Vitamin D In Pediatric Patients With Obesity And Arterial Hypertension

Živa Radulović (zivaaradulovic@gmail.com)
University of Maribor
Zarja Polak Zupan
University of Maribor
Aljoša Tomazini
University of Maribor
Nataša Marčun Varda
University Medical Centre Maribor

Research Article

Keywords: arterial hypertension, vitamin D, obesity, triglycerides

Posted Date: June 24th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-642607/v1

Abstract

Aim

The purpose of this study was finding potential discrepancies in vitamin D levels between different groups: overweight children with hypertension, normal-weight children with hypertension, overweight children and normal-weight children without hypertension –control group. We also wanted to determine whether there are correlations between vitamin D levels and other clinical laboratory parameters, to evaluate the need for substitution.

Methods

We measured vitamin D, homocysteine, total cholesterol, HDL, LDL, triglycerides, uric acid, glucose, apolipoprotein A1, apolipoprotein B, alkaline phosphatase, calcium, phosphate and magnesium serum levels in all groups. We also took anthropometric measurements (body weight, height, BMI) and observed patients' blood pressure. The results were analyzed with SPSS statistic tool with the use of independent t-test, Pearson correlation test and multi-variate analysis of variance (MANOVA).

Results

The study included 175 children between 5 and 18 years of age. 57 were healthy (group A – control group), 41 normal-weight with hypertension (group B), 44 overweight with hypertension (group C) and 33 overweight (group D). The results showed statistically significant distinction in values of vitamin D between all groups -– A and B ($p = 0.003$), A and C ($p = 0.000$), A and D ($p = 0.000$), B and D ($p = 0.043$), B and C (0.030), except for groups C and D ($p = 0.830$). There were statistically significant correlations between vitamin D and BMI ($r=-0.196$, $p = 0.010$), systolic pressure ($r=-0.190$, $p = 0.002$), diastolic pressure ($r=-0.149$, $p = 0.050$), homocysteine ($r=-0.208$, $p = 0.007$), triglycerides ($r=-0.196$, $p = 0.011$) and apolipoprotein A1 ($r = 0.222$, $p = 0.007$) among all groups.

Conclusion

The pilot study shows significant differences in serum vitamin D levels between all groups of children, apart from groups C and D. these results, combined with statistically significant correlations between vitamin D and systolic and diastolic blood pressure suggest the need for monitoring and potential substitution of vitamin D in in pediatric patients with hypertension and/or overweight children.

Introduction

Vitamin D is one of the most vital elements in the human body as it interferes with many physiological and, in some cases, pathological processes. Its role in bone metabolism has long been recognized,

however, newer studies have also revealed its importance in many other processes, such as autoimmunity, inflammation, angiogenesis as well as arterial hypertension. (2). There is also recent evidence of correlations between vitamin D and other important parameters and determinants of health in adults and children (3, 4).

The prevalence of childhood obesity in developed countries is still increasing, and the same goes for obesity-related health problems (5). The studies so far have shown vitamin D deficiency in overweight children, which is suggested to be the consequence of volume dilution and reduced sunlight exposure, which can further accelerate pathological processes. Because of large differences in weight between children of different sex and ages, we used body mass index percentiles for the purpose of our study, so we could compare measurements more accurately. The causes of obesity can be mainly attributed to lifestyle factors, which include over-eating and under-exercising, but they can also have genetic and hormonal basis (6, 7).

Arterial hypertension is also not uncommon in children. It affects 1–4 % of children, either as primary hypertension, which results from unhealthy lifestyle and genetic predispositions, or as secondary hypertension, which can be caused by different, most often nephrological, diseases. The former is more common in older children. On the other hand, different diseases can affect children of any age, therefore secondary hypertension can occur at any time (8). The studies have concluded that children with lower vitamin D levels have significantly higher blood pressure. This is the consequence of the effect vitamin D has on lowering the activity of the renin–angiotensin hormone system. It also affects many other parameters and risk factors such as blood lipid parameters through its actions on the vitamin D receptor (VDR) (9, 10).

