American Journal of Medicine and Medical Sciences 2025, 15(8): 2772-2778
DOI: 10.5923/j.ajmms.20251508.75

Character of Changes in Pro- and Anti-Inflammatory Cytokines in Women with Physiologically Proceeding Pregnancy

Turdieva Dilnavoz Olimovna*, Khamdamov Bakhtiyor Zarifovich, Makhmanazarov Orifjon Mirzonazarovich

Bukhara State Medical Institute, Bukhara, Uzbekistan

Abstract Studying the level of cytokines by weeks of the gestation period more accurately reflects changes in cytokine concentrations, provides important information about the state of the immune system not only at the time of examination, but can also allow predicting the further course of pregnancy and its outcome. The results obtained will allow them to be used as normative materials for the timely detection of immunological criteria for pregnancy pathology.

Keywords Physiologically proceeding pregnancy, Immune system, Pregnancy pathology

1. Introduction

Despite numerous studies in the field of reproductive immunology, pregnancy, "the most natural thing in the world," still remains an immunological mystery. Uncomplicated pregnancy is largely determined by a complex of immunological relationships between the mother and the fetus, which determine a certain level of tolerance of the pregnant woman's body to fetal alloantigens [2,3]. Traditionally, pregnancy is divided into three trimesters, and therefore all immunological indicators are usually given by authors by trimester. An analysis of published works shows that such a division is not informative enough for conducting immunological studies, since when dividing into trimesters it is not possible to study the relationships between immunological parameters and events occurring in the mother's and fetus's body during pregnancy, such as the formation of the placenta, the development of the fetal immunological system, hormonal changes in the mother's body, etc. [12,17].

In addition, disturbances in the immunological relationship between the mother and fetus can be the cause of spontaneous termination of pregnancy, and therefore knowledge of the physiological boundaries of immunological parameters in uncomplicated pregnancy by weeks of the gestation period provides important information for understanding the pathogenesis of a number of disturbances in the mother-placenta-fetus system [8,13]. Changes in immune status indicators during physiological and pathological pregnancy have interested scientists around the world for a long time, and many studies have been conducted on this topic. The literature data on the state of the immune system during pregnancy are contradictory. The inconsistency of immunological indicators may be due to differences and imperfections in methods, epidemiological features, and high variability of the physiological norm.

A number of mechanisms are believed to ensure that the fetus is not rejected during pregnancy: 1. Complete separation of the maternal and fetal circulatory systems; 2. The presence of an immunological barrier or buffer zone at the boundary between maternal and fetal tissues; 3. Masking of surface antigens on trophoblast cells by certain agents; 4. Synthesis by syncytiotrophoblasts and maintenance of a local (in the placenta) high concentration of hormones and other agents that act as immunosuppressants; 5. Production by the fetus of immunosuppressive agents or cells that enter the mother's body.

Production by the mother's body of immunoregulatory agents that prevent an immunological attack on the fetoplacental system. Recent studies have added to this such factors as apoptosis (CD 95 and its ligands), HLA-G, Th1/Th2 balance, leukemia inhibitory factor, annexin II [1,12,21].

Of course, the above list of possible mechanisms regulating the immunological relationship between mother and fetus during normal pregnancy is not exhaustive. There are probably other mechanisms of immunoregulation. Various aspects of the immune relationship that arises between the body of a pregnant woman and the fetus, which carries paternal antigens and, thus, represents a semi-allogeneic transplant, are the subject of close attention by researchers [4,7].

* Corresponding author:
turdiyeva.dilnavoz76@gmail.com (Turdieva Dilnavoz Olimovna)
Received: Aug. 9, 2025; Accepted: Aug. 27, 2025; Published: Aug. 30, 2025
Published online at http://journal.sapub.org/ajmms

