

Short report

The effect of medical and social factors on the health of children born as a result of ART in late reproductive age women

Kirill A. Kuzmichev¹, Olga V. Tyumina^{2,3}, Olga A. Khashina³, Valeria V. Sokolova³, Elizaveta A. Gusarova³

¹ Moscow State Medical Sechenov University, Moscow, Russia

² Regional Center of Reproductive Medicine DYNASTY, Samara, Russia

³ Samara State Medical University, Ministry of Healthcare of Russian Federation, Samara, Russia

Received 7 November 2023, Revised 14 May 2024, Accepted 17 May 2024

© 2023, Russian Open Medical Journal

Abstract: Background — This article is dedicated to the study of the effect of medical and social factors on the health of children born as a result of assisted reproductive technology (ART) in late reproductive age (LRA) women. Every year, there is a deterioration in the reproductive health of married couples, an increase in the frequency of infertile marriages, as well as an increase in the number of women over 35 years of age who gave birth to children as a result of ART.

Material and Methods — The study included 648 children (4-6 years old) born as a result of ART by women aged 35-45 years (the main group: MG). All children resided in the city of Samara. The control group (CG) included 648 children (4-6 years old) who were born from spontaneous conception and met the following criteria: their mother's age at birth exceeding 35 years, their age from 4 to 6 years, born from a singleton full-term (≥ 37 weeks of gestation) pregnancy. The main distinguishing feature between the MG and CG was birth after using ART. The children's health was assessed comprehensively, based on the results of physical and medical examinations, and a study of the child's development history. The course of pregnancy and childbirth, along with maternal morbidity, based on outpatient medical records, as well as their social and hygienic characteristics based on questionnaire data, were investigated. The following research methods were employed: sociological (questionnaire), direct observation, analytical, and statistical.

Results — We assessed children's health as follows: the subgroup with good health included 18.0% of children in the MG vs. 21.9% in the CG ($p=0.055$). The proportion of the subgroup of children with poor health was 56.2% in the MG vs. 36.1% in the CG ($p=0.048$).

Conclusion — We identified 18 significant risk factors that negatively affected the health of children born as a result of ART in LRA women.

Keywords: children's health, assisted reproductive technology.

Cite as Kuzmichev KA, Tyumina OV, Khashina OA, Sokolova VV, Gusarova EA. The effect of medical and social factors on the health of children born as a result of ART in late reproductive age women. *Russian Open Medical Journal* 2024; 13: e0306.

Correspondence to Olga V. Tyumina. Address: 159 Tashkentskaya St., Samara 443095, Russia. Phone: +79022912788. E-mail: centr123@bk.ru.

Introduction

Epidemiological studies conducted in Russia confirmed that the proportion of infertile marriages among the population of reproductive age (for women 15 to 49 years of age) ranges from 8 to 17% [1], which corresponds to the critical level sensu World Health Organization. On average, one in eighth couples faces this problem when planning their first child, and one in six couples face the challenge when planning their second child [2].

The increase in the frequency of infertile marriages and the successful correction of the reproductive health in married families using assisted reproductive technology (ART) in recent years have led to the worldwide increase in the number of children conceived through ART. In this regard, the issue of their development and health is very important [3]. At the same time, the health of children born as a result of ART is still insufficiently investigated. Existing studies were mainly aimed at examining the condition of children in infancy and early childhood. It was shown that children born after the use of ART are statistically significantly more likely to become ill and seek medical help [4, 5]. This can be explained as

follows: women of late reproductive age (LRA), i.e., 35-49 years old, who make up the bulk of women seeking ART, most often constitute a risk group, and the course of their pregnancy is complicated with diabetes mellitus, hypertension, etc. Thus, rather poor health of newborn offspring of such mothers is a reflection of maternal health: it can be explained by the aftereffects of pregnancy [6].

All published studies pointed out the critical impact of maternal factors, such as age at the time of conception, obstetric history, social wellbeing, etc. Taking into account the fact that women of LRA are increasingly seeking medical treatment for infertility, it is necessary to separately investigate the characteristics of the development of children's health in this group of women, and also to examine what medical and social factors affect the health of children born as a result of ART.

Hence, our **study goal** was to investigate the effect of medical and social factors on the health of children born as a result of ART by LRA women.

