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Association of Vitamin D Levels with the Metabolic Profile and Sexual Maturation Stage of Adolescents

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Abstract

The deficiency of Vitamin D (VD) is widely prevalent worldwide in adults, but many studies show that this deficiency also affects adolescents and may be considered a global public health problem. The VD levels are particularly significant in adolescents since it influences several aspects of growth, development, and puberty. During this phase of life, both girls and boys develop reproductive aspects, and secondary sexual characteristics and the adequate nutritional status appear to be the prerequisite for normal pubertal development. Due to the importance of VD in adolescents, the objective of this study was to investigate the association of the levels of this vitamin with glycemic, lipid, and anthropometric profile and sexual maturation stages of adolescents. Anthropometric (weight and height) and biochemical (fasting glycemia, total cholesterol, HDL-c, LDL-c, and triglycerides) data and VD levels were collected in 67 adolescents. 66% of the adolescents showed VD sufficiency, 28% insufficiency, and 6% showed the deficiency. There was a significant difference in VD levels between the stages of sexual maturation for boys and girls. Overweight patients had lower serum VD levels. The correlation analysis indicated a positive correlation between VD and fasting glycemia and HDL-c, but with no significant difference. A negative correlation was observed between VD and cholesterol, LDL-c and triglycerides, but also with no significant difference. Once VD is crucial for bone health, and as it seems it is necessary to the homeostasis of glycemia, lipids, and body weight, we suggest that more studies should be conducted to confirm the precise role of this vitamin in the promotion and maintenance of health in this population.

Keywords

Adolescents, Vitamin D, Glycemia, Lipids, Obesity

1. Introduction

Vitamin D (VD) is a fat-solublehormone that can be obtained from the diet or is synthesized in the skin under sunlight exposition. When produced in the skin, the 7-dehydrocholesterol undergoes activation by ultraviolet light, and further modifications occur in kidney and liver to produce VD3 (1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$) [1] [2].

In addition to being involved in skeletal health and calcium and phosphate homeostasis, VD also exhibits other essential functions, and its deficiency has been associated with altered insulin secretion, insulin resistance, type 2 diabetes (DM), obesity, dyslipidemia, high blood pressure and cardiovascular diseases [3] [4] [5].

The deficiency of VD is widely prevalent worldwide in adults, but many studies show that this deficiency also affects children and adolescents and may be considered a global public health problem [6]. Low VD status is related to the way of life of modern communities leading people to spend most of their time indoors and without sunlight exposition [7].

The VD levels are particularly significant in adolescents since it influences several aspects of growth, development, and puberty. During this phase of life, both girls and boys develop reproductive aspects, and secondary sexual characteristics and the adequate nutritional status appear to be the prerequisite for normal pubertal development [8] [9].

Due to the importance of VD in adolescents, the objective of this study was to investigate the association of the levels of VD with the glycemic, lipid, and anthropometric profile and sexual maturation stages of adolescents.

2. Methods

This study is primary, analytical, observational, transversal, retrospective, quantitative and exploratory. The study population was composed of adolescents attending a Pediatric Center, located in the city of Marília, SP, Brazil.

We selected 67 patients who met the inclusion criteria: adolescents 10 to 19 years old, both sexes, who presented in the medical record, the results of the parameters required in our research. The exclusion criteria were patients presenting liver or renal diseases, resection of the jejunum, diseases that promote biliary flow alterations (cholestasis, decrease in the enterohepatic circulation of bile salts), non-absorbent diseases (celiac disease, Crohn's disease, short bowel syndrome), lupus erythematosus, hypo or hyperthyroidism, and patients that were ingesting vitamin supplements.

Anthropometric data (weight and height), VD levels, fasting glycemia, total

cholesterol, HDL-c, LDL-c, and triglycerides were collected. The classification of the stages of sexual maturation and the anthropometric data were previously collected and evaluated by the physician responsible for the Pediatric Center and subsequently recorded in the patient's chart. The nutritional state was evaluated according to the Body Mass Index/Age (Z Score). For the stage of sexual maturation, stage 1 corresponds to pre-pubertal development and growth, whereas stages 2 to 4 correspond to the progression from puberty to full maturation, and stage 5 includes the finalization of the sexual maturation [10].

As for the stage of sexual maturation, the adolescents were classified according to the Tanner criteria by medical evaluation and later they were grouped in three pubertal stages: Stage Tanner I (pre-pubertal); stage II - IV (pubertal) and stage V (post-pubertal). In this study, the adolescents were only in the pre-pubertal and pubertal stages.

