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СТАН ФОЛАТНОГО ЦИКЛУ ТА ЙОГО ЗВ'ЯЗОК З ТИРЕОЇДНОЮ СИСТЕМОЮ У ДІТЕЙ ПІСЛЯ ЛІСОВИХ ПОЖЕЖ У ЧОРНОБИЛЬСЬКІЙ ЗОНІ ВІДЧУЖЕННЯ

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THE STATE OF FOLATE METABOLISM AND ITS LINK WITH THYROID SYSTEM IN CHILDREN AFTER FOREST FIRES IN THE CHORNOBYL EXCLUSION ZONE

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Keywords: folate metabolism, homocysteine, hormones of hypophysis and thyroid gland, forest fires, Chornobyl exclusion zone.

Folate cycle (FC) is one of the main metabolic cycles in the human organinsm, folic acid derivatives are involved in its enzyme systems. Moreover, the biosynthesis of methionine, purine and pyrimidine nucleotides, and DNA methylation takes place [1]. Homocysteine (H_c) is a sulphur-containing amino acid which is a marker for the efficiency of FM functioning.

Blood H_c levels have exceeded physiological limits in more than 75.0% of the adolescents living in Ivankivskyi and Poliskyi districts, Kyiv region, in 30 years after the accident at the Chornobyl nuclear power plant (ChNPP) [2]. Disorders in the production of thyroid hormones have also been registered [3].

Taking into account a high prevalence of thyroid cancer among the inhabitants of the Ukrainian-Belarusian Polissia after accident at the Chornobyl nuclear power plant [4], a determination of the FC state and its linkwith the thyroid system in children, constantly living under radiation risk due to the ChNPP accident, is of high priority.

The forest fires at the territory contaminated with radionuclides may be one of the causes of radiation exposure. In total, 4.0 millions hectares of the forest lands were contaminated with radioactive elements in Ukraine. Zhytomyr region (974.3 thousands hectares), Kyiv region (416.4 thousands hectares), Chernihiv region (725.5 thousands hectares), and Rivne region (728.8 thousands hectares) are the most suffered regions [5]. The greatest amount of radioactive fall-out, in particular ^{137}Cs – 4.4 PBq, ^{90}Sr – 4.0 PBq, $^{239/240}Pu$ – 32 TBq, fell within 30-km Chornobyl exclusion zone [6].

Thus, the soils of suffered areas, the forest trees, shrubs, and grasses, growing in these areas, currently contain a huge amount of radioactive elements.

Forest fires, often occurring in the Chornobyl exclusion zone, are one of the most powerful sources of secondary air pollu-

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***Мета дослідження:** визначення стану фолатного циклу та його зв'язку з тиреоїдною системою у дітей українського Полісся після лісових пожеж у Чорнобильській зоні відчуження.*
***Методи дослідження.** Імунохімічний, математико-статистичний.*
***Результати**. У підгрупі дітей-носіїв алелі ризику Т генетичного поліморфізму MTHFR:C677T, які проживають в Іванківському і Поліському районах, рівень гомоцистеїну у крови був достовірно вищим, ніж у підгрупі дітей, позбавлених даної алелі.*
Обстеження дітей із районів, прилеглих до Чорнобильської атомної електростанції, дозволило виявити у них зміни метаболічних процесів у вигляді підвищеної продукції гомоцистеїну у зв'язку з лісовими пожежами у зоні відчуження. У групі дітей із Іванківського району, обстежених після пожежі у Чорнобильській зоні відчуження, рівень гомоцистеїну у крови вищий, ніж у групі дітей із Поліського району, обстежених до пожежі, у тому числі у більшості генетичних підгруп, за винятком генетичної підгрупи з випадками гомозиготного носійства алелі Т.
У групі дітей із Іванківського району з більш високим рівнем гомоцистеїну у крови порівняно з групою дітей із Поліського району реєструвався прямий кореляційний зв'язок між вмістом у крови гомоцистеїну і тиреотропного гормону гіпофіза, гомоцистеїну та трийодтироніну. Можна обґрунтовано припускати негативний вплив пожеж у Чорнобильській зоні відчуження на процеси функціонування фолатного циклу дитячого організму.

