Revista O Mundo da Saúde

DOI: 10.15343/0104-7809.202347e11842021

Association between serum vitamin D level and insulin resistance in overweight adolescents

Fabricio Sbroglio Lando[1] **Deisi Maria Vargas**[2]

[1]Universidade do Vale do Itajaí – UNIVALI. Itajaí/SC, Brasil.
[2]Universidade de Blumenau – FURB. Blumenau/SC, Brasil.
E-mail: deisifurb@gmail.com

Abstract

The maintenance of glycemic homeostasis and insulin secretion is considered one of the metabolic effects of vitamin D (VD). Traditionally, obesity is the main cause of insulin resistance (IR) and an important risk factor for VD deficiency. Therefore, adolescents with obesity and VD deficiency may be faced with a doubled risk of developing IR. The objective of this study was to evaluate the association between serum levels of 25-hydroxyvitamin D [25(OH)D] and IR parameters in overweight adolescents. This is an observational study of 42 overweight adolescents followed in a secondary care service. Overweight was defined by the criteria of the World Health Organization and serum levels of 25(OH)D were categorized as normal (≥ 30 ng/mL) and low (< 30 ng/mL) according to the Brazilian Society of Nutrology. In the assessment of IR, the homeostatic model of IR assessment (HOMA-IR), the glucose/insulin ratio and fasting insulinemia were used. The studied group was characterized as being predominantly young adolescents (88.1% between 10 and 14 years old), in puberty (83.5%), and having central obesity (80%), and hypovitaminosis D (85.7%). Adolescents with low VD showed a higher occurrence of IR according to the HOMAR IR index (one-tailed Fisher test, $p < 0.05$), suggesting a relationship between vitamin D status and insulin sensitivity; hence, there was a positive association between low VD and high HOMA-IR.

Keywords: Vitamin D. Obesity. Insulin resistance. Metabolic syndrome.

INTRODUCTION

For several decades, it was thought that the organic functions of vitamin D were restricted to the skeletal system, including the regulation of bone metabolism and mineral homeostasis[1]. However, in recent decades, several studies have demonstrated the role of vitamin D in the regulation of other organic processes such as cell proliferation and apoptosis, the regulation of the immune and reproductive systems, as well as vascular and metabolic effects[1,2].

The regulation of glycemic homeostasis and insulin secretion is considered one of the metabolic effects of vitamin D[3]. Studies indicate that vitamin D participates in insulin secretion and glucose homeostasis[4] and

Revista O Mundo da Saúde

DOI: 10.15343/0104-7809.202347e11842021I

that vitamin D deficiency may be associated with the pathogenesis of insulin resistance (IR) and dysfunction of pancreatic β cells[5].

Obesity in adolescence leads to insulin resistance (IR)[6], becoming a trigger for the subsequent development of metabolic syndrome (MS), diabetes mellitus (DM2), and cardiovascular disease (CVD)[7]. On the other hand, obesity is a risk factor for vitamin D deficiency. Several mechanisms explain this phenomenon, one of which is the seizure of vitamin D by adipose tissue[8]. Therefore, children and adolescents with both obesity and vitamin D deficiency may face a doubled risk for developing IR and associated conditions such as MS and DM2.

Studies have shown an association between vitamin D deficiency and metabolic changes in overweight adolescents and young adults[1,9]. In obese adolescents, an inverse correlation was found between serum levels of vitamin D and elevated fasting glycemia and a positive association between vitamin D deficiency and MS[10,11], especially with the altered fasting glycemia criterion[12]. This indicates a possible metabolic activity of vitamin D on glycemic regulation in obese adolescents. However, other studies conducted with obese adolescents did not show an association between vitamin D deficiency and MS[12,13]. These controversies may be related to the fact that these studies analyze the MS components, which include glycemic alterations and not IR parameters specifically. Therefore, this study aimed to study associations between serum vitamin D and IR in overweight adolescentes.