VD wasclassifiedaccordingtoHolick *et al.* [11]. Value for sufficiency was 30 - 100 ng/mL; insufficiency was 21 - 29 ng/mL; deficiency was less than 20 ng/mL, and toxicity was higher than 100 ng/mL.

Approval for the execution of this study was provided by the Research Ethics Committee (University of Marilia, UNIMAR) under Protocol number 2,083,552 on 05/25/2017.

The statistical treatment of the quantitative data was performed with the support of the Bio Estat 5.0 program (Significance level of 5%). Test T of independence, Mann-Whitney, Anova 1 criteria and Pearson Correlation were used to study the parameters.

3. Results

The sample consisted of 67 adolescents (52.24% were female and 47.76% male). Regarding the classification of nutritional status according to BMI/AGE, 1.49% presented thinness, 52.24% presented eutrophy, 22.39% were overweight, and 23.88% presented obesity. Short stature for age was found in 2.99%, and 97.01% presented adequate height for age. The adolescents showed a mean body weight of 48.57 ± 13.96 kg. Body mass index (BMI) is shown in **Table 1**. This table also shows the results for VD levels and biochemical parameters.

According to the guidelines of VD, 66% of the adolescents showed VD sufficiency, 28% insufficiency, and 6% showed a deficiency. Test T indicated that there was no significant difference between VD levels in girls and boys.

There was a significant difference in VD levels between the stages of sexual maturation ($p < 0.0001$) for both males and females, as can we observe in **Table 2**.

Table 3 shows that the nutritional status of adolescents according to BMI/age interferes with serum VD levels, indicating a significant difference between them. Furthermore, overweight patients had lower serum VD levels. When comparing the distribution of VD levels and BMI/age in girls, there was no significant difference. However, when compared to boys, VD levels and BMI/age presented a significant difference, as can be observed in **Table 3**.

Table 1. Age, body weight, BMI, Vitamin D, anthropometricand biochemicalparameters of the studied adolescents.

Parameters	Total of adolescents		Girls		Boys	
	Mean ± SD	Median	Mean ± SD	Median	Mean ± SD	Median
Age (months)	144.24 ± 17.76	139.00	139.46 ± 17.76	137.00	149.47 ± 20.40	140.50
Weight (kg)	48.57 ± 13.96	46.50	45.27 ± 11.84	43.30	52.18 ± 15.34	53.50
BMI (kg/m²)	20.68 ± 3.85	20.08	20.27 ± 4.13	18.79	21.13 ± 3.52	20.58
Vitamin D (ng/mL)	33.66 ± 7.94	33.40	32.82 ± 7.58	31.70	34.57 ± 8.35	34.87
Fasting blood glucose (mg/dL)	90.27 ± 7.83	89.50	90.84 ± 6.84	91.00	89.67 ± 8.84	88.00
Total cholesterol (mg/dL)	166.27 ± 31.50	162.00	172.84 ± 35.30	166.00	159.09 ± 25.38	159.65
LDL-c (mg/dL)	97.64 ± 24.02	96.60	102.77 ± 26.67	100.90	92.04 ± 19.66	92.00
HDL-c (mg/dL)	51.53 ± 11.92	51.00	52.29 ± 14.73	51.00	50.69 ± 7.94	51.50
Triglycerides (mg/dL)	82.38 ± 37.51	75.00	85.50 ± 38.31	78.00	78.95 ± 36.92	71.00

BMC: Body Mass Index.

Table 2. Comparison of age, anthropometric and biochemical parameters in different stages of sexual maturation in girls and boys.