Material and Methods

Study subjects and sampling procedure

This study of the effect of medical and social factors on the health of children born as a result of ART by LRA women included 648 preschool-age children (4-6 years old). They constituted the main group (MG). All children resided in the city of Samara and were observed in children's polyclinics. The control group (CG) included 648 children (4-6 years old) who were born from spontaneous conception and met the following criteria: their mother's age at birth between 35-45 years, their age from 4 to 6 years, born from a singleton full-term (≥ 37 weeks of gestation) pregnancy. The main distinguishing feature between the MG and CG was birth after using ART. Donor gametes were not used. The study also included mothers of all these children; hence, the total sample of mothers included 648 mothers of children from the MG with a mean age of 39.11 ± 0.5 years and 648 mothers of children from the CG with a mean age of 38.95 ± 0.76 years.

Methods

We employed the following research methods: sociological (questionnaires), direct observation, analytical, and statistical. To

participate in the study, voluntary informed consent was signed by all legal representatives of the children (i.e., their mothers). The health of children in the MG and CG was assessed comprehensively, based on polyclinic visits, medical examinations, and a study of the child's development history. The analysis included the following parameters characterizing the health of the children under study: annual frequency of illnesses, duration of illnesses during the year, and a number of chronic diseases per child. Depending on the value of the above criteria, all examined children were distributed among three health assessment subgroups.

The subgroup with good health (subgroup I) included children for whom all listed criteria had positive values. The subgroup with fair health (subgroup II) included children with intermediate values of all listed criteria. The subgroup III included children with poor health. They were characterized by an annual frequency of four or more cases of illness, sickness for 40 days or more per year, and three or more chronic diseases per child. This subgroup included children for whom two of the listed signs had positive values.

Table 1. Comparative analysis of obstetric and gynecological history, and social and hygienic characteristics of women in the main (MG) and control (CG) groups (per 100 women)

Data from women's anamneses and questionnaires	Groups of mothers		p
	MG (n=648)	CG (n=648)	
Obstetric and gynecological history of the examined mothers			
Operations on the pelvic organs	49.0	14.6	-
- Undergone one surgery on pelvic organs	30.1	14.6	0.037
- Undergone two surgeries on pelvic organs	6.6	0	0.061
- Undergone three surgeries on pelvic organs	12.3	0	0.001
Treated sexually transmitted infections once	50.5	35.1	0.039
Treated sexually transmitted infections twice	14.6	5.1	0.001
Treated sexually transmitted infections ≥ 3 times	2.1	0	0.001
Have not encountered manifestations of sexually transmitted infections	32.8	59.8	0.043
Noninflammatory diseases of the genitals	61.3	20.3	0.039
Inflammatory diseases of the genitals	43.9	14.1	0.042
Benign neoplasms of the uterus and ovaries	31.5	5.5	0.023
History of abortions	29.9	10.1	0.019
History of nonviable pregnancy	9.8	4.1	0.021
Recurrent pregnancy loss	10.5	4.3	0.034
Preterm birth	12.3	1.8	0.001
Ectopic pregnancies	10.2	5.1	0.029
Anemia during pregnancy	41.5	12.5	0.028
Gestosis	32.1	18.1	0.033
Acute diseases during pregnancy	32.7	14.7	0.033
Vaginal infection during pregnancy	31.2	12.1	0.038
Caesarean section	41.2	13.4	0.042
Complications in the first half of pregnancy	62.1	13.4	0.039
Complications in the second half of pregnancy	52.3	19.8	0.042
Social and hygienic characteristics of the examined mothers			
The woman is married or is in civil partnership	91.5	82.3	0.067
The woman is not married	8.5	17.7	0.041
The work is associated with occupational hazards	31.3	13.2	0.042
- work on a computer	61.2	41.3	0.048
- work in conditions of noise pollution	23.1	11.3	0.043
- work with chemicals	7.8	1.3	0.034
The place of employment and the position correspond to the education	55.7	68.4	0.055
Regular workplace conflict situations	65.5	31.3	0.036
Experience nervous and mental stress and take sedatives	85.2	13.1	0.023
Experience fear, anxiety, sleep disorder, tearful crying	75.8	19.5	0.042
The woman is a smoker	15.9	4.1	0.018

Table 2. Rank distribution of medical and social factors affecting the health of children born as a result of ART by LAR women

