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Estimation of vitamin D status in infants with obesity

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The aim of the study was to assess the status of vitamin D, bone metabolism and the role of VDR gene mononucleotide polymorphism Bsm I in infants with obesity.

Materials and methods. Complex clinical and laboratory examinations of 120 children aging from 3 to 12 months were conducted. The main study group consisted of 90 infants whose physical development was above normal for age. The control group consisted of 30 infants whose physical development fell within standard deviation. The serum amounts of 25(OH)D and osteocalcin were measured for all the patients. Polymorphic variants of VDR – rs1544410 (Bsm I, A/G transition) was evaluated by PCR-RLFP.

Results. The main group infants had a significant difference in the levels of vitamin D. Obese infants had the lowest serum levels of 25(OH)D. An increase in vitamin D deficiency was associated with significant decrease in serum osteocalcin. A significant negative correlation between serum 25(OH)D and body mass index has been found in infants with the highest values in children with obesity. It was also shown that the alleles and the genotype of VDR gene influence the serum amount of vitamin D.

Conclusions. Obese infants have a higher risk of vitamin D deficiency compared to overweight children, those who had the risk of overweight and normal for age physical development. Among all the examined children, bone metabolism intensity according to serum osteocalcin was significantly lower in obese children as compared to children who had the risk of overweight and normal physical development. Homozygous children for mutant allele B had higher risk of vitamin D deficiency with the lowest content of serum 25(OH)D compared to heterozygous and homozygous for allele b carriers.

Key words: infant, vitamin D, obesity, osteocalcin, single nucleotide polymorphisms Bsm I in VDR gene.

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Аналіз статусу вітаміну D у дітей першого року життя з ожирінням

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Мета роботи – визначення показників статусу вітаміну D, кісткового метаболізму, ролі однонуклеотидного поліморфізму Bsm I гена VDR у дітей першого року життя з ожирінням.

Матеріали та методи. Виконали клінічне та лабораторне обстеження 120 дітей віком від 3 до 12 місяців. Основна група (n = 90) – діти, показники фізичного розвитку яких перевищували вікову норму. Контрольна група (n = 30) – діти з показниками фізичного розвитку, які перебували в межах ліній стандартного відхилення. Усім дітям проведено визначення концентрації 25(OH)D та остеокальцину в сироватці крові. Поліморфні варіанти гена VDR – rs1544410 (Bsm I, A/G transition) визначали методом ПЛР-RLFP.

Результати. У дітей основної групи спостерігали вірогідну різницю за частотою виявлення дефіциту вітаміну D. У дітей першого року життя на тлі ожиріння виявили найнижчий вміст 25(OH)D у сироватці крові. Збільшення дефіциту вітаміну D супроводжувалося вірогідним зниженням вмісту остеокальцину в сироватці крові. Встановили вірогідні зворотні кореляційні зв'язки між рівнем 25(OH)D у сироватці крові та індексом маси тіла в дітей першого року життя із максимальними значеннями в дітей, які мали ожиріння. Проаналізували асоціацію алелей і генотипів Bsm I поліморфізму гена VDR з рівнем вітаміну D у сироватці крові.

Висновки. У дітей першого року життя дефіцит вітаміну D реєструють вірогідно частіше на тлі ожиріння, ніж у дітей із надмірною масою тіла, ризиком надмірної маси тіла та осіб із фізичним розвитком, який відповідає віковій нормі. Серед обстежених дітей інтенсивність кісткового обміну за показниками сироваткового остеокальцину була вірогідно зниженою при ожирінні порівняно з дітьми, які мали ризик надмірної маси тіла та нормальний фізичний розвиток. У гомозигот мутантного алеля B вірогідно частіше реєструють дефіцит вітаміну D із найнижчим значенням сироваткового 25(OH)D, ніж у гетерозигот і гомозигот алеля b.

Ключові слова: діти першого року життя, вітамін D, ожиріння, остеокальцин, однонуклеотидний поліморфізм Bsm I гена VDR.

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Анализ статуса витамина D у детей первого года жизни с ожирением

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Цель работы – определение показателей статуса витамина D, костного метаболизма, роли однонуклеотидного полиморфизма Bsm I гена VDR у детей первого года жизни с ожирением.