As a result, we can see how recognizing the key role of vitamin D in various pathological processes can help us understand and potentially treat different pathologies, some of which that start in early childhood and can affect health much sooner than previously expected (10).

The purpose of this study was to find potential discrepancies in vitamin D serum levels between three groups of patients: overweight children, normal-weight children with hypertension and overweight children with hypertension. We also wanted to determine whether there are any correlations between vitamin D and other clinical laboratory parameters, to evaluate the need for substitution.

Materials And Methods

The study included 175 children between 5 and 18 years of age. 57 were healthy, 41 had hypertension, 44 were overweight with hypertension and 33 were just overweight. The measurements were obtained between November 2019 and November 2020 under the supervision of the Department of Paediatrics, University Medical Centre Maribor. The study was approved by Ethics Committee of the University Medical Centre Maribor in November 2019. All methods were carried out in accordance with relevant guidelines and regulations. We have obtained an informed consent from all parents and/or legal guardians of the children that have participated in the study.

The blood samples were obtained from children in the fasted state and were used to determine specific laboratory parameters under standard procedures: homocysteine, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides (TG), uric acid, glucose, apolipoprotein A1 (apo A), apolipoprotein B (apo B), alkaline phosphatase, calcium, phosphate, and magnesium.

We also took anthropometric measurements (body weight and height) and calculated every patient's body mass index (BMI). We measured blood pressure under the Second Task Force recommendations, which we also used in diagnosing our patients (11). We also conducted ambulatory 24-hour blood pressure monitoring (8). The BMI scores were modified to reflect accurate percentiles for patients' sex and age (12, 13). Serum vitamin D levels were determined through standard methods (14).

The results were statistically analyzed with the help of SPSS Statistics software (IBM, version 25) using Pearson correlation test, multi-variate analysis of variance (MANOVA) and independent samples t-test. A value of $p < 0.05$ was considered statistically significant.

Results

The study included 175 children and adolescents (76 girls and 99 boys) between 5 and 18 years of age. Among these, 57 were healthy children that represented our control group (group A). Group B was comprised of 41 children with hypertension, group C included 44 overweight children with hypertension and group D was represented by 33 overweight children with normal blood pressure. The descriptive statistics of each group and parameters observed are presented in Tables 1–4. Tables 2–4 include comparison of variables with the control group, with independent samples t-test in the last columns.

Table 1
Descriptive statistics of the control group (group A); BMI Percentile = body mass index percentile, LDL cholesterol = low-density lipoprotein cholesterol, HDL cholesterol = high-density lipoprotein cholesterol, TG = triglycerides, ApoA = apolipoprotein A1, ApoB = apolipoprotein B.

Variable	Median (minimum, maximum)	Interquartile range
Age [years]	14.0 (6.0, 18.0)	16.5
Vitamin D [nmol/L]	75.0 (35.9, 148.5)	35.4
BMI percentile	63.0 (2. 95)	55.0
Systolic pressure [mmHg]	111.0 (97.0, 130.0)	11.0
Diastolic pressure [mmHg]	65.0 (54.0, 94.0)	4.5
Homocysteine [µmol/L]	7.1 (1.8, 15.2)	3.65
Total cholesterol [mmol/L]	4.3 (2.9, 6.95)	1.04
LDL cholesterol [mmol/L]	2.6 (1.38, 4.9)	0.9
HDL cholesterol [mmol/L]	1.55 (0.76, 2.25)	0.50
TG [mmol/L]	0.775 (0.34, 1.67)	0.61
Uric acid [µmol/L]	264.0 (121.0, 424.0)	111
Glucose [mmol/L]	4.8 (1.42, 6.4)	0.6
ApoA [g/L]	1.45 (1.04, 6.87)	0.35
ApoB [g/L]	0.66 (0.4, 1.10)	0.16
Alkaline phosphatase [µkat/L]	3.2 (1.04, 6.87)	3.05
Calcium [mmol/L]	2.4 (2.23, 2.75)	0.11
Phosphate [mmol/L]	1.39 (0.85, 1.85)	0.37
Magnesium [mmol/L]	0.9 (0.73, 1.28)	0.08

Table 2

Descriptive statistics of the patients with hypertension (group B); BMI Percentile = body mass index percentile, LDL cholesterol = low-density lipoprotein cholesterol, HDL cholesterol = high-density lipoprotein cholesterol, TG = triglycerides, ApoA = apolipoprotein A1, ApoB = apolipoprotein B.

