BG Pulse Journal USA
ISSN:1947-2536 http://www.bgpulseusa.com/index.php/bg
BG PULSE JOURNAL

FEATURES OF CHANGES IN IMMUNE AND CYTOKINE INDICATORS DURING REPRODUCTIVE AGE IN WOMEN

F.A. Mustafaeva
Abu Ali ibn Sino Bukhara State Medical Institute, Bukhara, Uzbekistan
E-mail: mustafayeva.feruza@bsmi.uz
https://orcid.org/0009-0009-6211-4330

Resume. This study investigated changes in immune parameters in women at different stages of reproductive aging — premenopause, menopause, and postmenopause. A total of 90 women were examined (30 in each group). Blood levels of immunoglobulins (IgA, IgM, IgG, IgE), pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), anti-inflammatory cytokines (IL-4, IL-10), and C-reactive protein were measured. The results demonstrated an age-related shift of the immune system toward a pro-inflammatory profile. In postmenopause, IL-6, TNF-α, and C-reactive protein levels were significantly elevated, whereas IL-4 and IL-10 levels were decreased. These findings reflect mechanisms of immunosenescence and chronic low-grade inflammation.

Keywords: menopause, postmenopause, immune system, immunoglobulins, cytokines, immunosenescence, inflammation, IL-6, TNF-α, IL-10, C-reactive protein.

In recent decades, women's health, especially the somatic and immune changes that occur during menopause and postmenopause, have become a relevant scientific direction in world medicine. Menopause is a physiological state characterized by a decrease in the hormonal activity of the ovaries and a decrease in the secretion of estrogens. However, this process is not limited to the cessation of reproductive function, but also causes a profound restructuring of all body systems, in particular the immune system.

Estrogens are among the immunoregulatory hormones. They stimulate B-lymphocyte differentiation and antibody synthesis, affect T-cell balance, and maintain the cytokine profile in the anti-inflammatory direction. Under the influence of estrogens, the activity of anti-inflammatory cytokines such as IL-4 and IL-10 increases, while pro-inflammatory mediators are limited. Therefore, the immune response in women of reproductive age is more humoral and tolerant in nature.

With aging and hormonal deficiency, the immune system develops a condition called immunosenescence. This process is characterized by:

- decreased functional reserve of lymphocytes
- shift of cytokine balance towards pro-inflammation
- chronic low-grade inflammatory state
- increased susceptibility to autoimmune diseases

In modern literature, this condition is referred to as “inflammaging.” Inflammaging is the persistence of chronic, low-intensity inflammatory processes in the body as we age. This condition increases the risk of cardiovascular disease, osteoporosis, type 2 diabetes, neurodegenerative and autoimmune pathologies.

During menopause, estrogen depletion leads to a decrease in Th2-type immune responses and an increase in Th1-type pro-inflammatory responses. This is manifested by an increase in mediators such as IL-6, IL-1β, and TNF-α. IL-6 is a major cytokine associated with metabolic syndrome and

atherosclerosis, while TNF-α leads to endothelial dysfunction and tissue damage. At the same time, anti-inflammatory cytokines such as IL-4 and IL-10 decrease.

The immunoglobulin profile also changes with age. Decreases in IgA and IgM weaken mucosal immune defenses, which increases susceptibility to infections. Conversely, IgG may increase, which is a sign of chronic antigen exposure and impaired immune regulation.

Therefore, a comprehensive assessment of the immune status at the reproductive stages is of great importance for clinical diagnostics, identification of risk groups, and development of preventive measures. Determining the relationship between hormonal changes and the immune system in women is one of the important tasks of modern gerontology and immunology.

Objective:

To assess changes in immunoglobulin and cytokine profiles in women during premenopause, menopause, and postmenopause.

Materials and Methods:

90 women participated in the study and were divided into 3 groups.

Group Number Period

I 30 Domenopause

II 30 Menopause

III 30 Postmenopause

The following indicators were found in the blood

Immunoglobulins: IgA, IgM, IgG, IgE

Cytokines: IL-1b, IL-6, IL-4, IL-10, TNF-a

Inflammatory marker: S-reactive protein (CRO)

The tests were performed using the enzyme-linked immunosorbent assay (ELISA) method. The results are expressed as the arithmetic mean (M±m). The level of significance was set at $p<0.05$.

Results

1 Dynamics of immunoglobulins Index

Domenopause	Menopause	Postmenopause
IgA 3.3	2.8 ↓	2.2 ↓↓
IgM 1.25	1.34	1.05 ↓
IgG 10.7	11.8	18.5 ↑↑
IgE 165.2	98.6 ↓	72.1

Analysis: Decreased IgA and IgM indicate a weakening of mucosal immunity. Increased IgG is consistent with chronic antigen stimulation and signs of immune aging.

Proinflammatory cytokines Indicator

Domenopause	Menopause	Postmenopause
IL-1b 15.7	26.4 ↑	32.7 ↑↑
IL-6 13.9	27.8 ↑	39.3 ↑↑
TNF-α 10.2	18.7 ↑	25.3 ↑↑
CRO 5.5	10.3 ↑	13.6

Elevated IL-6 and TNF-α are markers of cardiovascular risk. Elevated CRO indicates subclinical inflammation.

Anti-inflammatory cytokines Indicator

Domenopause	Menopause	Postmenopause
IL-4 28.4	20.6 ↓	12.3 ↓↓
IL-10 35.6	26.9 ↓	17.8

Immunoglobulins A decrease in IgA and IgM was observed with age, indicating a weakening of mucosal immune defense. An increase in IgG during postmenopause indicates an increase in humoral immune response against the background of chronic antigen stimulation. IgE levels decreased in menopause and postmenopause, indicating a decrease in allergic reactivity.