Ключові слова: фолатний цикл, гомоцистеїн, гормони гіпофіза і щитоподібної залози, лісові пожежі, Чорнобильська зона відчуження.

tion with different radionuclides which have a negative impact on people's health [7].

Radioactive products of combustion of the forest plants move into the atmosphere with wind currents for long distances. The duration of the existence of radiation smoke aerosols and clouds is less than a week in the lower troposphere (the height up to 1.5 km), about a month – in the upper troposphere, and 1-3 years – in the stratosphere. At the same time, radioactive products of combustion are deposited on the radiation-free territories. Basically, radioactive aerosols contain ^{137}Cs [7].

The aim of this study was to determine a state of FC and its link with a thyroid system in the children of the Ukrainian Polissia after forest fires in the Chornobyl exclusion zone.

Material and methods. The study was conducted within the implementation of the projects of the European Commission in Ukraine "Health and Ecological Programmes around the Chornobyl Exclusion Zone: Development, Training, and Coordination of Health-Related Projects" and the Rhane-Alpes Regional Council (France).

178 children from Ivankivskyi district and 158 children from Poliskyi district of Kyiv region, underwent laboratory and instrumental examination. According to the findings of dosimetry certification of the settlements, the territory of the regions has remained contaminated with radioactive substances after the Chornobyl accident until the present day (the ^{137}Cs soil pollution density varies 0.17-1.9 Cu/km^2 [8]).

The average age of the children in the group from Ivankivskyi district was (13.6 ± 0.1) years old (95% CI 13.4-13.8 years old), and (14.8 ± 0.0) years old (95% CI 14.7-15.0 years old) in the group from Poliskyi district.

In the morning, all the children who attended school were taken the blood sampling in an empty stomach from the ulnar vein. Blood sampling among children from Poliskyi district was carried out on 02.04.2015 and in the children from Ivankivskyi district – on 18.12.2015.

The investigatons of blood samples were agreed with the parents, they were analysed at the laboratory, certified by quality standards. A content of pituitary thyroid-stimulating hormone (TSH), free triiodothyronine (T_3), free thyroxine (T_4), H_c, and the state of the FM genetic system were assessed.

TSH, T_3 and T_4 concentrations were determined with the help of electrochemiluminescent immunoassay method (ECLIA). Analyser and test kit: Cobas 6000; Roche Diagnostics (Switzerland).

Plasma homocysteine concentrations were measured with the chemiluminescent immunoassay method (CLIA). Analyser and test kit: Architect 1000 (ABBOT Diagnostics (USA)).

The following allelic variants were identified in genetic analysis of FM: C677T and A1298C of the MTHFR gene (synthesis of the methylenetetrahydrofolate reductase enzyme), A2756G of the MTR gene (synthesis of the B_{12}-dependent methionine synthase enzyme) and A66G of the MTRR gene (synthesis of the methionine synthase reductase enzyme). PCR method in a real-time regime was used. Analyser and test kit: DT-96 detecting thermocycler, DNA-Technology (Russia).

In order to carry out the correlation studies identifying a link between blood H_c levels and the frequency of genetic changes in the studied cases of each genetic polymorphism, we assessed genetic variants in points (0-3): "0" – homozygous carriership of a neutral allele; "1" – heterozygous carriership of a risk allele; "2" – homozygous carriership of a risk allele.

