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GENDER DIFFERENCES IN THE CONTENT OF THYROID HORMONES IN DIFFERENT GROUPS OF THE POPULATION OF THE ARCTIC

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The study of the gender characteristics of the thyroid gland functional activity take on particular significance in light of the increasing frequency of detecting various thyroid dysfunctions, especially in the Northern regions. Aim: to carry out a comparative analysis of the thyroid profile due to sex, taking into account the population groups of the North. Materials and methods. We examined 338 people born and living or wandering near the villages in the Arctic zone of the Russian Federation. The examined persons were divided by gender (men, women), age (21-44; 45-59 years) by gender and, population group (nomadic aborigines, sedentary aborigines, local Caucasoid population). The serum levels of thyroid hormones were determined by the method of enzyme immunoassay. Results and discussion. Analysis of sex differences in thyroid status by age groups showed a higher thyrotropin level in women of different age groups ($p = 0.049$; $p = 0.048$) compared with men (1.94 and 2.08 $\mu\text{IU/L}$ and 1.60 and 1.81 $\mu\text{IU/L}$, respectively). In addition, in the age group 21-44 years, there was an increase in thyroxine level (107.31 and 97.70 nmol/L , $p < 0.001$) and a decrease in the content of free triiodothyronine in women (4.79 and 5.36 pmol/L , $p = 0.002$) compared to men. There were shown a higher content of thyrotropin and thyroxine in the female aboriginal population compared with the male population. A higher level of thyroxine in women may be due to its reserve functions in relation to free fractions of iodothyronines, which play an important role in the reproductive health of women. The lower content of free fractions of triiodothyronine and thyroxine was shown in women belonging to the local Caucasoid population compared with men. Free fractions of thyroxine were lower in women - sedentary aborigines in relation to men of this group. The higher content of free fractions of iodothyronines in men may be due to longer-term effects from cold temperatures when working outdoors. Conclusion. Consequently, gender differences in the content of thyroid hormones among the local Caucasoid population are in the content of free fractions of iodothyronines, while the indigenous population has differences in the content of thyrotropin and total fractions of thyroxine. The sedentary aboriginal population, in addition to its own distinctive features characteristic, acquires the characteristics of the Caucasoid population with distinctive gender characteristics according to the free fractions of iodothyronines.

Keywords: thyroid gland, thyrotrophin, thyroxine, triiodothyronine, men, women, North.

Introduction. Thyroid pathologies occupy a leading position among diseases of the endocrine system, both in the world and in the Russian Federation, with a steady increase in the frequency of thyroid dysfunction registration in recent decades [6, 12]. It is well known about the age-related increase in the prevalence of thyroid diseases in both

sexes, which in women is more often associated with an autoimmune response [10, 11]. There are also shown gender differences in the content of hormones of the hypothalamic-pituitary-thyroid axis. Some authors indicate that the TSH level is higher in the female population [11], and there were no gender differences in its content in population aged 65 years or over [10]. Free fractions T3 and T4 were higher in the female population than in the male [10, 11]. In residents of the European North of Russia (Arkhangelsk), the contents of total T4 and T3 were higher in women than in men without significant differences in the TSH level [7].

The thyroid gland is involved in the maintenance of the body's metabolism [11], and therefore, human adaptation to the conditions of the North is undoubtedly associated with the stress of the thyroid gland function, which increases when moving to the North, and can lead to the development of its dysfunction [4, 9]. One of the methods for diagnosing thyroid dysfunction is to determine the levels of TSH, total and free fractions of iodothyronines. However, not all developers of test systems in the recommended standards for determining indicators of thyroid activity take into account the sex of the examined persons. In addition, the activity of the thyroid gland is main-

ly determined by both the geographical latitude of residence [9] and the racial or ethnicity of the surveyed individuals [3, 5, 10]. At the same time, in recent decades, the traditional way of life of northern peoples has changed, that is associated with their transition from a nomadic to a sedentary way of life [1]. In connection with the heterogeneous information available in the literature on gender differences in the content of thyroid hormones and the practical absence of such data among persons leading different lifestyles, the aim of the study was: to conduct a comparative analysis of the thyroid profile in different sexes, taking into account the population groups of the North.

