Vitamin D deficiency in children and adolescents with obesity: a meta-analysis

Verônica Indicatti Fiamenghi, Elza Daniel de Mello

Universidade Federal do Rio Grande do Sul (UFRGS), Programa de Pós-Graduação em Saúde da Criança e do Adolescente, Porto Alegre, RS, Brazil

Received 14 May 2020; accepted 3 August 2020
Available online 3 October 2020

KEYWORDS
Obesity; Vitamin D; Meta-analysis; Children; Adolescent

Abstract
Objective: To evaluate the prevalence of vitamin D deficiency in obese children and adolescents when compared to eutrophic controls.
Methods: Systematic review with meta-analysis covering studies with patients aged 0–18 years old diagnosed with obesity and vitamin D deficiency and control group of eutrophic patients. The studies were retrieved in the PubMed, Embase, and LILACS databases in December 2019. The search used the terms “obesity” in combination with “pediatric population” and “vitamin D”.
Results: Through the search 3155 articles were retrieved; and after analysis, 20 studies were selected according to the study objectives. A total of 24,600 children and adolescents were included. Through meta-analysis, the relative risk for the association between obesity and vitamin D deficiency in the pediatric population was 1.41 (95% CI: 1.26–1.59) (I² = 89%, p < 0.01).
Conclusion: Children and adolescents with obesity have higher risk of vitamin D deficiency. © 2020 Sociedade Brasileira de Pediatria. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction
Childhood obesity is a worldwide problem. It is known that overweight in childhood and adolescence is an important risk factor for obesity in adulthood, as well as for the development of comorbidities.

Regarding vitamin D (vit D), in addition to its role in bone health and calcium and phosphorus metabolism, its role in immune functions and in decreasing the risk of chronic illnesses has been considered. Vit D deficiency varies by geographic region, with an estimated prevalence of 15% in a study with the general pediatric population in the United States of America from 1 to 11 years of age. A similar
prevalence of 14% was found in a cross-sectional survey in a representative sample of adolescents from that country aged 12–19. The best indicator to assess vit D status is the metabolite 25-hydroxy vitamin D (25(OH)D). The relationship between hypovitaminosis D and obesity has been widely studied in the general population. A meta-analysis published in 2015 showed an association between vit D deficiency and obesity, with OR 3.43 (95% CI: 2.33–5.06). Vit D deficiency and excess body fat have mutual negative effects, resulting from metabolic processes that generate accumulation of inactive forms and decreased vit D bioavailability, in addition to decreased tissue secretion and sensitivity to insulin. There is no consensus as to why vit D levels are lower in obese individuals. The main hypothesis would be the absorption of vit D, which is fat soluble, by the adipose tissue.

Thus, it is known that obesity is related with hypovitaminosis D, with consequent greater chance of changes in glycemic control and metabolic syndrome in general population. Although this relationship is clear in the adult population, there is no consensus on the literature regarding a higher frequency of vit D deficiency in children and adolescents with obesity.

Methods

The literature search, study selection based on title and abstract, and data extraction were carried out independently by two trained reviewers. In cases of disagreement, it was resolved by the reviewers. In case of duplicate articles, only one was considered. The meta-analysis is registered on the PROSPERO Platform (PROSPERO, University of York, England) under number CRD42019137788.

Search strategy

The studies were identified through research in the PubMed, Embase, and LILACS databases, performed in December 2019. For the search, the term “obesity” was used in combination with “pediatric population” and “vitamin D”, through structured Medical Subject Heading (MeSH) key- words for PubMed, Emtree for Embase, and Health Science Descriptors (DeCS) for LILACS. The terms used in the search and the number of articles retrieved per database are depicted in Table S1 of the Supplementary material.

Eligibility criteria

The inclusion criteria were as follows: studies published in Portuguese, English, Spanish, or French, published on any date, evaluating patients aged 0–18 years old with diagnosis of obesity and vit D deficiency, with control group of eutrophic patients. Data related to patients with comorbidities that alter vit D metabolism (e.g., kidney, liver, gastrointestinal, or endocrine disease) or using medications that act in the metabolism of this vitamin (e.g., glucocorticoids), and studies with incomplete data or not published in full were excluded.

Data collection

After assessing the title, abstract, and full text of the studies according to the eligibility criteria, the data of interest were collected using a standard form. The following information was collected: authors, study place, design, year of publication, age of participants, 25(OH)D levels characterized as deficiency, method for assessing 25(OH)D levels, obesity definition by body mass index (BMI), number of patients with obesity and the respective number of patients with vit D deficiency, and number of eutrophic patients and the respective number of patients with vit D deficiency in this group.