Parameters	Pre-pubertal (n = 7)		Pubertal (n = 28)		p-value
Girls	Mean ± SD	Median	Mean ± SD	Median	
Age (months)	137.25 ± 13.88	134.00	148.28 ± 7.73	149.00	0.0177
BMI (kg/m²)	21.85 ± 5.75	22.00	19.14 ± 3.57	18.00	0.0616
Vitamin D (ng/mL)	22.57 ± 3.82	24.00	34.89 ± 6.02	34.00	<0.0001*
Fasting blood glucose (mg/dL)	89.28 ± 5.46	92.00	90.90 ± 6.96	90.00	0.2867
Total cholesterol (mg/dL)	183.85 ± 31.74	179.00	169.96 ± 36.14	161.50	0.1798
LDL-c (mg/dL)	105.42 ± 24.22	102.00	101.78 ± 27.84	99.00	0.3767
HDL-c (mg/dL)	55.42 ± 9.58	54.00	51.28 ± 15.82	49.00	0.2573
Triglycerides (mg/dL)	107.57 ± 57.48	87.00	79.82 ± 30.85	71.00	0.0381*
Parameters	**Pre-pubertal (n = 7)**		**Pubertal (n = 25)**		**p-value**
Boys	Mean ± SD	Median	Mean ± SD	Median	
BMI (kg/m²)	22.42 ± 4.03	23.00	20.04 ± 3.27	20.00	0.0573
Age (months)	139.71 ± 11.96	141.00	152.20 ± 21.59	140.00	0.1635
Vitamin D (ng/mL)	22.57 ± 2.63	23.00	37.36 ± 6.19	36.00	<0.0001*
Fasting blood glucose (mg/dL)	88.57 ± 7.20	86.00	89.80 ± 9.32	88.00	0.3751
Total cholesterol (mg/dL)	166.28 ± 37.55	165.00	156.96 ± 21.38	159.00	0.3161
LDL-c (mg/dL)	98.14 ± 28.10	94.00	90.00 ± 16.86	89.00	0.1699
HDL-c (mg/dL)	47.57 ± 6.13	44.00	51.44 ± 8.20	53.00	0.1285
Triglycerides (mg/dL)	98.85 ± 56.78	84.00	73.20 ± 28.41	69.00	0.1635

BMI: Body Mass Index; *Level of Significance: $p \leq 0.05$.

Table 3. Vitamin D levels and BMI classifications.

Parameters	Underweight (n = 1)	Normal (n = 35)	Overweight (n = 15)	Obese (n = 16)	p-value
All		Mean ± SD			
Vitamin D (ng/mL)	49.66	34.87 ± 7.87	28.84 ± 7.60	34.51 ± 6.21	0.0302*
Variables	**Underweight** (n = 0)	**Normal** (n = 20)	**Overweight** (n = 9)	**Obese** (n = 6)	**p-value**
Girls		Mean ± SD			
Vitamin D (ng/mL)	0	34.15 ± 7.52	29.88 ± 8.19	30.50 ± 5.75	0.3083
Variables	**Underweight** (n = 1)	**Normal** (n = 15)	**Overweight** (n = 6)	**Obese** (n = 10)	**p-value**
Boys		Mean ± SD			
Vitamin D (ng/mL)	49.66	34.80 ± 8.64	26.33 ± 6.53	36.30 ± 5.35	0.0339*

BMI: Body Mass Index. *Level of Significance: $p \leq 0.05$.

When the variables were correlated (Figure 1) the data show a positive correlation between VD and fasting glycemia and between VD and HDL-c, but without significant difference. Serum levels of VD and their correlations with cholesterol, LDL-c, and triglycerides were negative, but also with no significant difference. The sample was divided by sex for the correlation of the variables, but all the results did not show a significant difference.

4. Discussion

In this study, we evaluated the association between VD levels with anthropometric and biochemical parameters and pubertal stage of adolescents. According to our results, overweight was present in 46.27%, and 34% presented VD deficiency or insufficiency. The VD values were statistically different according to the nutritional status of the BMI/age index, and reduced levels were observed in overweight patients.

Deficiency of VD is observed worldwide at any age. According to Saggese *et al.* [12], the prevalence of VD deficiency ranges from 9% to 18%, and hypovitaminosis may reach 51% to 61%. A meta-analysis with almost 15,000 European pediatric patients showed that the deficiency might reach 4% to 7% in children with 1 - 6 years; 1% to 8% in 7 - 14 years, and 12% to 40% in 15 - 18 years. Authors suggested that particular attention should be directed to infants and adolescents. These data are similar to our results. The pre-pubertal period is the phase that precedes puberty, and it is associated with accumulation of adipose tissue as a form of energy storage for later growth. As the VD is associated with adipose tissue, its levels may be modified at this stage of life [13].

