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HEALTHY LIFESTYLE. PREVENTION

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THE ATTITUDE OF YOUNG PEOPLE OF REPRODUCTIVE AGE TO ETHICALLY CONTROVERSIAL ISSUES OF THE PRENATAL DIAGNOSIS OF HEREDITARY DISEASES

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The article discusses the results of a survey conducted among young people in the City of Yakutsk regarding ethically difficult issues of prenatal DNA-testing for hereditary diseases. Most respondents (74%) consider prenatal diagnosis a necessary procedure. Analysis of attitude of young people to morally ambiguous issues of prenatal diagnosis shows that the decision to terminate pregnancy after prenatal diagnosis is affected by the severity of damage to fetus. Compared to similar survey results in other countries, young reproductive age people in Yakutsk show lower values on the issue of pregnancy termination when confronted with Down's syndrome (49%) and an ethically ambiguous issue of pregnancy termination in case of a deaf child (19%). There is no connection between the opinions of respondents on prenatal diagnosis being a necessary or an unnecessary procedure, and their own desires to terminate pregnancy in case of a disorder.

Keywords: prenatal diagnosis, bioethics, survey, young people, hereditary diseases.

Introduction. Prenatal diagnosis (PND) is a modern means of diagnosing the state of a fetus and detecting possible disorders during pregnancy at different stages of gestation. Various diagnostic methods and their combinations are employed, such as ultrasound, biochemical, cytogenetic, molecular-genetic testing, including invasive and non-invasive methods of fetal examination [2].

According to European guidelines, the objective of PND is providing prenatal diagnostic testing services (for genetic conditions) that enable families to make informed choices consistent with their individual needs and values and which support them in dealing with the outcome of such testing [20].

When conducting a PND for hereditary monogenic disorders, fetal samples obtained via chorionic villus sampling at early stages of pregnancy are processed to extract DNA from cells, after which a molecular-genetic analysis is performed to detect damage (mutations) to genes. There are many different methods of genetic testing available today, from direct PCR diagnosis to detect mutations, to analysis of full genome sequencing of an individual's DNA. Modern genetic testing technologies can detect mutated gene variants and variations of genetic markers, which are connected to disorders based mostly on calculations of probability of disease manifestation. PND is a complicated and expensive procedure which often comes with moral and ethical dilemmas, both for geneticists and families that undergo PND and make a difficult decision to be tested [22]. Main bioethical issues include informed consent for PND, individual autonomy, right to reproductive choice [4]. In case of a risk of severe fetal disorder that makes it non-viable, or high probability of congenital genetic disease, families make emotionally difficult decisions to terminate pregnancy, and it is known that 80 to 90% of families decide to terminate [6,10,18]. The remaining families decide to continue pregnancy with an affected fetus due to their moral values or religious beliefs [13].

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There are many difficult and contentious ethical issues relating to prenatal diagnosis of fetal disorders that do not affect its viability. For example, is termination of pregnancy justified in case of disorders with variants of a gene (penetrance), when the detected mutation does not allow for definitive conclusion on development of a disease, or is it justified in cases of mutations with late onset, when the individual will develop a disease in adulthood [1].

The study of public opinion on genetic technologies in practical medicine of the Sakha Republic (Yakutia) is conducted in the form of sociological surveys. The study evaluates the perception and thoughts of the population, which is important for identifying a number of fundamental issues relating to regulation of human genome studies.

The objective of this article is to analyze the results of survey on contentious ethical issues of PND of hereditary diseases, and the attitude of young reproductive age people living in Yakutsk to PND.

Methods. The survey was conducted in Yakutsk using a standard method of sample survey that was done distantly. The number of respondents was 300 people. The objective of the sociological survey was to study the attitude of residents of Yakutsk to DNA-testing for hereditary diseases as a new method used in the practical medicine of the Sakha Republic (Yakutia). The questionnaire consisted of 24 different types of questions: multiple choice, binary (yes, no), matrix (questions in the form of a table where the necessary response should be marked with a tick). There were also a number of open questions, such as: "If you think that prenatal diagnosis should not be performed, could you explain why? (please write down your own answer)".

Questionnaire results were processed using IBM SPSS Statistics 22 software.

Confidence coefficient is 95%.

Confidence interval is (±%) 5.66.

When comparing groups by answers of respondents $\chi 2$ criterion and Fisher's criterion (F) for small samples were used.

Results of analysis of attitude of young people to DNA-testing (first part of the questionnaire) were published by us in International Journal of Circumpolar Health (2020) [12].

This article discusses the results of a survey conducted among young reproductive age people in Yakutsk regarding a number of issues related to prenatal DNA testing for hereditary diseases. Social and demographic profiles of respondents are shown in Table 1.

Most of the respondents (75%) were representatives of the Sakha people with an age of 29 years.

Results and discussion. The survey results are presented in Table 2. For respondents who answered "No" we gave an opportunity to voice their opinion using an open question "Why do you think prenatal diagnosis should not be performed?" This led to a number of different answers, with most respondents citing possible risks for the fetus, some saying "better not to know", or "I'm worried for my spouse", or "everything is in God's hands".

