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Scientific rationale for the indicators of biological urine monitoring in adolescents in Kazan City

Daniia Z. Gizatullina, Daniar R. Akberov, Tansu I. Gazieva, Emiliya R. Valeeva, Natalya V. Stepanova

Kazan (Volga Region) Federal University, Kazan, Russia

ABSTRACT

BACKGROUND: Biomonitoring is crucial for assessing the level of pollution in a population, identifying risks and studying the impact of changes in technology. Knowledge of the reference values of trace elements in biological material is critical in comparing exposed with non-exposed groups and accurate. The control values of trace elements are crucial for ensuring public health and occupational safety.

AIM: To study and analyze concentrations of priority chemical pollutants in the urine of adolescents aged 14–17 years in three zones in Kazan City and determine reference values for this age group.

MATERIALS AND METHODS: The concentration of elements in urine of 276 adolescents aged 14–17 years was measured by inductively coupled plasma mass spectrometry.

RESULTS: The upper 95 percentiles and their confidence intervals (RV95) were determined, which established the upper limit of the current background exposure to adolescents for 12 biomarkers, interpreted as "conditional" reference values for this age group. The following reference values for adolescents in Kazan City were obtained: Al, 12.80 μg/L; Cr, 1.02 μg/L; Mn, 3.53 μg/L; Hg, 0.65 μg/L; Cu, 110.91 μg/L, and Ni, 8.72 μg/L. In adolescents, the highest level of exceedance over background values was observed in zones 1 and 2 (Kirovsky and Privolzhsky Districts): Al exceeded by 1.4 times, Cr by 1.3 times in zone 1 (Kirovsky District), Mn by 1.5 times, Hg by 1.3 times, and Cu by 1.14 times in zone 2 (Privolzhsky District). The results are of interest for further analysis and identification of interrelations in the territory of the Republic of Tatarstan, Russia, where exposure levels may vary between regions or separate subgroups living in the same territory.

CONCLUSION: Research in the field of biomonitoring in Kazan established the levels of exposure to toxic elements among the studied population and provided means for comparing exposure for further research by population groups by age, sex, and ethnicity. Moreover, biomonitoring results can be used to determine research priorities, measure exposure trends over time, and verify effectiveness of individual measures to combat pollution and other measures in the field of the environment and public health. The study presents modern technologies for assessing exposure to chemical pollutants using human biomonitoring methods and demonstrates its advantages.

Keywords: biomonitoring; reference values; heavy metals; trace elements; adolescent health.

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Определение референсных значений приоритетных химических загрязнителей в моче подростков города Казани

Д.З. Гизатуллина, Д.Р. Акберов, Т.И. Газиева, Э.Р. Валеева, Н.В. Степанова

Казанский (Приволжский) федеральный университет, Казань, Россия

АННОТАЦИЯ

Обоснование. Биомониторинг является важным инструментом для определения уровня загрязнения в популяции и оценки экологической ситуации на отдельных территориях города. Знание референсных значений микроэлементов в биологическом материале необходимо для сравнения экспонированных и неэкспонированных групп, а точные контрольные значения микроэлементов важны для обеспечения здоровья населения и безопасности труда.

Цель исследования — изучение и анализ концентраций приоритетных химических загрязнителей в моче подростков в возрасте 14–17 лет в трёх зонах г. Казани с целью определения референсных значений для данной возрастной популяции.

Материалы и методы. Концентрации элементов в моче были измерены методом масс-спектрометрии с индуктивно связанной плазмой у 276 подростков 14–17 лет.

Результаты. Выявлены верхние 95-е перцентили (RV95) и 95% доверительные интервалы, определяющие верхний предел текущего фонового воздействия на подростков по 12 биомаркёрам, которые мы можем интерпретировать как «условные» референсные значения для данной возрастной популяции. Референсные значения для подростков г. Казани составили для Al — 12,80 мкг/л, Cr — 1,02 мкг/л, Mn — 3,53 мкг/л, Hg — 0,65 мкг/л, Cu — 110,91 мкг/л, Ni — 8,72 мкг/л. Наибольший уровень превышения показателей над фоновыми значениями определяется в 1-й и 2-й зоне (Кировский и Приволжский районы): Al — в 1,4 раза, Cr — в 1,3 раза в 1-й зоне (Кировский район); Mn — в 1,5 раза, Hg — в 1,3 раза, Cu — в 1,14 раза во 2-й зоне (Приволжский район). Полученные результаты представляют интерес для дальнейшего исследования по выявлению взаимосвязей на территории Республики Татарстан и в целом для Российской Федерации, где уровни экспозиции могут различаться между регионами или у отдельных подгрупп населения, проживающих на одной территории.