Material and methods. An analytical cross-sectional uncontrolled study of 388 people (aged 21-59 years) born and permanently residing in villages in the Arctic zone (village of Nelmin Nos NAO, village of Sovpolye, village of Soyana, village of Dolgoshchelye of the Mezensky district of the Arkhangelsk region (AR), village of Seyakha, village of Tazovsky, village of Gyda of the YaNAO), or wandering near these villages and the village of Pinega (AR)) of the Russian Federation was carried out. The surveyed were divided into groups according to the sex, age (21-44 and 45-59 years old), and groups of the population of the North (nomadic

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aborigines, sedentary aborigines, local Caucasoid population). The expeditions were carried out during the period of increasing daylight hours (March) from 2009 to 2016. The study was carried out in accordance with the Declaration of Helsinki of the World Medical Association "Ethical principles of scientific medical research with human participation." At the time of the study, those examined were not registered with an endocrinologist, had no exacerbations from cardiovascular and acute respiratory diseases. Blood collection was performed in the morning on an empty stomach after filling out the questionnaire and examining the doctor. On automatic plate analyzer ELISYS Uno ("Human GmbH", Germany) by enzyme immunoassay the serum concentrations of thyrotropin (TSH), total triiodothyronine (T3), total thyroxine (T4), free triiodothyronine (fT3), free thyroxine (fT4) were determined using test systems of LLC "Company AlcorBio" (Russia). The results were statistically processed using Statistica 10. The hypothesis of normal distribution was tested using the Shapiro – Wilk test. In accordance with the results, the medians and 10-90 percentile intervals of the studied hormones in the groups were determined. Comparison of groups was performed using the Mann-Whitney U-test.

Table 1

The content of hormones of the hypothalamic-pituitary-thyroid system in the blood of residents of the Arctic territories, taking into account gender and age

Variable	Men		Women	
	21-44 years old	45-59 years old	21-44 years old	45-59 years old
	1	2	3	4
	Me (10-90 %)	Me (10-90 %)	Me (10-90 %)	Me (10-90 %)
N	86	26	183	76
Age	41.0 (27.0; 44.0)	53.0 (45.0; 59.0)	41.0 (28.0; 43.0)	54.0 (46.0; 58.0)
TSH 0,23-3,4 uIU/mL	1.60 (0.60; 3.56)	1.81 (0.89; 3.04)	1.94 (0.90; 4.05) * (1)	2.08 (1.13; 7.22) * (2)
T3 1,0-2,8 nmol/l	1.76 (1.20; 2.62)	1.70 (1.01; 2.45)	1.70 (1.20; 2.68)	1.77 (1.20; 2.30)
T4 53-158 nmol/l	97.70 (63.2; 120.9)	103.50 (75.1; 122.5)	107.31 (82.5; 131.6) *** (1)	105.10 (71.8; 131.0)
fT4 10,0-23,2 pmol/l	14.80 (11.9; 20.1)	14.60 (11.6; 17.5)	14.40 (11.5; 18.1)	14.65 (10.9; 18.9)
fT3 2,5-7,5 pmol/l	5.36 (3.8; 7.0)	5.23 (3.7; 7.5)	4.79 (3.5; 6.4) ** (1)	4.80 (3.5; 7.2)

Notes: * - $p < 0.05$; ** - $p < 0.01$; *** - $p < 0.001$ - reliability of differences in relation to the data of the corresponding column in the table. The column number is given in bold.

Table 2

The content of hormones of the hypothalamic-pituitary-thyroid axis in the blood of residents of the Arctic territories according to gender and population group

Variable	Men			Women		
	nomadic aborigines	local Caucasoid population	sedentary aborigines	nomadic aborigines	local Caucasoid population	sedentary aborigines
	1	2	3	4	5	6
	Me (10-90 %)	Me (10-90 %)	Me (10-90 %)	Me (10-90 %)	Me (10-90 %)	Me (10-90 %)
N	33	56	23	32	118	109
Age	42.0 (28.0; 54.0)	46.0 (33.0; 53.0)	44.0 (25.0; 56.0)	43.0 (24.0; 56.0)	47.0 (34.0; 57.0)	44.0 (28.0; 59.0)
TSH 0,23-3,4 uIU/mL	1.73 (0.90; 4.30)	1.45 (0.62; 2.97)	1.94 (0.79; 3.04)	2.47 (0.90; 4.36)	1.50 (0.80; 4.29)	2.15 (1.21; 4.90) * (3)
T3 1,0-2,8 nmol/l	1.70 (1.20; 3.10)	1.80 (1.24; 2.40)	1.48 (1.13; 1.93)	1.80 (1.40; 3.24)	1.70 (1.20; 2.10)	1.70 (1.10; 2.90)
T4 53-158 nmol/l	88.65 (60.9; 116.0)	102.40 (71.6; 122.5)	101.70 (68.8; 120.6)	108.45 (70.7; 125.4) ** (1)	101.12 (70.0; 119.8)	110.10 (88.5; 134.4) ** (3)
fT4 10,0-23,2 pmol/l	13.50 (11.6; 17.2)	15.65 (12.5; 20.7)	15.53 (13.2; 19.3)	14.45 (11.3; 18.3)	14.70 (11.4; 18.9) * (2)	14.50 (11.5; 17.3) * (3)
fT3 2,5-7,5 pmol/l	5.32 (3.9; 7.9)	5.43 (3.8; 7.1)	4.23 (3.2; 5.6)	5.23 (3.6; 8.9)	4.85 (3.5; 6.3) ** (2)	4.60 (3.4; 6.1)