The statistical processing of the obtained results was performed with help of IBM SPSS Statistics 22 software (USA). The arithmetic mean (M), ± standard error of mean (m), confidence interval for the mean value (95% CI), median (Me), interquartile range (IR), minimum and maximum parameter values and percentiles were calculated for the analysed variables. The distribution hypothesis was tested (Kolmogorov-Smirnov criterion). All the parameters under study did not conform to the normal distribution law, thus, a non-parametric Mann-Whitney U-test was used to compare values. The statistical significance of variables was assessed by the determination of p significance level with the help of the statistical software programme.

The Student t-test was used to compare relative values. The critical level of significance for the null hypothesis (p) was taken as 0.05. An link between H_c, TSH, T_3 and T_4 levels in blood and variants of the carriership of risk alleles of folate metabolism genetic polymorphisms were identified with the help of the Spearman rank correlation coefficient (rxy). The strength of a link was assessed according to a typical scale: weak – from 0 to 0.299; moderate – from 0.3 to 0.699; strong – from 0.7 to 1.0.

Results and discussion. The investigations showed that blood H_c level was significantly higher in the subgroup of the children-carriers of the T risk allele of the MTHFR:C677T genetic polymorphism-MTHFR:677 C/T + MTHFR:677 genotypes, living in Ivankivskyi and Poliskyi districts of Kyiv region, than in the subgroup of the children without this allele – MTHFR:677 C/C genotype (tables 1-3).

H_c level was statistically significantly higher in the subgroup with the MTHFR:677 C/T + MTHFR:677 T/T genotypes in comparison with the subgroup that included the MTR:2756 A/G + MTR:2756 G/G genotypes in

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Objective. *We determined the state of folate cycle and its link with thyroid system in the children of the Ukrainian Polissia after forest fires in the Chornobyl exclusion zone.*

Methods*: Immunochemical, mathematical and statistical ones.*

Results. *Blood homocysteine levels were statistically significantly higher in the subgroup of the children who were the carriers of the T risk allele of the MTHFR:C677T genetic polymorphism living in Ivankovsky and Poliskyi districts than in the subgroup of the children without this allele. The examination of the children from the regions adjacent to the Chornobyl nuclear power plant allowed to identify in them the metabolic processes' changes in the form of increased production of H_c due to the forest fires in the exclusion zone. Blood H_c levels were higher in the children from Ivankivskyi district examined after fires in the Chornobyl exclusion zone than in those from Poliskyi district examined before fires, including the majority of genetic subgroups, with the exception of the genetic subgroup which included cases of homozygous carriership of the T allele.*

Direct links between blood homocysteine and pituitary thyroid-stimulating hormone levels, homocysteine and triiodothyronine levels were detected in the group of the children from Ivankivskyi district who had higher blood homocysteine concentrations compared to the group of children from Poliskyi district.

Conclusions. *It can be reasonably assumed that fires in the Chornobyl exclusion zone have a negative effect on the functioning of folate metabolism in a child's organism.*

Keywords: folate metabolism, homocysteine, hormones of hypophysis and thyroid gland, forest fires, Chornobyl exclusion zone.

Table 1

Statistical characteristics of blood H_c values of examined children from Poliskyi and Ivankivskyi districts

Genetic subgroups	Poliskyi district		Ivankivskyi district	
	Me	IR	Me	IR
MTR:2756 A/A	10.26	8.39-13.56	11.93	9.73-13.76
MTR:2756 A/G + MTR:2756 G/G	9.69	7.91-11.17	11.46	9.58-13.25
MTHFR:1298 A/A	10.14	7.99-13.04	11.53	9.64-14.22
MTHFR:1298 A/C+ MTHFR:1298 C/C	10.23	8.80-13.13	11.75	10.04-13.30
MTHFR:677 C/C	9.44	7.93-11.16	11.36	9.38-12.97
MTHFR:677 C/T + MTHFR:677 T/T	10.91	8.99-14.31	11.82	10.04-14.85
MTHFR:677 C/T	10.24	8.42-13.18	11.61	9.86-13.31
MTHFR:677 T/T	14.47	10.15-22.78	16.59	12.10-26.71
MTRR:66 A/A	9.26	8.03-3.13	10.86	9.19-13.23
MTRR:66 A/G + MTRR:66 G/G	10.26	8.32-13.10	11.79	9.74-13.52
Total group	10.17	8.30-13.10	11.62	9.69-13.39