Variable	Median (minimum, maximum)	Interquartile range	p-value
Age [years]	16.0 (8.0, 18.0)	3.5	0.002
Vitamin D [nmol/L]	60.0 (7.5, 113.2)	41.05	0.003
BMI percentile	74.0 (5.0, 94.0)	44.0	0.114
Systolic pressure [mmHg]	132.0 (124.0, 148.0)	7.0	0.000
Diastolic pressure [mmHg]	74.0 (61.0, 93.0)	8.5	0.000
Homocysteine [µmol/L]	7.9 (3.0, 18.2)	3.3	0.139
Total cholesterol [mmol/L]	4.14 (2.78, 6.10)	0.84	0.051
LDL cholesterol [mmol/L]	2.4 (1.5, 4.0)	0.83	0.091
HDL cholesterol [mmol/L]	1.45 (0.89, 2.53)	0.39	0.130
TG [mmol/L]	0.92 (0.45, 2.61)	0.48	0.089
Uric acid [µmol/L]	323.0 (101.0, 436.0)	132.0	0.006
Glucose [mmol/L]	4.7 (4.1, 5.6)	0.45	0.628
ApoA [g/L]	1.41 (0.99, 1.94)	0.22	0.101
ApoB [g/L]	0.69 (0.47, 1.1)	0.16	0.678
Alkaline phosphatase [µkat/L]	2.78 (0.91, 9.64)	3.58	0.995
Calcium [mmol/L]	2.42 (2.22, 2.64)	0.12	0.110
Phosphate [mmol/L]	1.25 (0.74, 1.80)	0.20	0.043
Magnesium [mmol/L]	0.9 (0.67, 1.05)	0.07	0.673

Table 3
Descriptive statistics of the overweight patients with hypertension (group C); BMI Percentile = body mass index percentile, LDL cholesterol = low-density lipoprotein cholesterol, HDL cholesterol = high-density lipoprotein cholesterol, TG = triglycerides, ApoA = apolipoprotein A1, ApoB = apolipoprotein B.

Variable	Median (minimum, maximum)	Interquartile range	p-value
Age [years]	14.0 (5.0, 18.0)	5.75	0.672
Vitamin D [nmol/L]	51.2 (13.5, 90.9)	21.05	0.000
BMI percentile	99.0 (91.0, 99.0)	2.75	0.000
Systolic pressure [mmHg]	127.5 (110.0, 140.0)	8.5	0.000
Diastolic pressure [mmHg]	70.0 (55.0, 77.0)	9.0	0.000
Homocysteine [µmol/L]	9.85 (5.7, 9.9)	0.45	0.000
Total cholesterol [mmol/L]	4.66 (2.29, 6.94)	1.12	0.472
LDL cholesterol [mmol/L]	3.05 (0.9, 5.10)	0.95	0.074
HDL cholesterol [mmol/L]	1.25 (0.8, 2.66)	0.56	0.002
TG [mmol/L]	1.13 (0.30, 4.18)	0.58	0.001
Uric acid [µmol/L]	344.0 (187.0, 534.0)	100.0	0.000
Glucose [mmol/L]	4.7 (3.6, 5.9)	0.6	0.666
ApoA [g/L]	1.36 (1.07, 1.77)	0.22	0.029
ApoB [g/L]	0.83 (0.29, 1.33)	0.28	0.003
Alkaline phosphatase [µkat/L]	2.63 (0.98, 6.24)	2.82	0.649
Calcium [mmol/L]	2.40 (2.20, 2.52)	0.11	0.741
Phosphate [mmol/L]	1.33 (0.75, 9.0)	0.45	0.472
Magnesium [mmol/L]	0.93 (0.71, 1.07)	0.10	0.228

Table 4

Descriptive statistics of the overweight patients (group D); BMI Percentile = body mass index percentile, LDL cholesterol = low-density lipoprotein cholesterol, HDL cholesterol = high-density lipoprotein cholesterol, TG = triglycerides, ApoA = apolipoprotein A1, ApoB = apolipoprotein B.

