IOP Conference Series: Earth and Environmental Science

PAPER • **OPEN ACCESS**

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To cite this article: M.S. Kabbani and L.S. Shchegoleva 2019 *IOP Conf. Ser.: Earth Environ. Sci.* **263** 012031

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Differentiated T-Cells Ratio in the Immune Response in Residents of Arctic and Middle Zone of the Russian Federation

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Abstract. The climate and environment of the northern and central regions of Russia have a significant impact on human health and, particularly, immune system, especially in women. Exposed to adverse conditions, the immune status is characterized by a short period of resistance, deficiency of T-cell population, weakened reserve capacity of immune homeostasis, and increased incidence of immune disorders. A study has been conducted to identify the ratio of differentiated T-cells in the immune response in healthy, working women aged 40–60, residing in the settlement of Pinega (Arkhangelsk Region) and the city of Vologda. The study has revealed leukopenia in 35.5% of Pinega women and lymphopenia in 31.8% of Vologda women. Regardless of the area of residence, 94.0% of the surveyed have deficit of mature T-lymphocytes (CD3+). The deficit of T-helper cells (CD4+) is suffered by 34.1% of Vologda women and 22.2% of Pinega ones. Furthermore, an increased content of cytotoxic T-lymphocytes and natural killer cells was detected in approximately 66% of Vologda and Pinega women.

1. Introduction

In recent decades, the immune system of people has been heavily burdened by stress, use of medicines, and ecological problems. Serving as an adaptation mechanism designed to restore the homeostasis disorders caused by anthropogenically altered environment, the strain in the immune system is known as anthropological-ecological, infectious immunological stress. Any uncompensated immunity stress is referred to as "fatigue", a condition relating to disrupted adaptation mechanisms that lead to unstable conditions and, ultimately, disease. The recent decades witness human body being exposed to pressure a variety of harmful factors and numerous foreign compounds, one being xenobiotics, that affect all levels of the immune system, causing mass allergies, prevalence of pathologies over acute conditions, and increase cancer incidence. [1,2,3].

Despite the multitude of life-supporting systems, the immune system works as a protection. Its unique nature consists in functional diversity, contributed to by its numerous defense mechanisms, resistance potential, and variety of reactions. A yardstick for the quality of the immune protection is human body's functional reserve and ability to adapt to the changing ambient conditions in prompt and quality manner [4,5].

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Changes in the duration of daylight lead to physiological, morphological and behavioral changes as mechanism for adapting to new conditions. The immune function responds to the changing duration of daylight, too. In general, shorter daylight enhances the immune responses, although the relating changes in all components of the immune function are not uniform. [6].

The effect of UV radiation on the human body leads to immunosuppression. The UV-induced immunosuppression activates regulatory T-cells that inhibit the proliferation of T-cells and the production of cytokines. The concentration of regulatory cells carrying CD4+ markers increases, while the concentration of cytotoxic T-lymphocytes (CD8+) and natural killer cells (CD16+) decreases [7, 8, 9]. The lack of ultraviolet radiation in the northern areas leads to an increase in sensitivity of the immune system and the spread of autoimmune diseases [9,10].

The climate and environment of the northern areas, as well as man-made impact on their ecosystems, manifest themselves in deteriorated ecology, that human body responds to by developing allergic diseases; delayed physical and psychological development in children; chronic degenerative diseases; oncopathology; repeated respiratory infections; and increased morbidity [11,12,13].

The unfriendly climatic factors of the northern areas affect the functional processes in the body, leading mainly to 3 groups of alterations that come down to increased metabolic load to maintain homeostasis and balanced metabolism; suppressed age-specific growth in a number of systems; and early reduction of reserve capacity [4].

The study of immune reactions in northern communities has revealed an increased level of immunodeficiency. Yet, any reduced immunological reactivity indicates to activation of cells and humoral mechanisms of the immune system, as well as to increase in concentrations of circulating immune complexes (CIC) and certain immunoglobulins and autoantibodies, that are products of the poorly-performing suppressor [15,16].

The purpose of this study is to evaluate the ratios of differentiated T-cells in the immune response in 40-60 year old women residing in the Arctic and the middle zone of Russia.

