CHAPTER «MEDICAL SCIENCES»

HYPERHOMOCYSTEINEMIA AND FOLATE CYCLE GENES IN GIRLS AND BOYS LIVING NEAR THE CHERNOBYL EXCLUSION ZONE

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Abstract. The state of hyperhomocysteinemia (the level of the sulfur-containing amino acid homocysteine – H_{cy} in the blood over 10 μmol/l) was first detected in a large number of adolescent children living in areas located near the Chernobyl Exclusion Zone (ChEZ) during the implementation of the European Commission's projects "Health and Ecological Programs around the Chernobyl Exclusion Zone: Development, training and coordination of health-related projects" and the Rhone-Alpes Regional Council (France). Since numerous studies have noted hyperhomocysteinemia in severe diseases in adults, it is necessary to investigate its etiopathogenesis in the body of children under constant radiation exposure. At the same time, it is important to determine the participation in this pathological process of the genes of the folate cycle, which exchanges H_{cy}. *The purpose of this study* was a comparative analysis of the manifestation of hyperhomocysteinemia in boys and girls living near the ChEZ, taking into account the genes that control the folate cycle. *Research methods.* The results of a laboratory examination of 690 children (368 girls and 322 boys) aged 8-17 from Ivankov and Polessky districts of the Kyiv region of Ukraine were used. Immunochemical, genetic and statistical research methods were used. *Results.* Statistical differences in the carriage of polymorphic alleles of the folate cycle (FC) genes, blood H_{cy} levels, the proportion of hyperhomocysteinemia levels,

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as well as correlations between H_{cy} values and B_6, B_9, B_{12} vitamins in the blood of the examined boys and girls were studied. Sex differences in the proportion of polymorphic alleles of the FC genes have not been established. In the general group of children, hyperhomocysteinemia was detected in 62.46 % of cases, while in the group of girls – in 53.80 % of cases, in the group of boys – in 72.36 % ($t = 5.16$; $p = 0.000001$). In most genetic subgroups of boys, the level of H_{cy} in the blood and the proportion of cases of hyperhomocysteinemia were statistically large compared with similar subgroups of girls. Despite the fact that the largest proportion of cases of hyperhomocysteinemia was associated with a homozygous variant of the T/T risk allele of the MTHFR:677 genetic polymorphism, in most genetic subgroups, including those that included only neutral FC alleles, this condition occurred in 50 or more % of cases. *Conclusions.* The high proportion of cases of hyperhomocysteinemia in children of both sexes may be associated with the constant exposure to long-lived radionuclides ^{137}Cs, ^{90}Sr, ^{241}Am contained in the soils and plants of the ChEZ and adjacent areas. The lower level of H_{cy} in the blood and the proportion of cases of hyperhomocysteinemia in the group of girls, compared with the group of boys, is associated with a higher content of vitamin B_{12} in their blood and a more intense functioning of the transsulfuration reaction cycle. The results obtained can be used in the organization of preventive and rehabilitation measures for the child population in the territory affected by radiation exposure.

1. Introduction

The state of hyperhomocysteinemia (the level of the sulfur-containing amino acid homocysteine – H_{cy} in the blood over 10 μmol/l) was first detected in a large number of adolescent children living in areas located near the Chernobyl Nuclear Power Plant (ChNPP) during the implementation of the European Commission's projects "Health and Ecological Programs around the Chernobyl Exclusion Zone: Development, training and coordination of health-related projects" and the Rhone-Alpes Regional Council (France) [1, p. 29].

A connection has been established between an increase in the level of H_{cy} in the blood of children and forest fires in the Chernobyl Exclusion Zone (ChEZ) [2, p. 35].

Since numerous studies note hyperhomocysteinemia in severe diseases in adults [3, p. 12; 4, p. 3; 5, p. 1087; 6, p. 8; 7, p. 49; 8, p. 4], it is necessary to investigate its etiopathogenesis in the body of children under constant radiation exposure [9, p. 5; 10, p. 12].