Rank	Risk factor	Odds ratio (OR)	Standard error of the odds ratio (S)	Lower limit of 95% confidence interval (CI)	Upper limit of 95% CI
1	Insufficient time spent outdoors with the child	18.8	0.87	1.98	17.82
2	Complicated delivery in mothers	9.8	0.81	1.11	87.91
3	Mother over 38 years old at the time of birth	7.6	0.66	2.07	27.89
4	Failure to follow doctor's prescriptions	7.0	0.62	2.04	24.01
5	Complications in the second half of pregnancy	5.3	0.87	3.13	29.25
6	Breastfeeding less than for six months	3.6	0.65	1.31	20.41
7	Low birth weight	3.5	0.78	1.21	15.34
8	Chronic diseases of the mother	3.5	0.75	3.12	15.34
9	Complications in the first half of pregnancy	3.2	0.68	2.13	12.16
10	Hereditary burden on the maternal side	3.1	0.79	3.12	14.66
11	Lack of daytime sleep in the child in the weekends	2.9	0.81	2.45	20.90
12	Smoking during pregnancy: father	2.4	0.45	2.12	17.18
13	Alcohol abuse by the father	2.2	0.81	1.14	8.56
14	Father over 40 years old at the time of birth	2.1	0.82	1.24	8.32
15	Lack of body hardening in the child	2.1	0.91	1.81	12.35
16	Smoking during pregnancy: mother	1.9	0.55	1.17	15.18
17	Alcohol abuse by the mother	1.8	0.65	1.15	7.89
18	Chronic diseases of the father	1.3	0.89	1.33	7.61
19	Hereditary burden on the paternal side	1.3	0.82	1.91	7.21
20	The child does not participate in sports	1.3	0.76	0.51	1.91
21	Infrequent outdoor walks with the child in the weekends	1.2	0.87	1.98	17.8
22	Lack of body hardening in the child	1.1	0.91	1.84	12.35
23	Failure to follow the doctor's prescriptions for follow-up care and treatment	0.9	0.82	1.11	8.32
24	Contacted the doctor only if the child was seriously ill	0.8	0.94	1.81	10.45
25	Parents do not carry out physical exercises with the child	0.7	0.92	1.77	7.25
26	Supplemented breastfeeding with formulas before the age of three months	0.7	0.72	1.51	3.34
27	Contacted the doctor only if the child felt unwell	0.6	0.91	0.98	5.38
28	Followed the doctor's prescriptions not very closely	0.5	0.64	1.22	7.71
29	Parents did not follow daily routine prescribed by the doctor	0.5	0.93	1.31	2.25
30	Practiced self-treatment	0.5	0.81	1.12	3.43

To analyze the features of the social and hygienic characteristics, as well as health and lifestyle of mothers raising the examined children, we developed a special questionnaire containing 63 questions, *Questionnaire for Medical and Social Examination of the Family of a Child Born in Late Reproductive Age*. The compiled questionnaire had the following sections: *Medical Activity* (11 questions), *Social Factors* (17 questions), *Medical and Biological Risk Factors for Pregnancy and Childbirth* (25 questions), and *Medical and Biological Risk Factors for Early Childhood* (10 questions). We studied the course of pregnancy and childbirth, as well as the morbidity of mothers, based on their questionnaires and outpatient medical records, followed by filling out sample medical records for studying the health of LRA women.

When analyzing the effect of medical and social factors as risk factors for the health of the examined children in the MG and CG, we used the method of assessing the odds ratios (OR). Children other than those with good health (health assessment subgroups II and III) born as a result of ART were compared with children with good health in the CG (health assessment subgroup I), using a four-field table for case-control studies.

Study design

At the first stage of our study, all children were characterized by three health assessment subgroups. At the second stage, we analyzed the features of the social and hygienic characteristics, health, the course of pregnancy and childbirth, as well as morbidity and lifestyle of mothers raising children of the MG and CG. Medical and social risk factors for the children's health were

identified. At the third stage of the study, we analyzed the effect of medical and social factors on the health of children born as a result of ART to LRA women in comparison with the CG.

Statistical data processing

Statistical data processing was carried out on a personal computer by the SPSS Statistics version 21 software using parametric and nonparametric statistics methods. For quantitative features, the normality of distribution was assessed; if the distribution was normal, parametric criteria (mean, error of the mean, Student's t-test) were used to characterize the feature. For qualitative features, the Pearson's chi-squared test with Yates's continuity correction was employed. To detect the statistical relationship between the studied independent features, we used correlation analysis and the Pearson's criterion. The critical significance level when testing statistical hypotheses was set at 0.05. To determine the strength of the relationship between the studied events, we used the OR calculation; a four-field table was used for case-control studies. OR>1 implied that there was a relationship between the events. OR≤1 suggested no relationship. For each OR value, we indicated the confidence interval (CI), along with the upper and lower limits of CI. 95% CI >1 or <1 implied statistical significance of the relationship between the examined features. 95% CI ≥1 or ≤1 (i.e., 1 was included in the CI values) indicated no relationship between the studied features. We also calculated the standard error of the relative risk (S).