2. Materials and methods

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

The immunological examinations covered two separate groups – 31 women residing in the settlement of Pinega, Arkhangelsk Region and 40 women residing in Vologda, Vologda Region (N=71), aged between 40 and 60 years.

The surveyed were practically healthy women with no acute conditions as of the time of blood sampling (according to the conclusions from the local doctors). Venous blood samples were taken in the morning on an empty stomach.

The immunological examinations targeted blood count and phenotyping of lymphocytes. The content of peripheral blood leukocytes, lymphocytes with receptors CD3+ (mature lymphoid cells), CD4+ (helper T-lymphocytes), CD8+ (cytotoxic T-lymphocytes), CD16+ (natural killers) was determined.

The content of leukocytes was determined using the standard method of counting cells in Goryaev chamber. Leukocyte formulas were determined by blood smear stained according to Romanovsky-Giemsa.

The percentage of T-lymphocyte subpopulations (CD3+, CD4+, CD8+, CD16+) was determined using the method of indirect immunoperoxidase reaction that involved monoclonal antibodies (MedBioSpektr, Sorbent, Moscow) on 'dried drop' preparations of lymphocytes, and chromogen solution-stained peroxidase required for immersion microscopy analysis.

Statistical processing of the results was performed using the Microsoft Excel 2016 and SPSS 20.0 for Windows. The normality of 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 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.

3. Results

The data analysis shows that the total number of leukocytes averages 5.04 ± 0.15 × 109 cells/L, regardless of region of residence (4.90±0.24 in Pinega women and 5.14±0.20 in Vologda women, p <0.01), which is within normal physiological range.

The interpretation of leukograms (Figure 1) has revealed that in Vologda women the average lymphocytes concentration is lower (2.01 ± 0.12 × 109 cells/L) than in Pinega women (2.44 ± 0.16 × 109 cells/L, p <0.05).

The average number of neutrophils in Vologda women is higher than in Pinega ones – 2.68 ± 0.14 and 2.02 ± 0.23 × 109 cells/L, p <0.01, respectively.

The total eosinophils content averages 0.10 ± 0.01 × 109 cells/L regardless of region of residence (0.10 ± 0.02 in Pinega women and 0.09 ± 0.01 in Vologda women, p <0.01). The average number of monocytes equals 0.37 ± 0.02 × 109 cells/L regardless of region of residence (0.36 ± 0.04 in Pinega women and 0.37 ± 0.03 in Vologda women, p <0.01).