Материалы и методы. Проведено комплексное клиническое и лабораторное обследование 120 детей в возрасте от 3 до 12 месяцев. Основную группу обследованных (n = 90) составили дети, показатели физического развития которых превышали возрастную норму. Контрольную группу (n = 30) составили дети, показатели физического развития которых находились в пределах линий стандартного отклонения. Всем детям проведено определение концентрации 25(OH)D и остеокальцина в сыворотке крови. Полиморфные варианты гена VDR – rs1544410 (Bsm I, A/G transition) определяли методом ПЦР-RLFP.

Результаты. У детей основной группы отмечена достоверная разница по частоте установления дефицита витамина D. У детей первого года жизни на фоне ожирения определяли наиболее низкий уровень 25(OH)D в сыворотке крови. Нарастание дефицита витамина D сопровождалось достоверным снижением содержания остеокальцина в сыворотке крови. Установлены достоверные обратные корреляционные связи между уровнем 25(OH)D в сыворотке крови и индексом массы тела у детей первого года жизни с максимальными значениями у детей с ожирением. Проведен анализ ассоциации аллелей и генотипов Bsm I полиморфизма гена VDR с уровнем витамина D в сыворотке крови.

Ключевые слова: дети первого года жизни, витамин D, ожирение, остеокальцин, однонуклеотидный полиморфизм Bsm I гена VDR.

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Выводы. У детей первого года жизни дефицит витамина D отмечают достоверно чаще на фоне ожирения, чем у детей с избыточной массой тела, риском избыточной массы тела и лиц с физическим развитием, отвечающим возрастной норме. Среди обследованных детей интенсивность костного обмена по показателям остеокальцина в сыворотке крови была достоверно снижена при ожирении в сравнении с детьми, которые имели риск избыточной массы тела и нормальное физическое развитие. У гомозигот мутантного аллеля B достоверно чаще регистрируют дефицит витамина D с наиболее низким значением 25(OH)D в сыворотке крови, чем у гетерозигот и гомозигот аллеля b.

Vitamin D deficiency is one of the most common conditions among infants. It causes a significant impact on the structure of infant pathology, as well as unfavorable influence on further development of the child and diseases origin in adolescents. Michael F. Holik, Professor of Medicine, Physiology and Biophysics, Director of the General Clinical Research Unit, Director of the Bone Health Care Clinic and the Director of the Heliotherapy, Light, and Skin Research Center at Boston University Medical Center considered that "Vitamin D deficiency – is a problem of the world. All the people are in a risk zone. Most of them do not think how important vitamin D is for the organism. Rickets that is known by the majority – is just the peak of the iceberg of the diseases that can appear in case of vitamin D deficiency. Other diseases are osteomalacia, diabetes mellitus, cardiovascular diseases, reactive arthritis, arterial hypertension, and oncology".

According to statistics 1 milliard people all over the world have deficiency or insufficient amount of vitamin D [1]. Vitamin D deficiency plays a leading role in all the main problems in pediatric population according to WHO data [2].

Taking into account modern knowledge concerning metabolism and physiological function of cholecalciferol, its deficiency, we should pay attention to its insufficient intake as well as peculiarities of vitamin D metabolism, which undergoes multiple both endogenous and exogenous factors that all lead to the pathology development [3]. It is known that vitamin D metabolism, storage, bioavailability and biological role are directly related to the body fat mass [4,5].

Pediatric overweight and obesity became a serious problem in most of the countries. Although there are a lot of technological and scientific achievements all over the world, the number of children with obesity is constantly rising [6,7]. Ukraine is one of the countries face such a problem. According to the Ministry of Public Health official data, we record up to 15,5 thousand children with newly diagnosed obesity every year. The statistics show that in 2016, more than 7 million 614 thousand obese children were registered in Ukraine, the prevalence of obesity among children as young as 17 years was 13.4 %, so 1 million 20 thousand children run into the problem [8]. The same results were presented by official data from the WHO. So, on 17 May 2017 at the 24th European Congress on Obesity in Porto, Portugal, the new WHO report was launched estimating high prevalence of obesity among the adolescent population in majority of EU countries.

"Despite sustained efforts to tackle childhood obesity, one in three adolescents is still estimated to be overweight or obese in Europe, with the highest rates found in southern European and Mediterranean countries. What is of particular concern is that the epidemic is on the rise in eastern European countries, where historically rates have been lower," stated Dr Zsuzsanna Jakab, WHO regional director for Europe.

We should indicate that somatic pathology severity is caused by the dominant role of obesity and overweight from infancy. Hypothesis concerning obesity-induced diseases and their complications in infants is based on the theoretical results and clinical studies [9].

