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Adaptive immune response in residents of the Russian Arctic zone and South Ossetia

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Abstract. The human body in adverse living conditions, such as in the Arctic, goes through the risk of impairing functional systems including the immune system. These disturbances lead to appear states of weakness or hyperactivity of the organism protective function. This study investigates the state of the adaptive immune response of 40-60-year-old women living in the Russian Arctic and South Ossetia. The indirect immunoperoxidase assay with monoclonal antibodies was used to analyze the immune parameters of lymphoid subpopulations in 40-60-year-old women living in Nadym city in the Yamalo-Nenets Autonomous Okrug and in Tskhinval city in South Ossetia. After analyzing the received data, the deficiency of mature T-lymphocytes (CD3⁺) was found in 96-100% of the examined individuals. We also revealed a decrease in the concentration of T-helper (CD4⁺) and B-activated (HLA-DR⁺) cells in 30% of Arctic zone cases and in 50% of the southern zone cases on the background of increasing concentrations of cytotoxic T-lymphocytes. A deficiency of cells with apoptosis receptors (CD95⁺) was registered mainly in Tskhinval women (80%). Thus, it can be assumed that the deficiency of mature lymphoid cells with a receptor (CD3⁺) leads to disruption of the T-cell pool of the immune response and delay of the adaptive immune response overall. The increase in the cytotoxic T-lymphocyte count indicates the stress state of the adaptive immune component to compensate for the lack of T-helper and B-activated cells concentration. Additional comprehensive studies are needed to identify environmental factors having a significant impact on the mechanism of the adaptive immune response development.

1. Introduction

Public health, including the state of the immune system, is an important indicator that should be used to track and monitor changes in human development depending on the place of residence [1]. Biological control of the human body includes a quantitative investigation of influencing factors and their effects on body fluids and tissues [2].

In recent decades, many efforts have been devoted to study the characteristics of pollution effects on the human body, especially in the Arctic regions. Currently, the scientific community has sought to epidemiological studies and assess the impact of pollution on human health, in particular on the immune and nervous systems [2].

Adverse environmental conditions directly affect the adaptive capacity of the organism functional systems, especially the immune system. These conditions ultimately lead to inadequate adaptative changes and the appearance of diseases. [3]. There are many factors that affect vital functions,



including immune homeostasis, such as mixtures of pollutants found in the Arctic, population, genetic susceptibility. In addition, the global geographical and climatic conditions put stress on the high latitude regions, and natural processes lead to changes in the total flow of pollutants to the Arctic [2,4,5].

The immune system considered to be the most sensitive system to environmental changes and an indicator of the body's adaptation reactions that reflect the level of stress in response to any stressful environmental impact. [6]. Additional researches and biomonitoring of the state of systems that provide vital functions, the immune system, in particular, are necessary to assess the impact of climatic and environmental conditions of the Arctic on the population. Furthermore, health vulnerabilities should be identified in high latitudes with the aim of development and improvement of adaptive mechanisms in order to reduce the impact of adverse living conditions on the human body and the occurrence of diseases. [7].

In 2015, the Arctic Monitoring and Assessment Program reported the emergence of new Arctic data in Russia for elevated levels of persistent organic pollutants (POPs) among indigenous coastal peoples. [8]. POPs are considered to be one of the factors associated with the development of autoimmune reactions by modulating the immune response, activating T-helper cells (CD4⁺) and suppressing cytotoxic cells (CD8⁺) [9,10].

The low ultraviolet index of high latitudes is an important cause of the spread of autoimmune diseases among the inhabitants of these regions since ultraviolet radiation plays the role of an immunosuppressant by activating regulatory T cells, suppressing cytotoxic cells (CD8⁺) and natural killer cells (CD16⁺) [11,12,13].