METHODS

This is an observational study carried out with 42 overweight adolescents of both sexes accompanied in a secondary healthcare service linked to the Unified Health System. Sequentially, overweight adolescents who went to a medical appointment between April 2018 and May 2019 were included in the study. Exclusion criteria were the presence of short stature (height for age and sex < -2 Z-score), the presence of alterations in neuropsychomotor development, and the use of supplements containing vitamin D.

Study variables were age, sex, Body Mass Index (BMI) z-score, degree of excess weight, blood pressure (BP), waist circumference (WC), presence of cervical acanthosis nigricans, fasting glucose (G), baseline insulin (I), homeostatic model of IR assessment (HOMA-IR), glucose/insulin ratio (G/I), and serum vitamin D. Vitamin D and insulin were measured using chemiluminescence and blood glucose using an enzymatic method (Prime 300+).

For the diagnosis of overweight, the criteria recommended by the World Health Organization (WHO) were used, which consider overweight a BMI Z-score between +1 and < +2, obesity a Z-score between ≥ +2 and < +3, and severe obesity, ≥ +3[14]. In the categorization of serum levels of 25(OH) D, the cutoff point defined by the Brazilian Association of Nutrology was used, which considers normal vitamin D a serum value of 25(OH)D > 30 ng/mL and low vitamin D values < 30 ng/ml[15]. HOMA-IR[16] index, fasting G/I ratio, and fasting insulin were used in the assessment of IR. Fasting insulin values ≥ 15 μU/ mL, HOMA-IR index ≥ 3,16, and G/I ratio < 6 were considered as IR.

Participants with systolic BP ≥ 130 and/or diastolic BP ≥ 85 were considered to have

DOI: 10.15343/0104-7809.202347e11842021I

high BP according to the recommendations of the Guidance Manual of the Department of Nephrology of the Brazilian Society of Pediatrics on Arterial Hypertension in Childhood and Adolescence[17]. WC was categorized according to the reference values of the National Health and Nutrition Examination Survey III (NHANES III)[18] as normal or high (≥ the 90th percentile). Acanthosis nigricans was assessed by inspection and was defined as the presence of any degree of skin darkening in the cervical region. Puberty staging was performed according to the Tanner criteria.

Descriptive statistics were used to present the results. Numerical variables were presented as mean, standard deviation (SD), amplitude and 95% confidence interval (CI), and categorical variables in relative frequencies. The Kolmogorov-Smirnov test was applied to evaluate the distribution of numerical variables. All numeric variables, except insulin and HOMA-IR, had a parametric distribution. Student's t test and Mann-Whitney U test were used to compare means between two categories, and the ANOVA test was used to compare means between three categories. The chi-square test and Fisher's exact test were used to compare frequencies between categories. Simple and multiple linear regression considered vitamin D as an independent variable and clinical and biochemical parameters as dependent variables.

The study was approved by the Human Research Ethics Committee of the University of Blumenau under the National Research Ethics Committee of the Ministry of Health under number 80540417.4.0000.5370 on 12/15/17. The research followed the ethical precepts required by Resolution No. 466/2012 of the National Health Council.

RESULTS

Table 1 describes the clinical profile of the participants. There was a predominance of males and the age group between 10 and 14 years old. Most participants were obese and had low vitamin D, showing a high occurrence of vitamin D deficiency in overweight adolescents. WC was elevated in approximately 80% of the adolescents, demonstrating a predominance of central obesity in the studied group. No participant had high vitamin D levels (above 100 ng/ml).

There was no evidence of an association between serum 25(OH)D and the clinical profile of the participants (Table 1). There was no difference in 25(OH)D serum levels in relation to gender and age group, and the BMI Z-score was higher in males (Table 2). Adolescents with low vitamin D had a higher occurrence of insulin resistance suggesting a relationship between vitamin D status and insulin sensitivity (Table 3).