Other authors also showed that VD is associated with obesity in adolescents. It is still not clear if the reduced levels of VD trigger or are a consequence for obesity. However, the increase in the adipose tissue is a factor that may be related with the reduction of VD in the pubertal stage. The association of VD and adipose tissue may occur due to the capacity of this tissue for storage of lipophilic

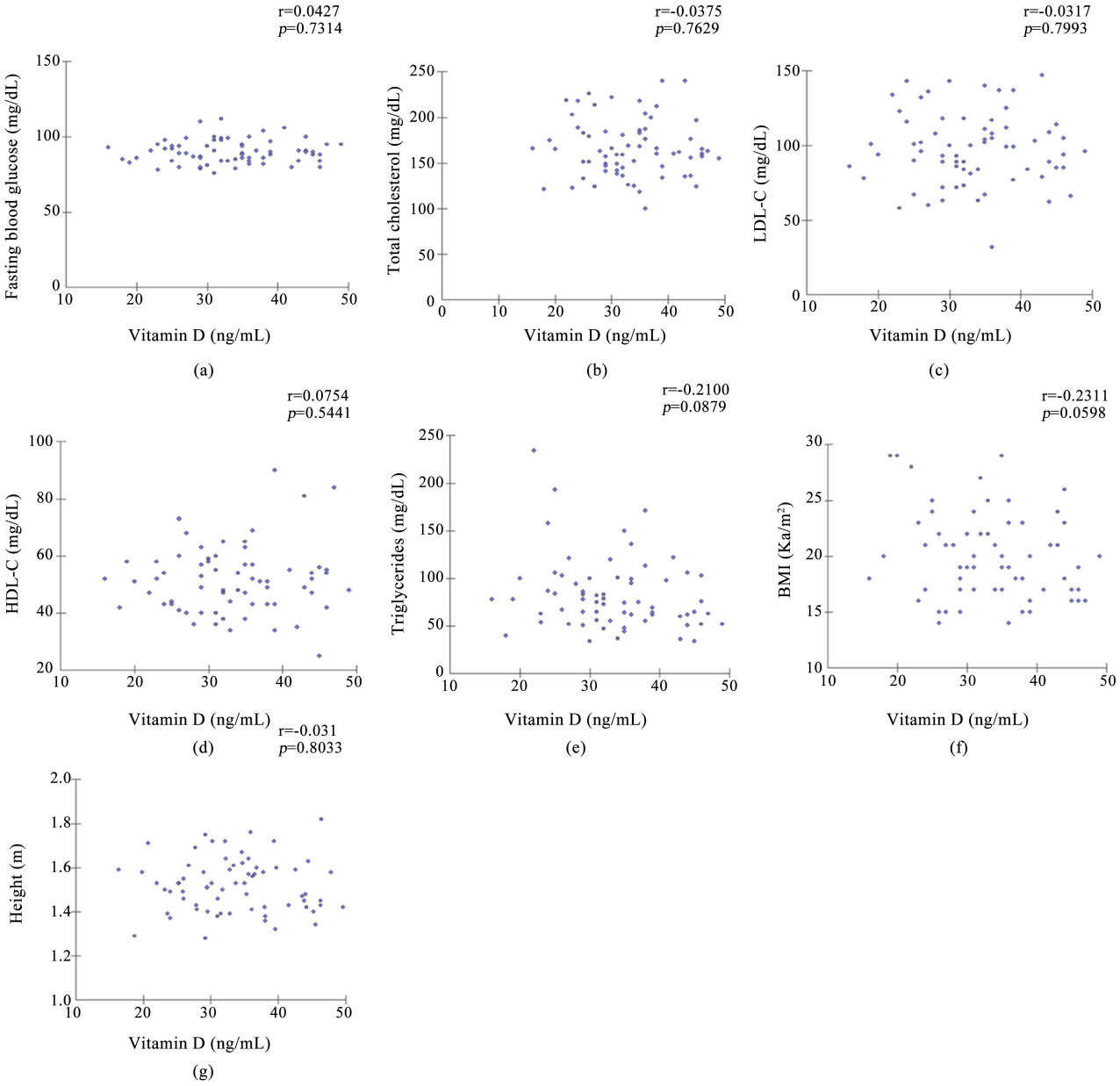

Figure 1. Correlation of serum vitamin D levels with (a) fasting glycemia; (b) total cholesterol; (c) LDL-c; (d) HDL-c; (e) triglycerides; (f) BMI; (g) height. Data evaluated by Pearson Correlation.

substances. This association has been shown by several authors regardless of age and latitude [14] [15] [16] [17].

On the other hand, the reduction of body weight barely improves VD status compared with the maintenance of weight under the same VD intake. Furthermore, studies with adult patients showed that the supplementation with this vitamin could not reduce adiposity. These findings show that hypovitaminosis D does not necessarily lead to obesity [12] [18] [19].

