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Reproductive genetic screening for heterozygous carriage of hereditary diseases in the Republic of Sakha (Yakutia)

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Motivation and Aim: On the territory of the Republic of Sakha (Yakutia), there is an accumulation of some hereditary diseases, their high frequency [1]. In this regard, genetic screening for heterozygous carriage of mutations in autosomal recessive diseases is of particular relevance in the RS(Y) in order to prevent them. The introduction of expanded screening requires a preliminary pilot study in populations, which makes it possible to analyze the merits and consequences of the program, for example, the clinical and cost effectiveness of screening, the psychological and social impact of the program [2]. The purpose of this study was to conduct a pilot project "Reproductive genetic screening for heterozygous carriage of hereditary diseases" to evaluate the effectiveness of genetic screening. The study included 7 autosomal recessive diseases that occur with a high frequency in Yakuts in the Republic of Sakha (Yakutia) – three M-syndrome 1, non-syndromic deafness type 1a, methemoglobinemia type 1, tyrosinemia type 1, SOPH syndrome, neuronal ceroid lipofuscinosis type 6 and mucopolysaccharidosis plus syndrome. For all these diseases, major mutations characteristic of the Yakut population have been established [1, 3].

Methods and Algorithms: During 2021, 915 women 11–13/6 weeks pregnant took part in the pilot project as part of early prenatal screening from 10 districts of Yakutia – Amginsky, Anabarsky, Verkhnevilyuisky, Megino-Kangalassky, Nizhnekolymsky, Nyurbinsky, Tattinsky, Tomponsky, Churapchinsky and Ust-Aldan. In terms of numbers, women of the Yakut nationality predominated – 847 (92.6 %), 52 (5.7 %) – representatives of the indigenous peoples of the North (Evenki, Evenki, Dolganki), 10 (1.1 %) – women of other nationalities. 6 participants (0.6 %) did not indicate their nationality. Genotyping was carried out using real-time PCR.

Before the start of the pilot project, a questionnaire survey was conducted to assess the attitude of the population towards genetic screening, in which 271 respondents over the age of 18 from different regions of Yakutia took part. The questionnaire included 21 questions to study the social status, family burden, awareness of the heterozygous carrier of hereditary diseases, and attitudes towards genetic screening of the respondents. Statistical analysis of the data was performed using Pearson's Chi-square test and hierarchical cluster analysis.

Results: According to the results of the pilot study, 193 heterozygous carriers were identified, the frequency of heterozygous carriage of 7 hereditary diseases among pregnant women from 10 districts was 21.1 %. 180 (93.3 %) women were of Yakut nationality, 9 (4.6 %) were representatives of the indigenous peoples of the North. 25

(13.0 %) women were carriers of several hereditary diseases: 3 – heterozygous carriers of 3 diseases, 22 – 2 diseases. Among the Yakuts, carriers for all 7 diseases were revealed, among the representatives of the indigenous minority of the North, carriers of the tri-M syndrome, type 1 methemoglobinemia and mucopolysaccharidosis-plus syndrome were identified.

The largest number of heterozygous carriers was found in areas with a predominance of the indigenous population – in the Amginsky, Nyurbinsky and Churapchinsky districts. Among them, the Nyurbinsky district stands out, where the maximum total number of heterozygous carriers of 7 hereditary diseases is recorded – more than 27 % of pregnant women.

The frequency of heterozygous carriage by disease was distributed as follows: non-syndromic deafness type 1a – 11 %, three M syndrome – 3 %, SOPH syndrome – 3 %, type 1 methemoglobinemia – 3 %, mucopolysaccharidosis-plus syndrome – 2 %, neuronal ceroid lipofuscinosis – 1 %, tyrosinemia type 1 – 1 %.

According to the results of a questionnaire survey, 89.3 % of respondents have a positive attitude towards genetic screening and agree to undergo DNA testing. At the same time, 93 % of rural residents, 100.0 % of respondents with a high level of awareness and planning to have children support screening. On the other hand, 22.5 % of respondents with children doubt their participation in DNA testing ($p = 0.025$). According to 24 % of respondents, they have a family history of hereditary diseases.

Conclusion: Thus, the results on the assessment of the frequency of heterozygous carriage of seven frequent hereditary diseases among the population of Yakutia, especially in ethnically homogeneous regions, are of great practical and theoretical significance. The results obtained confirm the need for further genetic screening with an increase in the number of participants, expanding the geography of the study. The results of the questionnaire survey showed that the strengthening of explanatory work among the population about the heterozygous carrier of hereditary diseases in the media, the Internet and in antenatal clinics can help increase the effectiveness of genetic screening for prevention.

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References

1. Genetic studies of the population of Yakutia. Puzyrev V.P., Tomskiy M.I. (Eds). Yakutsk, 2014.
2. Revazyan K.Z. Sociological aspects of genetic screening for the carriage of variants that cause the development of autosomal recessive diseases. *Med Genet*. 2020;19(10):86-88. doi: 10.25557/2073-7998.2020.10.86-88.
3. Maksimova N.R. Short Stature Diseases: 3-M syndrome and SOPH syndrome. M.: Nauka, 2021.