REVISTA O MUNDO DA SAÚDE

DOI: 10.15343/0104-7809.202347e11842021I

Table 1 - Serum level of vitamin D in relation to clinical profile of the participants.

Variables	n (%)	25(OH)D (ng/mL)			
		Mean ± SD	Range	CI(95%)	p
Sex					
Male	24 (57.1)	23.5 ± 6.2	12.9-33.4	20.9-26.1	0.69*
Female	18 (42.9)	24.2 ± 4.8	11.8-31.6	21.9-26.4	
Age group					
10-14 years	37 (88.1)	23.4 ± 5.7	11.8-33.4	21.5-25.3	0.23*
15-19 years	5 (11.9)	26.7 ± 4.3	20.9-30.8	22.9-30.4	
Degree of overweight					
Overweight	7 (16.7)	26.1 ± 3.9	20.9-31.6	22.5-29.7	0.51**
Obese	24 (57.1)	23.4 ± 6.1	11.8-33.4	20.8-25.9	
Severe obesity	11 (26.2)	23.4 ± 5.3	17.6-33.4	19.8-26.9	
Blood pressure					
Normal	32 (76.2)	23.8 ± 5.8	11.8-33.4	21.7-25.8	0.96*
Increased	10 (23.8)	23.9 ± 4.9	17.6-30.1	21.1-26.9	
Abdominal circumference					
Normal	9 (21.4)	25.2 ± 4.8	16.2-31.6	21.8-28.3	0.42*
Increased	33 (78.6)	23.5 ± 5.8	11.8-33.4	21.2-25.6	
Cervical Acanthosis nigricans					
Absent	23 (54.8)	23.6 ± 4.9	13.0-31.6	21.7-25.5	0.78*
Present	19 (45.2)	24.1 ± 6.4	11.8-33.4	20.9-27.1	
Pubertal stage					
Prepubescent	7 (16.7)	21.6 ± 4.0	16.2-26.8	18.7-24.9	0.25*
In puberty	35 (83.5)	24.3 ± 5.8	11.8-33.4	22.2-26.3	
Vitamin D (ng/mL)					
Normal (≥ 30)	6 (14.3)	31.6 ± 1.4	30.1-33.4	30.5-32.7	< 0.001***
Low (< 30)	36 (85.7)	22.5 ± 4.9	11.8-29.7	20.8-24.1	

Source: the authors. Notes: 25(OH)D: 25-hydroxyvitamin D; SD: Standard deviation; CI: Confidence interval; *Student's t test; **ANOVA; ***chi-square.

Table 2 - Anthropometric and biochemical data of participants categorized by gender.

Variables	Mean ± SD			Range	CI(95%)
	Overall	Male	Female		
Weight Z-score	2.1 ± 0.7	2.2 ± 0.5	1.9 ± 0.8	0.6-3.0	1.9-2.3
Height Z-score	0.8 ± 1.1	0.8 ± 0.9	0.8 ± 1.3	- 1.5-3.9	0.5-1.1
BMI Z-score	2.6 ± 0.7	2.8 ± 0.6*	2.3 ± 0.7*	1.0-4.2	2.4-2.8
25(OH)D (ng/mL)	23.8 ± 5.6	23.6 ± 6.2	24.2 ± 4.8	11.8-33.4	22.1-25.6
Insulin (µUI/mL)	15.1 ± 9.8	15.5 ± 10.8	14.5 ± 8.6	2.3-50.6	12.0-18.2
Glycemia (mg/dL)	88.9 ± 7.9	86.1 ± 7.2	92.8 ± 7.5	72-105	86.5-91.5
HOMA-IR	3.32 ± 2.19	3.03 ± 1.93	3.7 ± 2.51	0.47-10.86	2.63-4.00
G/I	8.5 ± 6.4	8.4 ± 6.9	8.6 ± 5.9	1.7-36.1	6.5-10.5

Source: the authors. Notes: SD: Standard deviation; CI: Confidence interval; BMI: Body Mass Index; 25(OH)D: 25-hydroxyvitamin D; HOMA-IR: Homeostasis-Insulin Resistance Assessment Model; G/I: Glucose/Insulin Ratio; *Student's t test; p < 0.05.

