DOI 10.25789/YMJ.2020.72.04

A A. Nikanorova, N.N. Gotovtsev, N.A. Barashkov, S.S. Nakhodkin, V.G. Pshennikova, A.V. Solovyev, S.S. Kuzmina, N.N. Sazonov, S.A. Fedorova

CIRCULATING LEVELS OF LEPTIN IN BLOOD OF YOUNG YAKUTS DEPENDING ON BODY MASS INDEX

Currently, adipose tissue is considered an endocrine organ that produces several hormonally active substances – adipokines, including a leptin hormone. This hormone plays a key role in regulating energy metabolism and body weight. Several studies have shown heterogeneity of leptin levels from the ethnic origin and the environment. It is possible that in indigenous populations living in extremely low climatic conditions, leptin levels may affect the development of diseases associated with impaired fat metabolism. In this regard, the purpose of this study is to assess the relationship of leptin circulating in the blood serum with body mass index groups in healthy Yakuts. The present study included 281 Yakuts (186 women and 95 men) with an average age of 19±2 years. The sample was divided into three groups according to the world health organization classification: underweight (n=37), normal (n=215), overweight/obesity (n=29). There were no statistically significant differences in body mass indices between men and women ($p>0.05$). As a result of comparative analysis, it was found that in women and men, leptin levels are statistically higher in individuals with overweight/obese ($p<0.01$), and in individuals with underweight and normal body weight, leptin levels do not statistically differ from each other in both women and men ($p>0.05$). Our results confirm that Yakuts with overweight/obesity body weight have an increased level of leptin against the background of leptin resistance. It is also possible that Yakuts with an underweight to protect the body from low temperatures develop a larger percentage of active brown adipose tissue and the level of leptin in the blood reaches equal values as in Yakuts with normal weight.

Keywords: leptin, underweight, overweight, obesity, adipose tissue, Yakut population.

NIKANOROVA Alena Afanasyevna – junior researcher, Laboratory of Molecular Genetics, Federal State Budgetary Scientific Institution "Yakut Science Center of Complex Medical Problems". Address: 677010, Sakha Republic, Yakutsk, Sergelyakhskoye Shosse, 4. Phone: 89244611585, e-mail: nikanorova.alena@mail.ru, http://orcid.org/0000-0002-7129-6633; **GOTOVTSEV Nyurgun Naumovich** – Scientific researcher, Laboratory of Molecular Genetics, Federal State Budgetary Scientific Institution "Yakut Science Center of Complex Medical Problems". Address: 677010, Sakha Republic, Yakutsk, Sergelyakhskoye Shosse, 4. Phone: 89141062015, e-mail: donzcrew@mail.ru, https://orcid.org/0000-0002-4710-1592. **BARASHKOV Nikolay Alekseevich** – Candidate of biological sciences, Head of laboratory of Molecular genetics, Federal State Budgetary Scientific Institution "Yakutsk Scientific Center of Complex Medical Problems". Address: 677010, Sakha Republic, Yakutsk, Sergelyakhskoye Shosse, 4. Phone: 8-(4112) 32-19-81, e-mail: barashkov2004@mail.ru, https://orcid.org/0000-0002-6984-7934. **NAKHODKIN Sergey Sergeyevich** – Engineer-researcher of the Research Laboratory of Molecular Biology Institute of Natural Sciences, Federal State Autonomous Educational Institution of Higher Education "North-Eastern Federal University M.K. Ammosov". Address: 677010, Sakha Republic, Yakutsk, Kulakovsky st. 46., e-mail: sergnahod@mail.ru, https://orcid.org/0000-0002-6917-5760. **PSHENNIKOVA Vera Gennadievna** – Candidate of Biological Sciences, Head of laboratory of Populational Genetics, Federal State Budgetary Scientific Institution "Yakutsk Scientific Center for Complex Medical Problems". Address: 677010, Sakha Republic, Yakutsk, Sergelyakhskoye Shosse, 4. Phone: 8-(4112) 32-19-81, e-mail: pshennikovavera@mail.ru, https://orcid.org/0000-0001-6866-9462; **SOLOVYEV Aisen Vasilyevich** – Candidate of Biological Sciences, junior researcher, of the Research Laboratory of Molecular Biology Institute of Natural Sciences, Federal State Autonomous Educational Institution of Higher Education "North-Eastern Federal University M.K. Ammosov". Address: 677010, Sakha Republic, Yakutsk, Kulakovsky st. 46., e-mail: nelloann@mail.ru, https://orcid.org/0000-0002-0664-4224; **KUZMINA Sargylana Semenovna** – Candidate of Biological Sciences, Associate Professor, Department of Biology, The Institute of Natural Sciences "North-Eastern Federal University M.K. Ammosov". Address: 677000, Sakha Republic, Yakutsk, Kulakovsky st. 48., e-mail: sskuzmina@bk.ru, https://orcid.org/0000-0002-4687-4868; **SAZONOV Nikolay Nikitich** – Doctor of biological sciences, Professor, Department of Biology, The Institute of Natural Sciences "North-Eastern Federal University M.K. Ammosov". Address: 677000, Sakha Republic, Yakutsk, Kulakovsky st. 48., e-mail: saznikol@mail.ru. **FEDOROVA Sardana Arkadievna** – Doctor of biological sciences, Head of the Research Laboratory of Molecular Biology Institute of Natural Sciences, Federal State Autonomous Educational Institution of Higher Education "North-Eastern Federal University M.K. Ammosov". Address: 677010, Sakha Republic, Yakutsk, Kulakovsky st. 46., e-mail: sardaanafedorova@mail.ru, https://orcid.org/0000-0002-6952-3868.