Statistical analysis

The studies were grouped in a meta-analysis. The summary measure used was relative risk (RR) with 95% confidence interval, weighted by the study power, using the random effect model. The inconsistency test ($I^2$) was used to assess heterogeneity between studies. A p-value <0.05 was considered to be statistically significant. The statistical analysis was performed using the “meta” package of the R program (R Core Team 2017: R: A language and environment for statistical computing. R Foundation for Statistical Computing, v. 3.5.1 — Vienna, Austria).

Results

During the search 3155 articles were retrieved, of which 20 studies were relevant to the objectives of this study (Table 1). The flowchart showing the search results and selection details is depicted in Fig. 1. A total of 24,600 children were included.

The studies were all carried out in countries located in the Northern Hemisphere. None of the studies performed in tropical countries fulfilled the inclusion criteria. The United States is the country with the most publications (n = 6), followed by three studies carried out in China.

Zhang et al. and Wakayo et al. evaluated 25(OH)D levels using chromatography, all others studies used immunoassay techniques. Regarding the cutoff point used to define 25(OH)D deficiency, the value of 20 ng/mL was the most frequently used, with only four studies using other cutoff points — Huang et al., Jari et al., Al-sadat et al., and Wang et al. There were also different definitions of obesity among the studies. Although most of them have used the definition of BMI equal or higher 95th percentile for age, Dylag et al. and Durá-Travé et al. used the 97th percentile for age the as cutoff point.

In meta-analysis, the relative risk for the association between vit D deficiency and obesity was 1.41 (95% CI = 1.26–1.59), ($I^2$ = 89%, p < 0.01), as shown in the forest plot (Fig. 2).

Heterogeneity was found among the studies, although the random effect model was used for meta-analysis. The study that contributed the most for heterogeneity was Turer et al. A sensitivity analysis was performed by excluding this study from the present analysis, and the relative risk did not change drastically.
Table 1  Characteristics of the studies included in the final analysis.

| Study          | Country       | Study type       | Age (years) | 25(OH)D cutoff point (ng/mL) | Method for evaluation of 25(OH)D | Definition of obesity by BMI | Obese (n) | Vit D deficiency in obese (%) | Control (n) | Vit D deficiency in control (%) |
|----------------|---------------|------------------|-------------|------------------------------|----------------------------------|-------------------------------|------------|--------------------------------|-------------|-------------------------------|
| Rajakumar et al. | United States | Cross-sectional  | 6–10        | <20                          | Immunoassay >p95                |                                | 21         | 57                             | 20          | 40                            |
| Elizondo-Montemayor et al. | Mexico        | Cross-sectional  | 6–12        | <20                          | Immunoassay ≥p97                |                                | 99         | 27                             | 99          | 13                            |
| Khor et al.     | Malaysia      | Cross-sectional  | 7–12        | <20                          | Immunoassay ≥p95                |                                | 66         | 90                             | 336         | 84                            |
| Rajakumar et al. | United States | Cross-sectional  | 8–18        | <20                          | Immunoassay ≥p95                |                                | 112        | 65                             | 125         | 47                            |
| Sacheck et al.  | United States | Cross-sectional  | 9–14        | <20                          | Immunoassay ≥p95                |                                | 65         | 80                             | 198         | 71                            |
| Absoud et al.   | England       | Cross-sectional  | 4–18        | <20                          | Immunoassay ≥p95                |                                | 247        | 39                             | 852         | 34                            |
| Olson et al.    | United States | Cross-sectional  | 6–16        | <20                          | Immunoassay ≥p95                |                                | 411        | 50                             | 87          | 21                            |
| Turer et al.    | United States | Cross-sectional  | 6–18        | <20                          | Immunoassay ≥p95                |                                | 2478       | 37                             | 9814        | 22                            |
| Bellone et al.  | Italy         | Cross-sectional  Pediatric patients |          | <20                          | Immunoassay >p95                |                                | 444        | 44                             | 113         | 31                            |
| Dylag et al.    | Poland        | Cross-sectional  | 1–5         | <20                          | Immunoassay ≥p97                |                                | 50         | 42                             | 50          | 22                            |
| Zhang et al.    | China         | Cross-sectional  | 7–11        | <20                          | Chromatography ≥p95             |                                | 164        | 69                             | 1324        | 55                            |
| Huang et al.    | China         | Cross-sectional  | 6–16        | <12                          | Immunoassay ≥p95                |                                | 348        | 18                             | 445         | 6                             |
| Jari et al.     | Iran          | Cross-sectional  | 10–18       | <10                          | Immunoassay ≥p95                |                                | 104        | 41                             | 986         | 40                            |
| Al-Sadat et al. | Malaysia      | Cross-sectional  | 12–13       | <15                          | Immunoassay ≥p95                |                                | 116        | 88                             | 1234        | 78                            |
| Wang et al.     | China         | Cross-sectional  | 8–18        | <12                          | –                               |                                | 103        | 4                              | 175         | 3                             |
| Wakayo et al.   | Ethiopia      | Cross-sectional  | 11–18       | <20                          | Chromatography Unavailable       |                                | 18         | 77                             | 156         | 39                            |
| Moore et al.    | United States | Cross-sectional  | 6–18        | <20                          | –                               | Immunoassay ≥p95               | 582        | 56                             | 1900        | 40                            |
| Barja-Fernandez et al. | Spain | Cross-sectional  | 2–18        | <20                          | Immunoassay ≥p95                |                                | 176        | 79                             | 295         | 108                           |
| Durá-Tráve et al. | Spain        | Cross-sectional  | 3.1–15.4    | <20                          | Immunoassay ≥p95                |                                | 119        | 32                             | 459         | 57                            |
| Shulhai et al.  | Ukraine       | Cross-sectional  | 12–17       | <20                          | Immunoassay ≥p95                |                                | 78         | 60                             | 131         | 84                            |

