International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 05, 2020
ISSN: 1475-7192

Vitamin D - Dependent Risk Factors of Formation of Essential Arterial Hypertension at School Children of Tashkent City

Akhmedova Firuza Mirzakirovna,
Agzamova Shoira Abdusalamovna,
Akhmedova Dilorom Ilxamovna and
Tashpulatova Fatima Kudratovna

Abstract--- *The study of vitamin D - dependent risk factors for the formation of essential arterial hypertension (EAH) based on the assessment of serum levels of calcidiol (25 (OH) D), calcium and vasoconstrictor factor endothelin-1-21 in 132 students aged 13 to 16 years (average age 14.64 ± 0.19 years) with normal, high normal blood pressure and essential arterial hypertension (EAH) established the priority effect of vitamin D supply on the level of diastolic blood pressure in the group of children with labile arterial hypertension and in the group of children with stable on the parameters of systolic blood pressure. In the mechanism of EAH formation in children, an interdependence between vitamin D deficiency and the severity of endothelial dysfunction by the level of endothelin -1-21 was revealed. The following vitamin D were determined by diagnostic efficiency - dependent risk factors for the formation of EAH in children in decreasing importance: endothein-1-21> 0.41fmol / ml; vitamin D <20ng / ml; Ca <2.22 mmol / L.*

Keywords--- *Essential Arterial Hypertension, School Children, Blood Pressure, Vitamin D (25 (OH) D), Endothelin-1-21.*

I. INTRODUCTION

Essential arterial hypertension (EAH) is one of the leading problems of modern medicine, being a significant cause of early disability and death in people of working age, the origins of which lie in childhood [1, 2]. In the structure of all registered diseases of the circulatory system in the Republic of Uzbekistan, the leading role belongs to diseases characterized by elevated levels of pressure (33.6-37, 8% in the country) [3]. It is generally recognized that the cardiovascular system is the leading effector system in the process of postnatal adaptation, through which the reactions of many regulatory systems of the body are mediated. The prevalence of EAH in childhood and adolescence is significant - from 2.4% to 20% or more [4, 5]. In recent years, there has been a tendency toward an increase in the frequency of EAH among schoolchildren, which is the result of an increase in the proportion of children with obesity and a behavioral stereotype that is far from a healthy lifestyle [6]. In children with blood pressure (BP) exceeding the norm, the tendency to its further increase increases with age and remains increased in 33-42% of them, and in 17-26% of children arterial hypertension (AH) progresses. In 50% of children, hypertension is asymptomatic, which makes it difficult to identify and, accordingly, timely treatment. Often, already in childhood,

Akhmedova Firuza Mirzakirovna, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan.
Agzamova Shoira Abdusalamovna, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan.
Akhmedova Dilorom Ilxamovna, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan.
Tashpulatova Fatima Kudratovna, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan.

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

target organ damage occurs: left ventricular hypertrophy, detected in 38-41% of children with hypertension [7, 8]. In this regard, the problem of prevention of modifiable risk factors in children and adolescents is a priority in pediatrics and pediatric cardiology.

To date, it has been irrefutably proven that vitamin D, as a hormone with the formation of its "hormone-like axis: calcidiol-calcitriol-VDR (vitamin D receptor)," is closely interconnected not only with parathyroid hormone and calcitonin, but also with the biological effects of insulin, estrogen, neurotrophic factors and cytokines [9, 10]. In this regard, it is possible to imagine the consequences of insufficient levels of vitamin D in the human body, ranging from growth retardation to a wide range of chronic diseases that take hundreds of millions of adults' lives [11, 12]. Evidence of the beneficial effects of vitamin D has stimulated the development and adoption of nationwide recommendations to address its deficiency in Poland (2009, 2013) [13, 14], Hungary (2012) [15], Germany, Austria and Switzerland (2012) [16], Russian Federation (2018) [17], USA (2011) [18]. In 2012, the European Food Safety Authority issued revised vitamin D levels (upper limits) for all relevant populations [19]. The level of calcidiol - 25 (OH) D in serum is accepted as a standard biomarker of vitamin D supply for the body. This metabolite is quite stable (half-life is 2-3 weeks), reflects the intensity of vitamin D synthesis in the skin and food intake [17, 20].

A meta-analysis of 11 placebo-controlled studies (5660 patients aged 6 months to 75 years) confirmed the protective effect of vitamin D intake against respiratory tract infections (influenza, pneumonia, acute respiratory infections) [17, 24]. Higher serum vitamin D levels correlated with improved lung function in patients with cystic fibrosis [25], with a 43% reduction in the risk of type 2 diabetes and metabolic syndrome (meta-analysis of 28 studies in 99,745 patients) [14].

Various studies have established a relationship between serum 25 (OH) D levels and blood pressure [21, 22, 23]. A meta-analysis of 7 cohort studies involving more than 43 thousand people established a relationship between a low level of 25 (OH) D and a high frequency of arterial hypertension (AH) for 7–8 years [26]. S. Pilz et al. in a randomized controlled study, it was recorded that taking vitamin D helps to reduce systolic blood pressure by 2-6 mm Hg. [27]. According to the results of a large-scale study of NHANES (National Health and Nutrition Examination Survey 2001-2004) in the USA, 61% of adolescents 12-19 years old (out of 4666) had insufficient levels of vitamin D (15-29 ng / ml) and 9% deficient (<15 ng / ml). These vitamin levels were associated with high systolic blood pressure and low levels of high density lipoproteins [28].

Low levels of vitamin D are associated with cardiac ventricular hypertrophy, endothelial dtsfunction, and activation of the renin-angiotensin system (RAS). It has been proven that in vitro the active form of the vitamin suppresses RAS, and the renin gene in the promoter region has a D-sensitive element, through which the vitamin has a direct regulatory effect on its transcription and renin production [29, 30, 31].

No relationship was found between vitamin A and vitamin D risk factors in children according to available literature data, which requires further research.