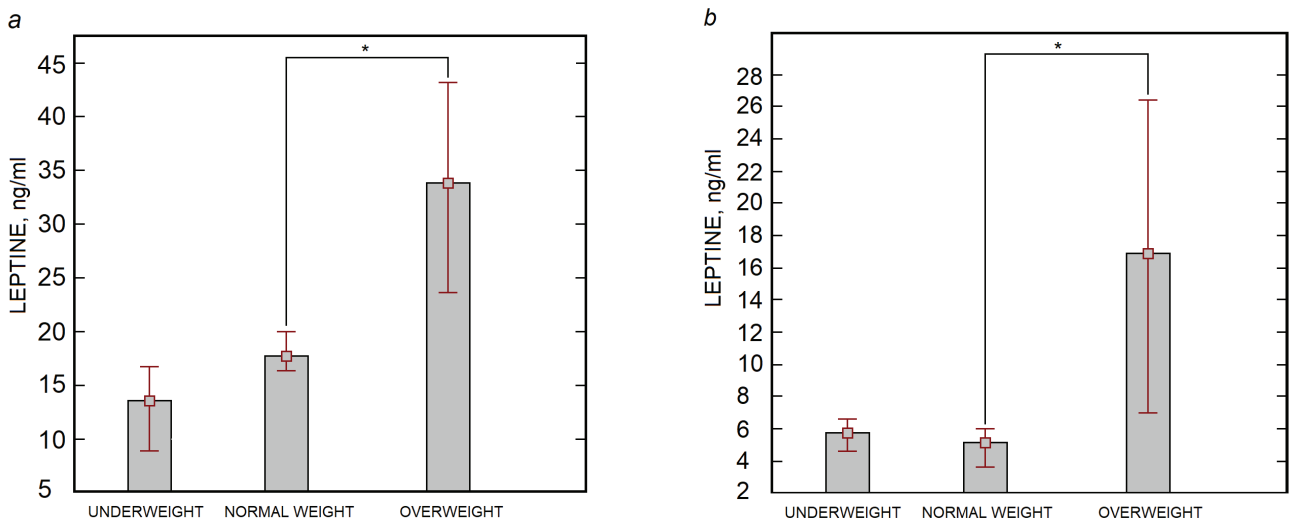
Introduction. Currently, almost one in three people suffer from at least one form of malnutrition: underweight, overweight, obesity, and non-communicable weight-related diseases [30]. Recently, the incidence of overweight, obesity, and type 2 diabetes has been particularly increasing among indigenous people living in circumpolar regions [7]. Thus, in the Republic of Sakha (Yakutia), the prevalence of obesity among Yakuts, Evenks, and evens living in the Olekminsky, Tomponsky, Gorny, and Zhigansky districts was studied. A total of 1,566 people (968 women, 598 men) was examined. As a result of this study, it was found that women (19%) are twice as obese as men (10%) [2, 3, 6]. The same data on the increased prevalence of obesity among women was found for other indigenous peoples of the North, such as the Sami (women 30%, men 23%), the Kven (women 26%, men 18%) [12] and the Inuit (women 25.5%, men 15.8%) [21].

