REGIONAL FEATURES OF ESSENTIAL ELEMENTS IN CHILDREN'S HAIR WITH CARDIOMYOPATHY

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Abstract. The study aimed to study the content of toxic and essential microelements in the hair of children with cardiomyopathy living in areas with different climatic and geographical conditions. 96 hair samples of children with cardiomyopathy living in different environmental conditions were examined. The research results showed that the problem of microelements is typical not only for the Aral Sea region but also for other regions: deficit and/or deficiency of 2 or more vital microelements is found in 96% of children with CMP. The frequency of trace elements in children in all regions was high in Ca, Cr, Co, Cu, He and Zn. Children living in the Aral Sea region were characterized by excessive levels of manganese, bromine, and iodine; children living in relatively advantaged regions were characterized by reliably high levels of potassium, chlorine, and iodine.

Keywords: children, cardiomyopathy, macro- and microelements, hair, Aral Sea region.

Introduction. At present, it has been established that success in protecting and promoting children's health depends largely on the environment. An "optimal environmental health level characterizes each region with significant environmental differences" and the presence of specific features of adaptation reactions of organs and systems in a specific environmental situation [10, 17, 19, 21, 23, 24]. Children, being in the process of growth and development, functional instability of the body's regulatory systems, are the most sensitive to changes in environmental conditions, so the health of the children's population can serve as a reliable indicator of the region's ecological well-being [1, 6, 10, 14].

The important role of microelements (ME) in the vital functions of the human body is beyond doubt. A significant number of studies are devoted to studying the influence of trace elements on metabolism [6, 7, 8, 18]. The attention of a wide range of researchers is focused on studying the content of macro- and microelements (ME) in human biosubstrates under various pathological conditions living in various environmental conditions. The microelement status of the population, especially children as the most sensitive part of the population, is one of the objective ecological and hygienic indicators of the territory's well-being [4, 5, 12, 22]. Among the conditions that contribute to the formation of inferior health of children, a special role is assigned to environmental disadvantage against the background of deteriorating social and living conditions, primarily malnutrition with insufficient protein and vitamin and mineral components [11, 12].

Deviations in the content of macro-and micronutrients caused by food, environmental, and climato-geographical factors of particular relevance contribute to the early formation of functional and structural cardiovascular disorders in children. The study of the role of elemental status changes in the formation of cardiovascular pathology is particularly relevant. Several studies have shown an essential role of macro- and microelements imbalance in the pathogenesis of heart and vascular diseases in residents of biogeochemical provinces [9, 15, 16, 17, 26]. In connection with the above, it is necessary to consider the diverse role of several chemical elements in complex mechanisms of cardiovascular pathology formation.

Recently, the study of hair to detect the state of metabolism of trace elements in the body and toxic effects of heavy metals is of increasing interest. Hair is a "mineral image" which is proportional to the composition of trace elements in the whole body [3, 11, 18].

The importance of complex research on the balance of micro- and macro elements is determined by the high biological activity and physiological significance of many of them, complex relationships between them in physiological and especially pathological conditions.

The study aims to study the content of toxic and essential microelements in the hair of children with cardiomyopathy living in areas with different climatic and geographical conditions.

Materials and methods. Regions with different climatic and geographical conditions and different ecological situation were selected for the study. Microelement composition of hair was studied in 96 children with cardiomyopathies, hospitalized cardioreumatological departments of the Republican Specialized Scientific-Practical Medical Center of Pediatrics and Republican Children's Multidisciplinary Medical Center of the Republic of Karakalpakstan. Depending on the region where children with cardiomyopathy live, the children were divided into 2 groups:

Group 1 - 54 children (56.2%) living in relatively favorable regions (children from all regions except Karakalpakstan Republic and Khorezm region);

2 group - 42 children (43.8%) living in an environmentally unfavorable Aral Sea region (Republic of Karakalpakstan and Khorezm region).