Results

Characterization of the examined children by health assessment subgroups

As a result of the comprehensive assessment of children's health, the subgroup I (good health) included 18.0% of children in the MG vs. 21.9% in the CG ($p=0.055$). The proportion of the subgroup including children with poor health in the MG was 56.2% vs. 36.1% in the CG ($p=0.048$). The remaining children in the MG (25.8%) and CG (42.0%) formed a subgroup with fair health (subgroup II, $p=0.046$). No age-based differences were found within the subgroups.

Analysis of health features, obstetric history, gynecological anamnesis, and social and hygienic characteristics of mothers raising the examined children

A study of the health status in mothers of the examined children showed that among women in the MG, the level of general morbidity was significantly higher: 2902.4 ‰ vs. 947.7 ‰ in the CG ($p<0.001$). As for the structure of morbidity in MG mothers, the top place is taken by diseases of the genitourinary system: 1082.6 ‰ vs. 146.9 ‰, i.e., 7.4 times higher ($p<0.001$). The second place is represented by diseases of the endocrine system: 586.3 ‰ vs. 90.0 ‰ in the CG (i.e., 6.5 times higher $p<0.001$). The third place belongs to respiratory diseases: 513.7 ‰ vs. 355.4 ‰ in the CG ($p=0.023$). In the MG, 270.1% of mothers have over three chronic diseases vs. 15.2% of mothers in the CG ($p<0.001$). The rate of comorbidity of chronic diseases per woman in the MG is 2.7 ± 1.2 vs. 0.4 ± 0.1 in the CG ($p=0.009$).

When studying the obstetric history and gynecological anamnesis of the examined mothers, we discovered that every second woman in the MG had undergone surgical interventions on the pelvic organs vs. every sixth mother in the CG. Sexually transmitted infections were diagnosed and treated in 69.6% of women in the MG, which is 1.7 times more often than in the CG. MG women had a history of abortions, noninflammatory and inflammatory diseases of the genitals 3 times more often. It was revealed that among mothers in the MG, compared with the CG, there was a significantly higher incidence of unfavorable course of previous pregnancies, as well as complications of pregnancy and childbirth, such as nonviable pregnancy, recurrent pregnancy loss, preterm birth, ectopic pregnancy, anemia during pregnancy, gestosis, acute diseases during pregnancy, vaginal infections during pregnancy, and complications of the first and (or) second half of pregnancy ([Table 1](#)).

Investigation of the social and hygienic characteristics in mothers revealed the following features: in the MG, women with higher education prevailed, whose professional activity was associated with various adverse workplace conditions, including the majority of mothers in the MG working on a computer, every fourth woman working in conditions of noise pollution, 7.8% of mothers working with chemicals. In the CG, more favorable workplace conditions were observed. Regular workplace conflict situations occurred in every second woman of the MG, along with an increased level of anxiety and stress. The majority of the examined children in both MG and CG were born to families where the parents were officially married. We established that mothers in the MG were smokers 3.9 times more frequently than in the CG ([Table 1](#)).

Effect of medical and social factors on the health of children born after ART by LRA women (vs. the control)

Analyzing the effect of medical and social risk factors on the health of children born after the use of ART by LRA women, we employed the odds ratio assessment method ([Table 2](#)). We classified the assumed risk factors into the following groups: indicators of parental health (complications in the first and in the second half of pregnancy, chronic diseases in the father and mother, alcohol abuse by the mother and father, hereditary burden), medical activity and lifestyle of families (failure to comply with medical recommendations, smoking during pregnancy by the mother and other family members, children's participation in sports, commitment to body hardening, being outdoors), and early childhood factors (complicated delivery, short breastfeeding or its absence, low birth weight).

We identified 18 significant risk factors that negatively affected the health of children born as a result of ART. They are listed below.

Indicators of parental health:

1. Father over 40 years old at the time of birth;
2. Mother over 38 years old at the time of birth;
3. Hereditary burden on the maternal side;
4. Complications in the second half of pregnancy;
5. Complications in the first half of pregnancy;
6. Alcohol abuse by the father;
7. Alcohol abuse by the mother;
8. Chronic diseases of the mother;
9. Chronic diseases of the father.