At the same time, it is important to determine the participation in this pathological process of the genes of the folate cycle, which exchanges H_{cy}.

The purpose of this study was a comparative analysis of the manifestation of hyperhomocysteinemia in boys and girls living near the ChEZ, taking into account the genes that control the folate cycle (FC).

2. Material and methods

During the implementation in Ukraine of the projects of the European Commission "Health and Ecological Programs around the Chernobyl Exclusion Zone: Development, training and coordination of health-related projects", the Regional Council of Rhone-Alpes (France) and the French public organization "Children of Chernobyl", were examined laboratory 690 children (368 girls and 322 boys) aged 8-17 living in the settlements of Ivankov and Polessky districts bordering the ChEZ, the soils and trees of which contain significant amounts of long-lived radioactive elements, including ^{137}Cs, ^{90}Sr, ^{241}Am [2, p. 9, 14].

Blood sampling from the cubital vein was performed in children attending school in the morning on an empty stomach.

The blood samples were tested in a quality-certified laboratory and agreed with the parents.

In all 690 children, H_{cy} was determined in the blood and allelic variants of genetic polymorphisms of the FC were registered.

The determination of H_{cy} in the blood was carried out using the immunochemical method with chemiluminescent detection (ECLIA). Analyzer and test system: Architect 1000 (ABBOT Diagnostics (USA)). The level of homocysteine in the blood of children over 10 μmol/l was defined as a state of hyperhomocysteinemia.

The genetic study of FC included the determination of allelic variants C677T and A1298C of the MTHFR gene (methylenetetrahydrofolate reductase), A2756G of the MTR gene (B_{12} – dependent methionine synthase), A66G of the MTRR gene (methionine synthase reductase). The method used was: PCR in Real-time mode. Analyzer and test system DT-96 detecting cycler; "DNA-Technology" (Russia).

In 179 children aged 12-17 years, the blood levels of vitamins B_6, B_9 and B_{12} were determined.

Determination of vitamin B_6 (HPLC) was carried out using the method of high performance liquid chromatography. Analyzer and test system: HPLC-System 1100, Agilent with fluoressence detection; Recipe complete kit (Germany).

Determination of vitamin B_9 – (folacin) was carried out using an immunochemical method with electrochemiluminescent detection (ECLIA). Analyzer and test system: Cobas e411; Roche Diagnostics (Switzerland).

The determination of vitamin B_{12} – holotranscobalamin (active vitamin B_{12}) was carried out using an immunochemical method with chemiluminescent detection (CLIA). Analyzer and test system: Architect 1000 (Abbott Diagnostics), USA.

The reference interval of extreme values indicated by the laboratory was: for vitamin B_6 – 8.7-27.2 μg/l, for folic acid (vitamin B_9) – 4.6 – 18.7 ng/ml, for vitamin B_{12} – 191, 0 – 663.0 pg/ml.

Statistical processing of the obtained results was carried out using the IBM SPSS Statistics 22 program (USA). In the course of it, for the analyzed indicators, the arithmetic mean (M) ± standard error of the mean (m), confidence interval of the mean value (95 % CI), median (Me), interquartile range (IR). The hypothesis about the type of distributions was tested (Kolmogorov-Smirnov criterion). All the studied parameters did not correspond to the normal distribution law, and therefore, the non-parametric Mann-Whitney U-test was used to compare the values.

The statistical significance of the indicators was assessed by determining the significance level p using a statistical program.

Student's t-test was used to compare relative scores. The critical confidence level of the null hypothesis (p) was taken as 0.05.

The relationship between the levels of H_{cy} and vitamins B_6, B_9, B_{12} was determined using the Spearman rank correlation coefficient (r_{xy}).

The strength of the correlation was assessed according to the traditional scale: weak – from 0 to 0.299; medium – from 0.3 to 0.699; strong – from 0.7 to 1.0.