BMI, body mass index.
Figure 1 Flowchart with the search results and selection details.

| Study                  | Obesity Events | Obesity Total | Control Events | Control Total | Risk Ratio | RR    | 95%-CI        | Weight |
|------------------------|----------------|---------------|----------------|---------------|------------|-------|--------------|--------|
| Rajakumar 2008         | 12             | 21            | 8              | 20            | 1.43       | [0.74; 2.74] | 2.2%   |
| Elizondo-Montermayor 2010 | 27            | 59            | 13             | 59            | 2.08       | [1.14; 3.78] | 2.5%   |
| Kohr 2011              | 60             | 66            | 284            | 336           | 1.08       | [0.98; 1.18] | 7.0%   |
| Rajakumar 2011         | 73             | 112           | 59             | 125           | 1.38       | [1.10; 1.74] | 5.7%   |
| Sacheck 2011           | 52             | 65            | 142            | 198           | 1.12       | [0.96; 1.30] | 6.5%   |
| Absoud 2011            | 98             | 247           | 289            | 802           | 1.17       | [0.98; 1.40] | 6.2%   |
| Olson 2012             | 205            | 411           | 19             | 87            | 2.28       | [1.52; 3.44] | 3.8%   |
| Turer 2013             | 930            | 2478          | 2227           | 9614          | 1.65       | [1.55; 1.76] | 7.1%   |
| Bellone 2014           | 197            | 444           | 36             | 113           | 1.39       | [1.04; 1.85] | 5.0%   |
| Dyag 2014              | 21             | 30            | 11             | 50            | 1.91       | [1.03; 3.53] | 2.4%   |
| Zhang 2014             | 113            | 164           | 726            | 1324          | 1.26       | [1.12; 1.41] | 6.8%   |
| Huang 2015             | 64             | 348           | 28             | 445           | 2.92       | [1.92; 4.45] | 3.7%   |
| Jarl 2015              | 43             | 104           | 393            | 986           | 1.04       | [0.81; 1.32] | 5.5%   |
| Al-Saad 2016           | 102            | 116           | 961            | 1234          | 1.13       | [1.05; 1.22] | 7.1%   |
| Wang 2016              | 4              | 103           | 6              | 175           | 1.13       | [0.33; 3.92] | 0.8%   |
| Wakayo 2016            | 14             | 18            | 59             | 156           | 2.06       | [1.50; 2.83] | 4.7%   |
| Moore 2016             | 328            | 682           | 757            | 1900          | 1.41       | [1.29; 1.55] | 7.0%   |
| Barja–Fernandez 2018   | 79             | 176           | 108            | 295           | 1.23       | [0.98; 1.53] | 5.7%   |
| Daru–Travé 2018        | 32             | 119           | 57             | 459           | 2.17       | [1.48; 3.18] | 4.1%   |
| Shulhai 2019           | 60             | 78            | 84             | 131           | 1.20       | [1.01; 1.43] | 6.2%   |

Random effects model: $5801 / 18799 = 0.31$; $I^2 = 89%$, $t^2 = 0.0479$, $p < 0.01$

Figure 2 Forest plot of the total study sample and the association between vit D deficiency and obesity.

Some studies reported other factors associated with vit D deficiency. Khor et al. demonstrated higher prevalence of vit D deficiency in girls (77.5%) than boys (66.1%), with statistical significance ($p = 0.01$). Rajakumar et al. and Turer et al. evidenced lower prevalence of hypovitaminosis D in individuals with white skin color, and in the summer and autumn seasons. The study by Shulhai et al. with Ukrainian children and adolescents reported a significant effect in the development of vit D deficiency in individuals who spend more than four hours a day in front of computer or television ($p = 0.027$).