The development of obesity is manifested by excessive accumulation of adipose tissue, which has recently been recognized as an endocrine organ that produces hormonal active substances – adipokines [13]. Leptin was the first adipokine discovered [9] and its main function is to participate in the regulation of energy metabolism and body weight [13]. The maximum amount of leptin is produced by white adipose tissue [18]. Therefore, it is believed that the levels of leptin circulating in the blood are directly proportional to the amount of adipose tissue in the body [24, 26]. Several studies have shown heterogeneity of leptin levels depending on ethnic origin and the environment [16, 17, 27]. It is possible that in indigenous populations living in extremely low climatic conditions, leptin levels may affect the development of diseases associated with impaired fat metabolism. In this regard, this study aims to assess the dependence of serum leptin levels on body mass index (BMI) in healthy Yakuts aged 18 to 30 years.

Materials and Methods. The present study included 281 Yakuts (186 women and 95 men) with an average age of 19.8±1.5 years. All participants were ethnic Yakuts who were healthy at the time of the study and passed a questionnaire indicating their gender, nationality, and age. The sample was made up of individuals who did not complain about their health status and were not registered in a dispensary for chronic diseases. All subjects gave written informed consent to participate in the study and to process their personal data. This work was approved by the local ethical Committee on biomedical ethics at the YNC KMP (Yakutsk, Protocol № 16 of December 13, 2014).

Average BMI values for each group divided by gender

UNDERWEIGHT(n=37)		U-критерий Манна Уитни	NORMAL WEIGHT (n=215)		t-критерий Стьюдента	OVERWEIGHT/OBESITY (n=29)		U-критерий Манна Уитни
WOMEN (n=26)	MEN (n=11)		MEN (n=11))	MEN (n=71)		WOMEN (n=16)	MEN (n=13)	
17.46±0.72	17.39+0.91	U_{test}=138; p>0.05	21.42±1.62	21.96±1.9	p>0.05	27.56±2.88	26.64±1.49	U_{test}=90; p>0.05



Levels of leptin, depending on the categories of BMI: a – female, b – male. Note: * – statistically significant difference

Venous blood for the study was collected in the morning after a 12-hour fast in all participants. Anthropometric indicators (body weight in kilograms, height in centimeters) were determined for all participants using standardized methods. Body mass index (BMI) was calculated by dividing body mass by the square of height. To determine the level of leptin circulating in the blood, an enzyme immunoassay kit "Leptin ELIS Akit"(Diagnostics Biochem Canada Inc., Canada) was used. The leptin concentration in the samples was measured at a wavelength of 450 nm in a VICTORX5 Multimode Plate Reader (Perkin Elmer Inc., USA).

Statistical analysis. The results were analyzed using a computer program for statistical data processing SPSS 18.0 (SPSS: An IBM Company, USA). p≤0.05 were considered statistically significant. All results were expressed as standard deviation (±). Anthropometric and hormonal characteristics between women and men were compared using the student's t-test. The Association of BMI with leptin levels was evaluated using multiple regression analysis.