Speaking about changes in immune parameters during pregnancy in the mother, it is impossible not to mention that a certain role is played by the development of the immune system of the fetus. As the immunocompetence of the fetus develops, maintaining the immunological balance between the organisms of the mother and the fetus becomes more difficult. Already in the 7th week of intrauterine life, the liver cells of the fetus are capable of reacting to alloantigens by blast transformation. In the 8th week, the first lymphocytes appear in the thymus rudiment, and after another 2 weeks, these lymphocytes are capable of reacting to PHA and alloantigens. In the 11-12th week, the liver cells of the fetus synthesize Ig M, A and G. Lymphocytes appear in the embryonic spleen in the 12th week of intrauterine life. However, the immaturity of the immunocompetent lymphoid tissue of the fetus and the macrophage digestion mechanism lead to the development of tolerance in response to maternal antigens, which is actively supported by fetal T-suppressors and humoral mechanisms of nonspecific suppression. Maternal immunoglobulin G, antigens, and immune complexes circulating in the fetal blood also have tolerogenic properties. The final establishment of fetal immunocompetence during normal pregnancy occurs in the postnatal period, but the fetal ability to respond to cellular immunity in the third trimester suggests the involvement of fetal immunological mechanisms in inducing timely labor [6,15,16,20].

The immunological relationships established between mother and child during pregnancy due to the direct contact of the syncytiotrophoblast and the basal decidua, and due to the constant influx of fetal cells into the maternal bloodstream, protect the fetus and its structures from the mother's immune mechanisms triggered by paternal fetal antigens. Studies have shown that the non-antigenic properties of the trophoblast are not the result of its invasive and destructive qualities, since they are also observed in the non-invasive trophoblast in the last stages of pregnancy. One explanation for this is the masking of its antigens by a "fibrinoid" layer consisting of acidic mucoprotein rich in tryptophan and sialic acid. This layer, which is a product of active secretion by the cytotrophoblast or the end product of cell and collagen fiber destruction, creates an electrochemical barrier between the maternal and fetal cells. Other authors [9,11] believe that this is associated with the expression of HLA-G, which provokes immunosuppression indirectly through cytokines. In experimental conditions, the trophoblast produces mediators that inhibit the growth of monocytes and cause T-cell suppression [10]. Recently, a regeneration and tolerance factor has also been identified - a protein produced by the cytotrophoblast, as well as expressed on peripheral B lymphocytes from the 7th to 9th week of pregnancy, which is capable of producing a suppressive immune response (in particular, the Th2 cytokine response), necessary for the initiation and development of fetal-maternal relationships [5,19].

Numerous studies of physiological pregnancy have shown the presence of cellular and humoral responses to paternal alloantigens expressed by the fetus. At the same time, it is known that physiological pregnancy is not accompanied by the development of an immune conflict between the mother and fetus, and fetal rejection does not occur [18,23]. Physiological blockade of transplantation immunity reactions occurs, ensuring long-term symbiosis of two genetically different and interrelated organisms [18], where an important role belongs to endogenous immunosuppressants, including serum and cellular blocking factors [19,22].

Physiologically occurring pregnancy is characterized by cyclic changes in the quantitative indices of the main lymphocyte populations, as well as the interferon system. A decrease in the indices of cellular immunity coincides with critical periods of fetal development. Changes in the immune status may be caused by hormones produced during pregnancy, specific proteins of pregnant women, antibodies to fetal egg antigens, antigen-antibody complexes, the population of suppressor cells of the mother's body, cellular elements of the fetus that mediate the immunosuppressive function, and, possibly, other factors [2,5,6]. Most researchers, although they do not find generalized T- and B-immunodeficiency, believe that some suppression of cell-mediated immunity during normal pregnancy protects the fetus from rejection, but poses a danger to the mother in terms of increased susceptibility to various infections [11].