Notes: * - $p < 0.05$; ** - $p < 0.01$ - reliability of differences in relation to the data of the corresponding column in the table. The column number is given in bold.

Results and discussion. Analysis of sex differences in thyroid status by age groups showed a higher TSH level in women of different age groups ($p = 0.049$; $p = 0.048$) compared with men. In women aged 21-44 years were shown an increase in the T4 level ($p < 0.001$) and a decrease in the content of fT3 ($p = 0.002$) compared with men (table 1).

Depending on the group of population a similar pattern of an increase in the TSH level in women compared with men was noted among the sedentary aboriginal population ($p = 0.037$) (table 2). An insignificant increase in TSH level was noted in women - nomadic Aborigines and no increase in it - among the Caucasoid population. Increased T4 levels in women compared to men were recorded in nomadic ($p = 0.008$) and sedentary aborigines ($p = 0.004$). There were no differences in the content of T4 in persons of different sexes among the Caucasian population. There was shown a decrease in fT3 level in Caucasoid women compared with men ($p = 0.002$). Despite the absence of reliable gender differences in the content of fT4 when analyzed taking into account gender and age, analysis depending on the population group and gender showed a decrease in fT4 in the female population - sedentary aborigines ($p = 0.024$) and the local Caucasoid population ($p = 0.030$).

Thus, in nomadic and sedentary aborigines, similar gender differences were revealed, consisting in higher levels of total thyroxine and TSH in the female population compared to the male population. Free thyroxine in women were lower than in men both in the sedentary Aborigines and in the local Caucasoid population, as were the free T3 fractions, the greatest differences in which were noted in the local Caucasoid population.

The presence of a higher T4 level in the female aboriginal population compared to men can be explained by its ability to be a deposition of blood free fractions of iodothyronines, which are active forms and provide the body's metabolism, which is especially important when adapting to cold temperatures. The reserve of iodothyronines is especially important for the woman's body, which by its nature must ensure the formation and growth of the fetus [8, 12]. It has been shown that an increase in estrogen is combined with an increase in TSH in the blood and a decrease in the concentration of fT4 [10], and a decrease in estrogen in postmenopausal women is accompanied by an increase in thyroid dysfunction [11]. Probably, it is precisely due to the difference in the content of sex hormones that the

greatest gender differences in the levels of thyroid hormones were revealed in the period of 21-44 years of age. Free fractions of iodothyronines are active forms that have a direct effect on various tissues and organs. There is information in the literature about the presence of sex differences in their content [11]. At the same time, it is known that their concentrations increase when exposed to cold [2]. One of the possible reasons for the higher levels of free fractions of iodothyronines in the male population of the North may be a longer exposure to low temperatures when working outdoors, which is accompanied by an activation of thyroid hormone metabolism with a decrease in the reserve of iodothyronines, namely, their total fractions [2].

Conclusion. In the population of the Arctic regions, gender differences in the content of hormones of the hypothalamic-pituitary-thyroid system were shown, consisting in a higher content of TSH, T4, a lower level of free fractions of iodothyronines in the female population compared to the male. Gender differences in the content of thyroid hormones among the local Caucasoid population are in the content of free fractions of iodothyronines, while the aboriginal population has differences in the content of TSH and total fractions of T4. The sedentary aboriginal population, in addition to the distinctive features of the content of TSH and T4, acquires the particular qualities of the Caucasoid population with distinctive gender characteristics by the free fractions of iodothyronines.

The data obtained are of interest in connection with the change in the lifestyle of indigenous peoples, with the possible impact of iodine deficiency conditions in the studied regions, and necessitate further studies on a representative sample on a large scale.

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