Table 2

Results of statistically significant differences when comparing blood H_c values of examined children from Poliskyi district

Comparison groups	Comparison group size	Average rank	Mann-Whitney U test value, significance level, p
MTHFR:677 C/T + MTHFR:677 T/T	79	90.16	U = 2278.5; p = 0.003
MTHFR:677 C/C	79	68.84	
MTHFR:677 C/T + MTHFR:677 T/T	79	73.48	U = 1621.0; p = 0.019
MTR:2756 A/G + MTR:2756 G/G	54	57.52	

Table 3

Results of statistically significant differences when comparing blood H_c values of examined children from Ivankivskyi district

Comparison groups	Comparison group size	Average rank	Mann-Whitney U test value, significance level p
MTHFR:677 C/T + MTHFR:677 T/T	98	96.67	U = 3217.0; p = 0.040
MTHFR:677 C/C	80	80.71	

the group of children from Poliskyi district (tables 1, 2).

There were no statistical differences in H_c levels between the subgroups of the children that included only cases of homozygous variants of a neutral allele and subgroups with a risk allele of the MTR:A2756G, MTHFR:A1298C and MTRR:A66G polymorphisms in the groups of childrens from both districts.

Blood H_c level was statistically significantly higher in the children from Ivankivskyi district than in those from Poliskyi district both in the total group and in the majority of genetic subgroups. There were no statistical differences between the above districts only in the MTHFR:677 C/T + MTHFR:677 T/T, MTHFR:677 T/T and MTRR:66 A/A subgroups (tables 1, 4).

No statistical differences were found in the proportions of risk alleles and neutral alleles of folate metabolism genetic polymorphisms when comparing the groups of children from Poliskyi and Ivankivskyi districts (tables 5, 6).

A weak direct link was found between H_c values and degree of the manifestation of the carriership of the risk allele of the MTHFR:C677T and MTRR:A66G polymorphisms in the groups of children from Poliskyi and Ivankivskyi districts (tables 8, 9).

There were no statistical differences in the frequency of cases of carriership of the T allele of the MTHFR:C677T polymorphism in the similar genetic subgroups of the children from Ivankivskyi and Poliskyi districts (table 7).

No link was observed between H_c values and a degree of the

manifestation of carriership of the risk allele of the MTR:A2756G and MTHFR:A1298C polymorphisms.

Direct links were detected between blood H_c and TSH levels, and H_c and T_3 levels in the group of children from Ivankivskyi district in contrast to the group of the children from Poliskyi district. A direct link was observed between TSH and T_3, and an inverse link was found between TSH and T_4 in both groups of children, which indicated a TSH participation in the formation of T_3 (tables 10, 11).

The obtained findings show that the presence of the T allele of the MTHFR:C677T genetic polymorphism contributes to the increased formation of H_c in the organism of the children living in the areas suffered from the accident at the ChNPP. Maximum H_c levels were reported in the group of the children who were the carriers of a homozygous variant of T allele.

Statistically significant differences between H_c values were found in both groups of the children under study between a subgroup with the 100 percent carriership of T allele and a subgroup without cases of carriership of T allele. However, blood H_c level was higher in the children from Ivankivskyi district than in those from Poliskyi district both in a total group and in the majority of genetic subgroups with the exception of a genetic subgroup which included cases of homozygous carriership of T allele.

It should be noted that 84 children from the examined group of Poliskyi district were examined again on 18.12.2015 simultaneously with the children from Ivankivskyi district. In this regard, an increase of H_c level in the blood was found in 78.6% of cases in comparison with the state on 02.04.2015 [9].