Variable	Median (minimum, maximum)	Interquartile range	p-value
Age [years]	14.0 (7.0, 18.0)	5.5	0.299
Vitamin D [nmol/L]	50.0 (7.5, 83.9)	28.0	0.000
BMI percentile	97.0 (86.0, 99.0)	5.5	0.000
Systolic pressure [mmHg]	120.0 (103.0, 135.0)	15.5	0.079
Diastolic pressure [mmHg]	66.0 (47.0, 79.0)	7.5	0.732
Homocysteine [µmol/L]	9.6 (7.6, 11.0)	0.79	0.000
Total cholesterol [mmol/L]	4.61 (3.35, 6.33)	1.10	0.830
LDL cholesterol [mmol/L]	2.95 (1.90, 4.50)	0.86	0.211
HDL cholesterol [mmol/L]	1.28 (0.81, 2.23)	0.38	0.001
TG [mmol/L]	1.1 (0.57, 3.31)	0.51	0.022
Uric acid [µmol/L]	332.0 (166.0, 477.0)	128.0	0.001
Glucose [mmol/L]	4.8 (3.6, 5.4)	0.5	0.957
ApoA [g/L]	1.38 (1.06, 1.62)	0.21	0.036
ApoB [g/L]	0.82 (0.40, 1.58)	0.21	0.009
Alkaline phosphatase [µkat/L]	2.27 (1.36, 6.83)	3.08	0.858
Calcium [mmol/L]	2.4 (1.57, 2.54)	0.15	0.173
Phosphate [mmol/L]	1.4 (0.77, 2.44)	0.32	0.471
Magnesium [mmol/L]	0.89 (0.32, 1.32)	0.09	0.648

Table 5

Comparison of parameters between the groups (independent sample T-test). Control group (A), children with hypertension (B), overweight children with hypertension (C) and overweight children with normal blood pressure (D); BMI Percentile = body mass index percentile, LDL cholesterol = low-density lipoprotein cholesterol, HDL cholesterol = high-density lipoprotein cholesterol, TG = triglycerides, ApoA = apolipoprotein A1, ApoB = apolipoprotein B.

	A and B	A and C	A and D	C and D	B and D	B and C	Total value of p
Vitamin D [nmol/L]	p = 0.003	p = 0.000	p = 0.000	p = 0.830	p = 0.043	p = 0.030	0.000
Systolic pressure [mmHg]	p = 0.000	p = 0.000	p = 0.079	p = 0.000	p = 0.000	p = 0.000	0.000
Diastolic pressure[mmHg]	p = 0.000	p = 0.000	p = 0.732	p = 0.026	p = 0.000	p = 0.001	0.000
Homocysteine [µmol/L]	p = 0.139	p = 0.000	p = 0.000	p = 0.658	p = 0.000	p = 0.001	0.000
Total cholesterol [mmol/L]	p = 0.051	p = 0.472	p = 0.830	p = 0.637	p = 0.045	p = 0.015	0.314
LDL cholesterol[mmol/L]	p = 0.083	p = 0.077	p = 0.211	p = 0.552	p = 0.004	p = 0.001	0.019
HDL cholesterol[mmol/L]	p = 0.130	p = 0.002	p = 0.001	p = 0.727	p = 0.040	p = 0.099	0.001
TG [mmol/L]	p = 0.103	p = 0.001	p = 0.022	p = 0.184	p = 0.503	p = 0.055	0.001
Glucose [mmol/L]	p = 0.628	p = 0.666	p = 0.957	p = 0.572	p = 0.517	p = 0.975	0.639
ApoA [g/L]	p = 0.101	p = 0.044	p = 0.049	p = 0.777	p = 0.132	p = 0.232	0.075
ApoB [g/L]	p = 0.678	p = 0.003	p = 0.009	p = 0.862	p = 0.019	p = 0.008	0.003
Alkaline phosphatase[µkat/L]	p = 0.995	p = 0.649	p = 0.858	p = 0.836	p = 0.888	p = 0.742	0.487
Uric acid [µmol/L]	p = 0.006	p = 0.000	p = 0.001	p = 0.461	p = 0.545	p = 0.154	0.000
Calcium [mmol/L]	p = 0.110	p = 0.741	p = 0.173	p = 0.222	p = 0.041	p = 0.063	0.082
Phosphate [mmol/L]	p = 0.043	p = 0.472	p = 0.471	p = 0.347	p = 0.389	p = 0.209	0.597
Magnesium [mmol/L]	p = 0.673	p = 0.228	p = 0.648	p = 0.207	p = 0.858	p = 0.099	0.316