The fast rate of bone remodeling during the first years of life leads to osteopenia development in children with obesity even in cases when primary prevention was performed correctly. There are analytical results of new studies concerning vitamin D receptors (VDR) influence on vitamin D deficiency [10].

The lack of special studies focused on risk factors assessment, namely obesity among the infant population for vitamin D deficiency development, continues to be a challenge.

The aim

Aim of the study: to assess the status of vitamin D, bone metabolism, role of VDR gene mononucleotide polymorphism Bsm I in infants with obesity.

Materials and methods

A complex clinical and laboratory examination of 120 children at the age from 3 up to 12 months (average age was (5.43 ± 1.4) months) was performed. The study was conducted during the period 2013–2016.

The main study group consisted of 90 infants whose physical development (body weight, weight-for-height and body mass index) was above normal for age. This study group was divided into 3 subgroups: the first subgroup included 30 children who had a risk of overweight; the second subgroup consisted of 30 overweight infants, and the third subgroup consisted of 30 infants with obesity.

Inclusion criteria: age from 3 up to 12 months, physical development above the mean normal for age. Exclusion criteria: prematurity, congenital and birth defects, severe injury of the nervous system, malnutrition, metabolic disorders, long-term intake of the drugs that can influence vitamin D metabolism; season from June to September.

The control group consisted of 30 infants whose physical development was scaled up to standard deviation adjusted for age.

Estimation of vitamin D status was done in accordance with the classification approved by experts of International Endocrine Society (The Endocrine Society, 2011) and a majority of the International Organizations. Based on the classification, serum hydroxyvitamin D concentration was measured without reference to child's age. Vitamin D deficiency was diagnosed in case if a serum concentration of 25(OH)D was lower than 20 ng/ml, relative vitamin D deficiency was defined as a 25(OH)D serum level from 21 to 29 ng/ml, and its concentration of 30 ng/ml and more – as sufficient amount. The measurements of 25(OH)D and osteocalcin serum concentrations were performed

using quantitative electrochemiluminescence method with the Elecsys COBAS test-system (Roche Diagnostics, Germany) according to the original instructions. Genomic DNA was extracted from whole blood by standard phenol-chloroform method. Polymorphic variants of VDR gene – rs1544410 (Bsm I, A/G transition) which is located in intron 8 was detected with method PCR-RLFP (restriction fragment length polymorphism) that provides detection of the point mutations with specific endonucleases. The results were statistically processed through standard programs Statistica for Windows 8.0.0. (SPSSI.N.C.; 1989–1997), Statistica V.6.0 (StatSoft Inc., 1984–1996), Microsoft Excel. Shapiro–Wilk test for small sample sizes was performed to test if the quantitative characteristics were normally distributed. A null hypothesis was considered if the studied deviation did not differ from the normal deviation. Estimation of the deviation hypothesis was done through an evaluation of the main tendency, mode and median, symmetrical characteristics, excess. Arithmetic means (M), standard deviations (S), standard errors of the mean (m), 95 % confidence intervals of the mean were taken into account to analyse the statistical data. Statistical significance of the differences was assigned at the $P < 0.05$ level.

The statistical significance of differences among independent groups was determined with the monofactor analysis of variance (ANOVA). The Kruskal–Wallis H-test was used to compare three independent groups. Characteristic of the qualitative parameters was done using Wilson method, with evaluation of relative frequency (P), its standard error (S) and 95 % confidence interval, as well as χ^2 tests and the corresponding significance level at a P-value < 0.05.

Results

It was revealed that more than half of the children from the main group were diagnosed with vitamin D deficiency (39 cases (43.33 ± 5.22) %), that exceeded frequency of vitamin D insufficiency (30 cases (33.33 ± 4.97) %, P > 0.05) and it was twice as high as the number of children with normal level of vitamin D (21 cases (23.33 ± 4.46) %, P < 0.01).

Vitamin D deficiency was significantly more common among obese infants ((63.33 ± 8.79) %), compared with overweight children ((36.67 ± 8.8) %, P < 0.05; OR = 2.98, S = 0.53, 95 % CI: 1.04–8.52), children with the risk of overweight ((30.00 ± 8.36) %, P < 0.05; OR = 4.03, S = 0.55, 95 % CI: 1.37–11.83) and those who had normal for age physical development ((26.67 ± 8.07) %, P < 0.05; OR = 4.75, S = 0.56, 95 % CI: 1.58–14.24).