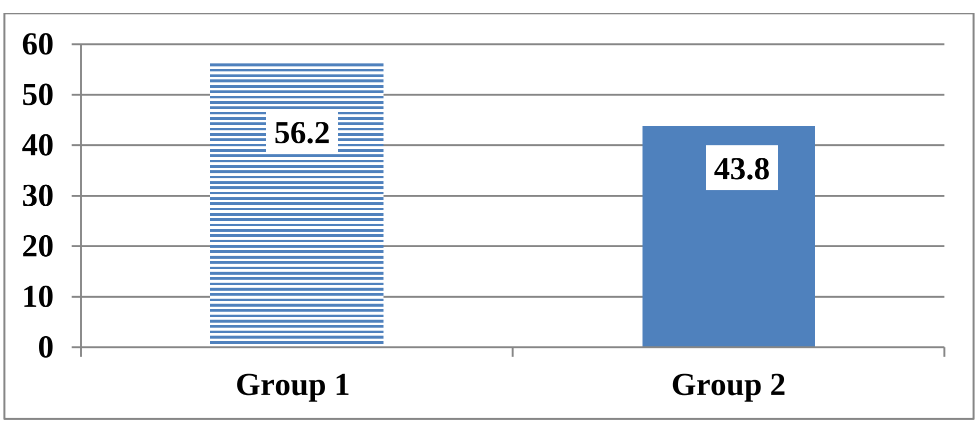

Fig.1. Distribution of children by region of residence

Evaluation of the content of chemical elements in the human body is the main issue in studying the impact on his health of deficiency, excess or redistribution of macro and trace elements.

The use of physico-chemical methods of research provides an opportunity to obtain data in the most unexpected areas of medical biology. Nowadays, in the world, different practice methods of quantitative determination of chemical elements in human hair are used.

The most used methods are atomic absorption spectroscopy, plasma mass spectrometry and neutron activation analysis. These methods allow for the simultaneous determination of several microelements in one sample of biosubstrate (blood, hair, nails, urine), which is very important for studying the mutual influence of these elements. Each of these methods has its advantages and disadvantages [21].

The Instrumental Neutron Activation Method (INAM) is also a multi-element method that allows the determination of a significant number of elements in various biosubstrates with too high sensitivity. An important advantage of the method is the simple sample preparation without sample decomposition, no correction for blank experience, low sample flow, high selectivity and exceptionally high throughput. The detection limits of the individual elements are up to 1 ng/g.

The study of hair samples for the content of macro - and trace elements were conducted in the Laboratory of Ecology and Biotechnology of the Institute of Nuclear Physics, Academy of Sciences of the Republic of Uzbekistan by instrumental neutron activation analysis (INAM).

Hair for analysis was cut with scissors from 3-5 places at the occipital part of the head. Hair length from root to distal part was 2-4 cm. Hair samples were thoroughly washed in acetone, dried, weighed and packed in marked polyethylene bags. The prepared samples were subjected to neutron-activation analysis. The technique of analysis is described in detail in paper 21.

Deviations of individual and group element profiles of children's hair from the norm were noted based on accepted reference values of chemical elements contained in the hair. Statistical processing was carried out using generally accepted methods using the universal application package Microsoft Excel 2007 and Statistica 6.0.

Results and discussion. Determination of chemical elements in hair serves as an objective indicator of the state of the organism as a whole. Hair has some advantages in comparison with other biosubstrates: a non-invasive prostate fence of the material, the possibility of stable storage at room temperature for an unlimited time, a higher concentration of trace elements in comparison with other bioobjects (blood, urine). Based on this, hair as a sufficiently informative substrate to confirm the diagnosis of microelementosis is widely used by many researchers [1, 11, 13].

In this connection, we determined the level of macro- and microelements in hair. The results of the studies presented in Table 1 show that the content of some potentially toxic and essential elements (Hg, Au, Ag, U, Sb, La, Na, Sc) in the hair is within the reference (biologically permissible) values.

Table 1: The element content of children with cardiomyopathy, µg/g

Element	Group 1	Group 2	P	References values
Sc	0,0039±0,00031	0,0047±0,00028	<0,01	0,06-0,015
Ag	0,075±0,013	0,15±0,083	<0,01	0,1-0,25
Sb	0,059±0,0081	0,028±0,0026	<0,01	<0,2
La	0,015±0,0014	0,018±0,0025	>0,05	0,02-0,04
Au	0,014±0,0017	0,011±0,0029	>0,05	0,025-0,075
Hg	0,046±0,0064	0,061±0,0054	<0,01	0,1-0,3
U	0,13±0,024	0,27±0,037	<0,01	0,1-0,3

*Note: * - validity of differences between children's scores relative to reference values; P - the validity of differences between the scores of compared groups.*

In other cases, various changes in the content of trace elements were noted, which are presented in the following tables 2 and 3.