With the onset of pregnancy and as it develops, the total number of leukocytes in the peripheral blood increases, and their relative or absolute number decreases. Moreover, the content of immunoregulatory cells in the blood of healthy pregnant women changes depending on the period of pregnancy development [21,23]. One of the most important mechanisms involved in preserving the fetus and protecting the mother's body from the damaging effects of fetal antigens is the cellular immunity system, with a special role in this mechanism played by a certain subpopulation of T cells - suppressors, namely an increase in their number and activity. Suppressor control of T lymphocytes over the development of humoral and cellular immune responses is carried out at several levels: circulating maternal T suppressors, T suppressors localized in the decidual membrane, T suppressors localized in regional lymph nodes, T suppressors penetrating the mother's body from the fetus [7,10]. The role of T-helpers, which act as assistants in the formation of cellular and humoral reactions, is also important. During pregnancy, there is an absolute decrease in the number of T-helpers (CD4) with an absolute increase in the number of T-suppressors (CD8), leading to a stable decrease in the CD4/CD8 ratio throughout pregnancy [14,19]. According to the latest data, one of the most important factors in the development of normal pregnancy is the T-helper1/T-helper2 ratio, namely, the lack of expression of Th1-specific cytokines (IL-2, IL-12) and the dominant expression of Th2-specific (IL-4, IL-6, IL-5, IL-10) in the peri-implantation endometrium and peripheral blood (presumably controlled by natural killers), which supports the successful development of pregnancy [3,15,20].

Beginning as early as the 5th to 8th week of pregnancy, suppressor lymphocytes are detected in the blood of pregnant women, and their specificity against the paternal, and not any

other HLA phenotype, has been noted. The importance of the early appearance of the suppressor function of lymphocytes for preventing spontaneous abortions and increasing the otherwise cytotoxic activity of T-lymphocytes has been proven experimentally [15]. These periods coincide with the onset of production of the regeneration and tolerance factor [20]. Some authors note an absolute and relative decrease in T-lymphocytes at the 5th to 7th and 13-16th weeks of pregnancy, which is apparently associated with critical periods of fetal, trophoblast, and placenta development. Many researchers find a decrease in the total pool of T-helpers, T-suppressors, a decrease in the activity of natural killers (NK), a decrease in the total number of B-lymphocytes and an increase in the content of their active fraction, a decrease in the level of immunoglobulin G and immunoglobulin. A by the third trimester of pregnancy, an increase in the concentration of IgM, the level of circulating immune complexes, the functional activity of neutrophils and monocytes [16,21]. At the same time, other authors [23] believe that during physiological pregnancy, a decrease in the percentage of T-lymphocytes with an unchanged absolute value, and the number of B-lymphocytes in absolute figures increases during all trimesters. A decrease in the number of molecules mediating apoptosis (CD95 +) and interleukin-2 factor (CD25 +) was revealed throughout pregnancy, and especially in the third trimester [1,9]. At the same time, the production of interleukin-4 increases throughout pregnancy and is significantly higher than in non-pregnant women [6]. The IL-4/IL-2 ratio reaches its maximum by the third trimester and is one of the main indicators of successful pregnancy development, as is the overall ratio of Th2 and Th1 specific cytokines [12,17].

Non-specific immunosuppression associated with pregnancy persists in the early postpartum period, but during the first 5 days, the indices of cellular and humoral immunity gradually recover to values close to normal [8,11,13,20,23]. Recovery of NK activity occurs within 6-10 days after delivery. According to other authors, the immunological effect of pregnancy persists for a longer period: from 4 months to a year after delivery. In cases where immunosuppression during pregnancy was more pronounced than normal, the early postpartum period is often complicated by the development of inflammatory processes, but timely application of adequate correction leads to a significant decrease in the incidence of postpartum inflammatory complications [10,16,18,19].