Заключение. Исследования в области биомониторинга химических загрязнителей в моче подростков в возрасте 14–17 лет г. Казани позволили установить уровни воздействия токсичных элементов среди исследуемой популяции и предоставить возможность сравнения экспозиции для дальнейших исследований по группам населения, возрасту, полу, этнической принадлежности. Результаты биомониторинга также могут использоваться для определения приоритетов исследований, для измерения тенденций воздействия в течение времени и для проверки эффективности отдельных мер по снижению загрязнения и других мероприятий в области окружающей среды и здоровья населения. В статье представлены современные технологии оценки экспозиции к химическим загрязнителям с использованием методов биомониторинга человека, а также показаны его преимущества.

Ключевые слова: биомониторинг человека; референсные значения; тяжёлые металлы; микроэлементы; здоровье подростков.

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ЭКО • ВЕКТОР

BACKGROUND

Human biomonitoring (HBM) is used to measure the concentrations of substances or their metabolites in body fluids and tissues. It is an effective method of measuring the influence of chemicals on humans. Global scientists are pursuing HBM research to develop a database of chemicals, including trace metals, to assess and manage their health risks. Studies have shown that deteriorating public health is directly related to exposure to environmental pollutants [1, 2].

The WHO European Center for Environment and Health, as part of its implementation of the Parma Declaration on Environment and Health, uses biomonitoring as a leading scientific tool [3]. The European Human Biomonitoring Initiative (HBM4EU), co-funded by Horizon 2020 (2017–2021), was launched to coordinate and promote biomonitoring of chemicals affecting human health in Europe. HBM4EU aims to support public health policy development by providing better evidence of actual exposure to chemicals and their mixtures and establishing links between these exposures and potential health consequences [4].

In this study, we selected a biological medium that would have the necessary information about the metal content and ease of biomaterial selection. According to Skalny et al. [5] and L.J. Casarett et al. [6], in addition to the qualities of the biological environment necessary for our study, up to 22 metals can be identified in urine, which determined our choice of this environment for study.

In accordance with generally accepted global practice, the reference value of biomarkers is defined as the 95th percentile (RV95) together with the 95% confidence interval (CI) of the substance concentration [7]. Simultaneous measurement of several elements in urine using inductively coupled plasma mass spectrometry enables the assessment of current exposure and determination of concentration ranges of these elements in the study population. Thus, changes in future exposures and associated risks to human health can be monitored, as is routinely done in North America [8] and Europe [9].

To date, the Russian Federation has not developed an HBM system at the federal and regional levels. Moreover, monitoring aimed at assessing changes in biomarker concentrations is mainly implemented in scientific research by individual scientific groups [4].

Such biomonitoring studies are important because reference concentrations reflect many factors, including geography, ethnicity, background pollution levels, lifestyle, and diet.

Studying the health status of adolescents aged 14–17 years is relevant given the recent deterioration in morbidity rates in this age group, and this will affect the ability to work, economic well-being, and demographic indicators of society [10].

To our knowledge, currently, no biomonitoring data are available to establish reference values in the Republic of Tatarstan, particularly for the city of Kazan.

This study aimed to investigate and analyze the concentrations of priority chemical pollutants in the urine of the adolescent population in Kazan to determine reference values for this age population.

METHODS

Study design

In 2021, a prospective study was conducted based on the results of a laboratory examination, which revealed the content of metals in the urine of adolescents aged 14–17 years in Kazan.

Compliance criteria

The selected groups of adolescents lived in three districts (zones) of the city, namely, Kirovsky, Privolzhsky, and Sovetsky. These areas demonstrated significant differences in the level of environmental well-being for heavy metals [11].

Conditions

The biological media were selected by an organization accredited for medical research, subject to the informed consent of the parents of adolescents for medical intervention (a standard informed consent form was used, and consent was obtained by the medical organization performing the research with the participation of department employees). Nurses and teachers from educational institutions organized the procedure and prepared the adolescents for urine collection. The biological material was collected in prepared containers before the start of classes.