One of the main risk factors for EAH is endothelial dysfunction (ED). Given the main functions of the endothelium, it is possible to distinguish vasomotor, hemostatic, angiogenic and adhesive forms of ED. With vasomotor ED, the synthesis of vasoactive substances is disrupted, and as a result, the vasomotor activity of the

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

endothelium is reduced. Markers of endothelial vasomotor dysfunction are blood levels of nitric oxide (NO) and endothelin-1, prostacyclin and thromboxane A2 [32, 33].

Endothelin-1 (E-1) is the strongest vasoconstrictor peptide synthesized in the body. Its vasoconstrictor potential is 10 times higher than that of angiotensin II and is considered as a marker of ED in cardiovascular diseases. E-1 is synthesized during stimulation of the endothelium by various factors - adrenaline, thrombin, angiotensin, vasopressin. The concentration of E-1 in the blood normally does not exceed 0.1-1.0 mmol / ml or may not be determined at all [34]. Currently, 3 endothelin isoforms consisting of 21 amino acid residues have been isolated: E-1, E-2 and E-3. They are identified in the tissues of the lungs, kidneys of the brain, placenta, etc. E-1, unlike E-2 and E-3, is produced by the endothelium [35, 36].

Thus, vitamin D deficiency refers to modifiable risk factors for many diseases. Insufficient vitamin supply is associated with a risk of developing pathology of the cardiovascular, bone, endocrine, immune and other systems. Vitamin D is becoming one of the most cost-effective supplements that can improve population health and reduce the cost of preventing non communicable diseases in both childhood and adulthood. In children, the data on the role of vitamin D and its relationship with ED in the occurrence and progression of EAH are sporadic, which is of interest for further scientific research.

Purpose of the Study

To study vitamin D-dependent risk factors for the formation of EAH in schoolchildren based on serum levels of calcidiol - 25 (OH) D, calcium and endothelin 1-21.

II. MATERIAL AND METHODS

We examined 132 schoolchildren aged 13-16 years (average age 14.64 ± 0.19) in Tashkent, selected by randomization. In the groups of children observed, there were 86 boys (65.2 ± 4.1%) and girls, respectively, 46 (34.8 ± 4.1%). The distribution by gender and age was uniform.

The examinations were carried out using standard research methods (questioning, collection of ante- and postnatal history, heredity, environmental factors, clinical and paraclinical studies (blood pressure (BP)); anthropometry according to WHO criteria (2009); determination of puberty according to Tanner's scheme (1962), etc.) The WHO recommendations and the Russian recommendations (second revision, 2009) [37, 38] were taken as a criterion for high blood pressure and establishing a diagnosis of EAH.

Criteria for Inclusion in a Clinical Trial

Children with essential grade I arterial hypertension (EAH) without target organ damage and children with normal and high normal blood pressure, without exacerbation of chronic foci of infection for 6 months. The inclusion criteria were: normal blood pressure - SBP and DBP, the level of which is ≥10th and <90th percentile of the distribution curve of blood pressure in the population for the corresponding age, gender and height; high normal blood pressure - average values of SBP and / or DBP at three visits of ≥90th percentile, but <95th percentile for a given age, gender and height, or ≥120 / 80mm Hg. (even if this value is <90th percentile. AH, I degree - average levels of SBP and / or DBP from three dimensions equal to or greater than the 95th percentile established for this

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

age group, provided that they exceed the 99th percentile no more than 5 mm Hg (Russian recommendations, 2009) [37] Provided that the elevated blood pressure during dynamic observation is not constantly recorded, the diagnosis of labile hypertension is made. Children are 13-16 years old.

Exclusion Criteria from a Clinical Trial

Exclusion criteria were congenital malformations of the kidneys, endocrine pathology, secondary or symptomatic hypertension, stage II EAH, somatic pathology in the acute stage.

In accordance with the goal, the distribution of children into groups was carried out taking into account blood pressure indicators: group 1 - children with normal blood pressure (BP) (control group) (n = 43), group 2 - children with high normal blood pressure (HNBP) (comparative - group 2) - 42, 2 main groups: group 3 - children with labile arterial hypertension (LAH) - 25 and group 4 - children with stable arterial hypertension (SAH) - 22.

The level of calcium was determined in blood serum using a Minray BS-200 biochemistry analyzer (China) using commercial Human kits (Germany). Serum concentrations of endothelin-1-21 and 25 (OH) D in blood serum were determined using commercial BIOMEDICA kits (Austria) for endothelin-1-21 (the reference value for endothelin-1-21 (for adults) was on the median 0.26 fmol / ml) and DIA source (Belgium) for 25 (OH) D using a Stat Fax 2100 analyzer (Israel) using ELISA.

The interpretation of the level of 25 (OH) D in the blood serum of children was carried out according to the National Vitamin D Provision Program, which was presented by I.N. Zakharova at the XX Congress of Russian Pediatricians with international participation, February 16, 2018 [17]. But vitamin D deficiency <10 ng / ml was characterized as “pronounced vitamin D deficiency” according to the 2017 classification. This interpretation is presented in table 1.

Table 1: Interpretation of Concentrations of 25 (OH) D (Zakharova I.N., 2018., RF)

Classification	**25 (OH) D in blood**
Vitamin D deficiency	<20 ng / ml (<50 nmol / L)
Vitamin D insufficiency	21-30 ng / ml (51-75 nmol / l)
Adequate Vitamin D levels	> 30 ng / ml (> 75 nmol / L)

In the statistical analysis, the mean values (M) were calculated, their standard error (m), and the 95% confidence interval (CI). The statistical significance of the differences was evaluated by Student's t criterion for dependent and independent samples, while the difference was considered significant at $p < 0.05$. An analysis of the relationship of variables was carried out with the calculation of the Spearman correlation coefficient. For the clinical and prognostic assessment of the risk of developing EAH in children, we calculated the values of the relative risk RR (relative risk - RR = Ie / Io = [a / (a + b)] / [c / (c + d)]). Potentially adverse effects of vitamin D-dependent factors during critical assessment of the risk of EAH formation in children calculated the values of sensitivity (sensitivity, Se, Se = a / (a + s)) and specificity (specificity, Sp, Sp = d / (b + d)) diagnostic tests. For an integrated assessment of the diagnostic effectiveness of the analyzed factors, the validity indicators (Validity = Se (%) + Sp (%) - 100%) and the diagnostic efficiency index (Diagnostic efficiency = (a + d) / (a + b + c + d)) were calculated [39].