Results. To assess the dependence of serum leptin levels on BMI, leptin concentrations were determined using enzyme immunoassay and BMI was calculated in a total sample of 281 people. The sample was divided into three groups according to the who classification [14, 29]: underweight (≤18.49 kg/m^2), normal weight (18.5-24.99 kg/m^2), overweight/obesity (≥25 kg/m^2) (Table 1). There were no statistically significant differences in BMI between men and women in the groups (p>0.05).

A comparative analysis of leptin levels was performed in individuals with normal BMI compared to individuals with underweight and overweight/obese (Figure 1). As a result, it was found that in comparison with the norm in both women and men, leptin levels are statistically higher in individuals with overweight/obese (p<0.01). There were no statistically significant differences in leptin levels (p>0.05) between the groups of individuals with a body mass deficit and the norm in both women and men.

Discussion. In the Yakut population, levels of leptin circulating in the blood of individuals over the age of 18 have previously been determined in several studies [5, 8]. In a study by Golderova et al., [5] it was shown that patients with unstable angina had significantly higher leptin levels compared to patients with stable angina. Klimova et al., [8] investigated associations of allelic variants of rs1799883 (*FABP2*) with metabolic syndrome and its components, including leptin, in a population sample of Yakuts. It was shown that the leptin level did not depend on the genotypes of the ALA54THR polymorphism of the *FABP2* gene [8]. In addition, we have recently published data on the dependence of leptin levels in young Yakuts depending on gender and body weight [1].

In this study, we evaluated for the first time the relationship of serum leptin levels with BMI groups (underweight, normal, overweight/obesity) in healthy Yakuts aged 18 to 30 years. We found that the level of leptin in Yakuts with overweight/obesity is significantly higher than in Yakuts with normal weight. It is believed that people suffering from obesity have leptin resistance, an overabundance of leptin against the background of immunity to its action [10, 20]. Thus, our results for the Yakut population are consistent with previous studies on other samples and confirm that overweight/obese individuals also have increased leptin levels against the background of leptin resistance.

Attention is drawn to the fact that in Yakuts with an underweight and normal weight, leptin levels in the blood serum do not statistically differ from each other. Several previous studies have found that people suffering from anorexia nervosa and eating disorders have significantly lower levels of leptin in their blood than healthy people [22, 23, 25, 28]. However, low leptin levels in underweight individuals are thought to signal a potentially

dangerous lack of energy resources to the brain [19]. Thus, in a study by Leonardo et al., [15] it was shown that the indigenous populations of Siberia have increased levels of energy metabolism and basal metabolism to protect the body from low temperatures. In addition, our recent study showed that men from the Northern regions recorded higher levels of leptin (10.03 ng/ml) than men from the southern regions (4.73 ng/ml) (p=0.00001) [27]. Although leptin is secreted mainly by adipocytes of white adipose tissue, in a study by Margetic et al., [18] it was shown that adipocytes of brown adipose tissue can also secrete it. In 2015, in Yakutia [4], for the first time in the world, a case of finding brown adipose tissue in an adult who was exposed to low temperatures most of the time was histologically confirmed. This indicates that people living in cold climates have active brown adipose tissue [4]. In a study by van Marken Lichtenbelt et al., [11] it was shown that in lean people, the number and activity of brown adipose tissue was 4 times higher compared to people who were overweight or obesity. Thus, it is possible that Yakut population with an underweight to protect the body from low temperatures develop a higher percentage of active brown adipose tissue and the level of leptin in the blood reaches the same values as in individuals with normal weight.

Conclusion. 1. In the Yakut population, overweight and obese individuals, both women and men, have higher leptin levels than normal weight individuals.

2. In individuals with low birth weight the levels of leptin in the serum were the same compared to the norm. Perhaps this is due to the protection of the body from low temperatures through the development of a greater number of active brown adipose tissue which secretes leptin additional.

Acknowledgements. The work was done within the scope of the Yakutsk scientific center for complex medical problems "Study of the genetic structure and burden of hereditary pathology of populations of the Republic of Sakha (Yakutia)", the base part of state assignment of Ministry of Science and Higher Education of the Russian Federation (FSRG-2020-0016) and Russian Foundation for Basic Research (grants #18-05-600035_Arctika).