Study description

As part of biomonitoring, 23 chemical elements were examined. Based on an analysis of data from the Agency for Toxic Substances and Disease Registry (ATSDR) 2023 priority pollutant list, 12 elements were identified for adolescents aged 14–17 years, namely, aluminum (Al), cadmium (Cd), cobalt (Co), manganese (Mn), copper (Cu), molybdenum (Mo), arsenic (As), nickel (Ni), mercury (Hg), lead (Pb), chromium (Cr), and zinc (Zn) [12].

Methods of outcome registration

Concentrations of chemical contaminants in the urine were measured using inductively coupled plasma mass spectrometry on an ISP-810MS PN 42897-09 spectrometer (Varian, USA) with atomic absorption spectrometry in the accredited laboratory “CityLab” in Kazan (Certificate ROSS RU.0001511481). Urine samples were collected in 125-mL polypropylene containers with a screw cap. Before collection, containers were washed in a 10% HNO_3 solution and then dried. Samples were delivered to the laboratory in a portable cooler bag, frozen, and stored at –20°C until laboratory testing.

For subsequent analysis of Hg, portions of collected urine were placed in 12-mL polypropylene tubes containing 0.1 mL of a 20% sulfamic acid solution and thoroughly mixed, and samples were placed in a mass spectrometer. To determine the remaining chemicals, samples were analyzed using international standards and control samples.

To assess health risks, the obtained biomarker results were compared with biomonitoring reference values.

Currently, the Human Biomonitoring Commission of the German Federal Office for the Environment has established the determination of biological exposure limits (HBM-I and HBM-II) as the most reliable method for biomonitoring [9]. In turn, the HBM-I indicator determines the limiting concentration of a biomarker, under which there is no risk to health, and the HBM-II indicator determines the concentration at which management decisions are required to minimize the risk to public health.

To date, the results were obtained as part of biomonitoring for the determination of minimum and maximum values at the RV95 level with 95% CI. RV95 indicates the level of background exposure to a certain chemical in the environment, where the obtained biomarker values can be used to develop regional (national) reference values for the studied substances [7].

Ethical considerations

The study was ethically approved based on the results of the meeting of the Local Ethics Committee of the Kazan (Volga) Federal University dated March 21, 2024 (extract from protocol No. 47), in which no ethical violations were identified.

Statistical analysis

Sample size calculation. The sample size was not preliminarily calculated and was determined during inclusion based on the eligibility criteria.

Statistical data analysis. Statistical data processing was performed using MS Excel for Microsoft 365 MSO (version 2312, build 16.0.17126.20132). The average, median, range (maximum and minimum values), and RV95 were calculated. For each data group, the normality of distribution was evaluated using the Kolmogorov–Smirnov test. Because the normality of distribution was not confirmed for most groups of data, a nonparametric criterion was chosen for comparison. Groups were compared using the Mann–Whitney test. The indicators at $p < 0.05$ were considered significant.

RESULTS

Study participants

The study population included 276 adolescents aged 14–17 years, who were students from three different districts of Kazan, namely, Gymnasium No. 4 of the Kirovsky District (n=83) as zone 1, School No. 100 of the Privolzhsky District (n=98) as zone 2, School No. 11 of the Sovetsky District (n=95) as zone 3. Participants were not separated by sex.

Main research results

In the analysis of the concentrations of chemical substances in the urine of adolescents examined, individual elements were characterized by a large range of absolute values. Thus, for Cd, the levels of HBM-I and HBM-II were 0.5 and 2 µg/L, respectively. In adolescents from the Kirovsky (RV95=1.054) and Privolzhsky (RV95=0.702) Districts, high Cd concentration (RV95) was registered relative to the established HBM-I values (Table 1).

Table 2 presents the RV95 of metals and trace elements found in the urine of the study participants and the achieved significance levels (p) in the Mann–Whitney test. The maximum concentrations of Al and Cr were recorded in zone 1 (Kirovsky District), with 18.136 and 1.297 µg/L and their minimum concentrations were recorded in zone 3 (Sovetsky District), with 9.233 and 0.901 µg/L, respectively (p=0.03 for Al and p=0.02 for Cr in both zones). The highest Ni content in the urine of adolescents (8.789 µg/L) was recorded in zone 3, whereas the lowest (8.773 µg/L) was in zone 1 (p=0.02).