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

III. RESULTS AND DISCUSSION

The frequency of occurrence of various levels of vitamin D provision for children depending on blood pressure parameters is presented in table 2.

Table 2: Frequency of Occurrence of Various Levels of Vitamin D Provision for Tashkent School Children Depending on Blood Pressure (abs /%, ng / ml)

25(OH)D_3 level	**Control group n=43**		**High normal blood pressure n=42**		**labile arterial hypertension n=25**		**stablearterialhypertensionn=22**	
	Abs	%	Abs	%	Abs	%	Abs	%
Adequate Vitamin D levels	20	46,5±7,6	-	-	-	-	-	-
Vitamin D insufficiency	21	48,8±7,6	17	40,5±7,6	3	12,0±6,5 ***	1	4,5±4,4 ***
Vitamin D deficiency	2	4,7±3,2	19	45,2±7,7 ***	11	44,0±9,9 ***	10	45,5±10,6 ***
Severe vitamin D deficiency <10 ng / ml	-	-	6	14,3±5,4	11	44,0±9,9 ^^	11	50,0±10,6 ^^
The average level of vitamin D, ng / ml	27,4±0,92		16,3±1,2***		12,35±1,1***		11,8±1,1***	

Note: the significance of differences in indicators at *** - p <0.001, relative to the control; ^ - p <0,01 in relation to the group with high normal blood pressure

According to the table, it can be seen that the frequency of insufficient vitamin D content in children of the main groups was significantly lower than in the control group (p <0.001 and p <0.001, respectively, in the 1st and 2nd main groups). The same trend, but with the opposite vector, was also noted in relation to the frequency of occurrence of vitamin D deficiency, starting with the comparison group with respect to the control. Severe deficiency or vitamin deficiency was diagnosed only in children with high normal blood pressure and AH, with a significantly high frequency in the main groups in relation to the comparison group.

Adequate vitamin D was only present in children in the control group. At the same time, the average concentration of 25 (OH) D in children of this group was evaluated as insufficient (Fig. 1).

Significantly low values of 25 (OH) D in children in the comparison groups (p <0.001) and the main (p <0.001 and p <0.001, respectively, in the 1st and 2nd main groups) with respect to the control, tended to be deficient.

An analysis of the vitamin D supply for schoolchildren depending on blood pressure indicators established a significantly high frequency of deficient vitamin D content in children with high normal blood pressure (p <0.001) and AH (p <0.001) in relation to children with a normal level of blood pressure. The diagnostic test, as vitamin D deficiency for the comparison group and the 1st main one, had 90% (Se = 0.90 = 90%) sensitivity, 68% (Sp = 0.68 = 68%) specificity and relative risk RR = 11, 25, for the 2nd main, 89% (Se = 0.89 = 89%) and 70% (Sp = 0.70 = 70%) of sensitivity, specificity, and RR = 10.0, respectively.

A pronounced deficiency was noted in children with high normal blood pressureand AH with a significant high frequency in the main groups in relation to the comparison group p <0.01 and p <0.01, respectively, in the 1st, (Se =

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

0.75, Sp = 0, 61, RR = 3.0) and in the 2nd, (Se = 0.75, Sp = 0.65, RR = 3.3,) main groups.

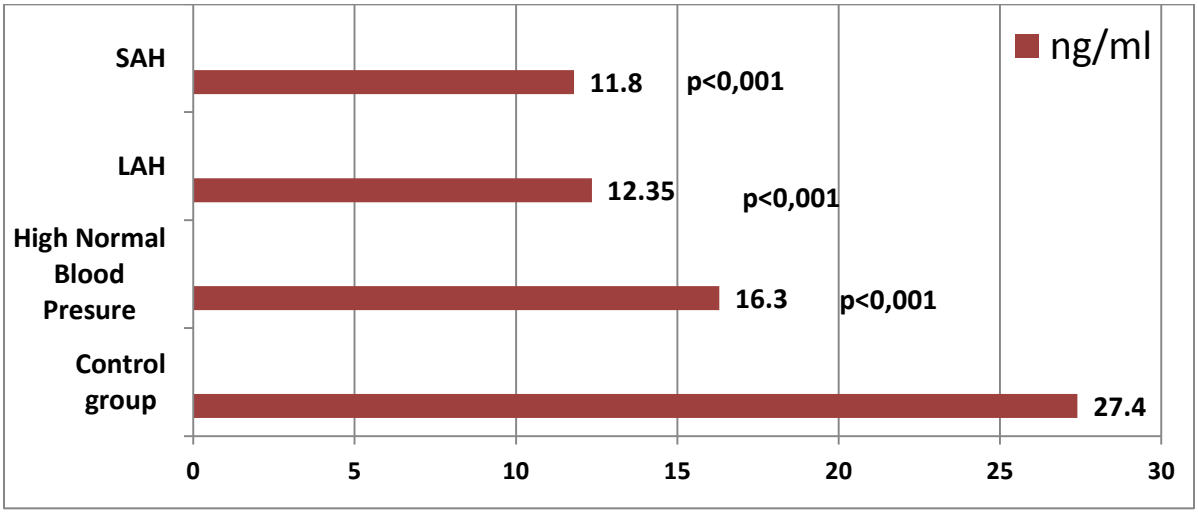

Figure 1: The Average Level of Vitamin D in the Analyzed Groups, ng / ml

A comparative analysis of the average parameters of serum calcium levels in children with different blood pressure levels is presented in figure 2.

