



## Dynamics of cytokine production during physiological pregnancy in women living in a hot climate

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### ABSTRACT

An increase in the production of cytokines in the body of pregnant women in the reproductive period and the main mechanisms of their action were studied. The article highlights their studies of cytokine production in women of the Bukhara population. The conducted studies study the conditions for the production of cytokines (IL-1b, IL-6, IL-8) and inflammatory cytokines (IL-4, IL-10) in the body of women living in a hot climate, and apply them in practice.

### Keywords:

Cytokines, IL-1b, IL-6, IL-8, inflammatory cytokines IL-4, IL-10.

**Reproduction** is a very important process for any species, as it ensures its continuation. An analysis of the regularities of regulation during physiological pregnancy can make it possible to approach the solution of many problems of clinical immunology and many medical problems.

At present, specialists working in the field of reproductive immunology have formed a definite opinion about the features of the construction of nonspecific and specific immune defenses. It is generally accepted that the normal development and functioning of the reproductive system is carried out in close interaction with the immune and endocrine systems.

The changes that occur during the menstrual cycle and pregnancy are controlled by the hypothalamic-pituitary system and are a direct result of hormone-induced tissue remodeling of the tissues of the ovary and uterine mucosa. The action of hormones at the cellular level is realized through the involvement of many peptide growth factors, among which a special role is given to lymphohemopoietic cytokines produced by immunocompetent cells (ICCs).

It has been established that ICC express receptors for sex hormones, luteinizing hormone (LH) and gonadotropin-releasing

hormone. Moreover, the change in the concentration of cytokines is cyclical, and a relationship is revealed between the level of sex hormones and the content of cytokines. For example, the expression of IL-1 $\beta$  mRNA in peripheral blood monocytes in the luteal phase of the cycle is 3 times higher than in the follicular phase.

The functions of ovarian-localized immune system cells are associated with their ability to produce cytokines and chemokines, which, either directly or through additional recruitment of various types of ICC, are involved in the regulation of follicular maturation, ovulation, development/atrophy of the corpus luteum, and steroidogenesis.

Immune cells are capable of expressing receptors for various hormones. Among them are receptors for corticosteroids, insulin, prolactin, estradiol, testosterone;  $\beta$ -adrenergic receptors, cholinergic receptors, receptors for enkephalins, somatostatin, etc.

Through these receptors, endocrine cell synthesis products can influence the function of immune cells.

Pregnancy, as a biological phenomenon, is a complex and understudied phenomenon. Since the middle of the 20th century, immunologists have been trying to establish the mechanisms

that allow a mother to bear an antigenically foreign fetus for 9 months. The mechanisms of non-response of the mother's immune system to the antigens of the developing fetus remain unclear.

The mechanisms of selective permeability of the placental barrier for various antigenic substances, often independent of their size, are also unclear. These questions force us to look for different approaches to the study of the mechanisms of preservation of the fetus, as an antigenically alien object, in the mother's body. An uncomplicated course of pregnancy is largely determined by a complex of immunological relationships between the mother and the fetus, which determine the known level of tolerance of the pregnant woman's body to alloantigens.

Numerous works highlight various aspects of cellular and humoral immunity, non-specific factors protecting women during pregnancy. Traditionally, pregnancy is divided into three trimesters, and therefore all immunological parameters are usually given by the authors by trimesters.

An analysis of published works shows that such a division is not informative enough, since when dividing into trimesters, it is not possible to study the relationship between immunological parameters and events occurring in the body of the mother and fetus during pregnancy, such as the formation of the placenta, the development of the fetal immunological system, and hormonal changes in the maternal body etc.

In addition, violations of the immunological relationship between mother and fetus can be the cause of spontaneous abortion and therefore knowledge of the physiological boundaries of immunological parameters (cellular, humoral immunity, as well as cytokine status) in an uncomplicated pregnancy in an arid zone by weeks of the gestational period provides significant information for understanding pathogenesis of a number of disorders in the mother-placenta-fetus system.

