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The role of vitamin D in metabolically unhealthy obesity in children

Abstract. ***Background.*** *Vitamin D deficiency is associated with impaired glucose tolerance, insulin resistance, metabolic syndrome, and an increased risk of developing type 2 diabetes. Aim: to study the role of vitamin D levels associated with single nucleotide variants (SNV) of the vitamin D receptor (VDR) gene in the development of metabolically unhealthy obesity (MUO) in children.* ***Materials and methods.*** *Two hundred and ten obese children aged 6–18 years were examined. The main group (n = 125) was represented by children with MUO. The control group (n = 85) included children with metabolically healthy obesity (MHO). Whole genome sequencing (CeGat, Germany) was performed in 31 randomly selected children of the main and 21 children of the control group. The level of serum 25-hydroxyvitamin D (Synevo, Ukraine) was measured in all children. Verification of results: calculation of Spearman's correlation coefficient (r) and p-value for each variable.* ***Results.*** *The mean serum level of 25-hydroxyvitamin D was significantly lower in children with MUO than in those with MHO: 14.57 ± 1.63 ng/mL versus 28.82 ± 1.93 ng/mL (t = 5.64, p = 0.00061). In patients with MUO, serum 25-hydroxyvitamin D levels are associated with the following predictors. Highly significant factors (0.7≤ |r| < 1): osteopenia (r = –0.73). Factors of average significance (0.3≤ |r| < 0.7): prolactinemia (r = –0.57); waist circumference/height ratio > 0.5 (r = –0.41); AA genotype SNP VDR rs12721365 (r = –0.41) and AA genotype SNP VDR rs2228572 (r = –0.39); metabolic-associated fatty liver disease (r = –0.39); physiological postprandial glycemia (r = 0.38); level of interkeukin-1β (r = –0.36); triglyceridemia (r = –0.34); body mass index (r = –0.33); adiponectinemia (r = 0.32); arterial diastolic hypertension (r = –0.32). Low-significant factors (0 < |r| < 0.3): polycystic ovary syndrome (r = –0.28); GG genotype SNP VDR rs2228570 (r = 0.27); waist circumference (r = –0.27); extreme obesity (r = –0.27); male sex (r = 0.26); hip circumference (r = –0.24); levels of high-density lipoprotein cholesterol (r = 0.24); serum gamma-glutamyl transpeptidase (r = –0.23); free thyroxine (r = 0.22); thyroid-stimulating hormone (r = –0.22); free triiodothyronine (r = 0.2).* ***Conclusions.*** *The development of cardiometabolic risk and vitamin D deficiency in obese children is associated with the presence of AA/AG genotypes SNV VDR rs12721365, rs2228572, rs2228570.*

Keywords: *children; metabolically unhealthy obesity; vitamin D receptor gene; single nucleotide variants; 25-hydroxyvitamin D*

Introduction

Currently, the global prevalence of overweight and obesity is 52 % (39 % for overweight and 13 % for obesity) and is expected to exceed 57 % by 2030. According to the World Health Organization [48], overweight and obesity are associated with premature death in 4 million people annually.

Obesity is a multifactorial disease, which is caused by the combined influence of both pathogenic exogenous factors, which include an unhealthy lifestyle, and genetic factors [2], such as single nucleotide variants (SNV) of the vitamin D receptor gene (*VDR*) (NR1I1, PPP1R163, ID: 7421) [3, 4, 31, 35].

The *VDR* gene (Baker et al., 1988), which encodes the vitamin D receptor, is located on the long arm of chromosome 12 (q12-q14), contains 11 exons, and spans a region of approximately 75 kb [41, 46].