REVISTA O MUNDO DA SAÚDE

DOI: 10.15343/0104-7809.202347e11842021I

Table 3 - Distribution of participants according to vitamin D status and insulin resistance parameters.

	Insulin (µU/ mL)*		HOMA-IR**		G/I Ratio***	
Vitamin D (ng/mL)	**< 15**	**≥ 15**	**< 3.16**	**≥ 3.16**	**≥ 6**	**< 6**
Normal (≥ 30)	6	0	6	0	6	0
Low (< 30)	22	14	20	16	21	15
	Total	42	Total	42	Total	42

Source: the authors. Notes: HOMA-IR: Homeostasis-Insulin Resistance Assessment Model; G/I: Glucose/Insulin Ratio; One-tailed Fisher test: *p = 0.08; ** p < 0.05; *** p = 0.06.

DISCUSSION

Adolescents with obesity are more likely to have lower values of 25(OH)D[19]. Although excess weight does not affect the cutaneous synthesis of vitamin D, excess body adipose tissue causes an increase in the sequestration of 25(OH)D, a liposoluble molecule, reducing its bioavailability[20]. This study confirms this predisposition as most participants had hypovitaminosis D.

The occurrence of hypovitaminosis D found in this study was higher than that found in Juiz de Fora, Minas Gerais (70%)[21] and in Blumenau, Santa Catarina (61.6%)[22], and was similar to that found in the city of Rio de Janeiro (90%)[10]. These studies were carried out with overweight adolescents and considered the same cut-off level for the definition of hypovitaminosis D. Some authors, in Brazil and in other countries, showed an inverse association between the degree of excess weight and serum values of 25(OH)D[20,21,22]. This association was not evident in this study. Although overweight adolescents had numerically higher means of serum vitamin D, the difference in relation to obese adolescents was not significant.

The metabolic syndrome (MS) is characterized by the aggregation of risk factors of metabolic origin that are related to a higher incidence of cardiovascular diseases and DM2 diabetes[23]. With the description of "Syndrome X" in the 80s, IR was defined as the main factor involved in the development of MS[24]. IR, the initial pathophysiological alteration of MS, can already be identified during adolescence. Approximately one third of the participants in this study had altered serum insulin and HOMA-IR index, which were present in overweight young adolescents. In a Brazilian multicentric study, these occurrences were similar, 38.6% for elevated HOMA-IR and 37.4% for elevated insulin[25]. In a municipality in the Middle Vale do Itajai, Santa Catarina, overweight children and teens between 6 and 14 years of age had a higher occurrence of high HOMA-IR, around 48%[26]. Although the appearance of T2DM is common in adults with obesity, its appearance in children and adolescents is infrequent[27]. However, the presence of IR predisposes individuals to its occurrence[28] and indicates an early appearance of metabolic risk, which, if maintained throughout life, will culminate in the occurrence of MS.

The relationship between vitamin D and insulin sensitivity is a controversial topic. As seen herein, other studies involving overweight adolescents have described an association between hypovitaminosis D and biochemical parameters of IR such as hyperinsulinemia[28,29,30] and elevated HOMA-IR index[9,21,29,31,32,33]. As there is no single method

REVISTA O MUNDO DA SAÚDE

DOI: 10.15343/0104-7809.202347e11842021I

capable of estimating the degree of individual sensitivity to insulin, it is not always easy to establish the diagnosis of IR[34]. The gold standard exam to assess IR is the hyperinsulinemic euglycemic clamp, but its complexity and high cost make its use unfeasible in epidemiological studies and in daily clinical practice[35]. As alternatives, there is the measurement of fasting blood glucose and insulin with calculations of HOMA-IR and G/I ratio. Fasting insulin ≥ 15 μU/ mL, HOMA-IR index ≥ 3.16, and G/I ratio < 6 are the criteria most used to identify IR in the pediatric age group, with the HOMA-IR index being the most reliable[16]. In this study, we observed that the IR parameter with the best association with vitamin D status was the HOMA-IR index compared to the G/I ratio and fasting insulin.