The following table 2. presents average values of macro- and micronutrients, the content of which had similar changes in both group 1 and group 2 patients.

These changes were characterized by lower contents of Ca, Cr, Co, Cu, and Ge compared to reference values, with higher values of Cl, Br, and I among children in both groups. More pronounced changes were common among children in group 1: their Cl was 2.2 times greater than allowed values, while children in group 2 were 1.5 times greater than allowed values ($p<0.001$); and, bromine was nearly 2 times greater than allowed values, while children in group 2 were 1.2 times greater than allowed values; iodine was also 10 times greater than the reference values of children in group 1 and 2 times greater than allowed values in comparison group 1 ($p<0.001$).

Table 2: The element content of children with cardiomyopathy, µg/g

Element	Group 1	Group 2	P	References values
Na	870±115	890±130	>0,05	400-900
Cl	5100,0±610,0*	3400,0±420,0*	<0,001	1200-2300
Ca	660,0±71,0*	930,0±135,0*	<0,001	1000-1500
Cr	0,24±0,024*	0,22±0,016*	>0,05	0,35-1,0
Co	0,031±0,0035*	0,030±0,0038*	>0,05	0,05-0,1
Cu	6,1±0,61*	6,9±0,41*	>0,05	10-15
Se	0,43±0,024	0,45±0,015	>0,05	0,35-1,0
Br	6,7±1,5*	4,1±1,3*	<0,001	1,0-3,5
I	10,0±4,3*	2,1±1,4*	<0,001	0,5-1,0

*Note: * - validity of differences between children's scores relative to reference values; P - the validity of differences between the scores of compared groups.*

Children in Group 1 had low Fe and Zn levels relative to both reference values and children in Group 2 ($p<0.001$). However, Aral Sea region children, in contrast to children in the

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comparison group, had significantly higher levels of manganese (-1.2±0.30 µg/g versus 0.64±0.061 µg/g, respectively).

Besides, children in Group 1 were characterized by excessive potassium and rubidium content ($p<0.001$), while children in the Aral Sea region were within reference values. And the level of potassium exceeded the permissible values (800-1500 µg/g) 1.3 times (2000.0±350.0 µg/g, $p<0.001$), and rubidium 1.6 times (1.6±0.30 µg/g, $p<0.01$).

Table 3: The element content of children with cardiomyopathy, µg/g

Element	Group 1	Group 2	P	References values
Mn	0,64±0,061	1,2±0,30*	<0,01	0,4-1,0
Fe	19,0±0,75*	24,0±1,0	<0,001	20-30
Zn	127,0±8,3*	153,0±8,1	<0,01	150-200
K	2000,0±350,0*	1200,0±200,0	<0,001	800-1500
Rb	1,6±0,30*	0,74±0,012	<0,001	0,5-1,0

*Note: * - validity of differences between children's scores relative to reference values; P - the validity of differences between the scores of compared groups.*

Rubidium has a physiological effect on muscle contractility and acid-base balance similar to potassium. The mechanisms of toxicity of elevated concentrations of rubidium are also similar to those of excess potassium toxicity [14].

Figures 2 and 3 show the frequency of microelementosis in sick children, depending on the region of residence.