It is interesting to assess the immune status of residents living in the adverse conditions in the southern region. The influence of a prolonged political and military conflict in South Ossetia is reflected not only in the deterioration of the economic, sociological situation, but also in the appearance of an environmental crisis. The combination of factors arising from this conflict has adverse effects on the psychological and physiological state of the human body [14,15,16].

Pollution levels and adverse living conditions in the Arctic are higher than in other regions. Thus, it can be assumed that the population of the Arctic is exposed to worse effects on the functional systems of the organism than the population of other regions. Although the impact of these conditions on health remains ambiguous, it is almost impossible to aggregate and isolate one of these factors to identify its effects [17].

However, the current investigation of the adverse effects of pollutants and the environment on the immune system is important to identify the reserve and adaptive capacity of immune components.

This paper aims to identify the state of the adaptive immune response of 40-60-year-old women living in the Russian Arctic and South Ossetia.

2. Materials and methods

The study was conducted in the immunocompetent cells physiology laboratory of Natural Adaptation Physiology Institute of the Federal Center for Integrated Arctic Research of Russian Academy of Sciences named after Academician N.P. Laverov, Arkhangelsk, Russia.

We investigated the immune parameters of 50 practically healthy women aged from 40 to 60 years. The examined persons were divided into 2 groups, the first group contained 30 women living in Nadym city in the Yamalo-Nenets Autonomous Okrug, the second group consisted of 20 women living in Tskhinval city in South Ossetia. Fasting blood samples of all volunteers were taken from the venous in the morning.

We assessed lymphocytes markers CD3⁺ (mature lymphoid cells), CD4⁺ (T-helper cells), CD8⁺ (cytotoxic T-lymphocytes), CD10⁺ (cells with receptors, reflecting lymphoproliferation), CD95⁺ (cells with receptors for apoptosis) and HLA-DR⁺ (activated B-cells with a receptor to the main histocompatibility complex of class II) in the peripheral blood.

The percentage of T-lymphocyte subpopulations (CD3⁺, CD4⁺, CD8⁺, CD10⁺, CD95⁺ and HLA-DR⁺) was determined by the method of indirect immunoperoxidase reaction with monoclonal

antibodies (MedBioSpektr, Sorbent, Moscow) on preparations of lymphocytes of the dried drop type using peroxidase conjugate staining with a chromogen solution for immersion microscopy analysis (Nikon microscope).

We performed statistical processing of the results by means of Microsoft Excel 2016 and SPSS 24.0 for Windows. The normality of the distribution of quantitative indicators was checked using the Shapiro-Wilk criterion. The mean values (M) and standard error of the mean (m) were calculated. The assessment of the significance of differences for paired independent samples was carried out using the Mann-Whitney test. The differences in the compared indicators were assumed to be reliable at a significance level of $p < 0.05-0.01$.

The work was carried out according to the state order № AAAA-A15-115122810184-6.

3. Results

The results of the analysis, which are presented in Table 1. and Figure 1, show a significant decrease in the concentration of mature T-lymphocytes in the examined women. The observed content of CD3⁺ in Nadym women was about 1.5 times higher than in Tskhinval women ($(0.53 \pm 0.03) \times 10^9$ cells/L, $(0.35 \pm 0.03) \times 10^9$ cells/L, $p < 0.01$), respectively. However, the deficiency of CD3⁺ was recorded in all the examined Tskhinval women, but only in 96.6% of examined women in Nadym city.

Table 1. The mean concentration of lymphocyte subpopulations in the peripheral blood of Nadym city and Tskhinval city 40-60-year-old women (M \pm m).