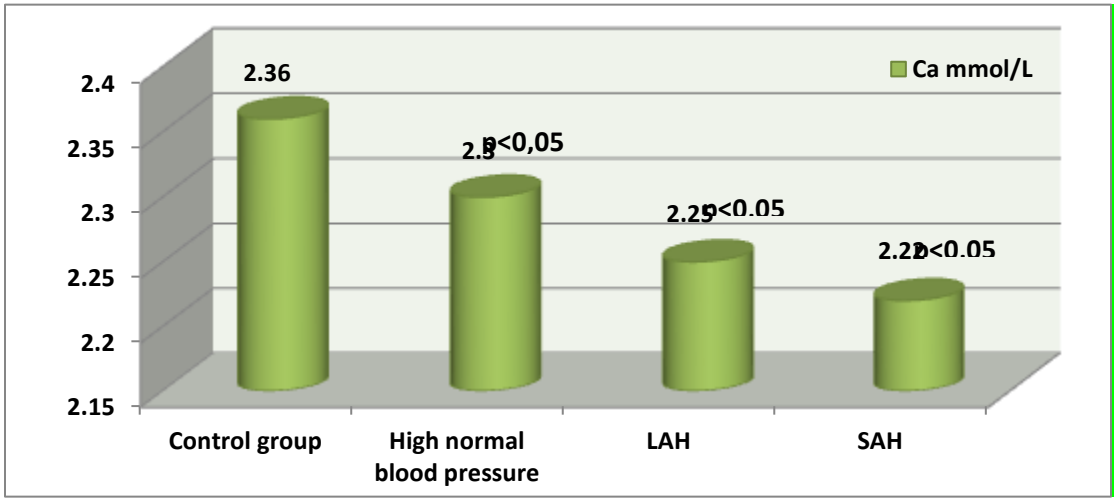

Figure 2: Averaged Serum Calcium Levels in Children of the Analyzed Groups

From the data of the figure it follows that the compared parameters of the level of calcium did not go beyond the normative range. But the average values of serum calcium concentration in children with high normal blood pressure ($p < 0.05$), with stable hypertension ($p < 0.05$) and with labile hypertension ($p < 0.05$) were significantly low compared to healthy children.

Endothelin-1-21 (E-1) is the most powerful vasoconstrictor factor, the main activators of the synthesis of which are hypoxia and local ischemia. E-1 enhances the production of cytokines and thereby initiates the inflammatory process [40].

As a rule, to realize its function, E-1 binds to two types of receptors: type A, localized on smooth muscle cells

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

(SMC) of blood vessels, and type B, localized on endothelial and SMC, the activation of these receptors causes a vasoconstrictor and mitogenic effect. The question of what place E-1 occupies in the pathogenesis of EAH in children and adolescents remains a controversial issue, which determines the relevance of further research in this area.

Our studies on the level of vasoconstrictor factor endothelin - 1-21 (E-1) in 78 schoolchildren showed an increase in its values in blood serum in groups with high normal blood pressure and AH (Figure 3).

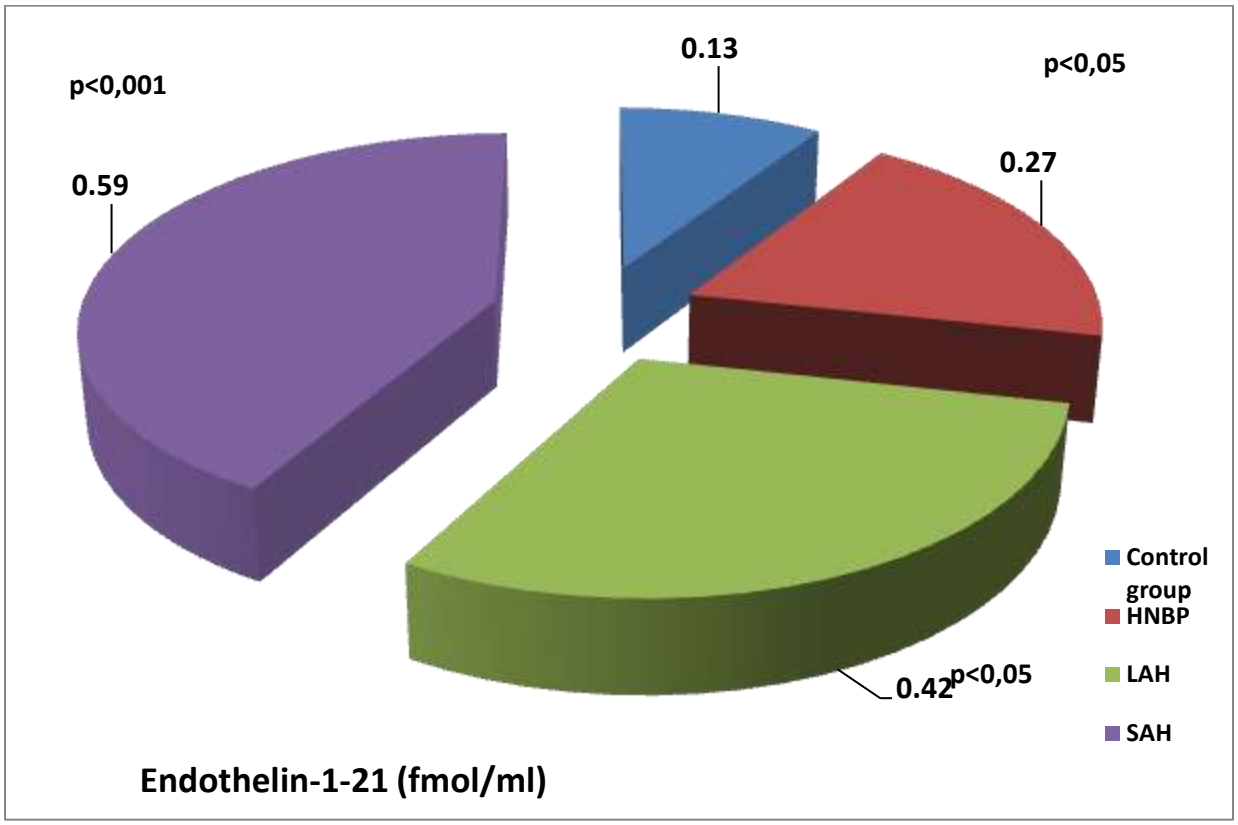

Figure 3: Comparative Analysis of the Level of Endothelin 1-21 in Children in the Analyzed Groups

According to the data presented, it was found that in children of the control group the level of E-1-21 did not exceed the reference values (<0.26 fmol / ml), whereas in children with HNBP (0.27 ± 0.05 fmol / ml, $p < 0.05$) LAH (0.42 ± 0.1 fmol / ml, $p < 0.05$) and SAH (0.59 ± 0.1 fmol / ml, $p < 0.001$) this level was significantly high compared to the control (0.13 ± 0.02 fmol / ml).