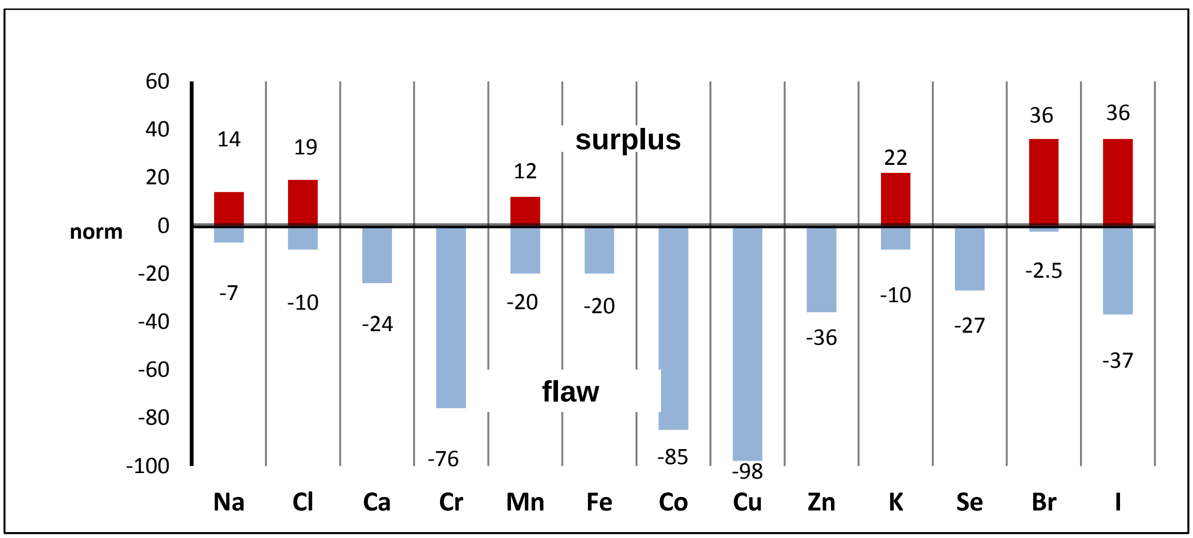

Fig. 2. Microelement frequency in sick children living in a relatively favorable region.

As the research results showed, the problem of trace elements is typical not only for the Aral Sea region but also for other regions. The conducted studies of microelements in hair showed that 96% of children with IUC had a deficit or insufficient content of 2 or more vital microelements relative to reference values.

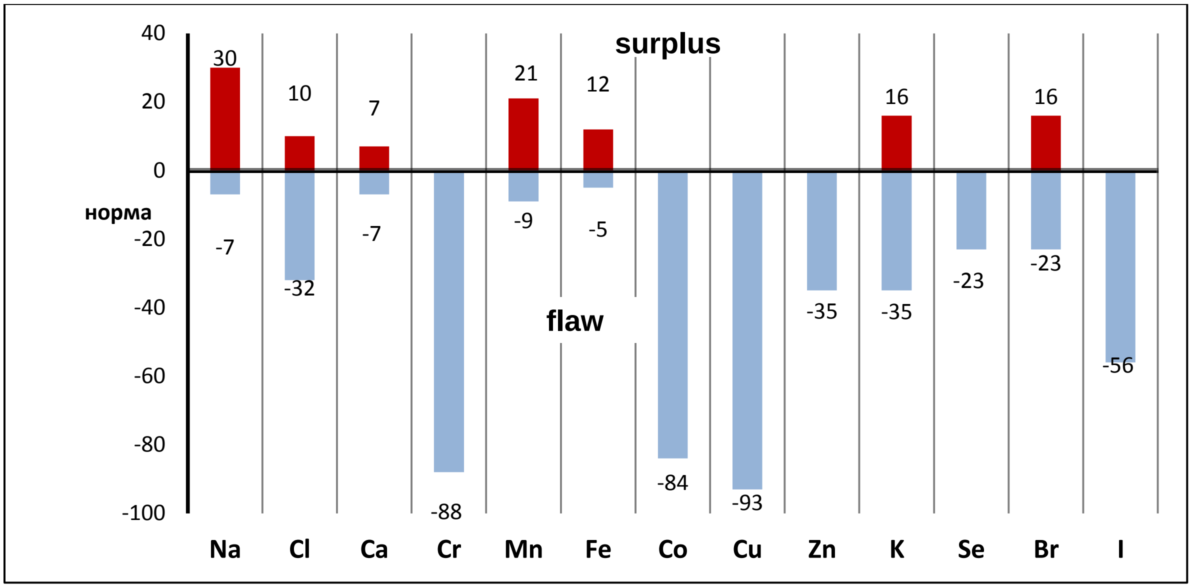

Fig. 3. Microelement frequency in children with CMP living in the Aral Sea region

A detailed analysis of children's macro- and micronutrient levels revealed that almost all of the study subjects, regardless of their region of residence, had a deficit or insufficient copper content in their hair (Figure 4).