There were no statistical differences between blood H_c levels in the children with the MTHFR:677 T/T genotype at the marked differences in the children with the MTHFR:677 C/C genotype in this study as well (table 12) [9].

An increase of H_c level was registered in 78.6% of cases among the children of Poliskyi district at the examinations on 02.04.2015 and 18.12.2015.

Thus, it should be stated that a worse course of H_c metabolism is observed in the children from Ivankivskyi district examined on 18.12.2015 in comparison with those from Poliskyi district examined on 02.04.2015.

In addition, the direct links were reported between the Hc and TSH, H_c and T_3 levels in the group of children from Ivankivskyi district. Thus, H_c can cause an increase in the production of TSH, and thereby affect the thyroid gland contributing to proliferative processes in its tissues. The correlative links between TSH and T_3, T_4 registered in both groups of children indicate that the pituitary hormone is involved in the metabolism of thyroid hormones.

In addition, in the presence of carriership of the G allele of the MTR:2756 polymorphism, H_c can be converted to cysteine through cystathionine β-synthase, and then to selenocysteine, which forms the active center of deiodinase 5-DI, which catalyzes the conversion of T_4 to T_3. Due to this mechanism, H_c levels are lower in this genetic subgroup than in others. At the same time, increased production of T_3 can cause serious cardiac abnormalities.

The absence of statistical differences in the occurrence of FC

Table 4

Results of statistically significant differences when comparing blood H_c values of examined children from Poliskyi[1] and Ivankivskyi[2] districts

Genetic subgroups	Comparison groups	Comparison group size	Average rank	Mann-Whitney U test value, significance level, p
MTR:2756 A/A	1	104	94.65	U = 4384.0; p = 0.010
	2	106	116.14	
MTR:2756 A/G+ MTR:2756 G/G	1	54	50.25	U=1228.5; p=0.0001
	2	72	73.44	
MTHFR:1298 A/A	1	82	73.93	U=2659.5; p=0.002
	2	89	97.12	
MTHFR:1298 A/C+ MTHFR:1298 C/C	1	76	72.19	U=2560.5; p=0.007
	2	89	92.23	
MTHFR:677 C/C	1	79	66.18	U=2068.5; p=0.0001
	2	80	93.64	
MTHFR:677 C/T + MTHFR:677 T/T	1	79	81.53	U=3281.0; p=0.082
	2	80	95.02	
MTHFR:677 C/T	1	60	62.45	U=1917.0; p=0.019
	2	83	78.90	
MTHFR:677 T/T	1	19	17.05	U=134.0; p=0.768
	2	15	18.07	
MTRR:66 A/A	1	32	26.33	U=314.5; p=0.074
	2	27	34.35	
MTRR:66 A/G + MTRR:66 G/G	1	126	119.97	U=7115.0; p=0.0001
	2	151	154.88	
Total group	1	158	145.64	U =10450.5; p = 0.0001
	2	178	188.79	

Table 5

Presence of polymorphic alleles of folate metabolism genes in examined children from Poliskyi district

Gene, polymorphism	"Neutral" allele		Risk allele	
	Absolute number (n)	Percentage, %	Absolute number (n)	Percentage, %
MTR:A2756G	104	65.8	54	34.2
MTHFR:A1298C	82	51.9	76	48.1
MTHFR:C677T	79	50.0	79	50.0
MTRR:A66G	32	20.3	126	79.7

genetic variants among examined groups allows to suggest that an increase in H_c concentrations in the body of children may be associated with the effect of an environmental factor during the period between the two examinations. This factor is related to forest and peat fires in the Chornobyl exclusion zone in an area of 10.127 ha during the period 26-27.04.2015 and 28-29.04.2015 [10] and in an area of 130 ha during the period from 29.06.2015 to 05.07.2015 [11].

In spring and summer of 2015, air currents containing products of combustion of wood, peat, and grass, including radioactive elements spread over long distances from fire sites and affected the population of Ivankivskyi and Poliskyi districts of Kyiv region.