Table 5 presents comparison of variables between the groups studied. The largest number of statistically significant differences was found between the control group and groups of overweight patients with hypertension and overweight patients.

Table 6
Correlation between vitamin D levels and different parameters in all of the observed groups; BMI Percentile = body mass index percentile, LDL cholesterol = low-density lipoprotein cholesterol, HDL cholesterol = high-density lipoprotein cholesterol, TG = triglycerides, ApoA = apolipoprotein A1, ApoB = apolipoprotein B.

Variable	Vitamin D
BMI	r=-0.196, p = 0.010
Systolic pressure [mmHg]	r=-0.190, p = 0.002
Diastolic pressure[mmHg]	r=-0.149, p = 0.050
Homocysteine [µmol/L]	r=-0.208, p = 0.007
Total cholesterol [mmol/L]	r = 0.040, p = 0.604
LDL cholesterol[mmol/L]	r=-0.017, p = 0.832
HDL cholesterol [mmol/L]	r = 0.124, p = 0.115
TG [mmol/L]	r=-0.196, p = 0.011
Glucose [mmol/L]	r=-0.090, p = 0.249
ApoA [g/L]	r = 0.222, p = 0.007
ApoB [g/L]	r=-0.042, p = 0.621
Alkaline phosphatase [µkat/L]	r = 0.096, p = 0.258
Uric acid [µmol/L]	r=-0.156, p = 0.060
Calcium [mmol/L]	r = 0.050, p = 0.950
Phosphate [mmol/L]	r=-0.104, p = 0.189
Magnesium [mmol/L]	r=-0.027, p = 0.730

Table 6 presents correlations between different variables and vitamin D in all the observed patients. Statistically significant correlations were found between vitamin D levels and body mass index, systolic pressure, diastolic pressure, homocysteine, triglycerides, and apolipoprotein A1.

Table 7
Vitamin D values in comparison to BMI percentile. Obesity is defined as a BMI at or above the 95th percentile.

	BMI below 85th percentile	BMI between 85th and 95th percentile	BMI above 95th percentile
Minimal vitamin D value [nmol/l]	7.5	18	7.5
Maximal vitamin D value [nmol/l]	148.5	126.8	90.9
Average vitamin D value [nmol/l]	70.84	64.89	52.1
Median [nmol/l]	71.0	58.0	48.6

Table 7 presents vitamin D levels in relation to different BMI values. The higher the BMI, the lower the average levels of vitamin D are. There is statistically significant difference between the group with BMI below the 85th percentile and the group with BMI above the 95th percentile ($p = 0.000$). There is also statistically significant difference between the patients whose BMI ranges from the 85th to 95th percentile and the group of patients with BMI above the 95th percentile ($p = 0.004$). There was no statistically significant difference between the group with BMI below the 85th percentile and the group with BMI ranging from the 85th to 95th percentile ($p = 0.229$).

By using the multi-variate analysis of variables, we concluded that the variables in our model can be used to explain 40.3% of the phenotype. The model is therefore statistically significant ($p = 0.001$).

Table 8
Model of multi-variate analysis of variables which proved significant in univariate analysis; BMI percentile = body mass index percentile, TG = triglycerides, ApoA = apolipoprotein A1.