3. Results and discussion

There were no statistical differences between the groups of girls and boys in the proportion of polymorphic alleles of the FC genes (Tables 1, 2).

Table 1

The frequency of polymorphic alleles of folate cycle genes in girls from Ivankovsky and Polessky districts

Gene, polymorphism	Genotype variants					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Risk allele" Homozygous variant	
	Abs. number	%	Abs. number	%	Abs. number	%
MTR:A2756G	234	63.59	115	31.25	19	5.16
MTHFR:A1298C	176	47.83	164	44.56	28	7.61
MTHFR:C677T	166	45.11	170	46.19	32	8.70
MTRR:A66G	74	20.11	171	46.47	123	33.42

Table 2

The frequency of polymorphic alleles of folate cycle genes in boys from Ivankovsky and Polessky districts

Gene, polymorphism	Genotype variants					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Risk allele" Homozygous variant	
	Abs. number	%	Abs. number	%	Abs. number	%
MTR:A2756G	193	59.94	111	34.47	18	5.59
MTHFR:A1298C	152	47.20	133	41.30	37	11.50
MTHFR:C677T	154	47.83	141	43.79	27	8.38
MTRR:A66G	58	18.01	157	48.76	107	33.23

In both groups of children, the proportion of cases with the neutral allele of the MTR:A2756G polymorphism exceeded the proportion of cases with the risk allele of the same polymorphism.

In the subgroups of polymorphisms MTHFR:C677T and MTHFR:A1298C, the proportion of cases with the risk allele was higher than with the neutral allele. At the same time, the proportion of cases with

heterozygous variants, including the risk allele, exceeded the proportion of cases with homozygous variants, with the same allele.

The MTRR:A66G subgroup differed in that the proportion of cases with the neutral allele was significantly less than with the risk allele (Tables 1, 2).

In the general group of children (n = 690), hyperhomocysteinemia (H_{cy} > 10 μmol/l) was registered in 431 cases, or in 62.46 % of cases.

In the group of girls, hyperhomocysteinemia occurred in 198 cases, or 53.80 %, while in the group of boys – in 233 cases, or 72.36 % (t = 5.16; p = 0.000001).

In most genetic subgroups of girls, the proportion of cases of hyperhomocysteinemia was in the range of 50-55 %. The maximum level of cases of hyperhomocysteinemia was recorded in the subgroup with the base genotype T/TMTHFR:677 – 71.87 %, the minimum level of cases of hyperhomocysteinemia – in the subgroup with the base genotype C/CMTHFR:1298 – 35.71 % (Table 3).

Table 3

The proportion of cases of hyperhomocysteinemia in subgroups of girls with genetic polymorphisms of the folate cycle

Gene, polymorphism	Hyperhomocysteinemia					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Neutral" allele Homozygous variant	
	Abs. number	%	Abs. number	%	Abs. number	%
MTR:A2756G	130	55.55	58	50.43	10	52.63
MTHFR:A1298C	97	55.11	91	55.49	10	35.71
MTHFR:C677T	83	50.00	92	54.12	23	71.87
MTRR:A66G	41	55.40	92	53.80	65	52.84

In most genetic subgroups of boys, the proportion of cases of hyperhomocysteinemia exceeded the 70 % threshold. The exceptions were subgroups with basic genotypes C/CMTHFR:1298, C/CMTHFR:677 and A/AMTRR:66.

The largest proportion of cases of hyperhomocysteinemia was recorded in the subgroup of boys with the basic genotype T/TMTHFR:677 – 81.48 % (Table 4).

Comparative analysis revealed statistical differences between groups of girls and boys in most subgroups, except for subgroups with genotypes G/GMTR:2756, C/CMTHFR:1298, T/TMTHFR:677, and A/AMTRR:66 (Table 5).