It is possible that overweight accompanied by central obesity and associated with hypovitaminosis D, a frequent condition in overweight adolescents, cooperate in the genesis of insulin resistance and may, over time and according to their magnitudes, trigger metabolic syndrome. The high occurrence of hypovitaminosis D and central obesity associated with a significant occurrence of IR found in the adolescents of this study, point to a metabolic risk in this earlier age group. Studies designed to evaluate the participation of each of these elements in the occurrence and evolution of IR and MS during and after adolescence would be of great interest.

In terms of application in clinical practice, the inclusion of the assessment of serum vitamin D in overweight adolescents is suggested. Maintaining a serum vitamin D above 30 ng/mL through lifestyle changes and supplementation, if needed, could be considered a treatment goal in this population group.

As limitations of this study, we highlight the transversality of the data, which limits the establishment of a temporal relationship and a causal relationship between the events, the use of a non-probabilistic sample, which does not guarantee the representativeness of the population of overweight adolescents, and the absence of a group of eutrophic adolescents for comparison purposes.

CONCLUSION

Low vitamin D affected a significant portion of overweight adolescents and was positively associated with elevated HOMA-IR, an indicator of insulin resistance, a pathophysiological mechanism that precedes the occurrence of metabolic syndrome.

There was also a high occurrence of central obesity, a clinical condition associated with insulin resistance, and a mandatory criterion for the diagnosis of metabolic syndrome in adolescents according to current criteria.

Author Statement CREdiT

Conceptualization: Vargas DM; Lando FS. Methodology: Vargas DM; Lando FS. Validation: Vargas DM; Lando FS. Statistical analysis: Vargas DM; Lando FS. Formal analysis: Vargas DM; Lando FS. Research: Vargas DM; Lando FS. Resources: Vargas DM; Lando FS. Writing-preparation of the original draft: Vargas DM; Lando FS. Writing-revision and editing: Vargas DM; Lando FS. Visualization: Vargas DM; Lando FS. Supervision: Vargas DM; Lando FS. Project management: Vargas DM; Lando FS.

All authors have read and agreed with the published version of the manuscript.