Vitamin D exerts its effect on target tissues by binding to the cytosolic/nuclear *VDR*, which is a member of the steroid/thyroid hormone receptor family. After binding to the ligand, *VDR* forms a heterodimer with the retinoid X

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receptor (RXR), the formed complex $1,25(OH)_2D_3$-VDR-RXR functions as a transcription factor that changes the transcriptional activity of numerous genes involved in the regulation of metabolism substances, modulation of the immune, cardiovascular and other systems of the human body [8, 12, 13, 15, 25, 32]. From an evolutionary point of view, vitamin D plays a more significant role in energy metabolism than in osteogenesis. An inverse correlation has been demonstrated between low serum levels of 25-hydroxyvitamin D (25(OH)D) and obesity [10]. Including the activity of the *VDR*, receptor modulates carbohydrate metabolism. Thus, it has been found that the vitamin D receptor is expressed in all nucleated cells, including pancreatic β-cells. In turn, vitamin D not only stimulates the synthesis of insulin by the pancreas, but also reduces the level of insulin resistance by activating the expression of insulin receptors [14, 44]. Vitamin D modulates lipid and glucose metabolism in the liver, inhibits the activity of inflammation and chronic oxidative stress caused by hyperglycemia [9, 47]. Thus, the formation of a metabolically unhealthy obesity (MUO) in childhood may be due to SNV of the *VDR* gene.

Currently, 111 different *VDR* gene SNVs have been identified, described in 41 studies, but the effect of *VDR* gene SNVs on *VDR* protein function and signaling is largely unknown. Of these, the potential effects on the formation of MUO, type 2 diabetes mellitus are most significantly represented in four adjacent SNV *VDR*: *ApaI, BsmI, TaqI, FokI* [37].

Aim: to study the role of vitamin D levels associated with SNV of the *VDR* gene in the development of MUO in children.

Materials and methods

Participants provided written informed consent, and research protocols and procedures were approved according to the ethical standards of the Helsinki Declaration 2013 and by the Human Research Ethics Committee of Dnipro State Medical University (ethical approval DSMU/EC/19/1107). Time of data collection: January 2020 — December 2022.

Design: observational, analytical, longitudinal, cohort study.

Inclusion criteria: polygenic obesity (body mass index (BMI) ≥ 97th percentile), age 6–18 years. Exclusion criteria: monogenic and/or syndromic obesity, pregnancy.

Two hundred and ten obese children aged 6–18 years were examined. The main group (n = 125) was represented by patients with MUO. The control group (n = 85) included children with metabolically healthy obesity (MHO). For inclusion in the main observation group, the presence of abdominal obesity and two of the following criteria were taken into account: 1) fasting glycemia ≥ 5.6 mmol/L [18] and/or, according to the recommendations of the IDEFICS Study, the level of basal insulinemia above the 90th percentile [40]; 2) high density lipoprotein cholesterol (HDL-C) ≤ 1.03 mmol/L or less than the 10th percentile of the age norm [19]; 3) triglycerides (TG) ≥ 1.7 mmol/L or more than the 90th percentile of the age norm; 4) systolic blood pressure and diastolic blood pressure (DBP) above the 90th percentile for a given age, gender and height [22]. The abdominal type of obesity was determined according to the consensus of the International Diabetes Federation, based on the excess of the waist circumference over the 90th percentile for children 6–15 years old or more than 94 cm for boys aged 16–18 years and more than 80 cm for 16–18-year-old girls [5].

The level of 25(OH)D in blood serum was studied by the immunochemical method with chemiluminescent detection using the Architect i2000 analyzer and the ABBOTT Diagnostics test system (USA). Reference values indicating risk of insufficient intake < 30 ng/mL, vitamin D deficiency of 20 ng/mL.

To study the role of proinflammatory markers in the development of meta-inflammation in children with obesity, the serum levels of interleukin-1β (IL-1β), IL-6, C-reactive protein (CRP) were evaluated. IL-1β was detected by the immunochemical method with chemiluminescence immunoassay. Analyzer and test system: Immulite (Siemens AG, Germany). The reference value of IL-1β level was 0–5 pg/ml. IL-6 was determined by an enzyme-linked immunosorbent assay (ELISA) using a Cobas 6000/Cobas 8000 kit provided by Roche Diagnostics (Switzerland). The reference value of IL-6 level was 1.5–7.0 pg/ml. The level of CRP was measured using the turbidimetric immunoassay method. Analyzer and test system: Cobas 6000 (with 501 modules), Roche Diagnostics (Switzerland). The CRP of 0–5 mg/dl was considered the reference value. Leptin was determined using ELISA. Analyzer and test system: Tecan Sunrise (LDN, Germany). The reference value of leptin level for boys was 2–5.6 ng/ml, for girls — 3.7–11.1 ng/ml. Adiponectin was tested using ELISA. Analyzer and test system: Mediagnost GmbH (Germany). Interpretation of the results was carried out as follows: low cardiovascular risk — more than 10 μg/ml; moderate cardiovascular risk — 7–10 μg/ml; high cardiovascular risk — 4–7 μg/ml; very high cardiovascular risk — less than 4 μg/ml.