Table 4

The proportion of cases of hyperhomocysteinemia in subgroups of boys with genetic polymorphisms of the folate cycle

Gene, polymorphism	Hyperhomocysteinemia					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Neutral" allele Homozygous variant	
	Abs. number	%	Abs. number	%	Abs. number	%
MTR:A2756G	141	73.06	79	71.17	13	72.22
MTHFR:A1298C	112	73.68	100	75.19	21	56.76
MTHFR:C677T	104	67.53	107	75.89	22	81.48
MTRR:A66G	34	58.62	117	74.52	82	76.63

Table 5

Statistical differences in the proportion of cases of hyperhomocysteinemia in groups of girls and boys with genetic polymorphisms of the folate cycle

Gene, polymorphism	Comparison indicators of the proportion of cases of hyperhomocysteinemia					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Neutral" allele Homozygous variant	
	t	p	t	p	t	p
MTR:A2756G	3.85	0.000151	3.27	0.001363	1.26	0.222990
MTHFR:A1298C	3.59	0.000418	3.65	0.000339	1.73	0.94758
MTHFR:C677T	3.24	0.001417	4.15	0.000050	0.90	0.374200
MTRR:A66G	0.37	0.711617	4.02	0.000083	3.91	0.000141

Note. t – Student's t-test; p – significance level.

Statistical differences in the level of Hcy in the blood of girls and boys were also determined in most genetic subgroups, with the exception of subgroups with basic genotypes G/GMTR:2756, T/TMTHFR:677 and A/AMTRR:66 (Tables 6, 7, 8).

Table 6

Statistical indicators of the content of H_{cy} in the blood of girls with genetic polymorphisms of the folate cycle

Gene, polymorphism	Statistical indicators of the content of H_{cy} in the blood					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Neutral" allele Homozygous variant	
	Me	IR	Me	IR	Me	IR
MTR:A2756G	10.57	8.99-12.41	10.01	8.65-11.13	10.38	7.40-13.01
MTHFR:A1298C	10.55	9.04-12.58	10.30	8.64-12.02	9.12	8.12-10.40
MTHFR:C677T	10.01	8.69-12.05	10.34	8.70-11.81	12.8	9.46-16.45
MTRR:A66G	10.40	8.89-12.20	10.30	8.71-12.30	10.20	8.80-12.10

Note. Me – median; IR – interquartile range.

Table 7

Statistical indicators of the content of Hcy in the blood of boys with genetic polymorphisms of the folate cycle

Gene, polymorphism	Statistical indicators of the content of H_{cy} in the blood					
	"Neutral" allele Homozygous variant		"Risk allele" Heterozygous variant		"Neutral" allele Homozygous variant	
	Me	IR	Me	IR	Me	IR
MTR:A2756G	12.00	9.70-14.14	11.70	9.50-14.84	11.27	9.57-12.98
MTHFR:A1298C	11.64	9.73-15.11	12.02	10.05-14.20	11.45	9.05-14.72
MTHFR:C677T	11.48	9.12-14.02	11.93	10.12-14.24	13.83	10.26-26.71
MTRR:A66G	10.78	8.79-13.82	11.80	9.84-13.65	12.60	10.20-16.35

Note. Me – median; IR – interquartile range.

In the blood of girls, compared with boys, a decrease in the level of H_{cy} was accompanied by an increase in the level of vitamin B_{12} (Tables 9, 10).

At the same time, in the group of boys, inverse correlations were found between the values of H_{cy} and vitamin B_9, H_{cy} and vitamin B_{12}, while in the group of girls only an inverse relationship was determined between the values of H_{cy} and vitamin B_9, however, an inverse relationship was found between the values vitamins B_{12} and B_6 (Tables 11, 12).

Thus, it should be noted the high proportion of cases of hyperhomocysteinemia in the surveyed group of children living near the ChEZ 30 years after the accident at the ChNPP.