References

1. Анализ уровня циркулирующего в крови лептина в популяции якутов / А.А. Никанорова, Н.А. Барашков, С.С. Находкин // Вопросы биологической, медицинской и фармацевтической химии. – 2020. – Т. 23. – № 5. – С. 10-14. [Analysis of circulating levels of leptin in the population of Yakutia / A. A. Nikanorov, N. And. Barashkov, S. S. Nakhodkin // Questions of biological, medical and pharmaceutical chemistry. – 2020. – Vol. 23. – №. 5. – P. 10-14. (in Russ.)].

2. Артериальное давление и ожирение среди сельской коренной популяции Якутии / В.И. Федорова, Т.М. Климова, М.Е. Балтахинова [и др.] // Якутский медицинский журнал. – 2014. – №. 1. – С. 4-6. [Blood pressure and obesity among the rural indigenous population of Yakutia / I. V. Fedorov, T. M. Klimova, M. E. Baltakhinova [et al.] / / Yakut medical journal. – 2014. – №. 1. – P. 4-6. (in Russ.)].

3. Барсуков А.П., Антонов А.Р., Соренсен М.В. Антропометрические особенности коренного населения республики Саха (Якутия) // Вестник НГУ. Серия Биология, клиническая медицина. – 2009. – Т. 7. – № 1. – С. 54-61. [Barsukov A. P., Antonov A. R., Sorensen M. V. Anthropometric features of the indigenous population of the Republic of Sakha (Yakutia). Series Biology, clinical medicine. – 2009. – Vol. 7. – № 1. – P. 54-61. (in Russ)].

4. Бурая жировая ткань и экстремально холодный климат / М.И. Томский, С. Чинти, Д.Г. Тихонов [и др.] //Якутский медицинский журнал. – 2015. – № 1. – С. 44-45. [Brown adipose tissue and extremely cold climate / M. I. Tomskiy, S. Centi, D. G. Tikhonov [et al.] //Yakut medical journal. – 2015. – № 1. – P. 44-45. (in Russ.)].

5. Взаимосвязь уровня лептина с факторами кардиоваскулярного риска при стабильной и нестабильной стенокардии / А.С. Гольдерова, А.Н. Романова, С.Д. Ефремова [и др.] // Якутский медицинский журнал. – 2015. – № 1. – С. 9-12. [The relationship of leptin levels with cardiovascular risk factors in stable and in unstable angina / A. S. Goldirova, A. N. Romanov, S. D. Efremova [et al.] / / Yakut medical journal. – 2015. – № 1. – P. 9-12. (in Russ.)].

6. Липидный профиль и дислипопротеинемии у коренного сельского населения Якутии / Т.М. Климова, В.И. Федорова, М.Е. Балтахинова [и др.] //Сибирский медицинский журнал (Томск). – 2012. – Т. 27. – №. 3. [Lipid profile and dyslipoproteinemia in the indigenous rural population of Yakutia / T. M. Klimova, V. I. Fedorova, M. E. Baltakhinova [et al.] //Siberian medical journal (Tomsk). – 2012. – Vol. 27. – №. 3. (in Russ.)].

7. Метаболический синдром у коренного населения Якутии / В.Л. Осаковский, Л.Г. Гольдфарб, Т.М. Климова [и др.] //Якутский медицинский журнал. – 2010. – №. 2. – С. 98-102. [The metabolic syndrome in indigenous population of Yakutia / V. L. Osakovsky, L. G. Goldfarb, T. M. Klimova [et al.] //Yakut medical journal. – 2010. – №. 2. – P. 98-102. (in Russ.)].\

8. Полиморфизм ALA54THR гена FABP2 и метаболический синдром в якутской популяции / Т.М. Климова, Р.Н. Захарова, А.И. Федоров [и др.] // Якутский медицинский журнал. – 2017. – №. 3. – С. 24-27. [The ALA54THR FABP2 gene polymorphism and metabolic syndrome in the Yakut population / T. M. Klimova, R. N. Zakharova, A. I. Fedorov [et al.] / / Yakut medical journal. – 2017. – №. 3. – P. 24-27. (in Russ.)].