Measurement of bone mineral density (BMD) was performed on the calcaneus by ultrasonic densitometry using the Osteosys Sonost 2000 apparatus (Korea). Osteoporosis was defined as a BMD Z-score of 2.5 SD or more below the mean. Osteopenia was defined as a BMD Z-score from –1.0 to –2.5 [29, 30].

The whole genome sequencing (NGS, Illumina CSPro®, CeGaT, Germany) was performed in 31 children of the main and 21 children of the control group, the sample was qualitatively homogeneous in relation to the general population. Average amount of DNA (μg) in samples — 0.875. Library preparation: a quantity used is 50 ng. Library preparation kit: Twist Human Core Exome plus Kit (Twist Bioscience). Sequencing parameters: NovaSeq 6000; 2 × 100 bp.

Bioinformatic analysis — demultiplexing of the sequencing reads was performed with Illumina bcl2fastq (version 2.20). Adapters were trimmed with Skewer, version 0.2.2 [26]. DNA-Seq: trimmed raw reads were aligned to the human reference genome (hg19-cegat) using the Burrows-Wheeler Aligner, BWA-mem version 0.7.17-cegat [33]. ABRA version 2.18 and Genotype Harmonizer v. 1.4.20 were used for local restructuring of readings in target regions to improve more accurate detection of indels in the genome during mutagenesis [17, 36].

Reference sequence obtained from the National Center for Biotechnology Information RefSeq database (http://www.ncbi.nlm.nih.gov/RefSeq) [43].

Statistical analysis of the obtained results was carried out using a package of application programs Statistica 6.1 (number AGAR909E415822FA) with the help a personal computer based on an Intel processor Pentium 4. Depending on the test result, parametric and non-parametric statistical methods were used. Correlation analysis was used to analyze 100 indicators of clinical, laboratory-instrumental and molecular genetic examinations in 210 children. To assess the relationship between quantitative traits, correlation analysis was used according to the Pearson method, and between qualitative traits, a non-parametric ranking method was used according to Spearman's analysis (r). Only essential connections were taken into account ($p < 0.05$).

Results

The mean age of patients in the main and control groups was 12.15 ± 0.09 and 12.24 ± 0.73 years, respectively. The proportion of boys in the main group was 56.14 ± 6.61 %, while in the control group, it was 48.17 ± 6.86 % ($p \geq 0.05$).

In obese children, the average serum level of 25(OH)D was 21.70 ± 1.78 ng/mL and was regarded as a risk of insufficient intake of vitamin D. The average level of 25(OH)D in blood serum of children with MUO (14.57 ± 1.63 ng/mL) was significantly lower than in those with MHO (28.82 ± 1.93 ng/mL); $t = 5.64$, $p = 0.00061$.

The correlation galaxy of associations between the level of 25(OH)D in the blood serum and metabolic, molecular genetic parameters in MUO is shown in Fig. 1.

Anthropometric criteria

Based on the analysis, a direct correlation was found between the level of 25(OH)D in the blood serum and child's height ($r = 0.28$, $p < 0.05$). At the same time, there is a negative correlation between the serum level of 25(OH)D and anthropometric indicators characterizing a positive energy balance: waist circumference/height ratio > 0.5 ($r = –0.41$); BMI ($r = –0.33$); waist circumference ($r = –0.27$); extreme obesity ($r = –0.27$); hip circumference ($r = –0.24$), $p < 0.05$.

Gender and age criteria

A direct relationship was found between the level of 25(OH)D in the blood serum and the age of the child ($r = 0.3$), as well as the male gender of the examined patients ($r = 0.26$, $p < 0.05$).

Proinflammatory status

Based on a molecular immunological study, we found a positive correlation between serum levels of 25(OH)D and adiponectin ($r = 0.32$), which is known to be produced by adipocytes of white adipose tissue and is characterized by antidiabetic, antiatherogenic and anti-inflammatory properties. In turn, we found that the concentration of the pyroptosis marker IL-1β is inversely proportional to the level of 25(OH)D in the blood serum ($r = –0.36$, $p < 0.05$).