Table 8

Results of statistically significant differences when comparing the level of Hcy in the blood of boys[1] and girls[2] within genetic subgroups

Parameters	Groups comparisons	Comparison group size	Average rank	U Mann-Whitney test, statistical significance, p
A/AMTR:2756	1	193	241.49	U = 17274.500; p = 0.00001
	2	234	191.32	
A/GMTR:2756	1	111	137.12	U = 3760.500; p = 0.00001
	2	115	90.70	
G/GMTR:2756	1	18	20.47	U = 144.500; p = 0.421
	2	19	17.61	
A/AMTHFR:1298	1	152	184.38	U = 10354.000; p = 0.00001
	2	176	147.33	
A/CMTHFR:1298	1	133	178.35	U = 7002.000; p = 0.00001
	2	164	125.20	
C/CMTHFR:1298	1	37	38.36	U = 319.500; p = 0.009
	2	28	25.91	
C/CMTHFR:677	1	154	182.48	U = 9397.500; p = 0.0001
	2	166	140.11	
C/TMTHFR:677	1	141	186.08	U = 7743.500; p = 0.0001
	2	170	131.05	
T/TMTHFR:677	1	27	33.93	U = 326.000; p = 0.107
	2	32	26.69	
A/AMTRR:66	1	58	70.03	U = 1941.000; p = 0.347
	2	74	63.73	
A/GMTRR:66	1	157	187.45	U = 9821.000; p = 0.0001
	2	171	143.43	
G/GMTRR:66	1	107	141.95	U = 3750.000; p = 0.0001
	2	123	92.49	

Note. [1] – group "1"; [2] – group "2".

The largest proportion of cases of hyperhomocysteinemia was determined in the case of homozygous variants of the T/T risk allele of the MTHFR:677 genetic polymorphism.

Under conditions of constant radiation exposure, the activity of the body's enzyme systems is reduced [11, p. 79], and therefore, even in the absence of risk alleles for genetic polymorphisms of FC in the child's

Table 9

Statistical characteristics of indicators of metabolic processes in the blood of the examined children

Parameters	Boys		Girls	
	Me	IR	Me	IR
H_{cy}, μmol/L	12.20	10.87 – 15.86	11.13	9.28 – 12.57
B_6, mcg/L	18.30	14.87 – 24.00	19.50	15.05 – 22.15
B_9, ng/mL	6.54	4.96 – 8.03	6.52	5.18 – 7.68
B_{12}, pg/mL	293.20	234.30 – 352.65	350.60	274.15 – 463.10

Table 10

The results of statistically significant differences when comparing the parameters of metabolic processes in the blood of the examined boys[1] and girls[2]

Parameters	Groups comparisons	Comparison group size	Average rank	U Mann-Whitney test, statistical significance, p
H_{cy}, μmol/L	1	86	105.25	U = 2687.500; p = 0.0001
	2	93	75.90	
B_6, mcg/L	1	86	89.30	U = 3939.000; p = 0.862
	2	93	90.65	
B_9, ng/mL	1	86	91.76	U = 3847.500; p = 0.662
	2	93	88.37	
B_{12}, pg/mL	1	86	75.71	U = 2770.000; p = 0.0001
	2	93	103.22	

Note. [1] – group "1"; [2] – group "2".

genome, there is an increase in the content of Hcy in the blood. In the group of girls with a combination of neutral alleles of FC genetic polymorphisms, the proportion of hyperhomocysteinemia was 50.00-59.09 %, in the same group of boys – 44.44-66.33 % (Table 13, 14).

The conducted studies indicate statistical differences in the content of Hcy in the blood of girls and boys.

In the general group of girls, compared with the general group of boys, the level of H_{cy} in the blood, as well as the proportion of cases of hyperhomocysteinemia, was significantly lower. A similar situation was recorded in most genetic subgroups.