As pregnancy develops, a temporary organ is formed – the placenta, which produces pregnancy hormones, acts as an absorbent of anti-paternal antibodies and an immunological barrier, and this barrier function is extremely important for maintaining pregnancy. The placenta has specific receptors for the Fc part of immunoglobulins, facilitating the transfer of IgG from mother to fetus. There is much evidence that stimulators of the formation of specific suppressor immunity during pregnancy are formed in the placenta. Placental substances, acting directly or indirectly on various targets in the maternal immune system, cause a wide range of immune reactions: immunosuppressive, immunostimulating and immunomodulatory. Pregnancy hormones play a very important role in immunosuppression [17,21]. Human chorionic gonadotropin, human chorionic somatotropin, cortisol, progesterone, estrogens (which are produced in pregnant women in tens of times greater amounts than in non-pregnant women), as well as some proteins of the blood serum of pregnant women, in particular alpha2-glycoprotein, alpha-fetoprotein, have properties that contribute to the suppression of transplant immunity to varying degrees. In particular, it has been established that estradiol, produced in large quantities as pregnancy progresses, has a suppressive effect on natural killers as gestation increases, which ceases immediately after childbirth, as evidenced by a sharp decrease in the estradiol level to normal and restoration of NK activity to the level of non-pregnant donors. Progesterone, in turn, stimulates the production of IL-4 and other Th-2 specific cytokines and a decrease in the production of Th-1 specific cytokines, which contributes to a normal systemic immune response during physiological pregnancy. It has been established that, under normal conditions, the whole extract of soluble trophoblast proteins suppresses the reactivity of T- and B-cells in non-pregnant women, with the greatest inhibitory activity being exhibited by the alpha- and beta-globulin fractions and their subfractions, as well as the interleukin-10 produced by it [20,22].

As can be seen from the above, the literature data on the indices of cellular and humoral immunity during physiological pregnancy are quite ambiguous. Taking into account all the above information, it can be said that in order to obtain sufficiently complete information on the state of the immune system, it is necessary to study the dynamics of immunological indices not only by trimesters of pregnancy, but also by weeks of the gestation period. The study conducted in this way will allow us to determine risk groups among pregnant women, in particular, those living in the Bukhara region, the normative indices of immunity, and will create a basis for preventing possible complications. It should be noted that the study of cytokine status indices by weeks of the gestation period during normal pregnancy in our republic has not been conducted.

Thus, the study of changes in cytokine status parameters during physiological pregnancy in women living in the Bukhara region is of theoretical and practical interest.

The aim of the study: to study changes in the parameters of cytokine status during physiological pregnancy in women living in the Bukhara region.

2. Materials and Methods

Based on the above, we conducted a study to examine the level of cytokines, both proinflammatory (IL-1β, IL-6, IL-8, and anti-inflammatory, in women with physiologically progressing pregnancy by weeks of the gestational period. The study involved 245 women. The main group consisted of 180 pregnant women at various gestational stages and 28 women in the delivery period (38–40 weeks). For a more accurate analysis of changes in the immune status, the

participants were distributed by gestational period: 5–7 weeks – 12 women, 8–11 weeks – 14 women, 12–15 weeks – 13 women, 16–19 weeks – 21 women, 20–23 weeks – 15 women, 24–27 weeks – 23 women, 28–31 weeks – 29 women, 32–35 weeks – 25 women and 36–40 weeks – 28 women. The control group consisted of 37 women of reproductive age outside of pregnancy.

3. Results and Discussion

Proinflammatory cytokines (IL-1β, IL-6, IL-8 and TNFα) activate the processes of the cellular immune response, playing a key role in early pregnancy. They promote embryo implantation, angiogenesis and tissue remodeling. Anti-inflammatory cytokines (IL-4 and IL-10) provide immunological tolerance, suppressing excessive inflammatory reactions and preventing immune conflict between the mother and fetus. Assessment of cytokine levels allows us to determine the nature of immune adaptation at different stages of gestation and promptly identify possible risks of pregnancy development disorders. IL-1β is one of the key mediators of the inflammatory response and plays an important role at all stages of pregnancy. Its main function is to activate the immune system, stimulate angiogenesis and tissue remodeling, which is necessary for embryo implantation and placenta formation. However, excessive production of IL-1β can contribute to the development of pathological processes, including pregnancy complications. Studying the dynamics of this cytokine during gestation allows us to determine the main mechanisms of immune adaptation.

In the early gestation period, there is a gradual increase in the IL-1β level associated with the active restructuring of the mother's body to maintain pregnancy. In the control group, consisting of 37 women outside pregnancy, the IL-1β level was 22.7 ± 1.2 pg / ml, which is the physiological norm for the absence of an active inflammatory process. Already at 5-7 weeks (n = 12), the IL-1β level increased significantly and was 59.6 ± 3.5 pg / ml, which is more than 2.6 times higher than the control group values. This is due to the need to activate innate immunity to ensure the processes of implantation and chorion development. IL-1β stimulates the secretion of other proinflammatory cytokines and growth factors involved in the formation of primary placental vessels. At 8–11 weeks (n=14), the IL-1β concentration continues to grow, reaching 97.3±4.2 pg/ml, which is 4.3 times higher than the level in women outside pregnancy. This is due to the completion of the placental attachment processes and increased angiogenesis. During this period, IL-1β plays an important role in stimulating cell proliferation and trophoblast migration.