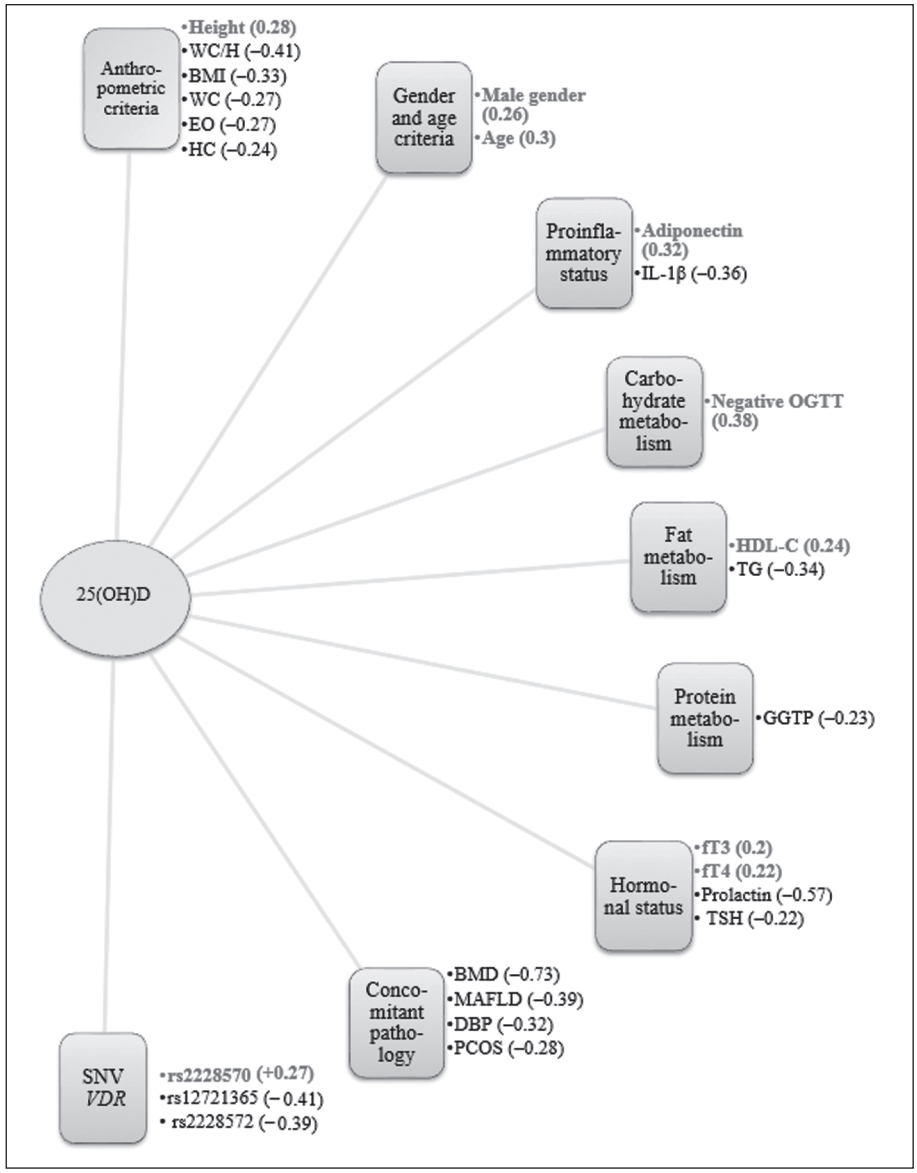

Figure 1. Correlation galaxy of associations between the level of 25(OH)D in blood serum and metabolic, molecular genetic parameters in children with MUO

Notes: WC/H — waist circumference/height ratio; EO — extreme obesity; HC — hip circumference; OGTT — oral glucose tolerance test; GGTP — gamma-glutamyl transpeptidase; fT4 — free thyroxine; fT3 — free triiodothyronine; TSH — thyroid-stimulating hormone; PCOS — polycystic ovary syndrome; MAFLD — metabolic-associated fatty liver disease.