Thus, infants with obesity had the 25(OH)D serum concentration of ((21.72 ± 2.92) ng/ml, 95 % CI: 16.02–27.44 ng/ml), that was significantly different from the results of patients with the risk of overweight ((30.66 ± 3.12) ng/ml, 95 % CI: 24.55–36.77 ng/ml, P < 0.05) and infants with normal for age physical development ((31.15 ± 2.80) ng/ml, 95 % CI: 25.67–36.63 ng/ml, P < 0.05). Infants of the control group had vitamin D level ((61.42 ± 2.06) ng/ml) within the laboratory reference values for 25(OH)D (from 30 ng/ml to 100 ng/ml). A normal value of 25-hydroxyvitamin D was estimated as 95 % CI (57.39–65.45 ng/ml) for means of 25(OH)D in the control group infants. Comparative analysis confirmed that mean levels of 25-hydroxyvitamin D were significantly lower in the main group of patients; however the comparison group results were consistent with the control group results (P < 0.001).

Overweight infants had higher prevalence of vitamin D insufficiency (13 infants) (43.33 ± 9.05) %, P < 0.05; OR = 0.51, S = 0.56, 95 % CI: 0.17–1.58) than infants with the risk of overweight (11 infants (36.67 ± 8.79) %, P > 0.05).

Data analysis showed that the number of infants with sufficient vitamin D supplementation did not differ between the study groups. So, among all the examined children, 5 with obesity (16.67 ± 6.8. %), 6 (20.00 ± 7.30 %) with overweight and 10 (33.33 ± 8.60 %) with the risk of overweight had sufficient amount of vitamin D (P > 0.001).

It was found that increased BMI in infants with obesity was accompanied by a marked decrease in serum 25(OH) D (r = -0.48, P < 0.01).

The analysis of the diagnostic significance of serum 25(OH)D in infants, depending on the study group, showed that the highest sensitivity of the method (Se) was defined for children of the third subgroup (83.38 %, 95 % CI: 72.6–83.38 %). The results of Se for the first and second subgroups were: 80.05 % (95 % CI: 69.1–80.05 %) and 66.71 % (95 % CI: 55.5–66.71 %), respectively. Sensitivity of the method in the comparative group was 73.38 % (95 % CI: 62.20–73.38 %). Specificity (Sp) and prognostic value of positive test (PVP) of the method in infants of the main group, as well as of comparison group were 100 %. Negative prognostic value (PVN) was the highest in the group of patients with obesity (85.7 %, 95 % CI: 76.50–97.31 %). PVN for the first and second subgroups of infants was 83.38 % (95 %CI: 74.20–95.51 %) and 2 75.05 % (95 % CI: 66.60–88.42 %), respectively. PVN for the comparison group was 78.99 % (95 % CI: 65.98–91.91 %).

It was found that intensity of the bone metabolism by osteocalcin levels was significantly lower in infants of the main study group compared with the healthy infants. Patients of the first subgroup had osteocalcin level of (67.85 ± 3.44) ng/ml (95 % CI: 61.11–74.59 ng/ml), the second subgroup – (65.58 ± 3.29) ng/ml (95 % CI: 59.14–72.02 ng/ml), the third subgroup – (56.15 ± 4.02) ng/ml (95 % CI: 48.28–64.02 ng/ml), which showed a significant difference in indicators of bone metabolism between children of each subgroup and infants of the control group – (94.26 ± 2.96) ng/ml, (95 % CI: 88.46–100.06 ng/ml, P < 0.001). Among the main group infants, the intensity of bone metabolism was significantly decreased in infants with obesity compared to infants who had the risk of overweight or normal physical development ((71.27 ± 3.29) ng/ml; 95 % CI: 64.83–77.71, P < 0.05).

High levels of vitamin D deficiency was followed by a significant decrease in serum osteocalcin (P < 0.05).

Detected disorders were by far more severe in infants with obesity in comparison to the results of infants with the risk of overweight and normal physical development. Comparison of the mean osteocalcin levels among the main group children revealed a significant difference between subgroup of children with obesity and subgroup with the risk of overweight, ((47.01 ± 2.98) ng/ml and (59.6 ± 2.2) ng/ml, P < 0.01), respectively.