In particular, the ^{137}Cs concentration amounted to $2.5x10^{-3}$ Bq/m^3 in an air sample taken directly in the fire area on the outskirts of the Poliskyi settlment, which substantially exceeded the reference level established by the exposure standards "Basic reference, clearance and action levels with regard to the radioactive contamination of the facilities of the zone of exclusion and zone of unconditional (obligatory) resettlement" [11].

It is known that inhalation of combustion products, as well as smoking, induces the formation of H_c in the organism [1, 12].

Taking into account the calculations of the collective radiation dose of the critical group of the population, the contingent residing at the territories contaminated with radionuclides in Kyiv, Zhytomyr, and Chernihiv regions have the highest risk of cancer due to the forest fires [5].

Thus, a deterioration of H_c metabolic processes in the children from Ivankivskyi district in comparison with those from Poliskyi district is not associated with homozygous carriership of the T allele of the MTHFR:C677T polymorphism. One can reasonably suggest that there is a connection between fires in the Chornobyl exclusion zone and abnormal functioning of FM in a child's organism resulting in increased blood levels of H_c.

The impact of the forest fires in the Chornobyl exclusion zone as an environmental factor on the developing organism contributes to hyperhomocysteinemia and identification of direct link between H_c and TSH, H_c and T_3.

Table 6

Presence of polymorphic alleles of folate metabolism genes in examined children from Ivankivskyi district

Gene, polymorphism	"Neutral" allele		Risk allele	
	Absolute number (n)	Percentage, %	Absolute number (n)	Percentage, %
MTR:A2756G	106	59.6	72	40.4
MTHFR:A1298C	89	50.0	89	50.0
MTHFR:C677T	80	44.9	98	55.1
MTRR:A66G	27	15.2	151	84.8

Table 7

Proportion of cases of carriership of T allele of MTHFR:C677T polymorphism in genetic subgroups of children from Ivankivskyi and Poliskyi districts

Genotype	Number of cases of carriership of T allele of MTHFR:C677T polymorphism in groups of children			
	Ivankivskyi district		Poliskyi district	
	Absolute number	%	Absolute number	%
MTR:2756 A/A	61	57.55	50	48.08
MTR:2756 A/G + MTR:2756 G/G	37	50.69	29	53.70
MTHFR:1298 A/A	60	66.67	54	65.85
MTHFR:1298 A/C + MTHFR:1298 C/C	38	42.70	25	32.90
C/C MTHFR:677	0	0	0	0
MTHFR:677 C/T + MTHFR:677 T/T	98	100	79	100
MTRR:66 A/A	14	51.85	14	43.75
MTRR:66 A/G + MTRR:66 G/G	84	55.26	65	51.59

Table 8

Results of correlation analysis between H_c values and variants of genotypes of folate metabolism polymorphisms in a total group of children from Poliskyi district

Parameter	Correlation coefficient	Parameter			
		1	2	3	4
H_c	Spearman's	-0.109	0.040	0.283**	0.170*
	Sign. (2-tailed), p	0.174	0.615	0.0001	0.033
	N	158	158	158	158

Table 9

Results of correlation analysis between H_c values and variants of genotypes of folate metabolism polymorphisms in a total group of children from Ivankivskyi district

Parameter	Correlation coefficient	Parameter			
		1	2	3	4
H_c	Spearman's	-0.108	-0.026	0.201**	0.177*
	Sign. (2-tailed), p	0.151	0.728	0.007	0.018
	N	178	178	178	178

*Note table 8-9: * – correlation is significant at the 0.05 level (2-tailed); ** – correlation is significant at the 0.01 level (2-tailed); 1 – MTR:A2756G; 2 – MTHFR:A1298C; 3 – MTHFR:C677T; 4 – MTRR:A66G.*

Conclusions

1. Blood H_c level were statistically significantly higher in the subgroup of the children who were the carriers of T risk allele of the MTHFR:C677T genetic polymorphism, living in Ivankivskyi and Poliskyi districts of Kyiv region, than in the subgroup of the children without this allele.