DOI: 10.15343/0104-7809.202347e11842021I

REFERENCES

1. Bouilon R, Marcocci C, Carmeliet G, Bikle D, White JH, Dawson-Hughes B, at al. Skeletal and Extraskeletal Actions of Vitamin D: Current Evidence and Outstanding Questions. Endocrine Reviews. 2019; 40(4): 1109-1151.
2. Zotarelli-Filho IJ, Garcia-Ramirez AV, Ribas-Filho D. Major Meta-Analysis, Randomized Clinical Studies, and International Consensus on Serum Levels and Importance of Supplementing Vitamin D: State of the art. Med Health Sci. 2021; 2(2): 54-66.
3.Han F, Lv Y, Gong L, Liu H Wan Z, Liu L. VDR gene variation and insulin resistance related diseases. Lipids Health Dis [revista em Internet] 2017; acesso em 28 de março de 2019; 16:157. Disponível em: https://doi.org/10.1186/s12944-017-0477-7 .
4. Hyppönen E, Power C. Vitamin D status and glucose homeostasis in the 1958 British birth cohort; the role of obesity. Diabetes Care, 2006; 29(10): 2244-2246.
5. Sung CC, Liao MT, Lu KC, Wu1CC. Role of Vitamin D in Insulin Resistance. J Biomed Biotech [revista em Internet] 2012; acesso em 27 de maio de 2019; volume 2012. Disponível em https://doi.org/10.1155/2012/634195
6. Medeiros CCM, Ramos AT, Cardoso MAA, França ISX, Cardoso AS, Gonzaga NC. Insulin resistance and its association with metabolic syndrome components. Arq. Brasil. Cardiol. 2011; 97(5): 380-389.
7. Assunção SNF, Boa Sorte NCA, Alves CAD, Mender PSA, Alvez CRB, Silva LR. Glucose alteration and insulin resistance in asymptomatic obese children and adolescents. J Pediatr. 2018; 94(3): 268-272.
8. Migliaccio S, Di Nisio A, Mele C, Scappaticcio L, Savastano S, Colao A. Obesity Programs of nutrition, Education, Research and Assessment (OPERA) Group. Obesity and hypovitaminosis D: causality or casualty? Int J Obes Suppl, 2019; 9(1):20-31.
9. Teixeira JS, Campos ABF, Cordeiro A, Pereira SE, Saboya SJ, Ramalho A. Vitamin D nutritional status and its relationship with metabolic changes in adolescents and adults with severe obesity. Nutr Hosp. 2018; 35(4): 847-853.
10. Kim YS, Hwang JH, Song MR. The association between vitamin D deficiency and metabolic syndrome in Korean adolescents. J Pediatr Nurs [revista em internet] 6 de dezembro de 2017; acesso em 27 de junho de 2022; 38; e7-e11. Disponível em: https://www.pediatricnursing.org/article/S0882-5963(17)30381-0/pdf
11. Fu J, Han L, Zhao Y, Li G, Zhu Y, Li Y, et al. Vitamin D levels are associated with metabolic syndrome in adolescents and young adults: The BCAMS study. Clin Nutr. 2019; 38(5): 2161-2167.
12. Cabral M, Araújo J, Teixeira J, Barros H, Martins S, Guimarães JT, et al. Vitamin D levels and cardiometabolic risk factors in portuguese adolescentes. Int J Cardiol. 2016;220:501-507.
13. Wojcik M, Janus D, Kalicka-Kasperczyk A, Sztefko K, Starzyk JB. The potential impact of the hypovitaminosis D on metabolic complications in obese adolescents - preliminary results. Ann Agric Environ Med. 2017; 24(4):636-639.
14. Organização Mundial da Saúde – OMS. Growth reference data for 5-19 years, [publicação na web]; 2007; acesso em 27 de junho de 2022. Disponível em: https://www.who.int/tools/growth-reference-data-for-5to19-years
15. Ribas-Filho D, Nogueira de Almeida AC, Oliveira Filho AE. Posicionamento atual sobre vitamina D na prática clínica: Posicionamento da Associação Brasileira de Nutrologia. Int J Nutrol. 2020; 12: 82–96.
16. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005; 115(4): 500-503.
17. Sociedade Brasileira de Pediatria. Departamento Científico de Nefrologia. Manual de Orientação. Hipertensão arterial na infância e adolescência. [publicação na web]; 2019; acesso em: 27 de junho de 2022. Disponível em: https://www.sbp.com.br/fileadmin/user_upload/21635c-MO_-_Hipertensao_Arterial_Infanc_e_Adolesc.pdf
18. Fernández JR, Redden DT, Peitrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of african-american, european-american, and mexican-american children and adolescentes. J Pediatr. 2004; 145(4): 439-444.
19. Lenders CM, Feldman HA, Von Scheven E, Merewood A, Sweeney C, Wilson DM, at al. Elizabeth Glaser Pediatric Research Network Obesity Study Group. Relation of body fat indexes to vitamin D status and deficiency among obese adolescents. Am J Clin Nutr. 2009; 90: 459-467.
20. Harel Z, Flanagan P, Forcier M, Harel D. Low vitamin D status among obese adolescents: prevalence and response to treatment. J Adolesc Health. 2011; 48: 448-452.
21. Oliveira RM, Novaes JF, Azeredo LM, Cândido AP, Leite IC. Association of vitamin D insufficiency with adiposity and metabolic disorders in Brazilian adolescents. Public Health Nutr. 2014; 17(4): 787–794.
22. Vargas DM, Lando FS, Fiegenbaum M, Bonmann NLF, Souza CA, Azevedo LC. Avaliação dos níveis séricos de 25-hidroxi-vitamina D em adolescentes com excesso de peso. Adolesc. Saúde. 2019; 16(2): 102-109.
23.Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, A, et al. Obesity and the metabolic syndrome in children and adolescents. N England J Med. 2004; 350(23): 2362-2374.
24. Reaven GM. Role of insulin resistance in the pathophysiology of non-insulin dependent diabetes mellitus. Diabetes Metab Res Rev. 1993; 9(1): 5-12.
25. Nogueira-de-Almeida CA, Mello ED. Correlation of body mass index Z-scores with glucose and lipid profiles among overweight and obese children and adolescentes. J Pediatr. 2018; 94(3): 308-312.
26. Rosini N, Moura SAZO, Rosini RD, Machado MJ, Silva EL. Síndrome metabólica e importância das variáveis associadas em crianças e adolescents de Guabiruba – SC, Brasil. Arq. Brasil. Cardiol. 2015; 105(1): 37-44.
27. Zambon MP, Antônio MARGM, Mendes RT, Barros Filho, AZ. Características clínicas e laboratoriais de crianças e adolescentes obesos. Rev Paul Pediatr. 2007; 25(1): 27-32.
28. Kurtoglu S, Hatipoglu N, Mazicioglu M, Kendirici M, Keskin M, Kondolot M. Insulin resistance in obese children and adolescents: HOMA-IR cut-off levels in the prepubertal and pubertal periods. J Clin Res Pediatr Endocrinol. 2010; 2(3): 100-106.