A correlation between serum levels of osteocalcin and 25-hydroxyvitamin D in the first subgroup children was (r = 0.58, P < 0.01), in the second subgroup (r = 0.37, P < 0.01) and in the third subgroup (r = 0.63, P < 0.01). A correlation between these indicators in the comparative

group patients (r = 0.47, P < 0.01) and the control group (r = 0.23, P < 0.05) was also significantly different. It should be noted that the highest correlation between serum osteocalcin and 25-hydroxyvitamin D was in infants with obesity. Nevertheless, the worst relation between these indicators was in the group of healthy children.

An association between Bsm I polymorphism in VDR gene and vitamin D deficiency in infants was analyzed. Heterozygous (Bb) genotype (53 patients (44.16 ± 4.53) %, 95 % CI: 35.60–53.11) was mainly detected in the overall structure of this condition. Children with homozygous mutant allele B (BB) (22 infants (18.33 ± 3.53) %, 95 % CI: 12.43–26.2) were the lowest population, as their number was significantly smaller than those with heterozygous (P < 0.001) and homozygous allele b (bb) (45 children (37.5 ± 4.41) %, 95 % CI: 29.35–46.42, P < 0.01).

Frequency of the allele b among all the examined patients was (59.6 ± 3.16) % (95 % CI: 53.4–65.79), that was 1,5 times higher than the allele B presence – (40.4 ± 3.16) % (95 % CI: 34.2–46.59, P < 0.01).

The difference between expected and real amount of the genotypes was statistically insignificant (χ^2 = 0.82, P = 0.36). Correlation of the alleles and genotypes in studied population demonstrated the Hardy–Weinberg equilibrium. This suggests that obtained study results can be representative for the real population.

Homozygotes for the mutant allele B appeared to be common in case of vitamin D deficiency ((59.09 ± 10.73) %, 95 % CI: 38.73–76.74, P < 0.05) with the lowest levels of serum 25(OH)D, than in heterozygous (OR = 2.8, S = 0.52, 95 % CI: 1.01–7.8) and homozygous allele b carriers (OR = 2.61, S = 0.53, 95 % CI: 0.91–7.45).

Significantly lower levels of serum 25(OH)D ((21.30 ± 3.31) ng/ml, 95 % CI: 14.82 – 27.78) and the highest prevalence of vitamin D deficiency ((59.09 ± 10.73) %, 95 % CI: 38.73–76.74) were more common among the homozygotes for the mutant allele B (P < 0.05).

Discussion

It is important to understand the influence of fat mass on bone tissue during the growth of organism and it is an important aspect for investigation. Even though we have got enough background information concerning the association between vitamin D deficiency and obesity, the data relate to adults and teenagers but not to infants. There are just a narrow range of studies concerning evaluation of vitamin D status and its association with obesity in infants. The analysis in the present study has shown that vitamin D deficiency is more often found in infants with obesity. The same results were obtained by other scientists who studied vitamin D status in obese infants. However, scientists from Poland got a conclusion that vitamin D deficiency is common mainly for obese children from 1 to 5 years during autumn and winter [11]. American scientists demonstrated that a high prevalence of vitamin D deficiency had been observed in obese children and insisted on routine vitamin D screening in such children [12]. It should be mentioned that the physical development of infants in this study was above the normal for age, however, the lowest 25(OH)D levels were found in obese infants. There is a high probability that a decrease in vitamin D biosimilarity occurs due to endogen factors which cause it to be stored in fat depots [13].

A significant negative correlation between serum 25(OH)D and BMI was found in the infants with obesity in the present study, as evidenced by the literature data [14], yet at the same time some investigators did not find any association at all [15].

In further evaluation, the serum osteocalcin level as a marker of osteoregeneration and bone tissue remodelling rate was examined. When reviewing the previous studies, no similar investigations of bone metabolism according to physical development of infants were found. But a lot of the studies illustrated such an association in older children. Some studies showed such an association, but others denied it. Thus, Korean scientists approved a negative correlation between serum osteocalcin level and obesity in children aged 9.78 ± 1.05 years old [16].

Pathophysiological association between obesity and bone tissue is challenging and still a dilemma facing researchers. According to the literature data, obesity may have an influence on the bone metabolism by several mechanisms. Since adipocytes and osteoblasts originate from the common multipotent mesenchymal cells, obesity can increase the differentiation of adypocytes and fat accumulation, but at the same time decrease the differentiation of osteoblasts and maturation rate of bone. Obesity is also associated with chronic inflammation. Increased concentrations of circulating and tissue inflammatory cytokines in obesity can influence the activity of osteoclasts and bone tissue resorption by changing the receptor activator of NF-kB / receptor activator of NF-kB ligand / osteoprotegerin (RANK / RANKL / OPG) pathway. Furthermore, leptin overproduction and/or decreased synthesis of adiponectin in adiposytes in case of obesity can indirectly influence the bone tissue formation or its resorption by means of inflammation cytokines synthesis [17].