Variable	F value	Sig.
BMI percentile	38.668	0.000
Systolic pressure	54.179	0.000
Diastolic pressure	10.082	0.000
Homocysteine	28.087	0.000
TG	2.939	0.036
ApoA	0.921	0.433

Table 8 presents a model of multi-variate analysis of variables that proved statistically significant in the univariate analysis.

Discussion

The purpose of this study was to find potential discrepancies and correlations between vitamin D levels and different parameters in groups of children with hypertension, overweight children, overweight children with hypertension and healthy control group. We discovered statistically significant differences in vitamin D levels in all groups in relation to the control group. There were also statistically significant differences between groups of overweight children and children with hypertension, as well as between children with hypertension and overweight children with hypertension. There were no significant differences in vitamin D levels between the groups of overweight children (group C and D). Our findings suggest there is a link between obesity and arterial hypertension, as well as vitamin D, which has also been proven by other studies in this department (10, 15, 16). Considering the statistically significant differences between patients with hypertension and both groups of overweight patients (group C and D), we conclude that obesity presents a bigger negative predictive factor for vitamin D values than hypertension. The effects of both factors combined were not proven to affect vitamin D values any more than each individual factor. Significantly low levels of vitamin D in children with hypertension and normal BMI suggest vitamin D affects blood pressure independently of obesity. Similar observations have been made in other studies (10, 15, 16, 17).

We discovered statistically significant correlations between vitamin D and various parameters in our research sample of 175 children. The correlation between BMI, measured in percentiles, and vitamin D was statistically significant, which supports our previous findings when comparing individual groups of children. The lower levels of vitamin D in overweight children are probably the result of volume dilution as well as reduced sunlight exposure (18). When supplementing vitamin D in overweight children, in order to achieve appropriate vitamin D serum levels, we usually have to administer higher doses than we would when treating children who are not overweight (6, 16).

Another statistically important correlation, albeit smaller, was discovered between vitamin D and systolic blood pressure. The reason for that likely being the presence of VDR in endothelial and smooth-muscle cells of blood vessels and cardiomyocytes. Studies in recent years have provided evidence of the role vitamin D has in reducing high blood pressure. This is achieved through inhibition of the renin-angiotensin hormone system, modulation of the endothelial function and reduction of oxidative stress in blood vessels.

Together with the fact that there is a statistically significant difference between the group of normal-weight children with hypertension and the control group, we can assume that vitamin D is a non-obesity-dependent negative predictive factor of arterial hypertension and that by supplementing it, we could potentially improve blood pressure. However, it is important to keep in mind that a healthy body weight is what helps maintaining sufficient levels of vitamin D in the first place (19).

Another correlation, which proved significant, was discovered between vitamin D and homocysteine, which is again in line with findings of other studies. This is most likely the consequence of vitamin D and its regulation of cystathionine-β-synthase (CBS), an enzyme which converts homocysteine into

cystathionine, which is further converted into cysteine. The net effect of this reaction is a reduction of total blood homocysteine. Because hyperhomocysteinemia can lead to endothelial disfunction, vitamin D can be seen as a potential protecting agent in preventing premature cardiovascular diseases (20, 21, 22).

We have noticed a statistically significant negative correlation between vitamin D and triglycerides (TG). Another negative correlation was found between vitamin D and LDL cholesterol and a positive one between vitamin D and HDL cholesterol, however it was statistically unsignificant. These results are in line with findings of other similar studies which proved correlation between low serum vitamin D levels and blood lipid abnormalities in children (16, 19). Statistically significant non-obesity-dependent correlation was established between vitamin D and TG, which means vitamin D is an independent negative predictive factor of hypertriglyceridemia. This is likely because vitamin D lowers fatty acid absorption in the intestine by increasing the absorption of calcium and higher calcium levels promote the hepatic conversion of cholesterol into bile. Vitamin D also reduces lipogenesis and promotes lipolysis through parathyroid hormone (PTH) inhibition, which additionally helps regulate blood lipid parameters (21, 22, 23).

