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# ENZYME ACTIVITY IN THE INDIGENOUS AND NON-INDIGENOUS POPULATION OF THE REPUBLIC SAKHA (YAKUTIA)

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In order to assess the metabolic state of the indigenous and non-indigenous population, the activity of certain enzymes in the blood serum was determined in 2259 people living in rural, industrial and Arctic groups of the regions of the Republic Sakha (Yakutia). Differences in the activity of serum enzymes in the indigenous and non-indigenous population of Yakutia are associated primarily with the various energy needs of the body.

Significantly higher activity of enzymes involved in bioenergy in the indigenous population is consistent with the opinion of researchers about a more intense energy exchange of the indigenous population acquired in the process of long-term adaptation to the harsh conditions of the North.

**Keywords:** North, indigenous and non-indigenous population, adaptation, enzymes.

Preservation of adaptation reserves of the human organism in the conditions of the North becomes a pressing problem of preventive measures for the development of methods of early, pre-nosological diagnosis of pathological conditions, preservation of health and working capacity of the population.

It is known that in conditions of high latitudes, normal human activity is associated with a transition to a new level of energy supply, which requires an increase in the spending of energy reserves to accelerate basic metabolism, which requires quantitative and qualitative transformations of enzyme systems. In the indigenous population, the restructuring of the physiological functions of the body is fixed genetically with the formation of a "systemic structural trace", in the newcomers the adaptive reaction is associated with the formation of a short-term phenotypic variant [2, 3, 5, 7].

Maintaining the constancy of the basic biochemical parameters of blood is achieved by the participation of key enzyme systems that catalyze the main streams of transamination, thermogenesis, gluconeogenesis. Aspartate aminotransferase (AST) (the process of catabolism) is involved in thermogenesis and bioenergy, and alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) (the process of anabolism) are involved in gluconeogenesis [9]. Alkaline phosphatase (ALP) is involved in the processes of transmembrane nonspecific dephosphorylation. The final reaction of anaerobic glycolysis is catalyzed by lactate dehydrogenase (LDH): the conversion of lactate to pyruvate and vice versa. Creatine kinase (CK) is involved in the transport of macroergic phosphates from mitochondria to cellular ATP (Na-K, Ca, myosin, etc.).

The activity of enzymes depends on the adaptive properties of the body. Over the past decades of socio-economic transformation and urbanization, there has been an increasing decline in the adaptation reserves of the North's population.

According to V.I. Khasnulin et al. (2015), objective indicators of the health of northerners are worse than those of residents in more southern regions. The morbidity of northerners by diseases of respiratory, blood circulation systems and malignant neoplasms is 2-3 times higher than in the Russian Federation [12].

One of the factors in the development of metabolic disadaptation observed in indigenous peoples is a moving away from the traditional way of life and the displacement of the northern type of diet with high consumption of carbohydrate products, which changes the northern type of metabolism [4, 6, 11].

In this regard, a comparative assessment of key enzymes' activity in the indigenous and expatriate population becomes important, having not only diagnostic but also metabolic significance. In addition, the frequency of changes in the enzymes' activity is relevant in assessing adaptive and maladaptive reactions of the body.

The purpose of the research is to assess the activity of the main blood enzymes in the indigenous and expatriate population of the Republic of Sakha (Yakutia).

**Materials and methods.** The material for biochemical research was gathered during biomedical expeditions through a single-stage examination of the population of Yakutia in the spring period. A random sample of 2,229 people aged 20 to 85 years old was examined with the average age of 46.38±0.28 years old. 1421 indigenous people (average age - 47.30±0.37; me-48), 808 expats (average age - 44.78±0.42; Me-46) were examined. Of these, 1,283 were women with the average age of 47.12±0.37 years old, and 1012 were men, their average age was 45.43±0.43 years old.

Blood for biochemical screens was collected in vacutainer tubes from the median cubital vein in the morning on an empty stomach, 12 hours after eating. The activity of alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), creatine kinase (CK), and creatine kinase-MB (CK-MB) was calculated by an enzyme assay on a "Labio" automatic biochemistry analyzer using "Analyticon" reagents (Germany).