By 12–15 weeks (n=13), the cytokine level reaches 122.8±4.9 pg/ml, indicating ongoing restructuring of the vascular network and stabilization of placenta formation. The peak of IL-1β activity at the end of the first trimester is an important factor for the full formation of the placental barrier and ensuring fetoplacental circulation. At 16–19 weeks (n=21), the IL-1β level continues to increase and reaches 171.4±5.8 pg/ml. This is 7.5 times higher than the control value. The increase in concentration at this stage indicates that the processes of angiogenesis and vascular remodeling continue, which is necessary to maintain the growing placental mass.

By 20–23 weeks (n=15), the cytokine level reaches 178.5±6.3 pg/ml, demonstrating stabilization at a high level. This confirms the importance of IL-1β for maintaining active placental blood flow and enhancing the immune response under conditions of increasing stress.

At 24–27 weeks (n=23), IL-1β increases to 195.6±5.2 pg/ml. This may be due to the increased need for adaptation of the vascular network for optimal blood supply to the fetus's organs and tissues, as well as an increase in the volume of circulating blood in the mother.

At 28–31 weeks (n=29), the IL-1β concentration reaches a peak (212.7±6.1 pg/ml), which is 9.4 times higher than the level in women in the control group. High cytokine activity at this stage is associated with an increased need for placental metabolism and preparation of the body for the final stage of gestation. However, by 32–35 weeks (n=25), the IL-1β level gradually decreases to 208.3±5.7 pg/ml, reflecting stabilization of the immune system and a decrease in inflammatory reactions.

At 36–40 weeks (n=28), the cytokine concentration drops to 189.6±6.4 pg/ml. This process is associated with the body's transition to regulating inflammation to prevent premature birth. However, in the prenatal period (n=28), there is a sharp jump in IL-1β levels to 273.6±7.5 pg/ml, which is associated with the activation of the prostaglandin system and the onset of labor. At this point, IL-1β stimulates uterine contractions and helps prepare the cervix for dilation.

Dynamics of IL-1β levels during pregnancy reflect phase activation and regulation of inflammatory processes. Study of IL-1β levels by trimesters of pregnancy. Analysis of data by weeks of the gestation period compared to data by trimesters clearly demonstrates how detailed the changes in the content of this cytokine are during the gestation period.

IL-6 is a universal cytokine involved in the regulation of both inflammatory and regenerative processes. It stimulates the cellular immune response by activating macrophages, neutrophils and other effector cells, and also plays an important role in the regulation of angiogenesis and tissue remodeling. In early pregnancy, an increase in IL-6 levels is necessary to ensure immune adaptation of the body to embryo implantation and placenta formation. As pregnancy progresses, the concentration of this cytokine gradually decreases, indicating phase regulation of the immune system. In the early stages of pregnancy (1–12 weeks), the IL-6 level increases significantly, which is associated with the active initiation of inflammation and angiogenesis processes. In the control group, the IL-6 level is 27.3±1.3 pg/ml, which corresponds to the normal immune status in the absence of pregnancy. However, at 5–7 weeks, this indicator increases to 54.5±2.8 pg/ml. This increase is due to the need to activate cellular immunity to ensure embryo protection and restructuring of blood vessels in the uterus. During this period, IL-6 promotes increased local inflammation, which is necessary

for successful implantation and adaptation of the mother's body to pregnancy. At 8–11 weeks, the cytokine concentration continues to increase and reaches 98.3±5.1 pg/ml. This increase is associated with the active phase of placenta development and the creation of full-fledged fetoplacental circulation. IL-6 enhances cell migration and promotes the production of growth factors necessary for the expansion of the vasculature.