Medical activity and lifestyle of families:

1. Insufficient time spent outdoors with the child;
2. Failure to follow doctor's prescriptions;
3. Lack of daytime sleep in the child in the weekends;
4. Lack of body hardening in the child;
5. Smoking during pregnancy: father.
6. Smoking during pregnancy: mother.

Early childhood factors:

1. Complicated delivery in mothers;
2. Breastfeeding less than for six months;
3. Low birth weight.

Preterm births and multiple pregnancies, as medical and social factors, were excluded from the study in compliance with the design of group recruitment.

Discussion

Studies examining the effect of ART, along with medical and social factors, on long-term health outcomes in offspring face multiple challenges. First, subfertility of the parents increases the risk of multiple health problems in the offspring, regardless of whether conception was medically assisted or not. The invasiveness of the required treatments probably increases the risk to the offspring. Besides that, it is difficult to control for factors that may also increase the risk of childhood morbidity, such as multiple embryo transfer, preterm birth, low birth weight, maternal chronic diseases, as well as maternal and paternal alcohol abuse and smoking. A challenge in collecting such data is

that it takes time to detect associations between rare events and ART. The results obtained in our study are consistent with those of other authors [4, 5, 8].

However, this is the first study conducted in a special group of children born to LRA women after ART and obtaining the data on the effect of parental health indicators, their medical activity, and early childhood factors on the health of children 4-6 years of age.

The field of reproductive medicine is slowly advancing from improving the efficacy of the interventions to focusing on optimizing the health of offspring born after the use of this method. Conducting more and better studies on the relationship between the use of ART and long-term health outcomes in children is essential [7, 8]. However, any increased risk observed among children born as a result of ART should be critically assessed [9, 10].

Over the past three decades, researchers were studying the potential perinatal health risks of children born using ART (4, 9, 10). Currently, a decrease in the number of adverse outcomes associated with a reduction in the number of multiple births is reported [5]. At the same time, it is essential to examine the long-term consequences for the health of children due to the possibility of an increased risk of somatic morbidity in childhood vs. children born after spontaneous conception [3, 11, 12].

Identification of the most important medical and social factors affecting the health of children born to LRA women is necessary for the development of an algorithm and a program for stratification of the health risk in children born as a result of ART. This is crucial for revealing a group of children with an increased risk of health deviations and for developing a differentiated approach to the formation of children groups that are in need of priority follow-up care.

Conclusion

We identified 18 significant medical and social risk factors that had an adverse effect on the health of children born to LRA women after using ART. The most important of these were insufficient time spent outdoors with the child, complications during childbirth for the mother, mother's age over 38 years at the time of childbirth, complications in the first and second halves of pregnancy, chronic diseases of the mother, duration of breastfeeding less than six months, and low birth weight of the child.

Limitations

Our study results are limited by the failure to use multivariate analysis methods due to the difficulty of taking into account the indirect impact of interdependent components under conditions of uncertainty. They are also limited by the nonlinear nature of the mutual influence of objects and processes; their insufficient consistency; as well as heterogeneity and inconsistency of information about objects and processes, and their influence on each other.

Acknowledgments

The authors thank the staff of the Regional Center of Reproductive Medicine DYNASTY in Samara, Russia, for the opportunity to review the medical records of women who were enrolled in the ART program at the center.

Conflict of interest

The authors declare no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in compliance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study protocol was approved by the Ethics Committee of the participating clinical centers. Written informed consent was obtained from all participants prior to their inclusion in the study.