Carbohydrate metabolism

The correlation diagram shows a direct relationship between the level of 25(OH)D in blood serum and the level of physiological postprandial glycemia after an oral glucose tolerance test ($r = 0.38$, $p < 0.05$).

Fat metabolism

Based on the study of lipid metabolism, a weak correlation was found between the levels of 25(OH)D and HDL-C content ($r = 0.24$) in blood serum. At the same time, an inverse proportional relationship was revealed between the level of 25(OH)D in blood serum and triglyceridemia ($r = –0.34$; $p < 0.05$).

Protein metabolism

Correlation analysis revealed a weak negative relationship between the levels of 25(OH)D and gamma-glutamyl transpeptidase enzyme in blood serum ($r = –0.23$; $p < 0.05$).

Hormonal status

The study of thyroid status in patients with MUO demonstrated a direct correlation between the levels of 25(OH)D and free thyroxine ($r = 0.22$), free triiodothyronine ($r = 0.2$) in blood serum. Interestingly, our study found a negative correlation between the level of 25(OH)D and thyroid-stimulating hormone ($r = –0.22$), as well as prolactinemia ($r = –0.57$), $p < 0.05$.

Concomitant pathology

The MUO phenotype in children was characterized by an inverse correlation between the level of 25(OH)D in the blood serum and the presence of comorbid pathology: bone mineralization associated with osteopenia ($r = –0.73$); metabolic-associated fatty liver disease ($r = –0.39$); the level of diastolic blood pressure associated with the risk of arterial hypertension ($r = –0.32$), polycystic ovary syndrome ($r = –0.28$; $p < 0.05$).

SNV VDR

The distribution of genotype frequencies was in Hardy-Weinberg equilibrium in both calculated groups. The association of AA genotype SNV *VDR* rs12721365 ($r = –0.41$), AA genotype SNV *VDR* rs2228572 ($r = –0.39$) and GG genotype SNV *VDR* rs2228570 ($r = 0.27$) with vitamin D deficiency was found in children with MUO, $p < 0.05$.

Thus, in children with MUO, the level of 25(OH)D in the blood serum is associated with genetic and clinical and laboratory factors. These factors were conditionally divided into three groups according to the degree of association with the level of 25(OH)D in blood serum.

The first group, which was characterized by a high level of dependence ($0.7 \le |r| < 1$) on the serum level of 25(OH)D, was represented by osteopenia ($r = –0.73$). The second group of factors that with mean strength ($0.3 \le |r| < 0.7$) correlated with serum 25(OH)D levels included: prolactinemia ($r = –0.57$); waist circumference/height ratio > 0.5 ($r = –0.41$); AA genotype SNP *VDR* rs12721365 ($r = –0.41$) and AA genotype SNP *VDR* rs2228572 ($r = –0.39$); metabolic-associated fatty liver disease ($r = –0.39$); physiological postprandial glycemia ($r = 0.38$); IL-1β ($r = –0.36$); triglyceridemia ($r = –0.34$); BMI ($r = –0.33$); adiponectinemia ($r = 0.32$); arterial diastolic hypertension ($r = –0.32$). And the third group of low-associated factors ($0 < |r| < 0.3$) included: polycystic ovary syndrome ($r = –0.28$); GG genotype SNP *VDR* rs2228570 ($r = 0.27$); waist circumference ($r = –0.27$); extreme obesity ($r = –0.27$); male sex ($r = 0.26$); hip circumference ($r = –0.24$); serum GGTP activity ($r = –0.23$); blood levels of HDL-C ($r = 0.24$); free thyroxine ($r = 0.22$); thyroid-stimulating hormone ($r = –0.22$); free triiodothyronine ($r = 0.2$).

Discussion

According to a meta-analysis by V.I. Fiamenghi and E.D. de Mello [21], obese children and adolescents have a higher relative risk of vitamin D deficiency than non-obese children of 1.41 (95% CI: 1.26–1.59, $p < 0.01$), which is consistent with our study demonstrating a direct association of hypovitaminosis D and MUO, including extreme obesity. According to various authors, hypovitaminosis D occurs in 76–90 % of patients with extreme obesity before bariatric intervention [6, 11]. Hypovitaminosis D is accompanied by a decrease in the activity of mechanisms for maintaining an optimal calcium level in the body, which leads not only to the development of osteopenia, but also to a violation of energy metabolism, cell differentiation and induction of low-level inflammation [43].