Table 11

Correlations between H_{cy}, vitamins B_6, B_9, B_{12} in the group of girls

Parameter	Correlation coefficient (r_{xy}), Significance, (p)	Parameters			
		H_{cy}	B_6	B_9	B_{12}
H_{cy}	Spearman's (r_{xy})	1.000	0.106	-0.369**	-0.184
	Sign. (2-tailed)	.	0.313	0.000	0.077
	N	93	93	93	93
B_6	Spearman's (r_{xy})	0.106	1.000	-0.136	-0.247*
	Sign. (2-tailed)	0.313	.	0.193	0.017
	N	93	93	93	93
B_9	Spearman's (r_{xy})	-0.369**	-0.136	1.000	0.114
	Sign. (2-tailed)	0.000	0.193	.	0.276
	N	93	93	93	93
B_{12}	Spearman's (r_{xy})	-0,184	-0.247*	0.114	1.000
	Sign. (2-tailed)	0.077	0.017	0.276	.
	N	93	93	93	93

Note. * – Correlation is significant at the 0.05 level (2-tailed).
** – Correlation is significant at the 0.01 level (2-tailed).

Table 12

Correlations between H_{cy}, vitamins B_6, B_9, B_{12} in the group of boys

Parameter	Correlation coefficient (r_{xy}), Significance, (p)	Parameters			
		H_{cy}	B_6	B_9	B_{12}
H_{cy}	Spearman's (r_{xy})	1.000	-0.017	-0.517**	-0.446**
	Sign. (2-tailed)	.	0.880	0.000	0.000
	N	86	86	86	86
B_6	Spearman's (r_{xy})	-0.017	1.000	0.138	-0.038
	Sign. (2-tailed)	0.880	.	0.205	0.731
	N	86	86	86	86
B_9	Spearman's (r_{xy})	-0.517**	0.138	1.000	0.426**
	Sign. (2-tailed)	0.000	0.205	.	0.000
	N	86	86	86	86
B_{12}	Spearman's (r_{xy})	-0.446**	-0.038	0.426**	1.000
	Sign. (2-tailed)	0.000	0.731	0.000	.
	N	86	86	86	86

Note. * – Correlation is significant at the 0.05 level (2-tailed).
** – Correlation is significant at the 0.01 level (2-tailed).

Table 13

Combinations of neutral genotypes of folate cycle, and associated hyperhomocysteinemia, in a group of girls

Genotypes	Number of cases in a group		H_{cy} > 10.0 µmol/L	
	n	%	n	%
C/CMTHFR:677-A/AMTR:2756	106	28.80	55	51.89
C/CMTHFR:677-A/AMTRR:66	35	9.51	18	51.43
C/CMTHFR:677-A/AMTHFR:1298	58	15.76	31	53.45
C/CMTHFR:677-A/AMTR:2756-A/A MTRR:66	22	5.98	13	59.09
C/CMTHFR:677-A/AMTR:2756-A/AMTHFR:1298	40	10.87	20	50.00
C/CMTHFR:677-A/AMTHFR:1298-A/A MTRR:66	12	3.26	7	58.33

Table 14

Combinations of neutral genotypes of folate cycle, and associated hyperhomocysteinemia, in a group of boys

Genotypes	Number of cases in a group		H_{cy} > 10.0 µmol/L	
	n	%	n	n
C/CMTHFR:677-A/AMTR:2756	98	30.43	65	66.33
C/CMTHFR:677-A/AMTRR:66	27	8.38	15	55.55
C/CMTHFR:677-A/AMTHFR:1298	47	14.60	31	65.96
C/CMTHFR:677-A/AMTR:2756-A/A MTRR:66	17	5.28	9	52.94
C/CMTHFR:677-A/AMTR:2756-A/AMTHFR:1298	30	9.32	18	60.00
C/CMTHFR:677-A/AMTHFR:1298-A/A MTRR:66	9	2.79	4	44.44

Non-significant differences in some subgroups were associated with a small number of comparisons.

A higher level of vitamin B_{12} in the blood of girls, compared with boys, suggests a better provision of the H_{cy} remethylation process in their body, and, consequently, the formation of internal methionine, which occurs with the participation of B_{12}-methionine synthase.