9. Adipokines: biofactors from white adipose tissue. A complex hub among inflammation, metabolism, and immunity/ J. Conde, M. Scotece, R. Gomez [et al.] // Biofactors. – 2011. – Vol. 37. – №. 6. – P. 413-420.

10. Associations of body mass index and insulin resistance with leptin, adiponectin, and the leptin-to-adiponectin ratio across ethnic groups: The Multi-Ethnic Study of Atherosclerosis (MESA) / L.J. Rasmussen-Torvik, C.L. Wassel, J. Ding [et al.] // Annals of Epidemioogy. – 2012. – Vol. 22. – №. 10. – P. 705-709.

11. Cold-activated brown adipose tissue in healthy men / W.D. van Marken Lichtenbelt [et al.] // New England Journal of Medicine. – 2009. – Vol. 360. – №. 15. – P.1500-1508.

12. Distribution of apoB/apoA-1 ratio and blood lipids in Sami, Kven and Norwegian populations: the SAMINOR study / T. Nystad, E. Utsi, R. Selmer [et al.] // Int J Circumpolar Health. – 2008. – Vol. 67. – №. 1. – P. 67-81.

13. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013 / M. Ng, T. Fleming, M. Robinson [et al.] //The lancet. – 2014. – Vol. 384. – №. 9945. – P. 766-781.

14. International Obesity Task Force. Managing the Global Epidemic of Obesity. Report of the World Health Organization (WHO) Consultation on Obesity; June 5–7, 1997; Geneva, Switzerland.

15. Leonard W.R., Snodgrass J.J., Sorensen M.V. Metabolic adaptations inindigenous Siberian populations // Annual Review of Anthropology 34. –2005. –P. 451–471.

16. Leptin and body composition of Nigerians, Jamaicans, and US blacks / A.H. Luke, C.N. Rotimi, R.S. Cooper [et al.] // Am J Clin Nutr. – 1998. – 67:391–396.

17. Leptin levels and nutritional status of indigenous tepehuán and mestizo subjects in durango, Mexico / D. Delgadillo Guzmán, L.A. Marchat Marchau, J.L. Reyes [et al.] //Disease Markers. – 2014. – Vol. 2014.

18. Leptin: a review of its peripheral actions and interactions / S. Margetic, C. Gazzola, G.G. Pegg [et al.] // International journal of obesity. – 2002. – Vol. 26. – №. 11. – P. 1407.

19. Milos G., Hebebrand J. Endocrine Consequences of Anorexia Nervosa //Praxis. – 2019. – Vol. 108. – №. 14. – P. 899-904.

20. Nelson D.L., Lehninger A.L., Cox M.M. Lehninger principles of biochemistry. – Macmillan, 2008.

21. Prevalence of obesity and its metabolic correlates among the circumpolar Inuit in 3 countries / T.K. Young, P. Bjerregaard, E. Dewailly [et al.] //American Journal of Public Health. – 2007. – Vol. 97. – №. 4. – P. 691-695.

22. Relationship between leptin level, body mass index and parathyroid hormone in chronic hemodialysis patients / I. Risovic, S.P. Pejicic, V. Vlatkovic [et al.] //21st European Congress of Endocrinology. – BioScientifica, 2019. – Vol. 63.

23. Restrained eating is associated with low leptin levels in underweight females / S. Von Prittwitz, W.F. Blum, A. Ziegler [et al.] //Molecular Psychiatry. – 1997. – Vol. 2. – №. 5. – P. 420-422.

24. Serum immunoreactive-leptin concentrations in normal-weight and obese humans / R.V. Considine, M.K. Sinha, M.L. Heiman [et al.] // New England Journal of Medicine. – 1996. – Vol. 334. – №. 5. – P. 292-295.