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Statistical processing was performed using the "SPSS Statistics 17.0" package from StatSoft Inc. (USA). The equality of sample means was checked using the parametric Student's t-test (in the case of a normal distribution) and the nonparametric Mann-Whitney U test for independent samples (in case of a deviation from the normal distribution). The data is presented as follows: M - mean value, ± m - standard error of the mean value, 95% confidence interval, median (Me), interquartile interval - 25th (Q1) and 75th (Q3) percentiles. Pearson correlation coefficient methods were used to identify the link between the studied indicators. The value $p < 0.05$ was taken as the threshold α-level of significance.

**Results and discussion.** The conducted analysis of the activity of blood serum enzymes in the entire surveyed population showed that the average activity of enzymes is within normal values, both in indigenous and expatriate population. However, the average activity of ALP, LDH, and GGT in native residents of Yakutia was 25; 9; 17.6% higher than in the expatriate population and had a negative correlation relationship: ALP ($r = - 0.435$; $p<0.01$), LDH ($r = - 0.234$; $p<0.01$), and GGT (- 0.154; $p<0.01$), which indicates a different intensity of adaptive metabolic processes (table 1). There were no significant differences in the ratio of LDH, CK, and AST activity. The higher activity of CK and CK-MB in the expatriate population is probably due to an increased need for energy essential for adaptive adjustment of metabolism in the North. In order to maintain homeostasis, activation of enzyme systems involved in thermogenesis and bioenergetics is required.

In different physiological and pathological conditions, the De Ritis ratio (AST/ALT) is used to determine the predominance of catabolic or anabolic pathways of metabolism. AST/ALT ratio is equal to 1.33– 1.5 at the equilibrium of metabolic pathways [1,9]. The De Ritis ratio (AST/ALT) had no significant differences, since the activity of ALT and AST in indigenous and non-indigenous people was relatively at the same level. For the indigenous population, the median of the De Ritis ratio was 1.50; for the non-indigenous population, it was 1.46, with a normal average of 1.33±0.42 or between 0.91 and 1.75.

A high percentage of cases of increased enzyme activity that does not correspond to the reference values was detected in 43% of the indigenous population for ALP, 35% for LDH and 20% for GGT, which accordingly exceeded the frequency of increased enzyme activity in the expatriate population by 4; 2; 1.4 times (Image 1).

Frequency of the high De Ritis ratio was slightly higher in the indigenous population, while percentage of the low De Ritis ratio was at the same level in both the indigenous and expatriate population (Image 2).

**Table 1**

**Enzyme activity in the population of indigenous and non-indigenous residents of Yakutia**

| E/l | Groups | N | M±m | 95% CI | Me (Q1-Q2) | *p* |
|---|---|---|---|---|---|---|
| Age years | Indigenous | 1447 | 47.30±0.37 | 46.57-48.03 | 48.00 (36.00-57.00) | |
| | Non-indigenous | 836 | 44.78±0.42 | 43.96-45.61 | 46.00 (35.00-54.00) | |
| LDH | Indigenous | 1421 | 394.60±2.07 | 390.53-398.67 | 389.00(344.00-436.75) | *0.000* |
| | Non-indigenous | 814 | 359.37±2.77 | 353.92-364.83 | 357.00 (308.00-399.00) | |
| CK | Indigenous | 1419 | 108.08±1.88 | 104.37-111.78 | 91.00 (65.00-127.00) | *0.005* |
| | Non-indigenous | 808 | 117.28±2.68 | 112.07-122.54 | 97.00 (71.25-138.00) | |
| $CK_{MB}$ | Indigenous | 1046 | 22.22±0.34 | 21.53-22.90 | 20.00 (15.00-27.00) | |
| | Non-indigenous | 438 | 23.13±0.53 | 22.08-24.19 | 21.00 (16.00-28.00) | |
| ALP | Indigenous | 1914 | 252.45±2.13 | 248.26-256.64 | 238.00 (196.00-293.00) | *0.000* |
| | Non-indigenous | 804 | 187.17±2.01 | 183.21-191.13 | 180.00 (148.00-214.00) | |
| GGT | Indigenous | 1421 | 40.14±0.78 | 38.60-41.68 | 30.00 (21.00-49.00) | *0.000* |
| | Non-indigenous | 808 | 33.00±0.90 | 31.22-34.78 | 25.00 (17.00-38.00) | |
| ALT | Indigenous | 1421 | 19.62±0.43 | 18.77-20.47 | 15.00 (10.00-22.00) | |
| | Non-indigenous | 808 | 18.32±0.52 | 17.30-19.34 | 14.00 (10.00-21.00) | |
| AST | Indigenous | 1421 | 25.62±0.34 | 24.95-26.30 | 23.00 (19.00-28.00) | |
| | Non-indigenous | 808 | 24.54±0.48 | 23.59-25.49 | 21.00 (18.00-26.00) | |
| K de Ritis | Indigenous | 1421 | 1.62±0.01 | 1.58-1.65 | 1.50 (1.14-2.00) | |
| | Non-indigenous | 808 | 1.59±0.02 | 1.55-1.64 | 1.46 (1.11-1.93) | |