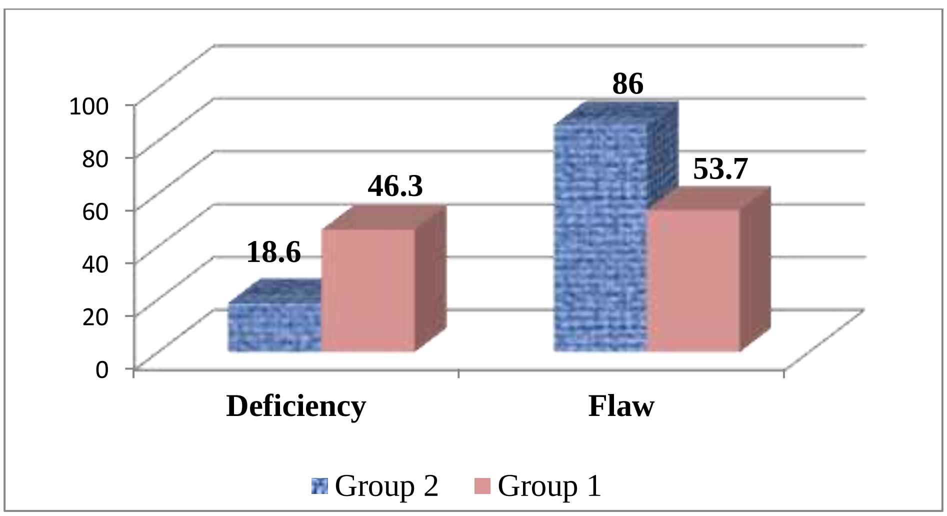

Fig.4. Number of children (%) with copper deficiency/insufficiency by region of residence

As revealed in Figure 5.5, children with a copper deficiency were 2.5 times more likely to be in Group 1 (46.3% vs 18.6%, $p<0.001$), while its deficiency prevailed in Group 2 (86% vs 53.7%, $p<0.001$). Its average values were 6.1±0.6 μg/g in the 1st group and -6.9±0.41 μg/g in the 2nd group, which is reliably below the reference values. At a low level of Cu in the organism, the risk of cardiovascular pathology increases significantly [13].

Ceruloplasmine enzyme containing Cu plays an important role in the mechanisms of antioxidant protection in myocardial ischemia; its content varies depending on the degree of coronary heart muscle damage. In case of Cu deficiency, the activity of lysiloxylase decreases, resulting in the normal formation of collagen and elastin, which in turn leads to pathological changes in the connective tissue structures of the heart and blood vessels [2, 9].

The vast majority of children living in the Aral Sea region had iodine deficiency (60.5%), while the number of children in group 1 was 1.4 times less and accounted for 43.9% ($p<0.01$). Overweight was found in 34.1% of group 1 children and 6.97% of children living in the Aral Sea region. Average iodine levels in children in the 1st group were significantly higher than comparison and reference values ($p<0.01$). However, the lack, as well as an excess of chemical elements, depresses protective mechanisms [2, 8].

Chromium deficiency was found among children in both the 2nd group and comparison group in almost equal amounts (30.2 and 29.3% respectively, $p>0.05$). However, its deficiency prevailed among children in the Aral Sea region (53.5% vs 43.9%, $p<0.001$).

The literature provides examples of hypocalcaemia and cardiomyopathy among children with rickets [15]. In our research, calcium deficiency prevailed in most children, regardless of their region of residence. However, there were 7.4 times more children with calcium deficiency in Group 1 (Figure 5). There was a more pronounced decrease in children in Group 1, compared to Group 2 (660.0±71.0 µg/g vs 930.0±135.0 µg/g, $p<0.001$).