Marker	Nadym city	Tskhinval city	Normal range
CD3 ⁺ $\times 10^9$ cells/L	0.53 \pm 0.03	0.35 \pm 0.03**	1 – 1.5
CD4 ⁺ $\times 10^9$ cells/L	0.47 \pm 0.03	0.37 \pm 0.04*	0.4 – 0.8
CD8 ⁺ $\times 10^9$ cells/L	0.49 \pm 0.03	0.37 \pm 0.04*	0.2 – 0.4
CD10 ⁺ $\times 10^9$ cells/L	0.44 \pm 0.03	0.39 \pm 0.04	0.05 – 0.6
CD95 ⁺ $\times 10^9$ cells/L	0.48 \pm 0.04	0.36 \pm 0.04*	0.45 – 0.55
HLA-DR ⁺ $\times 10^9$ cells/L	0.45 \pm 0.03	0.38 \pm 0.04	0.34 – 0.72

* $p < 0.05$, ** $p < 0.01$ Significance level in the comparison group of women Nadym with a group of women Tskhinval.

The concentration of T-helper (CD4⁺) in Tskhinval women is rather low, on average $(0.37 \pm 0.04) \times 10^9$ cells/L. However, it is significantly lower than the content of T-helper (CD4⁺) in Nadym women, which is within the normal range. It is on average $(0.47 \pm 0.04) \times 10^9$ cells/L, $p < 0.05$. A decrease in the T-helper concentration was found in Tskhinval women, 1.8 times higher than in Nadym women (55% and 30%, $p < 0.05$), respectively.

A high concentration of cytotoxic T-lymphocytes (CD8⁺) was found in Nadym women ($(0.49 \pm 0.03) \times 10^9$ cells/L) with a significant difference from the concentration (CD8⁺) in Tskhinval women ($(0.37 \pm 0.04) \times 10^9$ cells/L, $p < 0.05$), which is within the normal range. Considering the frequency of imbalances, a state of increased content (CD8⁺) was found in 60% of the examined women in Nadym and in 45% of the examined women in Tskhinval. A deficiency cytotoxic T-lymphocytes (CD8⁺) was recorded in 15% of Tskhinval women, South Ossetia.

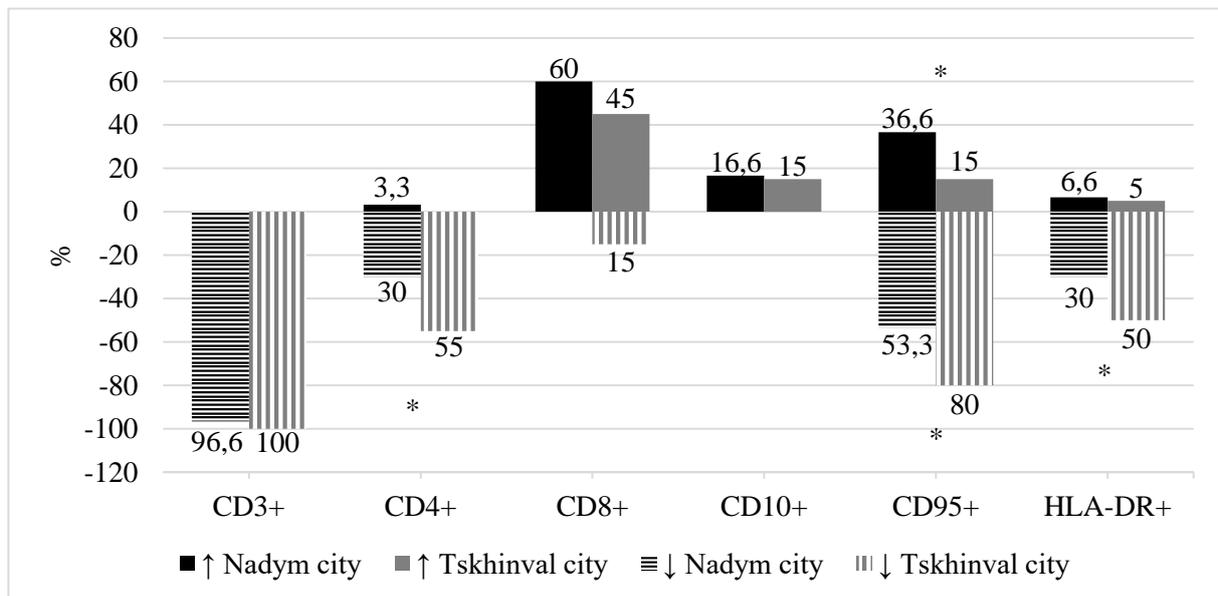


Figure 1. The frequency of imbalances registration of immunological parameters in women aged 40 - 60 years (residents of Nadym and Tskhinval),%, * $p < 0.05$.