There is as yet no consensus on the association between gene polymorphism and bone tissue, because some studies have confirmed this association, but others completely excluded it. The controversy between conducted studies can be explained by differences in the genome structure, feeding type and environmental factors influence in different parts of the world.

Genetic variants of the VDR gene (Bsm I polymorphism), which codes for vitamin D receptor, have shown the prevalence of heterozygous carriers among the examined infants. A number of homozygotes for mutant allele B was significantly lower than heterozygotes and homozygotes for allele b. The results we obtained were consistent with the results of similar previous studies. So, different geographical and ethnic populations around the world have a higher frequency of bb and Bb genotypes if compared to BB genotype. The situation is analogous with the distribution of allele b which is higher than frequency of allele B in different populations. Some studies presented data indicating that 16 % of white European population are homozygous for functionally incomplete allele BB and frequency of minor allele B among them is approximately 42 %. Similar results were obtained in adults concerning the risk of osteoporosis development. Meta-analysis of 26 studies on association between VDR

gene Bsm I nucleotide polymorphism and osteoporosis showed that bb genotype was associated with a significantly decreased risk of this disease development (bb against BB: OR = 0.61, 95 % CI, 0.40–0.92; bb against BB/Bb: OR = 0.70, 95 % CI, 0.52–0.95, respectively) [18]. Based on meta-analysis of 41 studies, other authors, however, did not prove a link between Bb genotype of VDR gene Bsm I polymorphism and osteoporosis in the general Asian population [19].

The same results were obtained after examination of 974 Brazilian children aged from 2.8 months to 10.4 years. The study showed an association between 25-hydroxyvitamin D average levels and VDR gene Bsm I, FokI, ApaI, TaqαI and Cdx2 mononucleotide polymorphisms, but only mutant allele B in the Bsm I polymorphic site of the VDR gene was the marker related to low serum concentration of 25(OH)D [20].

Heterogenous population and lack of prospective studies on the evaluation of genetic variations can explain the different results that were obtained in the studies.

Conclusions

1. Vitamin D deficiency was more common in infants with obesity ((63.33 ± 8.79) %) than in overweight ((36.67 ± 8.80) %, P < 0.05; OR = 2.98, S = 0.53, 95 % CI: 1.04–8.52), in infants with the risk of overweight ((30.00 ± 8.36) %, P < 0.05; OR = 4.03, S = 0,55, 95 % CI: 1.37–11.83) and in those with normal for age physical development ((26.67 ± 8.07) %, P < 0.05; OR = 4.75, S = 0.56, 95 % CI: 1.58–14.24). Infants with obesity had the lowest serum concentration of 25(OH)D ((19.11 ± 2.92) ng/ml, 95 % CI: 13.41–24.83 ng/ml), (P < 0,05), its moderate negative correlation (r = -0.48) with BMI and significant difference from this index in children with normal for age physical development ((31.15 ± 2.80) ng/ml, 95 % CI: 25.67–36.63, P < 0.05).

2. Among all the examined patients, the intensity of bone metabolism (according to serum osteocalcin level) was the lowest in case of obesity ((56.15 ± 4.02) ng/ml; 95 % CI: 48.28–64.02 ng/ml) compared with children who had the risk of overweight ((67.85 ± 3.44) ng/ml, 95 % CI: 61.11–74.59 ng/ml) and normal physical development ((71.27 ± 3.29) ng/ml, 95 % CI: 64.83–77.71 ng/ml), P < 0.05.

3. Homozygotes for mutant allele B had significantly higher frequency of vitamin D deficiency ((59.09 ± 10.73) %, 95 % CI: 38.73–76.74, P < 0.05) with the lowest level of serum 25(OH)D compared with heterozygotes (OR = 2.8, S = 0.52, 95 % CI: 1.01–7.80) and homozygotes for allele b (OR = 2.61, S = 0.53, 95 % CI: 0.91–7.45).

Recommendation for future research may include estimation of vitamin D status and bone metabolism in children with different genotypes.

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