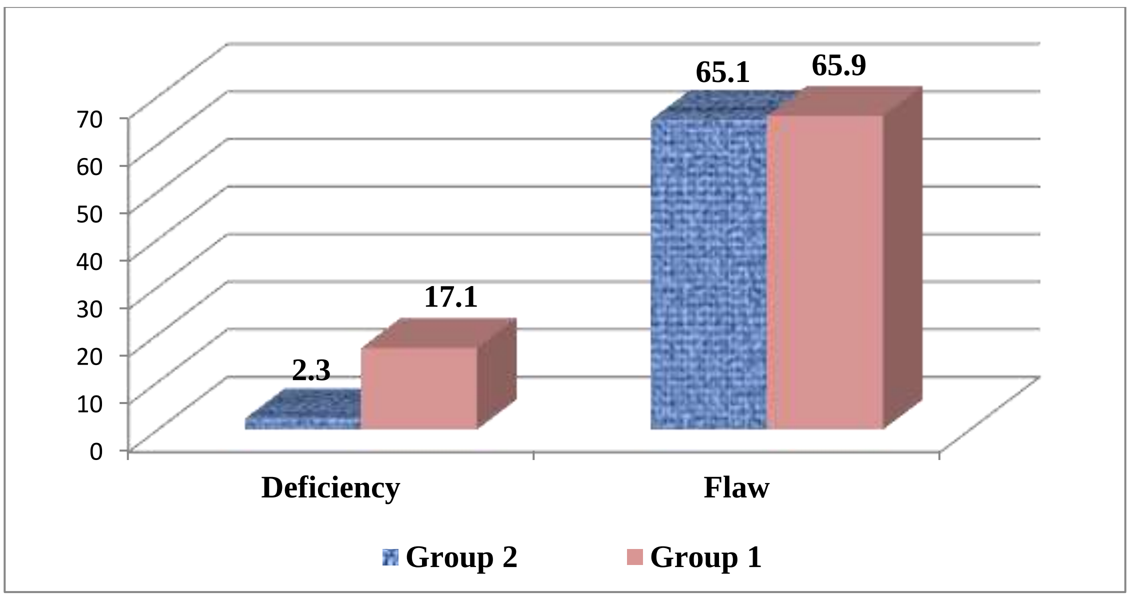

Fig.5. Percentage of children with calcium deficiency/insufficiency by region of residence.

According to the literature, in DCMP there is an increase in serum content of copper, the severity of which is inversely proportional to the size of the FM and heart index of such patients, as well as a decrease in zinc levels in comparison with healthy and sick other cardiovascular diseases, in particular coronary heart disease. However, the significance of these changes in the origin of the disease remains a subject of research so far [13].

It is known that the entry of calcium into cardiomyocytes occurs with the direct participation of such chemical elements as aluminum, copper, iron, lithium, manganese, molybdenum, lead, strontium, vanadium and zinc, and deviation from the norm of any of them in the body may cause the formation of diastolic dysfunction of the left ventricle [13], coronary circulation disorders and ventricular fibrillation. According to W. Nordhoy et al., calcium deficiency may be one of the causes of PQ interval shortening and QT elongation [27].

In case of deficiency of Co, heart rhythm disorders, asthenic syndrome develop, and its excessive intake into the body may lead to "cobalt" cardiopathy [2, 8].

In both Group 1 and 2, the insufficient content of cobalt was found in almost the same number of children (80.5% and 81.4%, $p>0.05$) and its average values were 0.031±0.0035 µg/g and 0.030±0.0038 µg/g, which is significantly lower than the acceptable values ($p<0.01$) (Table 2).

Potassium content was insufficient in 37.2% of children, and 30.7% of patients living in the Aral Sea region had a deficit. This indicator was 24.4% and 12.2% in Group 1, respectively. However, it was almost 3 times more prevalent among children in the 1st group, compared to children in the 2nd group (34.1% versus 11.6%, $p<0.001$). Its average values were 2000.0±350.0 µg/yr, which is reliably above the upper bound (800-1500 µg/yr) (Figure 6).