The concentration of lymphocytes with a receptor for lymphoproliferation ($CD10^+$) within the normal range and on average is $(0.41 \pm 0.02) \times 10^9$ cells/L, regardless of residence place. An increase in concentration ($CD10^+$) appeared in 16.6% and 15% of women in Nadym and Tskhinval, respectively.

The content of lymphoid cells with receptors for apoptosis ($CD95^+$) in Tskhinval women is low and on average is $(0.36 \pm 0.04) \times 10^9$ cells/L. The concentration ($CD95^+$) in women of Nadym ($(0.48 \pm 0.04) \times 10^9$ cells/L, $p < 0.05$) was significantly higher than in women of Tskhinval. The deficiency of lymphocytes with a receptor for apoptosis ($CD95^+$) was registered 1.5 times more often in Tskhinval women (80%) than in Nadym women (53.3%). Elevated concentrations of lymphocytes with a marker ($CD95^+$) were detected 2.4 times more often in Nadym women (36.6%) than in Tskhinval women (15%).

The total number of activated B-cells with a receptor to the main histocompatibility complex class II (HLA-DR⁺) is $(0.42 \pm 0.03) \times 10^9$ cells/L regardless of the place of residence ($(0.45 \pm 0.03) \times 10^9$ cells/L and $(0.38 \pm 0.04) \times 10^9$ cells/L in women of Nadym and Tskhinval, respectively). The frequency of registration of low concentrations of lymphoid cells with (HLA-DR⁺) receptor was found 1.6 times more often in women of Tskhinval (50%) than in women of Nadym (30%).

4. Discussion

The deficiency of lymphoid cells with a marker ($CD3^+$), which plays an important role in the transmission of the T-cell activation signal, leads to disruption of the T-cell immune response and suppression of the development of adaptive immune responses in almost all of the examined persons.

The lack of T-helper cells ($CD4^+$) and activated B-cells with a receptor to the main class II histocompatibility complex (HLA-DR⁺) in 30% of the Arctic region women and 50% of the Southern region women on the background of hyperactivation of cytotoxic T-lymphocytes ($CD8^+$) in 52% of the examined persons indicates the state of stress of the adaptive immune response, due to attempts to compensate for the pronounced deficiency of immune components.

It can be noted that the deficiency of cells with an apoptosis receptor ($CD95^+$) in 80% of Tskhinval women and 53.3% of Nadym women on the background of increasing their concentration in 1/3 of Nadym women and 1/6 of Tskhinval women was recorded. At the same time the number of cells with

a receptor (CD10⁺), reflecting lymphoproliferation, is within the normal range with an increase in activation in 15.8% of the examined persons. As a result, it can be assumed that due to deficiency (CD95⁺) on the background of normal or elevated concentrations (CD10⁺), women are more at risk of developing and growing tumors [4]. Especially it concerns Tskhinval women, whose deficiency (CD95⁺) can be explained by inadequate living conditions, due to political and military conflict and difficult social living conditions.

5. Conclusion

Adverse environmental and sociological living conditions have a great influence on the adaptive immune response. Moreover, it can cause depletion of the immune regulation reserve ability, which ultimately leads to the development of environmentally dependent immunodeficiencies and potential diseases.

Thus, additional comprehensive researches are required to determine the factor that has the greatest impact on the components of the immune system. The information obtained is necessary for taking measures to prevent and preserve the health of the population, as well as to develop and provide the necessary social compensation.

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