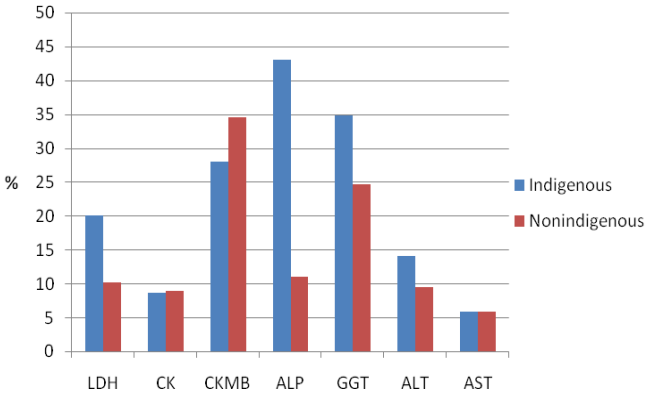


**Fig. 2.** The frequency of high enzyme activity in indigenous and non-indigenous inhabitants, E/l.

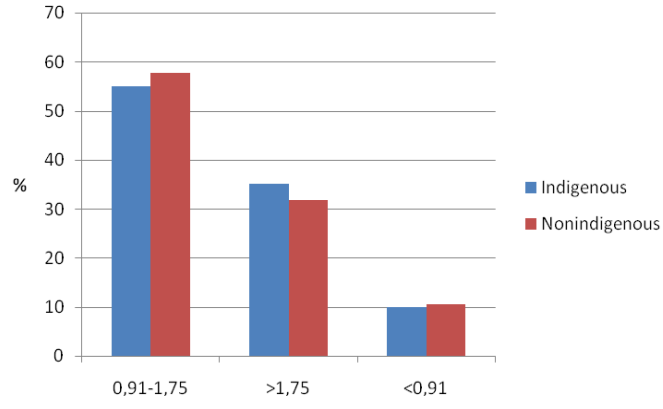


**Fig. 2.** The percentage of high and low K de Ritis in the indigenous and non- indigenous population

Table 2

**Indicators of normal enzyme activity in indigenous and non-indigenous populations within the reference values**

| Enzymes,E/l | Control values, E/l | Groups | N | M±m | 95% CI | Me (Q1-Q3) | $P_{I\text{-}Non\text{-}i}$ |
|---|---|---|---|---|---|---|---|
| LDH | 225-450 | Indigenous | 1116 | 367.07±1.53 | 374.07-340.85 | 370.00 (332.0-408.00) | 0.000 |
| | | Men | 504 | 368.01±2.29 | 363.51-372.51 | 371(333.50-409.00) | |
| | | Women | 612 | 347.76±2.81 | 342.22-353.29 | 348 (332.00-407.00) | |
| | | Non-indigenous | 723 | 344.77±1.99 | 340.85-348.69 | 345.00 (306.00-388.00) | |
| | | Men | 332 | 366.23±2.06 | 362.18-370.28 | 370.00 (312.00-388.75) | |
| | | Women | 381 | 341.39±2.84 | 335.80-346.99 | 340.00 (298.00-387.00) | |
| CK | <190 | Indigenous | 1293 | 47.28±0.39 | 46.51-48.05 | 48.00 (63.00-116.00) | 0.000 |
| | | Men | 524 | 110.37±1.78 | 106.86-113.88 | 107.50 (80.00-136.00) | |
| | | Women | 772 | 81.30±1.57 | 78.21-84.39 | 74.00 (56.25-97.00) | |
| | | Non-indigenous | 742 | 45.23±0.44 | 44.37-46.10 | 47.00 (69.00-125.25) | |
| | | Men | 320 | 115.12±2.39 | 110.41-119.83 | 111.00 (82.00-146.00) | |
| | | Women | 413 | 89.46±1.90 | 85.71-93.22 | 83.00 (63.50-110.50) | |
| CKMB | <25 | Indigenous | 763 | 17.11±0.20 | 16.70-17.52 | 17.00 (14.00-21.00) | - |
| | | Men | 308 | 17.65±0.35 | 16.95-18.35 | 18.00 (14.00-22.00) | |
| | | Women | 454 | 16.75±0.24 | 16.26-17.24 | 17.00 (13.00-21.00) | |
| | | Non-indigenous | 294 | 17.30±0.30 | 16.71-17.89 | 18.00 (14.00-21.00) | |
| | | Men | 145 | 18.21±0.41 | 17.40-19.02 | 18.00 (15.00-22.000 | |
| | | Women | 146 | 16.33±0.43 | 15.47-17.19 | 17.00 (13.00-21.00) | |
| ALP | До 258 | Indigenous | 827 | 201.35±1.34 | 198.71-204.00 | 204.00 (174.00-228.00) | 0.000 |
| | | Men | 329 | 208.76±1.98 | 204.84-212.67 | 208.00 (184.00-234.00) | |