25. Serum leptin and gonadotropin levels in patients with anorexia nervosa during weight gain / A. Ballauff, A. Ziegler, G. Emons [et al.] //Molecular psychiatry. – 1999. – Vol. 4. – №. 1. – P. 71-75.

26. The role of falling leptin levels in the neuroendocrine and metabolic adaptation to short-term starvation in healthy men / J.L. Chan, K. Heist, A.M. De Paoli [et al.] // The Journal of clinical investigation. – 2003. – Vol. 111. – №. 9. – P. 1409-1421.

27. The role of leptin levels in adaptation to cold climates / A.A. Nikanorova, N.A. Barashkov, S.S. Nakhodkin [et al.] //International Journal of Environmental Research and Public Health. – 2020. – Vol. 17. – №. 6. – P. 1854.

28. Time course of leptin in patients with anorexia nervosa during inpatient treatment: Longitudinal relationships to BMI and psychological

factors / E. Stroe-Kunold, M. Buckert, H.C. Friederich [et al.] //PloS one. – 2016. – Vol. 11. – №. 12. – P. e0166843.

29. WHO. Physical Status: The Use and Interpretation of Anthropometry: Report of a World Health Organization (WHO) Expert Committee. Geneva, Switzerland: World Health Organization; 1995.

30. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128 9 million children, adolescents, and adults / L. Abarca-Gómez, Z.A. Abdeen, Z.A. Hamid [et al.] // The Lancet. – 2017. – Vol. 390. – №. 10113. – P. 2627-2642.(WHO) Expert Committee. Geneva, Switzerland: World Health Organization; 1995.

31. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128· 9 million children, adolescents, and adults / L. Abarca-Gómez, Z.A. Abdeen, Z.A. Hamid [et al.] //The Lancet. – 2017. – Vol. 390. – №. 10113. – P. 2627-2642.

DOI 10.25789/YMJ.2020.72.05

O.N. Savelieva, A.S. Karunas, Yu.Yu. Fedorova, R.F. Gatiyatullin, E.I. Etkina, E.K. Khusnutdinova

ASSOCIATION ANALYSIS OF AMINOXIDASE 1 AOC1 AND HISTAMINE-N-METHYLTRANSFERASE HNMT GENE POLYMORPHISMS WITH THE DEVELOPMENT OF ASTHMA IN CHILDREN

SAVELIEVA Olga Nikolaevna – Post-graduate student, Bashkir State University; 450076, Ufa, st. Zaki Validi, 32; e-mail: olyasavelie@yandex.ru; ORCID: 0000-0002-9690-1481, **KARUNAS Aleksandra Stanislavovna** – Doctor of Biological Sciences, Candidate of Medical Sciences, Russian Academy of Education professor, Acting Director for science of the Institute of Biochemistry and Genetics - Subdivision of the Ufa Federal Research Centre of the Russian Academy of Sciences; 450054, Ufa, Pr. Oktyabrya, 71; Professor of the Chair of Medical Genetics and Fundamental Medicine of Bashkir State Medical University, 450008, Ufa, ul. Lenina, 3; Senior Researcher, Saint-Petersburg State University, ul. Universitetskaya embankment, 7/9; tel. +7 (347) 235-60-88; e-mail: carunas@list.ru; ORCID: 0000-0002-2570-0789, **FEDOROVA Yuliya Yurievna** – Candidate of Biological Sciences, Researcher, Institute of Biochemistry and Genetics - Subdivision of the Ufa Federal Research Centre of the Russian Academy of Sciences, 450054, Ufa, Pr. Oktyabrya, 71; Researcher, Saint-Petersburg State University, ul. Universitetskaya embankment, 7/9; tel. +7(347) 235-60-88; e-mail: fedorova-y@yandex.ru; ORCID: 0000-0002-9344-828X, **GATIYATULLIN Radik Fidagievich** - Doctor of Medical Sciences, Professor, Professor of the Chair of Hospital Pediatrics of Bashkir State Medical University, 450008, Ufa, ul. Lenina, 3; e-mail: radikfidagi@mail.ru, **ETKINA Esfir Isaakovna** - Doctor of Medical Sciences, Professor, Head of the Chair of Childhood Disorders of Bashkir State Medical University, 450008, Ufa, ul. Lenina, 3; e-mail: pedkaf@rambler.ru; ORCID: 0000-0003-1371-7927, **KHUSNUTDINOVA Elza Kamilevna** - Doctor of Biological Sciences, Professor, Associate Member of the Academy of Education of Russian Federation, Director of the Institute of Biochemistry and Genetics - Subdivision of the Ufa Federal Research Centre of the Russian Academy of Sciences, 450054, Ufa, Pr. Oktyabrya, 71; Chief Researcher, Saint-Petersburg State University, ul. Universitetskaya embankment, 7/9; e-mail: elzakh@mail.ru; ORCID: 0000-0003-2987-3334