Cytokines are traditionally the subject of special attention from researchers involved in the problems of reproductive immunology,

which is associated with their participation in almost all stages of the gestational process. They regulate the implantation of the blastocyst, the growth of the placenta and fetus, the production of placental hormones and specific proteins, cell apoptosis, the supervision of the microflora of the reproductive tract, preparation for childbirth and the unleashing of labor.

Moreover, during pregnancy, the significance of certain factors changes, which is due to the peculiarities of the stages of placenta formation and changes in the population composition of cytokine-producing cells in the dynamics of the gestational process.

Correspondence of the research topic with the priority areas of research in the Republic.

This dissertation topic corresponds to the priority area in allergology and immunology, and is also aimed at improving the health of the female population, in particular, assisting in supporting health care reforms, a safe motherhood program, integrated management of diseases of women of childbearing age, which is fruitfully implemented in the Republic of Uzbekistan.

Connection of work with government programs or R&D.

The topic is included in the research plan of the Bukhara State Medical Institute and approved by the Academic Council; Protocol No. ... dated ..... 2022

The degree of knowledge of the problem.

The aim of the study was to study the dynamics of pro- and anti-inflammatory cytokines, and growth factors in women of childbearing age and with uncomplicated, from an obstetric point of view, pregnancy by weeks of the gestational period in the conditions of the Bukhara region.

Research objectives:

To study the level of pro- and anti-inflammatory cytokines and growth factors in practically healthy women of reproductive age, depending on the phase of the menstrual cycle, living in the Bukhara region.

To evaluate the dynamics of pro- (IL-1 $\beta$ , IL-6, IL-8) and anti-inflammatory (IL-4, IL-10) cytokines by weeks of the gestational period in uncomplicated pregnancy in a hot climate.

To study the dynamics of growth factors (VEGF A and PGF) by weeks of the gestational period in uncomplicated pregnancy in a hot climate.

Assess the role of various cytokines in the development of normal labor activity.

To determine the most informative indicators of cytokine status by studying the dynamics of the gestational period of women in hot climates in order to create normative materials.

**Object of study.** It is planned to conduct a survey of 40 practically healthy women of reproductive age; 120 women with physiological pregnancy with different gestational age:

**Subject of study.** The subject of the study will be peripheral blood

A brief description of the significance of the scientific novelty of the expected results of the study

**Research novelty** The dynamics of various cytokines in women of reproductive age living in the Bukhara region will be assessed depending on the phases of the menstrual cycle. Prognostic criteria for the studied cytokines in pregnant women with a physiological course will be identified, on the basis of which normative data will be developed.

Expected plan of the research work to be carried out. Planned research methods:

**Clinical -Laboratory** - (general blood count, urinalysis, etc.) clinical and functional studies.

**Clinical and instrumental - ultrasound, dopplerometry.**

Immunological - determination of the level of pro- and anti-inflammatory cytokines (IL-1 $\beta$ , IL-4, IL-6, IL-8, IL-10) and growth factors (vascular endothelial growth factor - VEGF and placental growth factor - IGF).

**Stages of work:** 2022 - 2023 -Preparation of accounting and registration documentation and mastering research methods. Acquaintance with the literature on the topic of the dissertation. Conducting patent and information research to approve the topic of the dissertation for the degree of Doctor of Philosophy (PhD). Approval of the topic at the

department and the problem committee. Passage of the coordinating council. Collection of clinical material. Analysis of the results of the study. Writing articles and abstracts and making a presentation. Writing dissertation chapters: introduction and literature review, chapters of own research. Fulfillment of pedagogical load. Passing qualifying exams.

2024 - Statistical processing of the received data. Writing a dissertation and manuscript of the abstract. Approbation and scientific seminar, release of the dissertation abstract. Dissertation defense.

## Literature

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