The frequency of occurrence of high levels of e-1-21 depending on blood pressure in the analyzed groups is presented in table 3. According to the table it is clear that the frequency of indicators of e-1-21> 0.26 and> 1.0 fmol / ml in children with SAH was 2.4 and 1.6, respectively, times higher (OS = 2.4; RR = 1.5 and OS = 1.6; RR = 1.5, respectively) than in children with LAH. But in children with HNBP, the frequency of indicators of the level of E-1-21> 0.26 fmol / ml was identical compared to the group of children with SAH (60.0 ± 10.9%, against 61.1 ± 11.5%, respectively), which indicated early signs of ED in children with high normal blood pressure. This test has 100% sensitivity and 0% specificity in the early diagnosis of ED with EAH.

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

Table 3: The Frequency of Occurrence of High Levels of Endothelin level -1-21 Depending on Blood Pressure (abs /%, fmol / ml)

The level of endothelin is 1-21, fmol / ml	I group Normal blood pressure (control group) n = 20		II group HNBP (comparison group) n = 20		III group LAH (1st main group) n = 20		IV groups SAH (2nd main group) n = 18	
	Abs	%	Abs	%	Abs	%	Abs	%
<0,26	24	100,0	8	40,0±10,9	9	45,0±11,1	3	16,7±8,8
>0,26; <1,0	-	-	12	60,0±10,9	8	40,0±10,9	11	61,1±11,5
>1,0	-	-	-	-	3	15,0±7,9	4	22,2±9,8

We obtained results are comparable with literature data. In the studies of G. Aflyatumova et al. (2017) the level of E-1-21 in adolescents with a stable form of EAH was significantly higher than in the labile version (1.67 ± 0.12 versus 1.14 ± 0.13 fmol / ml, respectively) [41]. Also, the levels of E-1-21 in children with labile hypertension were significantly higher than in the control (1.38 ± 0.13 versus 0.8 ± 0.08 fmol / ml, respectively, p <0.001).

It was found that in physiological concentrations E-1 acts on endothelial receptors, causing the release of relaxation factors, and at higher levels it activates receptors on SMCs, causing their persistent vasoconstriction and proliferation of media. Thus, using the same factor, two opposite vascular reactions (dilatation and constriction) are controlled by the feedback mechanism [42].

The results form the basis for the development of measures for effective non-drug and drug therapy based on antagonists of E-1-21 receptors, which is especially important for children and adolescents with HNBP and AH as a way to prevent EAH and its complications in the adult period.

In our work, to identify causal relationships between factors providing vitamin D and levels of calcium, endothelin-1-21 in blood serum and physical development parameters in the formation of EAH in children, depending on the level of blood pressure, a mathematical correlation analysis was performed between the above values (Fig. 4).

According to Figure 3, it is seen that between the vitamin D level and endothelin -1-21, strong negative correlation relationships were established in the comparison groups (r = -0.80, p <0.001) and two main (r = -0.66, p < 0.01 and r = -0.79, p <0.001, respectively, in groups of children with LAH and SAH), which indicates the relationship between vitamin D deficiency and the severity of endothelial dysfunction.

Our results are comparable with published data. Kodensovoy V.M. et al. (2017), an association was established between the lack of vitamin D in the body and the occurrence of three mutually influencing processes: oxidative stress, inflammation, endothelial dysfunction [20].

The level of vitamin D provision had a positive associative relationship of medium strength with physical development parameters (with growth values: r = 0.45, p <0.05; weight: r = 0.62, p <0.01; BMI: r = 0 , 47, p <0.05) in children of the control group. But these interdependencies lost strength and reliable values in groups of children with HNBP and hypertension.