References

- Lebedev GS, Golubev NA, Shaderkin IA, Shaderkina A, Apolihin OI, Sivkov AV, et al. Male infertility in the Russian Federation: statistical data for 2000-2018. *Experimental and clinical urology* 2019; (4): 4-12. Russian. <https://doi.org/10.29188/2222-8543-2019-11-4-4-12>.
- Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reprod Biol Endocrinol* 2015; 13: 37. <https://doi.org/10.1186/s12958-015-0032-1>.
- Fauser BC, Devroey P, Diedrich K, Balaban B, Bonduelle M, Delemerre-van de Waal HA, et al. Health outcomes of children born after IVF/ICSI: A review of current expert opinion and literature. *Reprod Biomed Online* 2014; 28(2): 162-182. <https://doi.org/10.1016/j.rbmo.2013.10.013>.
- Pykhtina LA, Filkina OM, Gadzhimuradova ND, Malyskhina AI, Nazarov SB. Risk factors and predicting health disorders in infants born from monocyosis after in vitro fertilization. *Health Risk Analysis* 2017; (1): 56-65. Russian. <https://doi.org/10.21668/health.risk/2017.1.07>.
- Zhao J, Yan Y, Huang X, Li Y. Do the children born after assisted reproductive technology have an increased risk of birth defects? A systematic review and meta-analysis. *J Matern Fetal Neonatal Med* 2020; 33(2): 322-333. <https://doi.org/10.1080/14767058.2018.1488168>.
- Tyumina OV. Organization of medical care for women with infertility with low ovarian reserve. *Medical & Pharmaceutical Journal "Pulse"* 2022; 24(6): 110-114. Russian. <https://doi.org/10.26787/nydha-2686-6838-2022-24-6-110-114>.
- Rumbold AR, Moore VM, Whitrow MJ, Oswald TK, Moran LJ, Fernandez RC, et al. The impact of specific fertility treatments on cognitive development in childhood and adolescence: A systematic review. *Hum Reprod* 2017; 32(7): 1489-1407. <https://doi.org/10.1093/humrep/dex085>.
- Chen M, Heilbronn L. The health outcomes of human offspring conceived by assisted reproductive technologies (ART). *J Dev Orig Health Dis* 2017; 8(4): 388-402. <https://doi.org/10.1017/s2040174417000228>.
- Fruchter E, Beck-Fruchter R, Hourvitz RA, Weiser M, Goldberg S, Fenchel D, et al. Health and functioning of adolescents conceived by assisted reproductive technology. *Fertil Steril* 2017; 107(03): 774-780. <https://doi.org/10.1016/j.fertnstert.2016.12.001>.
- Morin SJ, Seli E. Assisted reproductive technology and origins of disease: The clinical realities and implications. *Semin Reprod Med* 2018; 36(3-04): 195-203. <https://doi.org/10.1055/s-0038-1677048>.
- Meister TA, Rimoldi SF, Soria R, von Arx R, Messerli FH, Sartori C, et al. Association of assisted reproductive technologies with arterial hypertension during adolescence. *J Am Coll Cardiol* 2018; 72(11): 1267-1274. <https://doi.org/10.1016/j.jacc.2018.06.060>.
- Bergh C, Wennerholm UB. Long-term health of children conceived after assisted reproductive technology. *Ups J Med Sci* 2020; 125(2): 152-157. <https://doi.org/10.1080/03009734.2020.1729904>.

Authors:

Kirill A. Kuzmichev – PhD, Head of Paid Medical Services, Moscow State Medical Sechenov University, Moscow, Russia. <https://orcid.org/0000-0002-5853-1838>.

Olga V. Tyumina – MD, PhD, Director, Regional Center of Reproductive Medicine DYNASTY; Professor, Department of Hospital Therapy, Samara

State Medical University, Samara, Russia. <https://orcid.org/0000-0002-5608-1925>.

Olga A. Khashina – Assistant Professor, Department of Public Health and Healthcare, Samara State Medical University, Samara, Russia. <https://orcid.org/0009-0005-4147-4100>.

Valeria V. Sokolova – Student, Samara State Medical University, Samara, Russia. <https://orcid.org/0009-0006-3096-8487>.

Elizaveta A. Gusarova – Student, Samara State Medical University, Samara, Russia. <https://orcid.org/0009-0004-2072-1646>.

Appendix 1

Questionnaire for Medical and Social Examination of the Family of a Child Born in Late Reproductive Age

Directions for filling the questionnaire: please, answer the questions by choosing only one, the most appropriate answer. In some questions, it is necessary to write a detailed comment.

Medical activity

1. How often do you visit a pediatrician?

1. Once a month
2. Once every 2-3 months
3. Once every six months
4. Other (specify)_____

2. What are the most common reasons for taking your child to the doctor?

1. Acute illness
2. Chronic illness
3. Periodic health examination
4. Other (specify)_____

3. When the first signs of illness appear in your child, do you:

1. Immediately contact a doctor?
2. Only contact a doctor if your child feels unwell?
3. Practice self-treatment?
4. Only seek help if you have no experience of self-treatment?