According to a previous study [13], Al is characterized by neurotoxicity, potential to affect the respiratory tract due to increased oxidative stress, decreased total antioxidant capacity, potential to trigger an inflammatory reaction, and disruption of lung function. Moreover, 80%–90% of absorbed Al is excreted in the urine, reflecting intake through various sources including digestion and respiration.

At high concentrations, the effect of Ni was manifested by respiratory toxicity in experimental animals and adverse effects on the respiratory and cardiovascular systems [14].

Concentrations of Mn, Cu, and Hg were higher in zone 2 (Privolzhsky District) than in zone 3 (Sovetsky District), with 5.248 and 1.511 µg/L (p=0.01), 126.864 and 90.228 µg/L (p=0.04), 0.842 and 0.421 µg/L in (p=0.04) in zones 2 and 3, respectively. Although Mn is an important trace element for the human body, its high concentration is neurotoxic and can lead to memory impairment, deterioration of information retention, decreased academic performance, impaired motor function, and visual perception [15]. Hg exposure is toxic and can damage the nervous system. In particular, the prenatal period is recognized as the most vulnerable period in human life because of adverse neurological influences; rapid and time-dependent programmed formation of the nervous system occurs during this period [16]. During early childhood and infancy, maturational processes including nerve cell migration, differentiation, synaptogenesis, and myelination occur in the nervous system of children; therefore, exposure to a neurotoxicant such as Hg during this period is associated with various health effects, including problems associated with growth and development of the nervous system, which influence behavior, cognitive abilities, and school performance [17, 18]. Exposure to high concentrations of Cu is associated with adverse health effects such as genotoxicity and pulmonary, nervous, and renal dysfunction [19].

Table 1. Indicators of metal and trace element content in the urine of adolescents in Kazan city based on biomonitoring data (µg/L)

Elements	Mean	Minimum	Maximum	Median	RV95
Zone 1: Kirovsky District					
Al	8.5901	4.992	25.39	6.5735	18.136
Cd	0.4528	0.147	1.215	0.4195	1.054
Co	1.4739	0.552	1.917	1.616	1.906
Mn	2.1308	1.087	3.24	1.986	3.834
Cu	53.5961	19.66	122.66	39.236	115.651
Mo	69.624	21.57	108.1	77.155	107.605
As	8.4303	1.82	35.55	5.218	24.975
Ni	6.9859	2.99	8.914	7.74	8.773
Hg	0.3428	0.135	0.73	0.274	0.700
Pb	3.6957	0.03	31.003	0.837	17.634
Cr	0.9029	0.414	1.343	0.958	1.297
Zn	766.441	257.9	1397.7	741.31	1293.705
Zone 2: Privolzhsky District					
Al	6.756	4.03	11.853	6.419	11.035
Cd	0.327	0.118	0.749	0.294	0.702
Co	1.307	0.657	1.834	1.328	1.760
Mn	0.3275	0.879	8.233	1.576	5.248
Cu	2.151	6.354	127.54	51.525	126.864
Mo	48.7525	17.98	108.8	39.265	92.795
As	8.14575	1.081	31.312	5.664	19.982
Ni	6.74	3.95	8.98	7.025	8.585
Hg	0.4145	0.012	1.047	0.357	0.842
Pb	0.496	0.035	1.628	0.314	1.470
Cr	0.612	0.37	0.844	0.614	0.865
Zn	635.97	157.3	1199.7	564.615	1150.255
Zone 3: Sovetsky District					
Al	5.7917	2.67	9.44	5.595	9.233
Cd	0.2854	0.144	0.508	0.2805	0.463
Co	1.2047	0.366	1.847	1.1525	1.897
Mn	0.9626	0.165	1.452	1.086	1.511
Cu	30.1067	5.36	76.414	15.553	90.228
Mo	55.199	21.7	104.9	47.6	105.010
As	13.5003	1.363	51.704	5.7845	45.607
Ni	5.0812	2.86	8.09	4.412	8.789
Hg	0.2396	0.092	0.326	0.2255	0.421
Pb	0.2885	0.072	0.564	0.2745	0.513
Cr	0.5027	0.179	1.086	0.503	0.901
Zn	541.515	159.2	1106.4	467.53	1084.125