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

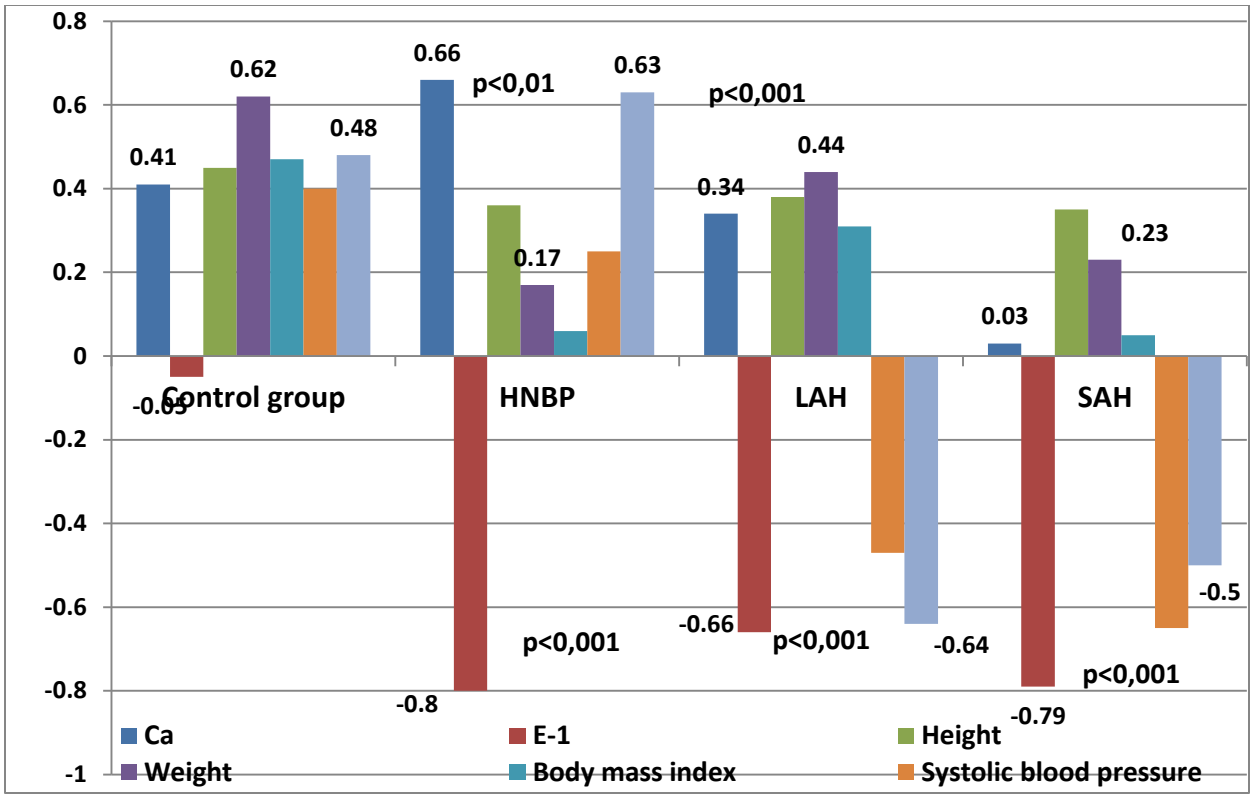

Figure 4: Features of the Correlation between the Level of Vitamin D and the Values of Ca, Endothelin -1-21 in the Blood Serum, the Parameters of Physical Development, Systolic and Diastolic Blood Pressure in the Analyzed Groups

Between the parameters of blood pressure and level 25 (OH) D, multidirectional correlation relationships were established, where the relationship between high blood pressure values and low levels of vitamin D in children of the main groups is logically traced.

In the control group (Fig. 4) of children, there was a direct correlation of weak strength between blood pressure ($r = 0.40$, $p > 0.05$ and $r = 0.48$, $p < 0.05$, respectively, for SBP and DBP) .

A rather specific dynamics of the connections is monitored in relation to the values of SBP and DBP in groups of children with HNBP, LAH and SAH. In the group of children with HNBD, a direct dependence of the level of diastolic blood pressure on the degree of provision with vitamin D appears ($r = 0.63$, $p < 0.01$). A change in the polarity of the bonds was noted in the relationships between the level of vitamin D and the values of SBP and DBP in the main groups: the priority influence of vitamin D supply on the level of DBP ($r = -0.64$, $p < 0.01$) in the group of children with LAH, but in group of children with SAH, this effect was directed to the parameters of systolic blood pressure ($r = -0.6$, $p < 0.01$).

A single reliable relationship was found between the levels of vitamin D and Ca ($r = 0.66$, $p < 0.01$) in the group of children with HNBP. In the control ($r = 0.41$, $p > 0.05$) and main ($r = 0.34$, $p > 0.05$ and $r = 0.03$, $p > 0.1$) groups of children, the described similar relationship was absent.

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

The only reliable relationship between the level of endothelin-1-21 and the values of Ca ($r = -0.68$, $p < 0.01$) in the blood serum with a negative vector in the second main group of children was revealed.

Potentially adverse effects of vitamin D - dependent factors in a critical assessment of the risk of EAH formation in children calculated the values of sensitivity (Se) and specificity (Sp) of diagnostic tests. Indicators of Ce and Sp of the analyzed vitamin D - dependent factors in diagnosing the risk of EAH formation are presented in table 4.

Table 4: The Values of Sensitivity (Se) and Specificity (Sp) Analyzed Diagnostic Tests

№	Analyzed Factors	Children with HNBP		Children with SAH	
		S_e%	S_p%	S_e%	S_p%
1	Deficiency Vit. D <20 ng / ml	90,0	68,0	89,0	70,0
2	0.17 <Endothelin 1-21 <0.41 fmol / ml	48,0	67,0	72,0	67,0
3	Endothelin 1-21> 0.41 fmol / ml	33,3	**82,7**	**100**	**82,7**
4	Ca<2,22mmol/L	50,0	67,4	51,2	67,4

The results indicate that a potentially adverse effect of the factor, such as a deficient vitamin D content in the blood, in diagnosing the risk of EAH in children has a fairly high sensitivity of 90%. Therefore, in 10% of cases, it is likely that people with a very high risk of developing the disease will be classified as low.

Moreover, this factor has moderate specificity, i.e. in 68% of cases, positive test results can correctly diagnose a very high risk of disease formation.

For an integrated assessment of the diagnostic effectiveness of the analyzed factors, the validity indices and the diagnostic efficiency index were calculated. Validity and diagnostic efficacy indicators of the analyzed vitamin D - dependent factors in diagnosing the risk of EAH formation are presented in table 5.

Table 5: Validity and Diagnostic Effectiveness of the Analyzed Diagnostic Tests

№	Analyzed Factors	Validity Assessment		Diagnostic efficiency	
		HNBP	SAH	HNBP	SAH
1	Deficiency Vit. D <20 ng / ml	50,3	**67,4**	**75,3**	**83,7**
2	0.17 <Endothelin 1-21 <0.41 fmol / ml	16,2	39,5	58,8	69,8
3	Endothelin 1-21> 0.41 fmol / ml	16,0	**82,7**	62,0	**87,8**
4	Ca<2,22mmol/L	17,4	18,6	58,8	59,3

An integral assessment of the factor - deficient vitamin D in the blood when diagnosing the risk of EAH formation showed moderate validity (67.4%) and a fairly high diagnostic efficiency (83.7).

Consequently, a critical assessment of potentially unfavorable vitamin D-dependent risk factors for the formation of essential arterial hypertension in children established the following diagnostic tests for diagnostic effectiveness in decreasing importance: endothelin 1-21> 0.41 fmol / ml - 87.8; vitamin D deficiency <20 ng / ml - 83.7; 0.17 <Endothelin 1-21 <0.41 fmol / ml - 69.8; Ca <2.22 mmol / L - 59.3.