2. The examination of the children from the regions adjacent to

the Chornobyl nuclear power plant allowed to identify changes in metabolic processes among them as the increased production of H_c due to the forest fires in the exclusion zone.

3. Blood H_c levels were higher in the children from Ivankivskyi district examined after the fires in the Chornobyl exclusion zone than in those from Poliskyi district examined before fires, including the majority of genetic subgroups, with the exception of the genetic subgroup which included cases of homozygous carriership of T allele.

4. Direct links were detected between blood H_c and TSH levels, and H_c and T_3 levels in the group of the children from Ivankivskyi district who had higher blood H_c concentrations in comparison with the group of the children from Poliskyi district.

5. It can be reasonably assumed that fires in the Chornobyl exclusion zone have a negative effect on the functioning of folate metabolism in a child's organism.

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Table 10

Links between metabolic variables in a total group of children from Poliskyi district

Parameter	Correlation coefficient	Parameter			
		H_c	TSH	T_3	T_4
H_c	Spearman's	1.000	-0.002	0.130	0.0001
	Sign. (2-tailed), p	.	0.984	0.102	0.998
	N	158	158	158	158
TSH	Spearman's	-0.002	1.000	0.211**	-0.239**
	Sign. (2-tailed), p	0.984	.	0.008	0.002
	N	158	158	158	158
T_3	Spearman's	0.130	0.211**	1.000	0.024
	Sign. (2-tailed), p	0.102	0.008	.	0.760
	N	158	158	158	158
T_4	Spearman's	0.0001	-0.239**	0.024	1.000
	Sign. (2-tailed), p	0.998	0.002	0.760	.
	N	158	158	158	158

Table 11

Links between metabolic variables in a total group of children from Ivankivskyi district

Parameter	Correlation coefficient	Parameter			
		H_c	TSH	T_3	T_4
H_c	Spearman's	1.000	0.206**	0.157*	0.095
	Sign. (2-tailed), p	.	0.006	0.037	0.207
	N	178	178	178	178
TSH	Spearman's	0.206**	1.000	0.236**	-0.149*
	Sign. (2-tailed), p	0.006	.	0.001	0.047
	N	178	178	178	178
T_3	Spearman's	0.157*	0.236**	1.000	-0.010
	Sign. (2-tailed), p	0.037	0.001	.	0.890
	N	178	178	178	178
T_4	Spearman's	0.095	-0.149*	-0.010	1.000
	Sign. (2-tailed), p	0.207	0.047	0.890	.
	N	178	178	178	178

*Note table 10-11: * – correlation is significant at the 0.05 level (2-tailed); ** – correlation is significant at the 0.01 level (2-tailed).*

Table 12

Statistical assessment of homocysteine levels in subgroups of examined children from Poliskyi district (n = 84)

Genotype	Number of cases	Hyperhomocysteinemia				Blood H_c levels, μmol/L			
		Measurement I		Measurement II		Measurement I		Measurement II	
		Abs.	%	Abs.	%	Me	IR	Me	IR
C/C MTHFR:677	44	20	45.5	31	70.5[1]	9.7	7.7-11.1	11.4	9.7-14.1[2]
T/T MTHFR:677	11	9	81.8	11	100	14.5	10.2-19.0	15.0	13.2-22.1[3]

Note: Measurement I - 02.04.2015; Measurement II - 18.12.2015;
1 - statistical differences between Measurements I and II, p<0.05;
2 - statistical differences between Measurements I and II (Wilcoxon T-test standardized score, Z – 4.773, asymptotic significance (two-tailed), p=0.0001);
3 - statistical differences between Measurements I and II (Wilcoxon T-test standardized score, Z – 1.156, asymptotic significance (two-tailed), p=0.248).

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