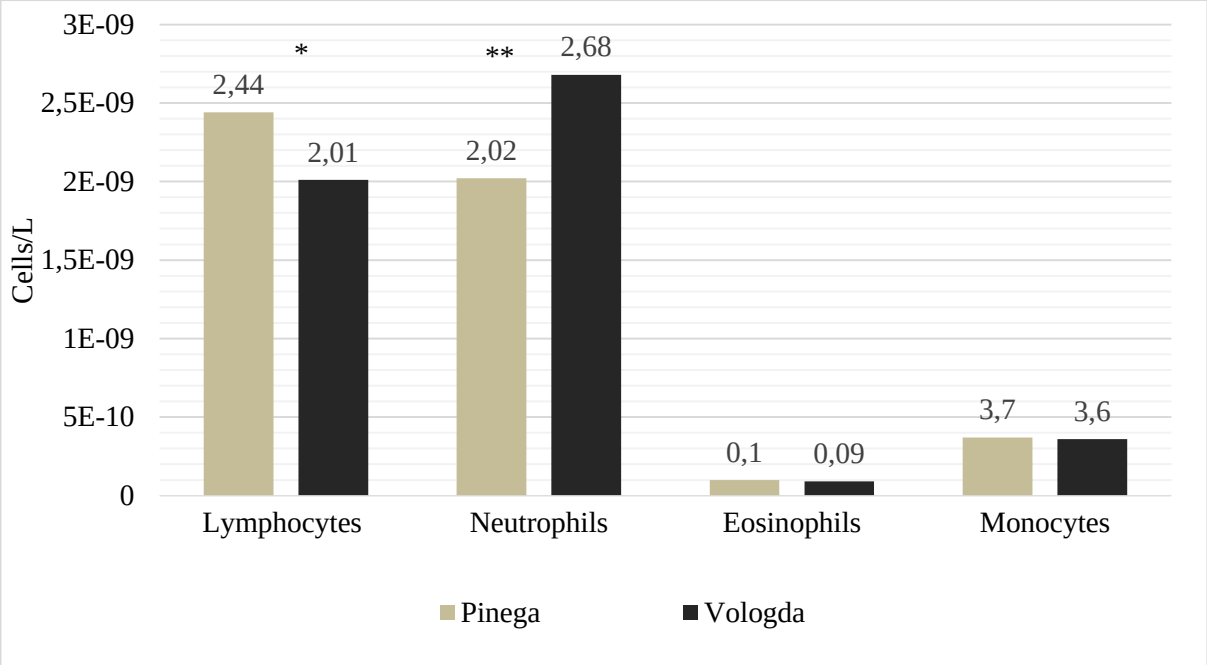


Figure 1: The leukogram of women living in Pinega settlement and Vologda city, age 40-60
* p < 0.05, ** p <0.01

The analysis of the imbalance rate (Figure 2) has shown a decrease in leukocyte concentration in 18.2% in Vologda women and 35.5% in Pinega women.

The Vologda women showed reduced number of neutrophils and lymphocytes – 11.4% and 31.8%, respectively, whereas in Pinega women this decrease equals 38.7% and 9.7%, respectively.

Increased concentrations of lymphocytes and monocytes was found in 2.2% and 12.9% of Vologda women and 9.7% and 13.6% of Pinega women, respectively.

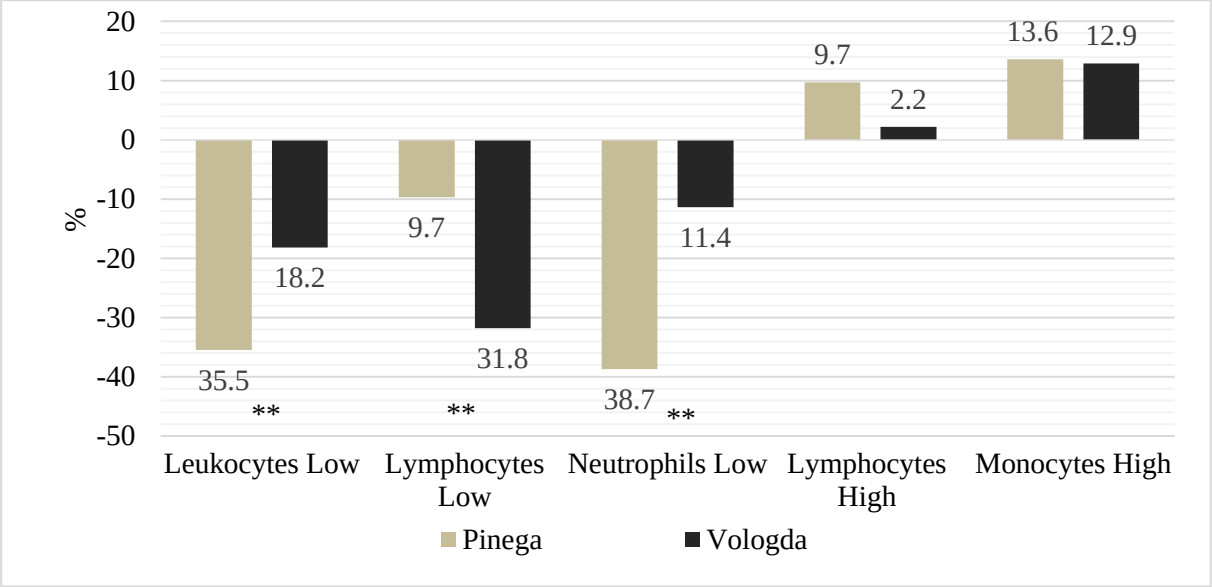


Figure 2: Leukogram imbalance rates in women living in Pinega settlement and Vologda city, age 40-60 ** p <0,01.

Our analysis of lymphoid subpopulations (Table 1) revealed that the content of T- lymphocytes with a CD3+ marker that activates T-cell signals and regulates the expression of TCR is, on average, below physiological standards, equaling 0.57 ± 0.03 ± 109 cells/L regardless of place of residence. T-lymphocyte deficiency with the CD3+ marker is found in 94.0% of the cohort (97.5% of Vologda women and 88.5% of Pinega women).