Our data on the association of 25(OH)D level with clinical, biochemical, molecular genetic parameters and data from instrumental research in children aged 6–18 years with MUO allow us to conclude that there is a positive relationship between vitamin D and such an anthropometric indicator, as a linear growth of a child, which determines physical development, and negative correlation with obesogenic indicators, including waist circumference/height ratio, waist circumference, hip circumference, BMI. In addition, our results demonstrate a direct correlation between physiological 25(OH)D levels, age, and male gender, confirming data from other studies on a higher risk of hypovitaminosis D in young girls [45] and obese women [23]. Samantha L. Huey et al. [27], reviewing 139 studies on the effect of vitamin D on linear growth in children under 5 years of age, concluded that oral vitamin D supplementation increased length/height Z-score for age.

Low serum levels of 25(OH)D in children with MUO, identified in our study, are associated with the risk of developing cardiometabolic disorders: an increase in TG levels, a decrease in HDL-C concentration, and the development of postprandial hyperglycemia. An increased risk of vitamin D deficiency dyslipidemia has been detected by Pei Xiao et al. [50]. The authors found that children with persistent vitamin D deficiency had significantly elevated serum levels of free cholesterol, TG, and low-density lipoprotein cholesterol. The atherogenic influence of vitamin D deficiency that accompanies obesity may be one of the decisive factors leading to the development of MUO. We also found an inversely proportional relationship between serum level of 25(OH)D in children with MUO and GGTP activity, which was also recorded by other researchers (OR 1.39, 95% CI 1.07–1.8) [20, 38]. Increased serum GGTP activity is a biomarker of increased oxidative stress in humans and plays a key role in atherogenesis [16].

Pei Xiao et al. [51] demonstrated that TG, serum insulin, and insulin resistance were inversely related to 25(OH)D concentration ($p < 0.05$) in obese children. The authors believe that 32 % of hyperglycemia cases in obese children are associated with a lack of vitamin D. It has been demonstrated that vitamin D-mediated increase in insulin sensitivity is due to the binding of calcitriol to *VDR*, induction of insulin receptor expression and excitation of the peroxisome proliferator-activated delta receptor [44].

Vitamin D is known to have anti-inflammatory effects. In particular, it has been demonstrated that vitamin D suppresses 10 out of 12 human leukocyte antigen class II genes and five S100 calcium-binding protein A genes, and also modulates the expression of six *CXCL* chemokine genes [24]. We found that the concentration of the proinflammatory cytokine IL-1β is inversely proportional to the level of 25(OH)D in the blood serum, which is probably due to the inhibitory effect of vitamin D on the activity of NLRP3/caspase-1/GSDMD-pyroptosis [28]. It should be noted that the activation of NOD-like receptor protein 3 induced by hyperglycemic stress is recognized as a key stage in the initiation of inflammation of pancreatic β-cells in the pathogenesis of type 2 diabetes mellitus [49].

Thyroid hormones such as fT4 and fT3 enhance the genomic action of $1,25(OH)_2D_3$ in the gut, promoting paracellular entry of Ca^{2+} into the body's internal continuum [7], which explains the direct correlation between the levels of vitamin D and fT4, fT3, as well as the reverse relationship between 25(OH)D and TSH, demonstrated in our study.

For the first time, D.N. Pahuja and H.F. DeLuca [39] described in 1981 the stimulatory effect of prolactin on active calcium transport in the gut in vitamin D-deficient rats. Prolactin can increase the expression of the CYP27B1 protein, thereby increasing $1,25(OH)_2D_3$ synthesis, regulates TRPV6 and PMCA1b in the duodenum independently of vitamin D, and also has a pleiotropic effect with $1,25(OH)_2D_3$ on the regulation of intestinal proteins that transport calcium — TRPV6 and calbindin-D_{9K} [7]. The inverse correlation found by us between the concentration of vitamin D in the blood serum and the level of prolactinemia probably opens up promising opportunities for supplemental vitamin D therapy for hyperprolactinemia in obese individuals [1, 42].

Unlike previous studies [4, 21, 34], we have shown for the first time an association of vitamin D deficiency determined by AA/AG SNV genotypes of the *VDR* gene rs12721365, rs2228572, rs2228570 with the development of MUO in children.