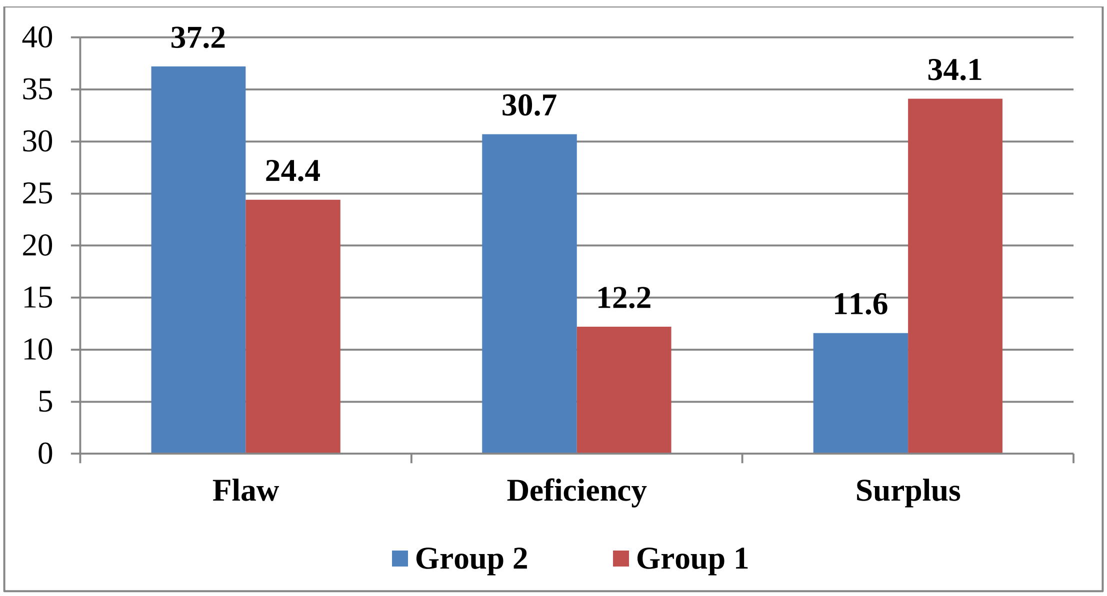

Fig.6. Percentage of children with potassium deficiency/insufficiency and overproduction, depending upon the region of residence.

Selenium (Se) is a cardioprotector protecting the myocardium from cardiotoxic substances, xenobiotics, viruses. It helps to normalize lipid metabolism and prevent the development of atherosclerosis. Se deficiency is a risk factor for the development of CHD, which is associated with the higher morbidity of this pathology in selendeficiency areas [15, 16]. Cardioprotective effect of Se on the reduction of frequency of reperfusion arrhythmias has been shown. Cardioprotective and angioprotective effect of Se is significantly related to the antioxidant role of this ME. Selenium-containing proteins are an essential component of the antioxidant protection system. An important role of selenoprotein P in maintaining normal function of the endothelium of vessel walls damaged by one of the products of oxidative stress peroxynitrite has been shown [15, 16].

Some studies have shown a connection between selenium deficiency and the development of cardiomyopathy and other cardiovascular diseases (myocardial infarcts, coronary heart disease) [13, 15, 16].

Studies found that selenium deficiency was found in only 2 (4.9%) of Group 1 patients, but was reported in nearly 1/3 of Group 2 children (32.6% vs. 21.95%; p<0.001). Average selenium was below the reference values in both groups: 0.29±0.024 µg/y in Group 1 children and 0.31±0.015 µg/y in Group 2 children (p>0.05).

Zinc deficiency was found in 34.9% of children in group 2 and 43.9% of children in group 1. In other patients, the average zinc content was comparable to the norm (150-200 µg/g) (Figure 7). Because of the large number of children with zinc deficiency in Group 1, its mean value was 127.0±8.3 µg/g, which is significantly lower than the norm and comparison group values (153.0±8.1 µg/g) (Table 3).

Zn deficiency is associated with the development of such pathological conditions as congestive heart failure, rheumatic heart disease. Zn and Cu deficiency limits the activity of antioxidant metalloenzymes, promotes the formation of endothelial dysfunction and vascular permeability disorder [2].