Table 1: The average content of lymphoid subpopulations in the peripheral blood in women residing in the settlement of Pinega and the city of Vologda, age 40-60 (M ±m).

Marker	Pinega settlement	Vologda city	Normal range
CD3+ × 10^9 кл/л	0,57 ± 0,0*5*	0,56 ± 0,04	1 – 1,5
CD4+ × 10^9 кл/л	0,54 ± 0,0*5*	0,49 ± 0,03	0,4 – 0,8
CD8+ × 10^9 кл/л	0,45 ± 0,03	0,50 ± 0,04	0,2 – 0,4
CD16+ × 10^9 кл/л	0,63 ± 0,05	0,52 ± 0,04	0,25 – 0,5
CD4+/CD8$^+$	*1,0*3 ± 0,05	*1,16* ± 0,05	1 – 4

The total concentration of helper T-lymphocytes (CD4+), known to play a crucial role in regulating adaptive immune responses, is 0.51 ± 0.03 × 109 cells/L regardless of place of residence (0.54 ± 0.05 in Pinega women and 0.49 ± 0.03 in Vologda women, p<0.01). The lack of T-helpers in women of Vologda occurs 1.5 times more often than in Pinega women (34.1% Vologda women and 22.2% of Pinega women).

The average number of cytotoxic T-lymphocytes (CD8+) is high, amounting to 0.47 ± 0.03 × 109 cells/L. No significant difference in the CD8+ content for found between Vologda women (0.45 ± 0.03) and Pinega women (0.50 ± 0.04). Increased concentrations of CD8+ is found in 50% of Vologda women and 67.9% of Pinega ones. Decreased concentrations of CD8+ is found in 9.5% of Vologda women and 3.6% of Pinega ones.

The content of natural killer T-cells (CD16+) averages 0.57 ± 0.03 × 109 cells/L, with no significant dependence on place of residence (0.63 ± 0.05 in Pinega women and 0.52 ± 0.04 in Vologda ones, $p < 0.01$), which exceeds the normal physiological range. In 50% of Vologda women and 65.4% of Pinega ones, CD16+ levels are higher than normal.

The helper/suppressor ratio (CD4+/CD8+), which reflects the level of the immune system, averages 1.11 ± 0.04 regardless of place of residence (1.03 ± 0.05 in Pinega women and 1.16 ± 0.05 in Vologda ones), which corresponds to the lower limit of normal physiological range. In Pinega women, the deficiency of CD4+/CD8+ ratio is 2 times higher than in Vologda women (25% and 52% respectively, $p<0.01$).

4. Discussion

Our investigation of the content and activity of immunocompetent cells in women aged 40-60 years residing in the Arctic and the middle zone of the Russian Federation, has revealed a number of distinctive features.

In Pinega women, the immune deficiency relates mainly to leukopenia and low neutrophil counts – 35.5% and 38.7%, respectively, Vologda women (31.8%) tend to show low lymphocyte count.
The deficit of mature T-cells CD3+ is found 94% of women aged 40 to 60 regardless of place of the residence.

The increased content of cytotoxic lymphocytes CD8+ and natural killer CD16+ was observed in 50.0% of Vologda women, and in 67.9% and 65.4% of Pinega women, respectively. The increase in CD8+ and CD16+ levels is related to a relative decrease in the count of T-helper lymphocytes (CD4+), regardless of residence area

The extremely low values of the helper/suppressor ratio (equals 1.11) result from the increased concentrations of T-lymphocytes (suppressors/killer CD8+) and the moderately decreased concentration of T-lymphocytes (CD4+ helpers) in peripheral blood. The deficiency of CD4+/CD8+ ratio indicates a decrease in the resistance to infections and an increase in the possibility of developing an autoimmune disease as a result of the disruption of the immune homeostasis [17,18].

5. Conclusion

The state of the immunological cellular components in the women examined is characterized as strained. The prolonged stress in T-cells leads to weakened immune homeostasis, manifesting itself in secondary immunodeficiencies caused by environmental factors. To problem identified requires systematic observation and the used of immunomodulators. Also, the existing benefits and compensations provided by the state to residents of the Far North and equated localities should remain in force.

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