Table 2. Values of RV95 for metals and trace elements in urine for adolescent in different zones of Kazan city (significance levels *p* by Mann–Whitney test)

Indicator	Zone 1	Zone 2	Zone 3	p_{1-2}	p_{1-3}	p_{2-3}
Al	18.136	11.035	9.233	0.53	0.03	0.41
Cd	1.054	0.702	0.463	0.31	0.16	0.97
Co	1.906	1.760	1.897	0.25	0.31	0.67
Mn	3.834	5.248	1.511	0.28	0	0.01
Cu	115.651	126.864	90.228	0.67	0.05	0.04
Mo	107.605	92.795	105.010	0.28	0.43	0.97
As	24.975	19.982	45.607	0.67	0.73	0.97
Ni	8.773	8.585	8.789	0.49	0	0.02
Hg	0.700	0.842	0.421	0.37	0.27	0.04
Pb	17.634	1.470	0.513	0.45	0.12	0.58
Cr	1.297	0.865	0.901	0.02	0.02	0.22
Zn	1293.705	1150.255	1084.125	0.49	0.21	0.45

Note: p_{1-2} — statistically significant differences in values between zones 1 and 2; p_{1-3} — between zones 1 and 3; p_{2-3} — between zones 2 and 3.

Regarding Cr concentrations, significant differences were found between zone 1 and zones 2 and 3. Thus, the Cr concentration in zone 1 was 1.297 μg/L, which is significantly higher than those in zones 2 (0.865 μg/L; p=0.02) and 3 (0.901 μg/L; p=0.02). Studies have shown that after human exposure to Cr, when excreted from the body by the kidneys, it accumulates in the proximal convoluted tubules, causing kidney damage as a result of oxidative stress, apoptosis, and disruption of mitochondrial dynamics, which causes its nephrotoxicity [20].

Table 3. Average values of metals and trace elements in urine of adolescents aged 14–17 years in Kazan (*n*=276) based on biomonitoring data (RV95)

Elements	RV95 (95% CI), μg/L	P95, μg/L
Al	12.80	11.22–14.38
Cd	0.74	0.64–0.84
Co	1.85	1.83–1.88
Mn	3.53	2.90–4.17
Cu	110.91	104.60–117.22
Mo	101.80	99.15–104.46
As	30.19	25.62–34.75
Ni	8.72	8.68–8.75
Hg	0.65	0.58–0.73
Pb	6.54	3.31–9.77
Cr	1.02	0.94–1.10
Zn	1176.03	1140.01–1212.04

The maximum concentrations of Pb, Zn, Co, Cd, and Mo were recorded in zone 1. However, differences in the indicators of these substances were not statistically significant.

The average concentrations of metals and trace elements at the RV95 level in the urine of adolescents living in Kazan districts were analyzed to determine reference values (Table 3). The results showed a statistically significant excess of RV95 over the background values of Al by 1.4 times and Cr by 1.3 times in zone 1 (Kirovsky District); Mn by 1.5 times, Hg by 1.3 times, and Cu by 1.14 times in zone 2 (Privolzhsky District); and Ni by 1.01 times in zone 3 (Sovetsky District). In the ATSDR list of priority substances, Hg ranks third, which requires further monitoring of its concentration in the urine of the adolescent population of Kazan [12].

DISCUSSION

Summary of main research result

In this study, the reference values were determined by calculating RV95 with 95% CI of priority chemical pollutants in the urine of adolescents living in Kazan. The reference values were 12.80 μg/L for Al, 1.02 μg/L for Cr, 3.53 μg/L for Mn, 0.65 μg/L for Hg, 110.91 μg/L for Cu, and 8.72 μg/L for Ni. Excesses of background values were detected in zones 1 (Kirovsky District) and 2 (Privolzhsky District).

Discussion of the main research result

The research algorithm was tested in accordance with the definition of the Human Biomonitoring Commission of the Federal Office for the Environment of Germany, WHO, and United States Environmental Protection Agency in Kazan

(Republic of Tatarstan, Russian Federation) to form an evidence base for group average indicators of the connection between adolescent health risks and environmental factors.