IV. CONCLUSIONS

1. An analysis of the availability of vitamin D for schoolchildren, depending on blood pressure, established a significantly high frequency of deficient vitamin D in children with HNBP ($p < 0.01$) and hypertension ($p < 0.01$) in relation to children with normal blood pressure. The diagnostic test, as vitamin D deficiency for the comparison group and the 1st main one, had 90% (Se = 0.90 = 90%) sensitivity, 68% (Sp = 0.68 =

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

68%) specificity and relative risk RR = 11, 25, for the 2nd main, 89% (Se = 0.89 = 89%) and 70% (Sp = 0.70 = 70%) of sensitivity, specificity, and RR = 10.0, respectively. A pronounced deficiency was noted in children with HNBP and AH with a significant high frequency in the main groups in relation to the comparison group $p < 0.01$ and $p < 0.01$, respectively, in the 1st, (Se = 0.75, Sp = 0, 61, RR = 3.0) and in the 2nd, (Se = 0.75, Sp = 0.65, RR = 3.3,) main groups.

2. Studies on the level of endothelium-dependent vasoconstrictor factor endothelin-1-21 (E-1-21) showed a significant increase in its values in blood serum in children with high normal blood pressure (0.27 ± 0.05 fmol / ml, $p < 0.05$) and arterial hypertension (0.42 ± 0.1 fmol / ml, $p < 0.05$ and 0.59 ± 0.1 fmol / ml, $p < 0.001$, respectively, in groups of children with LAH and SAH) compared with the control (0.13 ± 0.02 fmol / ml).
3. In the mechanism of EAH formation in children, the relationship between vitamin D deficiency and the severity of endothelial dysfunction in terms of endothelin levels of -1-21 ($r = -0.79$, $p < 0.001$), as well as the priority effect of vitamin D provision on the DBP level ($r = -0.64$, $p < 0.01$) in the group of children with LAH, but in the group of children with SAH this effect was directed to the parameters of systolic blood pressure ($r = -0.6$, $p < 0.01$).
4. A critical assessment of potentially unfavorable vitamin D-dependent risk factors for the formation of essential arterial hypertension in children has established the following diagnostic tests for diagnostic effectiveness in decreasing importance: endothelin 1-21> 0.41 fmol / ml - 87.8; vitamin D deficiency <20 ng / ml - 83.7; 0.17 <Endothelin 1-21 <0.41 fmol / ml - 69.8; Ca <2.22 mmol / L - 59.3.

REFERENCES

[1] Alexandrov A.A., Rozanov V.B., Pugaeva H.S., Ivanova E.I. The prognostic value of high blood pressure in children and adolescents (32 - year long-term follow-up). *Cardiovascular therapy and prevention.* 2018; 17 (4): 12-18.

[2] Arsentiev VG, SergeevYu.S., SeredaYu.V., Tikhonov VV High blood pressure in children and adolescents: an emphasis on diagnostic issues. *Pediatrics.* 2018; 97 (3): 119-124.

[3] TursunovD.Sh. The effectiveness of organizational forms of prevention and treatment of arterial hypertension in primary health care. Abstract. diss. Ph.D. Tashkent. 2012.23 s.

[4] Flynn J.T., Kaelber D.C., Baker-Smith C.M. et al. Clinical practice Guideline for screening and management of High Blood pressure in Children and Adolescents. *Pediatrics.* 2017.140 (3) e20171904.

[5] Williams B., Mancia G., Spiering W., AgabitiRosei E. et al. 2018 ESC / ESH Guidelines for the management of arterial hypertension: *the task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Eur. Heart J.* 2018. Sept. 1; 39 (3): 3021-3104. Doi: 10.1093 / eurheartj / ehy339.

[6] Agzamova Sh. A., Hasanova G.M. Obesity in children: frequency of occurrence and features of thickness of epicardial fat depending on indicators of body weight index and lipid spectrum. *International Journal of Psychosocial Rehabilitation* Vol. 24, Issue 05, 2020. p. 434-442. DOI: 10.37200 / IJPR / V24I5 / PR201709

[7] Jurko A. J., Minarik M., Jurco T., Tonhajzerova I. White coat hypertension in pediatrics. *Ital. J. Pediatrics.* 2016; 42: 4.

[8] Litwin M., Feber J., Ruzicka M. Vascular Aging: Lessons From Pediatric Hypertension. Canadian Journal of Cardiology. Volume 32. 2016.

[9] Dreval A.V., Kryukova I.V., Barsukov I.A. TevosyanL.Kh. Extra-bone effects of vitamin D (literature review). *Russian medical journal.* 2017; 1: 53-56.

[10] Bikle DD. Extraskeletal actions of vitamin D. Ann. N. Y. Acad. SCI. 2016; 1376: 29-52.