4. How often do you give your child medications without a doctor's prescription:

1. More than once a month
2. Once every 2-3 months
3. Less often than every 2-3 months
4. Other (specify)_____

5. What medications do you most often give your child on your own?

1. Antipyretics
2. Antibiotics
3. Antivirals
4. Vitamins
5. Other (specify)_____

6. Does your child attend a child care facility when showing signs of an acute viral infection (or other acute disease)?

1. All the time
2. Depending on the child's condition
3. Never

7. How closely do you follow the recommendations given to you by health workers regarding your child?

1. I always follow closely
2. I do not follow them sometimes or follow not very closely
3. I do not follow them at all

8. What kind of prescriptions you do not follow ever, sometimes, or do not follow closely?

1. The prescribed daily routine
2. I do not take (do not always take) medications
3. I do not attend scheduled appointment
4. I did not undergo the recommended diagnostic examination
5. I did not attend the recommended treatment procedures
6. Other (specify)_____

9. Why do you not follow at all (do not follow closely) the doctor's prescriptions?

1. I do not trust doctors
2. I think that the recommended treatment will not help my child
3. I forget to give my child medications
4. I have no time for examinations and treatment
5. I do not have the financial means to carry out treatment
6. I do not see the need for doing that
7. Other (specify)_____

10. How do you rate your child's health?

1. Bad/poor
2. Fair
3. Good
4. Excellent

11. Which medical institutions do you visit most often?

1. Outpatient clinic at my place of residence, [number/address] _____
2. Private clinic, [name] _____
3. Follow-up care by a private pediatrician at home
4. Other (specify)_____

Social factors

Please, answer the questions by choosing only one, the most appropriate, answer.

1. Living conditions:

1. Private apartment
2. Private house
3. Room in a communal apartment
4. Room in a dormitory

2. Number of children in the family:

1. 1
2. 2
3. 3
4. 4 and more

3. Family type:

1. Complete
2. Single-parent family: mother
3. Single-parent family: father
4. Guardian-ward family

4. Income per family member:

1. Above the subsistence minimum
2. Corresponds to the subsistence minimum
3. Below the subsistence minimum

5. Family environment:

1. Prosperous
2. Dysfunctional
3. Presence of disabled and seriously ill family members

6. Father's education:

1. Higher
2. Secondary
3. Incomplete secondary

7. Mother's education:

1. Higher
2. Secondary
3. Incomplete secondary

8. How much time does your child spend outdoors in the weekends?

1. 3 or more hours
2. 2-3 hours

3. Less than 2 hours

9. How much time do you spend on various activities with your child per day?

1. 3 or more hours
2. 2-3 hours
3. Less than 2 hours

10. Does your child do physical exercises or participates in sports outside of the child care facility?

1. Regularly
2. From time to time
3. Does not do at all

11. Does your child attend clubs/interest groups, or development groups?

1. Club _____ (specify)
2. Development group _____

12. Does your child have a daytime nap in the weekends?

1. Regularly
2. Sometimes
3. Never

13. Where does your child spend time during the summer vacations?

1. Outside the city (children's camp, dacha)
2. Countryside (relatives)
3. In the city
4. Other (specify) _____

14. How many times a day does the child eat at home in the weekends?

1. 5
2. 4
3. 3
4. Other (specify) _____

15. At what age did your child go to a child care facility?

1. 1.5 years
2. 2 years
3. 3 years
4. Other (specify) _____

16. How did the adaptation period go in the child care facility?

1. Well

- 2. Relatively well
 - 3. Unwell
 - 4. Other (specify) / Not applicable
-

17. Does your child eat at the child care facility?

- 1. According to the institution's daily operating routine
- 2. Does not eat
- 3. Not applicable (does not attend the child care facility)

Medical and biological risk factors during pregnancy and childbirth

Please answer the questions by choosing one relevant answer (or in some questions, several answers). In some questions, you must write a detailed comment.

1. What was your age at the time of this child's birth?

2. What was the father's age at the time of this child/s birth? _____

3. Serial number of the pregnancy:

- 1. 1st
- 2. 2nd
- 3. 3rd
- 4. 4th or higher

4. Serial number of the delivery:

- 1. 1st
- 2. 2nd
- 3. 3rd
- 4. 4th or higher

5. Was the first half of pregnancy accompanied by nausea and/or vomiting?

- 1. Yes
- 2. No

6. During your pregnancy, did you have any infectious diseases?

- 1. Yes
- 2. No

If you answered YES to this question, please specify what infectious diseases you had

7. During your pregnancy, did you have any noninfectious diseases?

1. Yes

2. No

If you answered YES to this question, please specify what diseases you had during your pregnancy

8. Was the second half of your pregnancy accompanied by any of the following conditions? (Select as many as applicable from the list unless you select NO):

- 1. Edema
- 2. Elevated blood pressure (> 140 / 90 mm Hg)
- 3. Impaired renal function
- 4. Anemia
- 5. No