| | | Women | 333 | 196.85±1.78 | 193.35-200.36 | 201.00 (171.00-225.00) | |
| | | Non-indigenous | 714 | 173.20±1.46 | 170.32-176.09 | 174.00 (144.00-200.00) | |
| | | Men | 333 | 178.71±2.13 | 174.52-182.90 | 180.00 (151.00-206.00) | |
| | | Women | 375 | 167.63±2.00 | 163.69-171.57 | 169.00 (138-196.00) | |
| GGT | women: 7-32; men: 11-50 | Indigenous | 932 | 25.02±0.30 | 24.42-25.63 | 23.00 (18.00-30.00) | 0.000 |
| | | Men | 416 | 28.75±0.44* | 27.88-29.61 | 27.00 (22.00-35.00) | |
| | | Women | 498 | 22.08±0.38* | 21.33-22.84 | 21.00 (17.00-26.00) | |
| | | Non-indigenous | 624 | 23.03±0.41 | 22.22-23.85 | 21.00 (16.00-28.00) | |
| | | Men | 333 | 27.41±0.69* | 26.05-28.78 | 25.00 (17.00-26.00) | |
| | | Women | 375 | 19.57±0.42* | 18.74-20.40 | 19.00 (14.00-24.00) | |
| ALT | До 30 | Indigenous | 1225 | 14.74±0.19 | 14.36-15.11 | 13.00 (10.00-19.00) | - |
| | | Men | 515 | 15.59±0.31 | 14.98-16.20 | 14.00 (11.00-19.00) | |
| | | Women | 709 | 14.14±0.24 | 13.67-14.61 | 12.00 (10.00-18.00) | |
| | | Non-indigenous | 737 | 14.82±0.22 | 14.38-15.27 | 14.00 () | |
| | | Men | 334 | 15.58±0.34 | 14.90-16.26 | 14.00 (11.00-19.00) | |
| | | Women | 398 | 14.28±0.30 | 13.69-14.81 | 13 (10.00-18.00) | |
| AST | До 40 | Indigenous | 1329 | 23.25±0.17 | 22.89-23.60 | 22.00 (19.00-27.00) | - |
| | | Men | 573 | 23.62±0.29 | 23.04-24.19 | 23.00 (19.00-27.00) | |
| | | Women | 760 | 22.98±0.22 | 22.54-23.42 | 22.00 (19.00-26.00) | |
| | | Non-indigenous | 754 | 21.73±0.22 | 21.29-22.17 | 21.00 (18.00-25.00) | |
| | | Men | 338 | 22.73±0.34 | 22.06-23.41 | 22.00 (19.00-26.00) | |
| | | Women | 406 | 20.80±0.29 | 20.22-31.27 | 20.00 (17.00-24.00) | |
| K de Ritis | | Indigenous | 778 | 1.33±0.01 | 1.31-1.35 | 1.33 (1.13-1.53) | - |
| | | Men | 361 | 1.34±0.01 | 1.31-1.37 | 1.35 (1.13-1.55) | |
| | | Women | 412 | 1.31±0.01 | 1.28-1.33 | 1.30 (1.11-1.50) | |
| | | Non-indigenous | 458 | 1.33±0.01 | 1.30-1.35 | 1.31 (1.11-1.53) | |
| | | Men | 213 | 1.33±0.01 | 1.30-1.37 | 1.30 (1.12-1.55) | |
| | | Women | 244 | 1.33±0.02 | 1.28-1.37 | 1.30 (1.10-1.50) | |