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

[11] Bergman P., Lindh A.U., Bjorkhem-Bergman L., Lindh J.D. Vitamin D and respiratory tract infections: *a systematic review and meta-analysis of randomized controlled trials. Plos one.* 2013; 8 (6): e65835.
[12] Zittermann A., Pilz S., Hoffmann H., Marz W. Vitamin D and airway infections: A European perspective. *European J. of Medical Research.* 2016: 21 (1): doi: 10.1186 / s40001-16-0208-y.
[13] Charzewska J., Chlebna-Sokol D., Chybicka A. et al. Prophylaxis of Vitamin D deficiency-Polish recommendation 2009. *Endocrinol.* Pol. 2010; 61: 228-232.
[14] Pludowski P., Karczmarewicz E., Bayer M., Carter G., Chlebnasokop D. et al. Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe - recommended vitamin D in takes im the general population and groups at risk of vitamin D deficiency. 30-50 ng of vitamin D in optimal - Central Europe consensus. Sept. 2013. EndocrinologiaPolska. 2013; 64 (4): 319-27. Doi: 10/5603 / EP2013.0012.
[15] Takacs I., Benko I., Toldy E. et al. Hungarian consensus regarding the role of vitamin D in the prevention and treatment of diseases. Orv. Hetil. 2012; 153 (Suppl.): 5-26.
[16] German Nutrition Society. New reference values for vitamin D. Ann. Nutr. Metab. 2012; 6: 214-246.
[17] Symposium "D-hormone - the opening of the XXI century". Review of I.N. Zakharova, L.Ya. Klimova, V.A. Kuryaninova, I.L. Nikitina et al. Pediatrics *(Addendum to Journal of Consilium Medicum).* 2018: 1: 23-30.
[18] IOM (Institute of Medicine): Dietary reference intakes for calcium and vitamin D. Washington (DC): National Academies Press (US); 2011.
[19] Holick M.F., Binkley N.C., Bischoff-Ferrari H.A., Gordon C.M. et al. Endocrine Society Evaluation treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. *J. Clin. Endocrinol. Metab. 2011*; 96: 1911-1930.
[20] Kodentsova V.M., Mendel O.I., Khotimchenko S.A., Baturin A.K., Nikityuk D.B., Tutelyan V.A. Physiological need and effective doses of vitamin D to correct its deficiency. *The current state of the problem. Nutrition issues.* 2017.V. 86. No. 2. S. 47-62.
[21] Karonova T.L., Andreeva A.T., Zlotnikova E.K., Grineva E.N. Vitamin D deficiency and hypertension: what is common? *Arterial hypertension.* 2017; 23 (4): 275-281.
[22] Nikitina I.L., Todeva M.M., Ilyina M.N., Budanova M.V. et al. Vitamin D treatment experience: is it possible to influence the metabolic and cardiovascular risk factors for obese children. *Arterial hypertension.* 2015; 21 (4): 426-435.
[23] Agzamova S. A., Akhmedova F, Shamansurova E. A., Evaluation of potentially removable risk factors of arterial hypertension in chiloren of Uzbekistan. *European science review.* No. 7 - 8. 2018. July-August: p. 72-75
[24] Bergman P., Lindh A.U., Bjorkhem-Bergman L., Lindh J.D. Vitamin D and respiratory tract infections: *a systematic review and meta-analysis of randomized controlled trials. Plos one.* 2013; 8 (6): e65835.
[25] Pashkevich A.A., Borisenko T.S., Kaystrya I.V., Orlov A.V. et al. Vitamin D deficiency in children with cystic fibrosis. *Treatment and prevention.* 2018; 8 (1): 5-12.
[26] Wang L., Song Y., Manson J.E., Pilz S. Circulating 25-hydroxyvitamin D and risk of cardiovascular disease: A meta-analysis of prospective studies. Circ. Cardiovas. *Qual. Outcomes.* 2012; 1; 5: 819-829.
[27] Pilz S, Gaksh M., Kienreich K., Grubler M. et al. Effects of vitamin D on blood pressure and cardiovascular risk factors: *a randomized controlled tried. Hypertension* 2015; 65 (6): 1195-120.
[28] Kumar J., Muntner P., Kaskei F.J., Hailpern S.M. MLM Prevalence and associations of 25- hydroxyvitamin D deficiency in US children. *NHANES* 2001-2004. Pediatrics. 2009; 124: 362-370.
[29] Dubova A.V., Pshenichnaya E.V., Bordyugova E.V., Onoprienko Z.S. The effect of vitamin D on the occurrence and progression of cardiovascular pathology in adults and children. *(Literature review). Bulletin of emergency and reconstructive surgery.* 2016; 1 (2): 292-298.
[30] Yakovleva L.V., Zeid S.S.K., Melititskaya A.V. The relationship between vitamin D levels, renin, and body mass index in adolescent children with primary hypertension. *Medical Bulletin of Bashkortostan.* 2017; T. 12. No. 5 (71): 65-69.
[31] Dudinskaya E.N., Tkacheva O.N. The role of vitamin D in the development of arterial hypertension // *Kariovascular therapy and prevention.* - 2012 .-- 11 (3). - S.77-81.
[32] Mayanskaya S. D., Grebenkina I. A. Structural and functional remodeling of the vessel wall in patients with a history of arterial hypertension. *Cardiology.* 2015.2.27-31.
[33] Samolyuk MO, GrigoryevaN.Yu., Assessment of endothelial dysfunction and the possibility of its correction at the present stage in patients with cardiovascular diseases. *Cardiology. Study of. Implementation. Practice.* 2019. №3. S. 4-9.

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020

[34] Sergeeva E.V., Sadykova D.I. Endothelin-1 as a marker of endothelial dysfunction in various forms of essential hypertension in adolescents. *Russian Bulletin of Perinatology and Pediatrics.* 2016.4.17-177

[35] Mikashinovich Z.I., NagornayaP.Yu., Kovalenko T.D. Biochemical indicators of endothelial damage of inflammatory genesis in adolescents with arterial hypertension. *Kuban Scientific Medical Bulletin.* 2012; 2: 123-125.

[36] Plotnikova I.V., Kovalev I.A., Suslova T.E., Bezlyak V.V. The relationship of endothelial dysfunction with the development of essential hypertension in adolescence. *Cardiology.* 2015; 3: 21-26.

[37] Diagnosis, treatment and prevention of hypertension in children and adolescents. Russian recommendations (second revision). *Appendix 1 to the journal Cardiovascular Therapy and Prevention.* 2009; 8 (4): 32 s.

[38] Global Status Report on noncommunicable diseases 2013 [http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf?ua=1]

[39] Kelmanson I.A. Principles of evidence-based pediatrics. - St. Petersburg: Tome, 2004.-240s.

[40] RyabchenkoA.Yu., Dolgov A.M., Denisov E.N. et al. Role of nitric oxide and endothelin-1 in the development of ischemic disorders of cerebral circulation. *Neurological Bulletin.* 2014. No1. S. 34-37.

[41] Aflyatumova G.N., Sadykova D.I., Nigmatullina R.R., Chibireva M.D. The nature of endothelial dysfunction in essential arterial hypertension in adolescents (clinical and experimental study). *Arterial hypertension.* 2017; 23 (2): 131-140.

[42] Golivets T.P., Dubonosova D.G., Osipova O.A., Petrova G.D. et al. Effects of endothelin-1 in the development and progression of metabolic syndrome and other socially significant non-infectious diseases (literature review). *Scientific reports of Belgorod State University.* Series: Medicine. Pharmacy. 2017. Electronic resource. https: // cyberleninka / article / n / effect ...

DOI: 10.37200/IJPR/V24I5/PR2020213
Received: 12 Mar 2020 | Revised: 28 Mar 2020 | Accepted: 06 Apr 2020