The maximum IL-6 value is observed at 12–15 weeks and is 113.6±4.5 pg/ml. This is more than 4 times higher than the control value and is associated with the completion of placental angiogenesis processes. At this stage, the cytokine maintains stable functioning of the placental barrier and immune tolerance. At 16–19 weeks, the cytokine level is 92.8±5.0 pg/ml. This concentration maintains the adaptation of the placenta to the increased need for oxygen and nutrients. By 20–23 weeks, the IL-6 level decreases to 88.1±4.2 pg/ml. Local inflammatory processes are regulated, which helps avoid excessive activation of the immune system. At 24–27 weeks, the cytokine concentration decreases to 59.4±3.7 pg/ml. This indicates the beginning of stabilization of metabolic processes and a decrease in inflammatory activity in the context of increasing metabolic load from the fetus. At 28–31 weeks, it reaches 45.6±2.9 pg/ml, which is 1.7 times higher than the control level. At this stage, the cytokine participates in maintaining placental metabolism and adaptation of the maternal immune system. At 32–35 weeks, the IL-6 level is 42.8±2.5 pg/ml. The decrease in concentration is associated with increased regulatory mechanisms aimed at maintaining immunological balance and preventing premature labor. By 36–40 weeks, the IL-6 level drops to 34.9±3.0 pg/ml. The immune system switches to a state of controlling inflammatory reactions, which is necessary to ensure a stable course of pregnancy at the final stage.

Data on pregnancy trimesters do not show the changes that occur weekly during the gestation period.

IL-8 is a chemokine cytokine, the main function of which is to attract and activate neutrophils at the site of inflammation. It plays an important role in angiogenesis, stimulating the proliferation and migration of endothelial cells, which is especially important in the early stages of pregnancy. IL-8 ensures the restructuring of the vascular network and supports immune processes during the formation of the placenta.

In women of the control group, the IL-8 level is 17.5 ± 0.9 pg / ml, which corresponds to a normal physiological state without signs of an active inflammatory response.

At 5-7 weeks of pregnancy, the concentration of IL-8 increases to 31.9 ± 2.1 pg / ml, which is associated with the need to activate local inflammatory mechanisms to support embryo implantation and placenta formation. The maximum level of IL-8 is reached in the period of 12-15 weeks and is 98.5±3.5 pg/ml. This peak is due to the intensive growth and development of the placental vascular network. The cytokine plays an important role in maintaining angiogenesis and migration of endothelial cells.

After 15 weeks, a gradual decrease in the concentration of IL-8 is observed. At 16-19 weeks, its level is 63.7±3.2 pg/ml, which is associated with the completion of active processes of vascular restructuring.

At 28-31 weeks, the concentration of IL-8 reaches 33.2±2.0 pg/ml and remains relatively low until the late stages of pregnancy. Minimum values (19.8±1.5 pg/ml) are noted at 36-40 weeks, indicating a decrease in inflammatory activity and preparation for childbirth.

Analysis of data obtained by trimesters of pregnancy showed that changes in the IL-8 level do not fluctuate much, but are approximately at the same level. Those surges in the IL-8 level that occur by weeks of the gestation period are not visible.

Thus, the obtained data show the importance of the cytokine level in ensuring the immune adaptation of the mother's body at various stages of pregnancy. The observed change in the levels of both pro- and anti-inflammatory mediators emphasizes their key role in regulating the processes of angiogenesis, placental blood flow and immune control, which is an important condition for the physiological course of pregnancy and its timely completion. Summarizing the data on the cytokine regulation of the mother's immune response during the gestation period, it should be noted that the local restructuring of the immune background, necessary for the normal implementation of the processes of blastocyst implantation, formation and growth of the placenta, is also accompanied by changes in systemic immunity. At the systemic level, priming of phagocytic cells occurs at the beginning of pregnancy, which is manifested by their ability to produce a high level of various cytokines. These results may indicate the participation of phagocytic cells in the regulation of the maternal immune response. Late gestation periods are accompanied by increased activity of peripheral phagocytic cells with a simultaneous stimulating effect of proinflammatory cytokines against the background of increased systemic and local cytotoxic reactions, possibly due to the synthesis of Th1 type cytokines. Thus, increased synthesis of proinflammatory cytokines and suppression of anti-inflammatory cytokines in the third trimester of uncomplicated pregnancy indicate that the development of labor is associated with increased production of cytokines that stimulate phagocytic cells and NK.