Conclusions

The serum level of vitamin D is an important modifiable exposome factor that is involved in the formation of the obesity phenotype in children.

Vitamin D deficiency in obese children is one of the key factors that form the MUO phenotype, contributing to the development of abdominal obesity, metabolic-associated fatty liver disease, arterial diastolic hypertension, dyslipidemia, postprandial hyperglycemia, proinflammatory type of cytokine status, as well as osteopenia and hyperprolactinemia.

The serum level of vitamin D in obese children is associated with the SNV of the *VDR* gene.

The risk of developing cardiometabolic disorders and vitamin D deficiency in obese children is associated with the presence of AA/AG genotypes SNV rs12721365, rs2228572, rs2228570 of the *VDR* gene.

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Роль вітаміну D при метаболічно нездоровому ожирінні в дітей

Резюме. Актуальність. Дефіцит вітаміну D пов'язаний із порушенням толерантності до глюкози, інсулінорезистентністю, метаболічним синдромом і підвищеним ризиком цукрового діабету 2-го типу. **Мета:** вивчити роль рівня вітаміну D, пов'язаного з однонуклеотидними варіантами (single nucleotide variants — SNV) гена рецептора вітаміну D (vitamin D receptor — *VDR*), у розвитку метаболічно нездорового ожиріння (МНО) у дітей. **Матеріали та методи.** Обстежено 210 дітей з ожирінням віком 6–18 років. Основну групу (n = 125) становили пацієнти з МНО. Контрольну групу (n = 85) представили діти з метаболічно здоровим ожирінням (МЗО). У рандомізовано обраних 31 дитини основної та 21 дитини контрольної груп проведено повногеномне секвенування (CeGaT, Germany). В усіх дітей вимірювали рівень сироваткового 25-гідроксивітаміну D (Synevo, Ukraine). Для верифікації результатів розраховували коефіцієнт кореляції Спірмена (r) і p-значення для кожної змінної, а також проводили біоінформаційний аналіз. **Результати.** Середній рівень 25-гідроксивітаміну D у сироватці крові був вірогідно нижчим у пацієнтів із МНО і становив 14,57 ± 1,63 нг/мл, а в дітей із МЗО — 28,82 ± 1,93 нг/мл (t = 5,64; p = 0,00061). При МНО рівень 25-гідроксивітаміну D у сироватці пов'язаний з наступними предикторами (p < 0,05). Високозначущі фактори ($0,7 \le |r| < 1$): остеопенія (r = –0,73). Фактори середньої значущості ($0,3 \le |r| < 0,7$): пролактинемія (r = –0,57); індекс співвідношення окружності талії до зросту > 0,5 (r = –0,41); АА генотип SNP *VDR* rs12721365 (r = –0,41) та АА генотип SNP *VDR* rs2228572 (r = –0,39); метаболічно-асоційована жирова хвороба печінки (r = –0,39); фізіологічна постпрандіальна глікемія (r = 0,38); рівень інтерлейкіну-1β (r = –0,36); тригліцеридемія (r = –0,34); індекс маси тіла (r = –0,33); адипонектинемія (r = 0,32); артеріальна діастолічна гіпертензія (r = –0,32). Низькозначущі фактори ($0 < |r| < 0,3$): синдром полікістозних яєчників (r = –0,28); GG генотип SNP *VDR* rs2228570 (r = 0,27); окружність талії (r = –0,27); екстремальне ожиріння (r = –0,27); чоловіча стать (r = 0,26); окружність стегон (r = –0,24); рівні ліпопротеїнів високої щільності (r = 0,24); гамма-глутамілтранспептидази сироватки (r = –0,23); вільного тироксину (r = 0,22); тиреотропного гормону (r = –0,22); вільного трийодтироніну (r = 0,2). **Висновки.** Розвиток кардіометаболічного ризику та дефіциту вітаміну D у дітей із ожирінням пов'язують із наявністю генотипів AA/AG SNV *VDR* rs12721365, rs2228572, rs2228570.

Ключові слова: діти; метаболічно нездорове ожиріння; ген рецептора вітаміну D; однонуклеотидні варіанти; 25-гідроксивітамін D