Most young people (74%) of Yakutsk consider prenatal diagnosis a needed and necessary procedure. Our data corresponds to Julian-Reynier (1993) study results, where reproductive age women from Italy also voiced the usefulness of PND for trisomy 21 syndrome (Down' syndrome), 78% of respondents would like to be tested even if there was a 1% chance of trisomy 21 syndrome [11]. One can imagine that most people would consider it a good thing to prevent birth of children with disabilities, however there are movements for rights of disabled people in our society that think that life with disabled traits should not necessarily damage the ability of "special" people or their families to have a decent life [15].

After a PND and getting information on severe disorder affecting a fetus, a pregnant woman or a couple is forced to make a difficult decision to terminate or to continue the pregnancy [16]. This is a very stressful process that requires additional information for parents and support from specially trained medical staff or clinical psychologists [6,9,19,21]. A survey of 207 married couples carried out by Quadrelli R (2007) with the objective of finding out the decisions of parents after a PND that identified chromosomal anomalies had the following results: in case of Down's syndrome or fetal aneuploidy with severe prognosis, 89% and 96% of patients respectively would terminate the pregnancy, while in case of chromosomal disorders with low risk of an anomalous clinical phenotype up to 90% of patients would continue the pregnancy [17]. In our survey, in case of Down's syndrome prognosis, 49% of respondents would terminate the pregnancy (figure 1).

A difficult and contentious ethical issue comes to the forefront when deciding to terminate pregnancy (based on PND results) in case of disorders which are not life-threatening (deafness, blindness), or in case of anomalous phenotypes such as short stature, short limbs, facial dysmorphism, etc. [5]. An example of a difficult bioethical issue is the possibility of PND for 3M syndrome or Yakut short stature syndrome (YSS), widespread in the Sakha population (12.72:100000). According to Maksimova et al., 2007, all affected by YSS have characteristic clinical features and phenotype: postnatal growth and physical development retardation, large head, facial dysmorphism, short and wide thorax, enlarged abdomen, lumbar lordosis, muscle hypo-

Table 1

Socio - demographic characteristics of respondents

characteristics of respondents	values (n=300)	%
Sex:		
Female	146	48.7
Male	154	51.3
Age:		
average value	29.7	
median	23	
moda	22	
Marital status:		
not married	170	56.7
married	84	28.0
Education:		
Higher	214	71.3
college	80	26.7
Having children:		
without children	197	65.7
One or more children	103	34.3
type of activity:		
Student	180	60.0
Working in various fields	143	47.7
Nationality:		
Sakha (Yakuts)	225	75.0
Other nationalities	75	25.0

tonia and others, but with no motor and sexual development retardation, normal intelligence and no mental deficiency [14]. In cases of prenatal diagnosis of 3M syndrome parents are informed of risks of having a child with this disorder and possible difficulties in the child's social life due to short stature. According to Gotovtseva (2014) there were 40 PND procedures for 3M syndrome performed in 5 years with 11 fetuses identified as carriers of CUL7 mutation [3]. There is no data on the number of terminated or continued pregnancies as the bioethical issues of this monogenic disorder have not been studied and there are no ethical rules for PND and DNA-testing for YSS.

Fu et al. (2016) studied the ethically ambiguous issues of DNA-testing and prenatal diagnosis for recessive forms of hereditary deafness by surveying college students in Shanghai. After a brief written information was presented to them with an example of GJB2, the most widespread recessive gene of deafness, 67.7% of respondents voiced their interest in undergoing genetic testing to find out if they were carriers of GJB2 mutation. In hypothetical scenario of carrying GJB2 recessive mutation, 86.9% of respondents would ask their partners to also take the test. If both partners were carriers, 88.7% would consider prenatal diagnosis, and 80.7% would consider terminating pregnancy [8]. In another study, Deng et al. (2018) conjecture that PND and genetic consultation protocol contain detailed information that can help couples from high risk families to prepare for childbirth and future family planning. For mutation carrying newborn, PND and genetic consultation would facilitate the implementation of strategy of "early screening, early diagnosis, early intervention" [7].