In addition, the inverse correlation between vitamins B_{12} and B_6 and the absence of an inverse correlation between H_{cy} and vitamin B_{12} indicates a close relationship between B_{12}-methionine synthase and cystathionine-β-synthase, representing the cycle of transsulfurization reactions. With an insufficient content of active forms of vitamin B_{12} in the blood, and therefore, insufficient activity of B_{12}-methionine synthase, the activity of cystathionine-β-synthase increases. Accordingly, the blood content of active forms of vitamin B_6, the coenzyme cystathionine-β-synthase, increases.

The inclusion of the compensatory mechanism of H_{cy} utilization through the cycle of transsulfuration reactions in the body of girls is evidenced by the results of comparing the level of hyperhomocysteinemia in subgroups with a combination of alleles of genetic polymorphisms of FC.

In the absence of the negative effect of the T allele of the MTHFR:677 genetic polymorphism and the carriage of the G risk allele in the MTR:2756 and MTRR:66 genetic polymorphisms, the combination of C/C MTHFR:677-A/G MTR:2756-G/GMTRR:66 genotypes, state hyperhomocysteinemia was detected in the group of girls in 6 out of 16 cases – 37.5 %, while in the group of boys in 13 out of 15 cases – 86.67 % ($t = 3.29$; $p = 0.004625$).

It was noted that in adult women, the concentration in the blood of H_{cy} is inversely proportional to the concentration of endogenous estrogens [12, p.8; 13, p. 618].

There is a reasonable assumption that estrogens affect the metabolism of thiol amino acids, most notably methionine. They interfere with the transsulfurization process by activating cystathionine-β-synthase, and thereby prevent the accumulation of H_{cy}. At the same time, the formation of reduced glutathione is enhanced, which has a beneficial effect on the walls of blood vessels [14, p. 580].

Thus, in the body of girls with hyperhomocysteinemia, increased amounts of H_{cy} are utilized in trans-sulfurization reactions, while, from the interaction of H_{cy} and serine, cystathionine is formed, and then cysteine and glutathione, which has an antioxidant effect.

In boys, the process of H_{cy} utilization through the cycle of transsulfurization reactions is less pronounced, as a result of which the level of this sulfur-containing amino acid in the blood is much higher than in girls.

In this regard, they have a great danger of the occurrence of destructive processes in the circulatory system and the central nervous system.

4. Conclusions

In the population of Ukrainian children living near the ChEZ 30 years after the accident at the ChNPP, there were no statistical differences between the groups of girls and boys in the proportion of polymorphic alleles of the FC genes.

In the general group of children, hyperhomocysteinemia was detected in 62.46 % of cases, while in the group of girls – in 53.80 % of cases, in the group of boys – in 72.36 % ($t = 5.16$; $p = 0.000001$).

In most genetic subgroups of boys, the level of H_{cy} in the blood and the proportion of cases of hyperhomocysteinemia were statistically large compared with similar subgroups of girls.

Despite the fact that the largest proportion of cases of hyperhomocysteinemia was associated with a homozygous variant of the T/T risk allele of the MTHFR:677 genetic polymorphism, in most genetic subgroups, including those that included only neutral FC alleles, this condition occurred in 50 or more % of cases.

The high proportion of cases of hyperhomocysteinemia in children of both sexes may be associated with the constant exposure to long-lived radionuclides ^{137}Cs, ^{90}Sr, ^{241}Am contained in the soils and plants of the ChEZ and adjacent areas.

The lower level of H_{cy} in the blood and the proportion of cases of hyperhomocysteinemia in the group of girls, compared with the group of boys, is associated with a higher content of vitamin B_{12} in their blood and a more intense functioning of the transsulfuration reaction cycle.

The results obtained can be used in the organization of preventive and rehabilitation measures for the child population in the territory affected by radiation exposure.

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