Proinflammatory cytokines IL-1β, IL-6, and TNF-α increased progressively from premenopause to postmenopause. This indicates that inflammatory processes dominate the immune system. In particular, increased IL-6 is a marker associated with cardiovascular risk and metabolic syndrome. CRO levels also increased with age, confirming a state of subclinical inflammation.

Levels of the anti-inflammatory cytokines IL-4 and IL-10 begin to decline at menopause and are significantly reduced in postmenopause, indicating that immune surveillance mechanisms are weakened and inflammatory processes are not limited.

Discussion

The results of the study clearly showed that the direction of immune system activity changes in women with age. While immune parameters are relatively balanced in the premenopausal stage, inflammatory processes begin to dominate during menopause and especially postmenopausal periods.

The gradual increase in the levels of IL-1β, IL-6 and TNF-α indicates the formation of a chronic inflammatory state in the immune system. This is of great clinical importance, since IL-6 is one of the main mediators in the development of cardiovascular pathologies, insulin resistance and osteoporosis. TNF-α, on the other hand, damages endothelial cells and accelerates the development of atherosclerosis.

The increase in CRO levels with age also confirms the state of subclinical inflammation. It has been repeatedly noted in the literature that an increase in this indicator is associated with an increased risk of somatic diseases during menopause.

A decrease in the levels of the anti-inflammatory cytokines IL-4 and IL-10 indicates a weakening of the control mechanisms in the immune system. IL-10 is the main cytokine that limits the activity of macrophages and T-cells, and its decrease leads to uncontrolled inflammatory processes. IL-4, on the other hand, controls humoral immunity and allergic responses, and its decrease indicates a loss of immune regulation.

The immunoglobulin profile also corresponded to these changes. Decreases in IgA and IgM indicate a weakening of mucosal immune defense, which is explained by an increased susceptibility to infections in postmenopause. An increase in IgG is characteristic of the phenomenon of immune aging and is associated with chronic antigen exposure and a tendency to autoimmune reactions.

The results are consistent with international studies and confirm the formation of Th1 dominance in the immune system during menopause. Estrogen deficiency leads to a decrease in anti-inflammatory cytokines and an increase in pro-inflammatory mediators, which leads to a state of inflammation in the immune system. This condition, if prolonged, creates the basis for the development of chronic diseases.

Thus, the results of the study showed that changes in the immune system in women during menopause and postmenopause are closely related to hormonal background. By monitoring the

immune system and implementing preventive measures, it is possible to reduce the risk of somatic diseases that occur during this period.

REFERENCES

1. Ф.А.Мустафаева. У.П.Набиева.Описание иммунного статуса женщин в пременопаузе, менопаузе и постменопаузе, новый подход к его био и иммунокоррекции (обзор литературы). // Тиббиётда янги кун. 3(77).2025.35-38.
2. Абдиева Г., Ташкенбаева Э., Музаффарова Ю. Факторы риска развития сердечнососудистых заболеваний у женщин в климактерическом периоде // Журнал проблемы биологии и медицины. 2016;4(91):156-158.
3. Гендерное сравнение клинико-ангиографических особенностей инфаркта миокарда у пациентов молодого возраста / Н.М. Балаян, М.М. Шебзухова, Н.С. Грачев [и др.]. - Текст: непосредственный // Вестник РГМУ. 2016;5:44-50.
4. Brunelli R, Frasca D, Perrone G, et al. Hormone replacement therapy affects various immune cell subsets and natural cytotoxity. // Gynecol. Obstet. Invest. 1996;88:25-8, 128-31.
5. White HD, Crassi KM, Givan AL, et al. CD3+ CD8+, CTL-activity within the human female reproductine tract: influence of stage of the menstrual cycle and menopause. // J. Immunolog. 1997;158:3017-27.
6. Исакова О.В. и др. Сывороточные уровни некоторых иммунорегуляторных белков и цитокинов при приеме менопаузальной гормональной и негормональной терапии / О. В. Исакова, Л. Г. Баженова, Р. М. Зорина [и др.] // Российский вестник акушера-гинеколога. 2015;4:7-11.
7. Huang W. et al. Circulating interleukin-8 and tumor necrosis factor-α are associated with hot fl ashes in healthy postmenopausal women / W. Huang, I. Hsin, D. Chen [et al.] // PLoS One. 2017;12(8):e0184011.
8. В.В. Симрок, Е.Д. Мирович, С.Е. Золотухин, К.Е. Ткаченко, Н.И. Костецкая, Д.Э. Майлян. Цитокиновый профиль у женщин с климактерическим синдромом и остеопорзом. Проблемы экологической и медицинской генетики и клинической иммунологии // Сборник научных трудов. Луганкс 2 (170).
9. Сметник В.П. Медицина климактерия / под ред. В.П. Сметник. Ярославль: ООО “Издательство Литера” 2006; 848 стр.
10. Хаитов Р.М. Иммунология / Р.М. Хаитов, Г.А. Игнатьева, И.Г. Сидорович / М.: Медицина, 2000; 250 стр.
11. Коркушко О.В. Пептидные препараты тимуса и эпифиза в профилактике ускоренного старения / О.В. Коркушко, В.Х. Хавинсон, Г.М. Бутенко // СПб., 2002; 31-51 стр.
12. Теппеева Т.Х. Изменения фагоцитарного и клеточного звена иммунитета у женщин с гиперплазией эндометрия на фоне патологического климакса 2020.
13. Теппеева Т.Х., Мусуралиев М.С., Тулебеков Б.Т. Результаты оценки системного иммунитета у женщин с различным течением климактерия. Международный научный журнал «Инновационная наука» 2016;9. ISSN 2410-6070.