The study results revealed differences in the effect of environmental factors on individual areas. The greatest excess of indicators over background values was determined in zones 1 and 2 (Kirovsky and Privolzhsky Districts, respectively). The maximum excesses of Al and Cr concentrations over the background values in adolescents in the Kirovsky District were 1.4 and 1.3 times higher, respectively. In the Privolzhsky District, the maximum excesses of Mn, Hg, and Cu were 1.5, 1.3 and 1.14 times higher, respectively, which indicates the need for measures to reduce or eliminate harmful effects.

Study limitations

Some limitations of this study should be acknowledged: unfeasibility of assessing dynamics by exposure levels at the regional level, lack of Russian programs for the standardization of procedures, and interlaboratory comparison of test results for biomarkers of exposure. The comparison of our values with the concentrations of heavy metals in the biological environment in other countries is not possible because of differences in ecological and hygienic environmental conditions, which raises the need for standardized methods and procedures of biomonitoring with international requirements.

CONCLUSION

Based on the results of a study of biomonitoring of chemical pollutants in the urine of adolescents aged 14–17 years in Kazan, exposure levels were established among the study population, and means were identified to allow for comparison of exposure in further studies of different age groups. Our results are of interest for further analysis and identification of relationships in the Republic of Tatarstan and the Russian Federation as a whole, where exposure levels differ among regions.

The study contributes to the targeted planning of sanitary and hygienic measures to prevent and eliminate the harmful effects of environmental factors on the health of the population by effectively using the obtained HBM data to reduce and minimize the levels of risk to the health of adolescents. The study results can be used to substantiate scientifically a regional system for ensuring sanitary and epidemiological well-being, managing health risks, and improving the quality of life of the population.

ADDITIONAL INFORMATION

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Competing interests. The authors declare that they have no competing interests.

Authors' contribution. D.Z. Gizatullina — literature review, collection and analysis of literary sources, conducting research, statistical processing of results; D.R. Akberov — literature review, collection and analysis of literary sources, preparation and writing of the article text; T.I. Gazieva — processing of primary data from analysis results; E.R. Valeeva — literature review, collection and analysis of literary sources, writing and editing of the article text, statistical processing of results; N.V. Stepanova — writing and editing of the article text. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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AUTHORS' INFO

*** Daniia Z. Gizatullina;**
address: 76 Karl Marx street, 420015 Kazan, Russia;
ORCID: 0009-0006-4698-7738;
eLibrary SPIN: 9673-4824;
e-mail: dzgizatullina@stud.kpfu.ru

Daniar R. Akberov;
ORCID: 0009-0007-5756-9491;
e-mail: adanik2007@yandex.ru.com

Tansu I. Gazieva;
ORCID: 0009-0006-8026-5173;
e-mail: tansu8888@gmail.com

Emiliya R. Valeeva, MD, Dr. Sci. (Medicine), associate professor;
ORCID: 0000-0002-8683-6241;
eLibrary SPIN: 3040-2258;
e-mail: ERValeeva@kpfu.ru

Natalya V. Stepanova, MD, Dr. Sci. (Medicine), associate professor;
ORCID: 0000-0002-2889-3109;
eLibrary SPIN: 3531-0262;
e-mail: NaVStepanova@kpfu.ru

ОБ АВТОРАХ

*** Гизатуллина Дания Зуфаровна;**
адрес: Россия, 420015, Казань, ул. Карла Маркса, д. 76;
ORCID: 0009-0006-4698-7738;
eLibrary SPIN: 9673-4824;
e-mail: dzgizatullina@stud.kpfu.ru

Акберов Данияр Рашидович;
ORCID: 0009-0007-5756-9491;
e-mail: adanik2007@yandex.ru.com

Газиева Тансу Ильнуровна;
ORCID: 0009-0006-8026-5173;
e-mail: tansu8888@gmail.com

Валеева Эмилия Рамзиевна, д-р. мед. наук, доцент;
ORCID: 0000-0002-8683-6241;
eLibrary SPIN: 3040-2258;
e-mail: ERValeeva@kpfu.ru

Степанова Наталья Владимировна, д-р. мед. наук, доцент;
ORCID: 0000-0002-2889-3109;
eLibrary SPIN: 3531-0262;
e-mail: NaVStepanova@kpfu.ru

* Corresponding author / Автор, ответственный за переписку