There was a statistically significant positive correlation between apolipoprotein A1 (apo A) and vitamin D. Apo A is one of the main components of HDL cholesterol, its presence is therefore an indicator of cardiovascular health. In terms of the role of apo A as a marker of cardiovascular health it is important to consider its relationship with apo B because higher values of the latter indicate an increased risk for cardiovascular disease. In our study we discovered a negative correlation between vitamin D and apo B, though unsignificant. These results reflect the role of vitamin D in regulating the hepatic synthesis of apo A through its action on the VDR receptor (23, 24, 25).

The negative correlation between vitamin D and uric acid, which we found to be just slightly below the limit of statistical significance, is most likely the consequence of 1-alpha-hydroxylase inhibition which is caused by higher levels of uric acid. 1-alpha-hydroxylase is an enzyme that converts 25(OH)D into its biologically active form $1,25(OH)_2D$ and therefore promotes its actions (28).

Despite many positive and promising findings of our study, there are still some things which could be improved. Ideally, the groups would be comprised of equal number of patients of the same sex and age. This would be very difficult to achieve in our situation, as we recruited our patients in an anterograde fashion. Another thing, which could provide us with more relevant results would be to include a larger number of participants.

We can conclude with relative certainty that the results of our study are in line with the findings of other recent studies, whether regional or international, and that they provide enough evidence to the theory that maintaining a healthy body weight and appropriate vitamin D levels is of vital importance, especially in patients subjected to cardiovascular diseases.

Conclusion

Our pilot study has shown statistically significant differences in vitamin D serum levels between groups of children who were overweight, normal-weight with hypertension, overweight with hypertension and the control group. There was also statistically significant correlation between vitamin D and blood pressure, BMI, and some blood lipid parameters. Our findings suggest the need for further research into vitamin D and its role in protecting cardiovascular health, as well as its use in therapeutic and preventive care for children with hypertension and/or obesity.

Declarations

AUTHOR'S CONTRIBUTION

All authors read and approved the final manuscript.

ŽR: measured the patients, collected the data, analyzed and interpreted the data, wrote the manuscript.

AT: measured the patients, collected the data, analyzed and interpreted the data, wrote the manuscript.
ZPZ: measured the patients, collected the data, analyzed and interpreted the data, wrote the manuscript.

NMV: planned the study, provided the patients, supervised and guided the study, revised the data analysis and the written manuscript, approved the version to be published.

STATEMENT OF COMPLIANCE WITH ETHICAL STANDARDS

The study has been approved by Ethics Committee of the University Medical Centre Maribor in the year 2019.

CONFLICT OF INTEREST AND FINANCIAL DISCLOSURE STATEMENT

The authors declare no conflict of interest and no specific funding.

References

1. Umar M, Sastry KS, Chouchane AI. Role of vitamin D beyond the skeletal function: a review od the molecular and clinical studies. Int J Mol Sci. 2018; 19(6): 1618.
2. Gallieni M, Cozzolino M, Fallabrino G, Pasho S, Olivi L, Brancaccio D. Vitamin D: physiology and pathophysiology. Int J Artif Organs. 2009; 32(2): 87–94.
3. Yang CY, Leung PSC, Adamopoulos IE, Gershwin ME. The implication of vitamin D and autoimmunity: a comperhensive review. Clin Rev Allergy Immunol. 2013; 45(2): 217–26.
4. Braegger C, Campoy C, Colomb V. Vitamin D in the healthy European paediatric population. J Pediatr Gastroenterol Nutr. 2013; 56(6): 692–701.
5. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes and consequences. J Family Med Prim Care. 2015; 4(2): 187–92.