In adolescents, hypovitaminosis D is also related to defective bone mineralization [20], increases the risk of urinary and respiratory infections, tuberculosis [21] [22], allergies [12] [23], asthma [24], celiac disease [25], inflammatory bo-

wel diseases [26], type 1 diabetes [27], obesity and metabolic syndrome [28].

VD also interferes with the secretion of insulin and affects the glycemia. This relationship with the development of diabetes is a serious worry once high levels of plasmatic glucose is related to other components of the metabolic syndrome, thus, increase the risk of cardiac issues in late stages of life [29] [30]. Thorsen *et al.* [31] also showed that maternal or neonatal levels of VD display a clinically significant effect on the risk of developing type 1 diabetes in childhood.

On the other hand, Brar *et al.* [15] used a high dose of VD in obese adolescent and did not find improvement on insulin secretion and sensitivity, and concluded that this supplementation did not appear to produce benefits on the homeostasis of the glucose on obese adolescents. Savastano *et al.* [32] and Gul *et al.* [33] found a negative correlation between VD levels and fasting glycemia.

The role of hypovitaminosis D in worsening the comorbidities in adolescence is, furthermore, related to the lipoprotein metabolism. Obese children with insufficiency of this vitamin exhibit a higher risk for reduced levels of HDL-c and hypertension [34]. Although without significance, our results showed a positive correlation between VD and HDL-c levels. Sriram *et al.* [34] and Prodam *et al.* [35] showed that VD levels are negatively correlated with total cholesterol, LDL-c, and triglycerides, corroborating our findings. VD receptors (VDRs) are found ubiquitously, including the adipose tissue. These receptors are related to the cholesterol levels by regulating bile acid synthesis. Studies on animal models and humans suggest that VDRs inhibit the expression of receptors, which usually acts indirectly by decreasing the expression of CYP7A1, a limiting enzyme in bile acid synthesis, increasing cholesterol levels.

Contradicting recent studies that have shown that supplementation with VD may improve glycemia and lipid profile in children with deficiency of this vitamin [36] [37] [38], Jamka *et al.* [39] and Jamka *et al.* [40] performed meta-analysis that showed no correlation between VD and glucose and lipid levels.

The stage of pubertal development affects the body composition in both sexes [41]. Although Fernández *et al.* [8] concluded that in the pubertal stage the children exhibited values significantly lower of VD than prepubescent children, our results indicate that when the sample is divided by stages of sexual maturation (pre-pubertal and pubertal stage), there is a significant difference in the serum levels of VD and BMI. This could be explained because lower serum value of this vitamin, also associated to greater adiposity, are present in the period of development and growth (pre-pubertal) when compared to the progression of puberty (pubertal).

Skin can synthesize most of the VD requirements (90%) due to the exposition of ultraviolet B radiation from the sunlight. Notwithstanding, this production may be influenced by latitude, season, skin pigmentation, time and area of exposure. During periods of less exposition to sun, the endogenous stores may provide the needs for this vitamin or supplementation should be performed [42]. As adolescents are in a critical phase of growth, bone formation and develop-

ment, the need for this vitamin is higher during puberty. Furthermore, this population is at augmented risk for deficiency of VD, and some authors recommend continuous supplementation in addition to the VD obtained from the diet or produced due to the exposition to the sunlight [43] [44].

Similarly to many other studies, our data suggest that adolescents are at higher risk of VD deficiency and insufficiency, mainly the obese. VD concentrations, BMI, and triglyceride values differed at puberty, with levels of this vitamin and higher adiposity during the pre-pubertal stage. As the role of this vitamin in the biochemical and anthropometric profile is not well established, we suggest that further studies are necessary to the standardization of supplementation in controlling metabolic risks.

This study had some limitations such as sample size. The data for this research were collected in medical records, which may have limited the number of information that could be relevant to the study.

5. Conclusion

The puberty phase increases the risk for hypovitaminosis D mainly in obese adolescents. Once this vitamin is crucial for bone health, and as it seems it is necessary to the homeostasis of glycemia, lipids, and body weight, its monitoring should be performed with rigor and caution. As our results are based in a short number of adolescents and literature is scarce on studies with individuals in pre-pubertal and pubertal stage, we suggest that more studies should be performed to confirm the precise role of vitamin D in the promotion and maintenance of health.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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