The De Ritis ratio above 2 indicates a cardiac involvement associated with the destruction of cardiomyocytes. On the contrary, below 1 indicates liver damage and is a prognostically unfavorable sign of the course of the disease. In this case, any deviations in the "cardiac" (> 1.5) and "liver" (< 1.5) variations of the ratio mean a change in the direction of metabolic pathways with an according predominance of catabolic or anabolic reactions [1,13].

In laboratory diagnostics, ALP along with GGT is an indicator enzyme of various liver pathologies, and

the presence of a large percentage of individuals with hyperactivity of these enzymes indicates metabolic maladaptation and the development of pathologies. A moderate increase in the activity of ALP, as a powerful regulator of energy metabolism, is an adaptive reaction of the body with changes in the intensity of substrate pathways through the membranes and indicates compensation for a decrease in the level of phosphorus by dephosphorylation. Increased GGT activity indicates more intensive borrowing of amino acids from tissues to maintain gluconeogenesis, but only after spending other sources. In addition to participating in the end reaction of anaerobic glycolysis, LDH regulates the acid-base homeostasis of the blood and is involved in maintaining and preserving a constant pH level.

In order to assess the regional characteristics of the key enzyme activity, a comparative analysis of data from indigenous and expatriate populations (with normal indicators of enzyme activity) has been conducted. Thus, the average activity of ALP, GGT, and LDH in the native population was significantly higher than that of the expatriate population. This difference is also shown by the medians of these enzymes, which accordingly were higher than those of the expatriate population by 14.7, 8.7, and 6.7% (table 2).

During the adaptation to the conditions of the North, increased gluconeogenesis requires optimal intake of free amino acids into the blood as necessary substrates for glucose synthesis. The intake of amino acids from tissues provides GGT, the transmembrane enzyme, but only after utilizing other sources. In addition, GGT is a component of one of the detoxifying systems of the body; it is involved in the destruction of serotonin and histamine, in the metabolism of GABA, and proteolysis of denatured proteins. As one of the key enzymes in bioenergetics, ALP provides a sufficient content of phosphates in the blood, which in turn are consumed to maintain the appropriate circulatory buffer system and to synthesize high-energy bonds (ATP, ADP). Thus, ALP plays an important role in the regulation of transmembrane metabolic pathways. Increased LDH activity provides more intense glycolysis and easier dissociation of oxygen and hemoglobin, which allows more intensive blood circulation and high tissue oxygenation. As a result, substrates pass through metabolic pathways faster and more intensively [10], which requires high activity of all enzymes.

In the expatriate population, a significantly higher level of CK than in the indigenous population may be associated with an increased need for an endogenous membrane protector - creatine phosphate, which plays an important role in maintaining the ATP/ADP ratio in the cell. CK is the most sensitive enzyme of metabolism, an integral part of the CPK-system, which includes creatine, creatine phosphate (CP), and creatinine. CK is a more beneficial form of high-energy's transport than adenosine triphosphate (ATP). In addition, CK is considered a stress enzyme.

Thus, the average activity of enzymes in the entire research population did not exceed the control values. The high frequency of hyperactivity of alkaline phosphatase, gamma-glutamyltransferase, and lactate dehydrogenase among the indigenous population indicates the presence of greater metabolic maladaptation than in the expatriate population. It is possible that changes in the quality of life and Europeanization of the diet of the Northern population have the greatest negative impact on the health of the indigenous population. A regional characteristic of the activity of the main enzymes within the reference values is a significantly higher activity of alkaline phosphatase, gamma-glutamyltransferase, lactate dehydrogenase in the indigenous population, and a higher activity of CK in the expatriate population. This is associated with the various energy needs of the body and indicates a greater adaptation of the indigenous population to the climatic and geographical conditions of Yakutia.

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