6. Peterson CA, Belenchia AM. Vitamin D deficiency & childhood obesity: a tale of two epidemics. Mo Med. 2014; 111(1): 49–53.
7. Zakharova I, Klimov L, Kuryaninova V, Nikitina I, Malyavskaya S, Dolbnya S, et al. Vitamin D insufficiency in overweight and obese children and adolescents. Front Endocrinol (Lausanne). 2019; 10: 103.
8. Rus R, Marčun Varda N. Novelties in the management of arterial hypertension in children and adolescents in accordance with US (2017) and European guidelines (2016). Zdrav Vestn. 2020; 89(9–10): 498–514.
9. Guoying W, Liu X, Bartell TR, Pearson C, Cheng TL, Wang X. Vitamin D trajectories from birth to early childhood and elevated systolic blood pressure during childhood and adolescence. Hypertension. 2019; 74: 421–30.
10. Kao KT, Abidi N, Ranasinha S. Low vitamin D is associated with hypertension in paediatric obesity. J Paediatr Child Health. 2015; 51(12): 1207–13.
11. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the diagnosis and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555–76.
12. Heaney RP. Vitamin D in health and disease. Clin J Am Soc Nephrol. 2008; 3(5): 1535–41.
13. Kromeyer-Hauschild K, Wabitsch M, Kunze D, Geller F, Geiß HC, Hesse V, et al. Perzentile für den Body-mass-Index für das Kindes- und Jugendalter unter Heranziehung verschiedener deutscher Stichproben. Monatsschr Kinderheilkd. 2001; 149: 807–18.
14. Pilz S, Zitterman A, Trummer C, Theiler-Schwetz V, Lerchbaum E, Keppel MH, et al. Vitamin D testing and treatment: a narrative review of current evidence. Endocr Connect. 2019; 8 (2): 27 – 43.
15. Nair R, Maseeh A. Vitamin D: the “sunshine” vitamin. J Pharmacol Pharmacother. 2012; 3(2): 118–26.
16. Kim MR, Jeong SJ. Relationship between vitamin D level and lipid profile in non-obese children. Metabolites. 2019; 9(7): 125.
17. Min B. Effects of vitamin D on blood pressure and endothelial function. Korean J Physiol Pharmacol. 2013; 17(5): 385–92.
18. Patel N, Walker N. Clinical assessment of hypertension in children. Clin Hypertens. 2016; 22: 15.
19. Greene-Finestone LS, Garriguet D, Brooks S, Langlois K, Whiting SJ. Overweight and obesity are associated with lower vitamin D status in Canadian children and adolescents. Paediatr Child Health. 2017; 22(8): 438–44.
20. Drincic AT, Armas LAG, Van Diest EE, Heaney RP. Volumetric dilution, rather than sequestration best explains the low vitamin D status of obesity. Obesity (Silver Spring). 2012; 20(7): 1444–8.
21. Vaidya A, Forman JP. Vitamin D and hypertension. Hypertension. 2010; 56: 774–9.
22. Amer M, Qayyum R. The relationship between 25-hydroxyvitamin D and homocysteine in asymptomatic adults. J Clin Endocrinol Metab. 2014; 99(2): 633–8.

23. Dibaba DT. Effect of vitamin D supplementation on serum lipid profiles: a systematic review and meta-analysis. Nutr Rev. 2019; 77(12): 890–902.
24. Glueck CJ, Jetty V, Rothschild M, Duhon G, Shah P, Prince M. Association between serum 25-hydroxyvitamin D and lipids, lipoprotein cholesterols, and homocysteine. N Am J Med Sci. 2016; 8(7): 284–90.
25. Jaimundal S, Wehmeier K, Mooradian AD, Hass MJ. The emerging evidence for vitamin D-mediated regulation of apolipoprotein A-I synthesis. Nutr Res. 2011; 31(11): 805–12.
26. Turan S, Topcu V, Gokce I, Guran T, Atay Z, Omar A. Serum alkaline phosphatase levels in healthy children and evaluation of alkaline phosphatase z-scores in different types of rickets. J Clin Res Pediatr Endocrinol. 2011; 3(1): 7–11.
27. Kubota M. Hyperuricemia in children and adolescents: present knowledge and future directions. J Nutr Metab. 2019; 2019: 3480718.
28. Thakkinstian A, Anothaisintawee T, Chailurkit L, Ratanachaiwong W, Yamwong S, Sritara P, Ongphiphadhanakul B. Potential causal associations between vitamin D and uric acid: bidirectional mediation analysis. Sci Rep. 2015; 5: 14528.