9. Did you have any chronic diseases that developed before your pregnancy?

- 1. Yes
- 2. No

If you answered YES to this question, please specify what diseases

10. Did the child's father have any chronic diseases before your pregnancy?

- 1. Yes
- 2. No

If you answered YES to this question, please specify what diseases

11. Did you experience harmful workplace-related factors during pregnancy (chemicals, noise, vibration, etc.)?

- 1. Yes
- 2. No

If you answered YES to this question, please specify what harmful workplace-related factors you experienced

12. Did you take any medications during pregnancy?

- 1. Yes
- 2. No

13. During your pregnancy, did you experience stress, unpleasant emotions associated with the loss of loved ones, conflicts in the family or at work, or for other reasons?

- 1. Yes

- | | |
|---|---|
| <p>2. No</p> | <p>1. Up to 2.5 kg
 2. 2500-4.0 kg
 3. Over 4.0 kg</p> |
| <p>14. Did you consume alcohol during pregnancy?</p> <p>1. Yes
 2. No</p> | <p>23. Specify the baby's height at birth:</p> <p>1. Less than 50 cm
 2. 50 cm or more</p> |
| <p>15. Did you smoke before pregnancy?</p> <p>1. Yes
 2. No</p> | <p>24. Did the baby have a birth injury?</p> <p>1. Yes
 2. No</p> |
| <p>16. Did you smoke during your pregnancy?</p> <p>1. Yes
 2. No</p> | <p>25. Were there any signs of neonatal hypoxic ischemic encephalopathy in the baby?</p> <p>1. Yes
 2. No</p> |
| <p>17. Did the child's father smoke before your pregnancy?</p> <p>1. Yes
 2. No</p> | <p>25. Were there any signs of neonatal hypoxic ischemic encephalopathy in the baby?</p> <p>1. Yes
 2. No</p> |
| <p>18. Did the child's father smoke during your pregnancy?</p> <p>1. Yes
 2. No</p> | <p><i>Medical and biological risk factors of early childhood</i></p> <p><u>Please, answer the questions by choosing only one, the most appropriate, answer.</u></p> |
| <p>19. Do any relatives on your side have hereditary diseases?</p> <p>1. Yes
 2. No</p> <p>If you answered YES to this question, please specify hereditary diseases _____</p> | <p>1. How long did you only breastfeed your baby?</p> <p>1. Less than 6 months
 2. 6 months or more
 3. None at all</p> |
| <p>20. Do relatives on the child's father's side have hereditary diseases?</p> <p>1. Yes
 2. No</p> <p>If you answered YES to this question, please specify hereditary diseases _____</p> | <p>2. When did you start supplementing breastfeeding with formulas?</p> <p>1. Before 3 months of the child's age
 2. From 3 to 6 months of the child's age
 3. After 6 months of the child's age
 4. From birth</p> |
| <p>21. How did the delivery go?</p> <p>1. Vaginal without complications
 2. Vaginal with complications
 3. Cesarean delivery without complications
 4. Cesarean delivery with complications</p> <p>If you responded "with complications" to this question, please specify complications _____</p> | <p>3. At what age did you start introducing complementary foods?</p> <p>1. Before 6 months of the child's age
 2. From 6 months of the child's age
 3. Other (specify) _____</p> |
| <p>22. Specify the baby's weight at birth:</p> | <p>4. Approximately how many hours a day did you spend outdoors with your child in the first year of life?</p> <p>1. Less than 5 hours
 2. 5-6 hours</p> |

3. More than 6 hours

4. Other (specify) _____

5. Did you perform body hardening procedures in the first year of the child's life?

1. Yes, regularly

2. Yes, from time to time

3. No

6. At what age did the baby get the first baby teeth?

1. At 6 months of age

2. Before 6 months of age

3. After 6 months of age

7. At what age did the baby start talking in syllables?

1. At 8 months of age

2. Before 8 months of age

3. After 8 months of age

8. At what age did the baby start walking?

1. At 12 months of age

2. Before 12 months of age

3. After 12 months of age

9. At what age did the baby's large (anterior) fontanelle close?

1. At 12-15 months of age

2. Before 12 months of age

3. After 15 months of age

10. How often was the baby sick in the first year of life?

1. Never sick

2. Less than 4 times

3. 4 times or more

Thank you for your time!

In the course of questionnaire scoring, if there were several response options, the selected option was assigned 1 point, while all unselected response options were scored as 0 points. For yes/no questions, a yes answer was given 1 point, while a no answer was scored 0 points.