Asthma is a common multifactorial disease characterized by chronic inflammation of the respiratory tract, and respiratory symptoms such as wheezing, shortness of breath (dyspnea), coughing, that vary over time and intensity. The main goal of asthma management is to achieve and maintain clinical control of the disease over a long period of time, considering the safety of therapy and potential adverse reactions. At present, total asthma control is achieved in less than half of patients, and 10-20% of patients show signs of therapeutic resistance to certain groups of drugs. Several studies have revealed that heredity has a significant effect on the individual sensitivity to asthma therapy. In this regard, it is actual to study the genes involved in the metabolism of major groups of drugs used to asthma treatment. Antihistamines are frequently prescribed in the treatment of allergic diseases, it blocks the binding of histamine to its receptors by the mechanism of competitive inhibition, it has antipruritic, antiedema, antispasmodic and local anesthetic effect.

The aim of this work was to analyze associations of polymorphic variants of amine oxidase, copper-containing 1 *AOC1* and histamine N-methyltransferase *HNMT* genes involved in the histamine metabolism with the development of asthma in children living in the Republic of Bashkortostan. **Material and methods.** DNA samples of 430 unrelated individuals aged 2-17 years living in the Republic of Bashkortostan were used as the study material. Genotyping of polymorphic variants is carried out by PCR-RFLP method. **Results.** The associations of rs1049793**CC* genotype and rs1049793**C* allele of the *AOC1* gene with asthma development, with significant decreases in spirometry measures in Russians were revealed. The associations of rs1801105**CT* genotype and rs1801105**T* allele of the *HNMT* gene with significant decrease of MEF25 in asthma patients of Tatar ethnicity were established. **Conclusion.** The results of the study suggest that *AOC1* and *HNMT* polymorphic variants are involved in asthma development.

Keywords: bronchial asthma, polymorphic variant, association, aminoxidase 1 *AOC1* gene, histamine N-methyltransferase *HNMT* gene.

Introduction. Asthma is a severe heterogeneous disease characterized by chronic airway inflammation. The global prevalence of asthma is 1-18% [4]. Despite the rapid development of modern medicine in 10-20% of Russian patient's severe course of asthma with the signs of therapeutic resistance to various groups of drugs are diagnosed [2]. Genetic variability has a significant influence on the patient's sensitivity to the prescribed therapy [5]. Histamine is a biogenic amine that plays an important role in the development of inflammatory processes. The activation of histamine receptors in the lungs leads to bronchospasm and airway obstruction. Histamine is metabolized by two main enzymes, which are histamine-N-methyltransferase (HNMT) and aminoxidase (DAO, AOC1) [7]. Several studies have shown that polymorphic loci in the genes encoding histamine metabolizing enzymes are associated with allergic diseases [1, 7]. **The aim** of this work was to assess the significance of amiloride-sensitive amine oxidase *AOC1* and histamine-N-methyltransferase *HNMT* genetic polymorphisms involved in the histamine metabolism in the prediction of asthma developing in children of different ethnicities living in the Republic of Bashkortostan (RB).

Materials and methods. DNA samples of 430 unrelated individuals aged 2-17 years old from the RB were used in this work. The group of patients included