of the main pro-inflammatory cytokines produced by macrophages, epithelial and endothelial cells. Plays an important role in the innate immune system, acting as a chemoattractant for neutrophils, macrophages, lymphocytes, eosinophils, and is a key inducer of an acute inflammatory response. Local action of IL-8 results in increased infiltration of activated macrophages, which may contribute to placental dysfunction.

The prognostic value of IL-6 and IL-8 was 86.6% in 39 cases and coincided with the clinical picture of decompensated FPN against the background of IUI with preeclampsia in AFD. Analysis of the data obtained showed that the initial increase in the level of pro-inflammatory cytokines in pregnant women with a complicated course of labor indicates the presence in the body of a pronounced immune response to the development of degenerative-inflammatory processes; after the completion of labor, already on the 2-3rd day, with a favorable course of the pathological process began reliably decrease.

Conclusion:

The increased initial level of pro-inflammatory cytokines and their subsequent pronounced decrease in patients with preeclampsia during AFD may reflect a change in the direction of the immune response during treatment as a result of a switch from the initially dominant Th-1 cell type to humoral, which should be regarded as a favorable prognostic indicator .

A significant increase in the levels of IL-6 and IL-8 in patients with preeclampsia and AFD allows them to be used as additional criteria for immunodiagnosis and help to urgently terminate pregnancy.

In general, the predictive value of proinflammatory cytokines in perinatal pathologies is high and varies from 62.2% to 81%, which can be recommended as one of the reliable markers for diagnosing FPN and as a way to monitor the course of the inflammatory process, which may possibly develop during childbirth and postpartum period, as well as to predict the outcome of the pathological condition of the fetus and mother during pregnancy.

Literature:

1. Anderssohn M., Maas L.M., Diemert A. Severely decreased activity of placental dimethylarginine dimethylaminohydrolase in pre-eclampsia. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2012; 161 (2): 152-6.
2. Abrahams V.M. Mechanisms of antiphospholipid antibody-associated pregnancy complications. *Thromb Res.* 2009 Nov; 124 (5): 521-5.
3. Adizova S.R., Ashurova N.G. Izuchenie effektivnosti i priemlemosti kontratseptivnykh sredstv u mnogorozhavshikh zhenshchin // Молодежный инновационный вестник. - 2016. - Vol. 5. - N. 1. - P. 193-194.
4. Adizova S. R. Vitamin d, homocysteine and their impact on maternalfetal outcomes in pregnancy with preeclampsia //Art of Medicine. International Medical Scientific Journal. – 2022. – T. 2. – №. 4.
5. Adizova , S., Ibrohimova , D., & Ikhtiyarova , G. (2023). Peculiarities of hemostasis in pregnant women with preeclampsia. *Prospects for the Development of Medicine*, 1(1), 25.
6. Akhmedov F.K., Negmatullaeva M.N., Avakov V.E. Features of renal blood flow and dynamics of uric acid concentration in women with pregnancy complicated by preeclampsia // *Clinical nephrology.* - 2018. - N. 1. - P. 38-40.
7. Makarov O.V., Tkacheva O.N., Volkova E.V. Preeclampsia and chronic arterial hypertension. *Clinical Aspects.* Moscow, 2010; 136 p.

8. Poletayev, A.B.; Morozov, S.G. ELYPTESTHES methods in the estimation of the reproductive health condition of women of fertile age. Moscow, 2008; 16 p.
9. Ikhtiyarova G.A., Ayupova F.M., Negmatova G.M. Risk factors of perinatal complications according to the retrospective analysis data. Zh; Pediatrics Toshkent 2019, - № 1. - С. 223 – 229
10. Адизова С. Р., Ихтиярова Г. А. Морфологическая характеристика плаценты у женщин с преэклампсией //Новый день в медицине. – 2020. – №. 2. – С. 26-30.
11. M.N. Negmatulleva., D.I. Tuksanova, M.S Nosirova. Features of the state of the circulatory system mother and fetus in the second trimester of pregnancy in women with mitral stenosis of rheumatic etiology - European Journal of Biomedical and Pharmaceutical ..., 2020
12. Hutcheon J.A., Lisonkova S., Joseph K.S. Epidemiology of pre-eclampsia and the other hypertensive disorders of pregnancy. Best. Pract. Res. Clin. Obstet. Gynaecol. 2011 Aug; 25 (4): 391-403.
13. Lamarca B. Endothelial dysfunction. An important mediator in the pathophysiology of hypertension during pre-eclampsia. Minerva Ginecol. 2012; 64 (4): 309-20.
14. McSharry C. Chronic kidney disease: Early CKD increases the risk of adverse outcomes in pregnancy. Nat. Rev. Nephrol. 2010 Jul; 6 (7): P. 385.
15. Rizokulovna , A. S. (2022). Blood Homocysteine Level and its Prognostic Value in Pregnant Women with Preeclampsia. *Central Asian Journal of Medical and Natural Science*, 3(5), 51-57.
16. Tuksanova D. I. et al. Osobennosti pochechnogo i pechenochnogo krovotoka u beremennyh s preeklampsiej //Rossijskij vestnik akushera-ginekologa. – 2013. – T. 13. – №. 5. – С. 41-43.
17. Levine R.J., Lam C., Qian C., Yu K.F., Maynard S.E., Sachs B.P. et al. Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. N. Engl. J. Med. 2006; 355(10): 992-1005.