Thus, changes in the immune system of a woman occurring during pregnancy are aimed at ensuring immunologically conflict-free development of a semi-allogeneic fetus. The development of the gestational process is accompanied by suppression of the reactivity of T-lymphocytes and T-helpers. Pregnancy leads to the elimination of fetoreactive clones of T- and B-lymphocytes. At the same time, there is an increase in the role of non-specific resistance mechanisms, which apparently not only compensates for the insufficiency of immunological reactivity, but also increases the efficiency of blood purification, which contains excess concentrations of immune complexes. In the second half of gestation, the transfer of immune humoral factors to the fetus begins, which ensures its protection both during the period of intrauterine development and in the first months after birth. Such significant changes are largely due to the appearance of a

"new" organ in the pregnant woman – the placenta. Proteins and hormones synthesized by the placenta and fetus apparently play a leading role in the adaptation of the mother's body to pregnancy. Thus, studying the level of cytokines by weeks of the gestation period more accurately reflects changes in cytokine concentrations, provides important information about the state of the immune system not only at the time of examination, but can also allow predicting the further course of pregnancy and its outcome. The results obtained will allow them to be used as normative materials for the timely detection of immunological criteria for pregnancy pathology.

4. Conclusions

1. Studying the concentration of cytokines by weeks of the gestation period more accurately reflects the physiological boundary of changes occurring during pregnancy.
2. The maximum increase in the proinflammatory cytokine IL-1β in women with a physiologically proceeding pregnancy is observed at 28-31 weeks of gestation.
3. The maximum increase in the level of IL-6 and IL-8 in women with a physiologically proceeding pregnancy is observed at 12-15 weeks of gestation.

REFERENCES

[1] Botasheva T.L., Rymashevsky A.N., Mikhelson A.F., Fabrikant A.D., Khloponina A.V., Zheleznyakova E.V., Zavodnov O.P. Production of Some Angiogenic Factors and Cytokines in Physiological and Complicated Pregnancy Depending on the Sex of the Fetus // V.F. Snegirev Archives of Obstetrics and Gynecology. 2020. Vol. 7. No. 4. P. 195–200. doi: 10.17816/2313-8726-2020-7-4-195-200.

[2] Dobrokhotova Yu.E., Gankovskaya L.V., Bakhareva I.V., Svitich O.A., Malushenko S.V., Magomedova A.M. The role of immune mechanisms in the pathogenesis of miscarriage. Obstetrics and Gynecology. 2016; 7: 5-10. https://doi.org/10.18565/aig.2016.7.5-10.

[3] Zamyatina S.V., Elchaninova S.A., Raevsky V.M., Dudareva Yu.A., Rachenkova T.V. Cytokines in normal pregnancy and miscarriage. Problems of reproduction. 2024; 30(1): 72 81 https://doi.org/10.17116/repro20243001172.

[4] Kapustin E.A., Botasheva T.L., Linde V.A., Avrutskaya V.V., Kaushanskaya L.V. The influence of fetal sex on the functional state of women's blood during physiological pregnancy // Modern problems of science and education. 2014. No. 2. URL: http://Archive of Obstetrics and Gynecology named after V.F. Snegirev. 2020, 7(4). DOI http://doi.org/10.17816/2313-8726-2020-7-4-195-200.

[5] Kruglyakova M.V., Smirnova O.V., Titova N.M. Characteristics of the cytokine profile in physiological and complicated pregnancy // Culture. Science. Education: Problems and Prospects IX International Scientific and Practical Conference., 2021, pp. 549 – 556. https://doi.org/10.36906/KSP-2021/79.

[6] Ketlinsky S.A., Simbirtsev A.S. Cytokines. St. Petersburg. "Foliant"., 2008, 560 p.