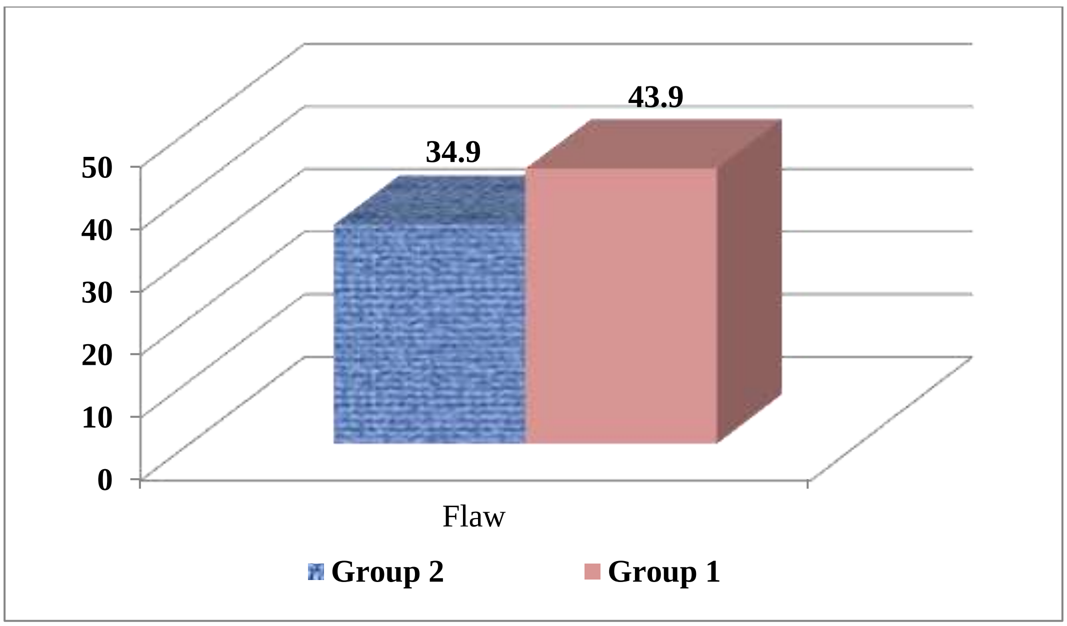

Fig.7. Percentage of children with zinc deficiency, by region

Bromine was excessive among children in the 1st group (39% vs 13.9%), and it was deficient among children in the 2nd group (18.6% vs 2.4%). Group 1 children (6.7±1.5 µg/y) were 1.9 times more likely to have bromine, while Group 2 children (4.1±1.3 µg/y) were 1.2 times more likely to have bromine (1.0-3.5 µg/y).

Iodine content in group 1 was 10±4.3 µg/g, which was 10 times higher than the reference values (0.5-1.0 µg/g). In children in Group 2, its value was 2 times higher than the reference values of 2.1±1.4 µg/g.

Insufficient or excessive content of other elements (iron, manganese) was insignificant in children. Most children's scores were similar to reference values regardless of their region of residence. Analysis of the macronutrient and trace element indices in the hair suggests that most children have a physiological level in their bodies. Concentrations of the elements were either at or below acceptable limits.

But it should be noted that manganese plays a significant role in myocardial energy supply [11]. Studies have shown that myocardial infarction is selectively activated by MPPSOD [11]. High cardioprotective activity of Mn synthetic preparations in myocardial ischemia has been noted [2].

When studying the micronutrient status of each child with cardiomyopathy regardless of the region of residence, it can be assumed that in addition to the main disease, 16% of children have disorders of the nervous system, 15% have disorders of the immune system, and 12% have disorders of the urinary tract.

Thus, the data obtained indicate a significant role of deficiency, excess and imbalance of some macro- and microelements in the development of cardiomyopathy in children.

Conclusions.

1. Microelements are typical not only for the Aral Sea region but also for other regions: deficit and/or deficiency of 2 or more vital microelements are found in 96% of children with IUC.

2. The frequency of trace elements in children in all regions was high in Ca, Cr, Co, Cu, He and Zn. Children living in the Aral Sea region were characterized by excessive levels of manganese, bromine, and iodine ($p<0.01$); children living in relatively favorable regions were characterized by reliably high levels of potassium, chlorine, and iodine ($p<0.01$).

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