REVISTA O MUNDO DA SAÚDE

DOI: 10.15343/0104-7809.202347e11842021I

29. Flores Ruelas Y, Equihua MDT, Solís NAJ, Rodríguez LMB, Enciso ID, Ramírez, CAS. Vitamin D status and its relation to insulin resistance in a Mexican pediatric population. J Pediatr Endocrinol Metab. 2020; 33(4): 481-486.
30. Williams R, Novick M, Lehman E. Prevalence of hypovitaminosis D and its association with comorbidities of childhood obesity. Perm J. 2014; 18(4):32-39.
31. Durá-Travé T, Gallinas-Victoriano F, Peñafiel-Freire DM, Urretavizcaya-Martinez M, Moreno-González P, Chueca-Guindulain MJ. Hypovitaminosis D and cardiometabolic risk factors in adolescents with severe obesity. [publicação na web]; Children (Basel). 2020; acesso em 27 de junho de 2022. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7072215/
32. Denova-Gutiérrez E, Munoz-Aguirre P, Lopez D, Flores M. Low serum vitamin D concentrations are associated with insulin resistance in Mexican children and adolescents. [publicação na web]; Nutrients. 2019; acesso em 27 de junho de 2022. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6770751/pdf/nutrients-11-02109.pdf
33. Slyper AH, Kashmer L, Huang W, Re´em Y. Acanthosis nigricans, vitamin D, and insulin resistance in obese children and adolescents. J Pediatr Endocrinol Metab. 2014; 27(11-12):1107-1111.
34. Romualdo MCS, Nóbrega FJ, Escrivão MAMS. Insulin resistance in obese children and adolescents. J Pediatr. 2014; 90(6): 600-607.
35. Einhorn D. American College of Endocrinology position statement on the insulin resistant syndrome. Endocr Pract. 2003; 9(3): 9-21.

Received: 22 october 2021.
Accepted: 23 november 2022.
Published: 01 march 2023.