[7] Kolesnik N.N. Local and systemic cytokines in isthmic-cervical insufficiency at different gestational periods. Women's Health. 2015; 10 (106): 108.

[8] Levkovich M.A., Nefedova D.D., Tsaturyan L.D., Berdichevskaya E.M. Immunological aspects of the problem of miscarriage. Modern problems of science and education. 2016; 3: 186. (In Russ.).

[9] Lebedeva E.I., Yavorskaya S.D., Momot A.P., Fadeeva N.I., Kuznetsova T.A. Improving perinatal outcomes in patients with miscarriage by correcting fibrinolytic reactions. Bulletin of Medical Science. 2021; 3(23): 4-10. https://doi.org/10.31684/25418475_2021_3_4.

[10] Moskalov A.V., Rudoy A.S., Apchel V.Ya. Chemokines, their receptors and features of the development of the immune response // Bulletin of the Russian Military Medical Academy. 2017. No. 2 (58). P. 182–187.

[11] Nacharov Yu.V., Sokolova T.M., Usova A.V. The content of pro- and anti-inflammatory cytokines in women with miscarriage after maintenance therapy. Bulletin of new medical technologies. 2008; 15(2): 50-52.

[12] Nefedova D.D., Linde V.A., Levkovich M.A. Immunological aspects of pregnancy (literature review). Med. vestn. of the South of Russia. 2013; 4: 16–21.

[13] Petrov Yu.A., Arndt I.G., Bakhtina A.S. Immunological aspects of miscarriage. Chief physician of the South of Russia. 2021; 1(76): 38-41.

[14] Pogorelova T.N., Gunko V.O., Nikashina A.A., Alliluyev I.A., Botasheva T.L. Posttranslational modifications and differential expression of proteins in placental insufficiency // Problems of reproduction. 2016. Vol. 22. No. 6. P. 115–119.

[15] Pogorelova T.N., Gunko V.O., Nikashina A.A. Influence of modification of the primary structure of cytoplasmic and membrane proteins of the placenta on the development of its insufficiency // Russian Bulletin of Obstetrician-Gynecologist. 2017. Vol. 17. No. 1. P. 4–8. doi: 10.17116/rosakush20171714-8.

[16] Sotnikova N.Yu., Kudryashova A.V., Antsiferova Yu.S. et al. Systemic and local mechanisms of regulation of the immune response in uncomplicated pregnancy // Mat. IV Russian Forum "Mother and Child" (Moscow, October 12-15, 2004) - M., 2004. - P. 323.

[17] Sukhikh G. T., Vanko L. V. Immunology of pregnancy. M., RAMS Publishing House, 2003., 340 p.

[18] Tesakova M. L., Nebyshinets L. M., Melnik E. V., Maloletkina O. L., Ivanchik G. I. Prediction of the outcome of labor induction by cytokine levels in cervical secretions // J. Maternity and Childhood Protection., 2013., No. 2 (22)., P. 47-51.

[19] Tetruashvili N. K., Sidelnikova V. M., Veryasov V. N., Sukhikh G. T. Cytokine ratio in early gestation in patients with a history of habitual miscarriage // Proceedings of the IV Russian Scientific Forum "Mother and Child". Moscow, 2002. P. 102.

[20] Tetruashvili N.K. The role of immune interactions in the early stages of physiological pregnancy and in habitual miscarriage // Immunology. 2008. No. 2. P. 124–129.

[21] Ali S., Majid S., Ali M.N., Taing S., Rehman M.U., Arafah A. Cytokine imbalance at materno-embryonic interface as a potential immune mechanism for recurrent pregnancy loss. Int. Immunopharmacol. 2021; 90: 107118. doi: 10.1016/j.intimp.2020.107118.

[22] American College of Obstetricians and Gynecologists et al. (2020) Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222/ Obstetrics and gynecology 2020. Vol. 135 No6. P. e237-e260. https://doi.org/10.1097/AOG.0000000000003891.

[23] Auvinen A-M, Luiro K, Jokelainen J, et al. Type 1 and type 2 diabetes after gestational diabetes: a 23 year cohort study. Diabetologia 2020; 63.