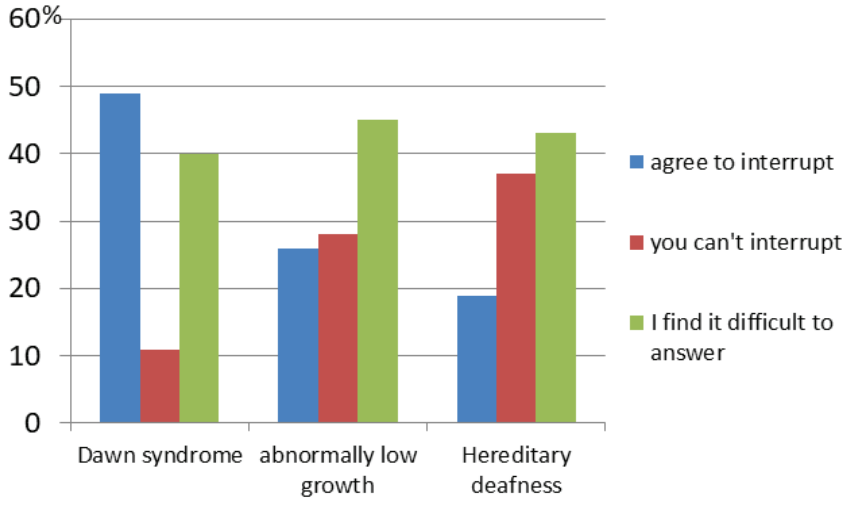
Using questionnaires we studied the attitude of young people in Yakutsk to morally ambiguous issues of terminating pregnancy as a result of PND. A hypothetical question "How justified do you think is the termination of pregnancy as a result of prenatal diagnosis?" in the form of a table was divided into more specific parts: Down's syndrome, the most well-known and severe disorder, and morally ambiguous reasons for terminating pregnancy: anomalously short stature (dwarfism), as well as possible hereditary deafness.

The results of our survey show that the decision to terminate pregnancy after a PND is affected by the severity of a fetal disorder. 49% of young reproductive age respondents think that pregnancy termination is justified if there is a risk of Down's syndrome; 26% think it is justified if there is a risk of anomalously short stature (dwarfism). By contrast to high numbers of Chinese young people who think that termination of pregnancy in case of possible deafness is justified (80.7%), only 19% of our respondents consider such a possibility in similar circumstances. Another distinctive result of our survey is that in all three cases (Down's syndrome – 40%, dwarfism – 45%, deaf-

Table 2

Respondents' answers to the question: "How do you feel about prenatal DNA diagnostics?

answer options	number of people	%
I consider it useful and necessary	222	74
I think that it does not need to be done	30	10
I find it difficult to answer	43	14.3
Other answers	5	1.7
Total	300	100



Respondents' answers to the question: "How do you think termination of pregnancy is justified based on the results of prenatal diagnosis?"

Table 3

Comparison of the opinions of two groups of respondents on termination of pregnancy according to the results of PD

How do you feel about prenatal DNA diagnostics?	I consider PD useful and necessary				I think that PD does not need to be done				X2	p	F(p)
How do you think termination of pregnancy based on the results of prenatal diagnosis is justified?	I agree to terminate the pregnancy		You can't interrupt		I agree to terminate the pregnancy		You can't interrupt				
number of respondents	n	%	n	%	n	%	n	%			
Down syndrome	119.000	83.217	24.000	16.783	13.000	72.222	5.000	27.778	0.607	0.435	0.608
Abnormally low growth	70.000	52.632	63.000	47.368	9.000	52.941	8.000	47.059	0.000	0.980	1.000
Hereditary deafness	46.000	34.586	87.000	65.414	7.000	43.750	9.000	56.250	0.520	0.470	0.581

ness – 42%) many respondents had no answers to morally difficult questions of terminating pregnancy if hypothetical disorders were present. In our opinion this once again confirms the conclusion that all children have special value and significance for the Sakha people as part of the ethnic mindset, considering that 75% of respondents were representatives of the Sakha people (table 1). We divided the respondents into two groups by positive and negative answers to the question of "What is your opinion on prenatal DNA-testing?" and compared them by their answers to the questions on terminating pregnancy in case of Down's syndrome, dwarfism, and hereditary deafness (table 3). We did not find any statistically significant differences when comparing these groups, which shows that there is no connection between the respondents thoughts on prenatal diagnosis being a necessary or an unnecessary procedure, and their own desires to terminate pregnancy in case of a disorder.

Conclusion. Analysis of attitude of young people in Yakutsk to morally ambiguous issues of prenatal diagnosis shows that the decision to terminate pregnancy after PND is affected by the severity of damage to fetus. Compared to similar survey results in other countries, young reproductive age people in Yakutsk show lower values on the issue of pregnancy termination when confronted with Down's syndrome (96% in Italy, 49% in Yakutsk) and an ethically ambiguous issue of pregnancy termination in case of a deaf child (80.7% in Shanghai, 19% in Yakutsk).

Conclusion on the special value and significance placed on any child among the Sakha people as part of an ethnic mindset was confirmed, as 75% of respondents of representatives of the Sakha people.

There is no connection between the respondents opinions on prenatal diagnosis being a necessary or an unnecessary procedure, and their own desires to terminate pregnancy in case of a disorder.

Development and practical application of genetic technologies, such as using prenatal diagnosis for "selecting" healthy fetuses and, in the future, editing genomes to change the genes of embryos, leads to discussions on the ethics of applying advances in genetics. Is there a line where we should stop applying the advances in genetic technology and where should it be drawn? Which kind of genetic testing is useful and necessary, and which should be declared ethically unacceptable? In order to find answers to these questions we need to study public opinion.

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