Two studies also evaluated insulin resistance and its relationship with hypovitaminosis D. Wang et al. used fasting glucose and serum insulin measurements to estimate
insulin resistance through homeostatic model assessment (HOMA-IR) in 278 children and adolescents. In multiple linear regression, there was association among HOMA-IR, BMI, and vit D deficiency (p < 0.001). Huang et al. also reported negative association between serum vit D and HOMA-IR in obese children and adolescents.

The severity of obesity also seems to be related with 25(OH)D levels. Turer et al. demonstrated that half of the children with severe obesity presented with hypovitaminosis D and even after statistical adjustment for confounding variables, these children have more than double the risk to present with vit D deficiency compared to eutrophic controls.

A funnel plot analysis showed the presence of publication bias (Fig. 3).

Discussion

This meta-analysis summarized the data from 20 cross-sectional studies that assessed vit D deficiency in obese and also in eutrophic children and adolescents, comprising a total of 24,600 patients.

The hypothesis that children and adolescents with excess weight present higher prevalence of vit D deficiency when compared to control group of eutrophic patients was confirmed. The most accepted physiopathologic basis is that vit D, being fat-soluble, is over-absorbed by adipose tissue. The data that excessive screen time (television, computers, and tablets) is also related to lower vit D levels reinforces the idea that the association between childhood obesity and hypovitaminosis D appears to be multifactorial, also influenced by diminished exposure to outdoor activities and sunlight.

It should be noted that all studies included in the review were carried out in the Northern Hemisphere. Although in Brazil the majority of the population resides in regions with adequate sun exposure, hypovitaminosis D is also a common problem. A study with 135 healthy Brazilian adolescents showed a prevalence of vit D deficiency of 60%. In another Brazilian study performed with healthy infants aged between six and 24 months, 6% presented deficient serum vit D concentration, which suggests that vit D deficiency may also vary with age. The Brazilian Society of Pediatrics recommends the prevention of deficiency through the supplementation of vit D in children on exclusive breastfeeding, children using fortified milk formula that ingest volumes less than 1000 mL/day, children and adolescents who do not ingest at least 600 IU/day of vit D in the diet or that are not exposed to the sun regularly, regardless of the region of the country.

Epidemiological data on the prevalence of childhood obesity and hypovitaminosis D in pediatrics are worrying. Knowing the immunological functions of vit D and its influence on insulin resistance mechanisms, it is necessary to discuss therapeutic measures that can minimize the consequences on the current and future health of children and adolescents with excess weight and disability from vit D deficiency.

Studies show that the obese pediatric population does not show the same response to vit D supplementation in the doses routinely used when compared with eutrophic controls. There is no consensus on the universally recommended dose for the treatment of hypovitaminosis D in this population; however, authors suggest an increase in the dose used regularly.

It is also essential to reinforce the importance of lifestyle changes in the pediatric population. It is necessary to encourage the practice of physical exercise, the reduction of screen time, and the adoption of healthy eating habits in order to reduce the prevalence of overweight and obesity in children and adolescents and the impact of associated comorbidities, including vit D deficiency.

Limitations

Some limitations of this meta-analysis must be recognized. The systematic review was limited to the published literature and the publication bias should be considered. There was high heterogeneity between the studies evaluated, which was minimized by the use of the random effect model. The studies used different cutoff points for 25(OH)D deficiency, a factor involved in heterogeneity. Also, hypovitaminosis D has a known multifactorial etiology, which is a possible confounding factor in the analysis. As it is a meta-analysis of cross-sectional studies, it is not possible to infer a cause-effect relationship between the variables studied. Despite the language limitation in inclusion criteria for the convenience of the researchers, the impact was minimal, since only two studies were excluded due to this criterion.

Conclusion

This meta-analysis demonstrated an association between obesity and vit D deficiency in the pediatric population. This finding reinforces the importance of stimulating healthy lifestyle habits and highlights the need to assess levels of 25(OH)D in obese children and adolescents.

Conflicts of interest

The authors declare no conflicts of interest.
Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi: https://doi.org/10.1016/j.jpeds.2020.08.006.

References

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017;390:2627–42.

2. Dankers W, Colín EM, van Hamburg JP, Lubberts E. Vitamin D in autoimmune: molecular mechanisms and therapeutic potential. Front Immunol. 2017;7:697.

3. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;115–27.

4. Mansbach JM, Ginde AA, Camargo CA Jr. Serum 25-hydroxyvitamin D levels among US children aged 1 to 11 years: do children need more vitamin D? Pediatrics. 2009;124:1404–10.

5. Saintonge S, Bang H, Gerber LM. Implications of a new definition of vitamin D deficiency in a multiracial us adolescent population: the National Health and Nutrition Examination Survey III. Pediatrics. 2009;123:797–803.

6. Maeda SS, Borba VZ, Camargo MB, Silva DM, Borges JL, Bandeira F, et al. Recommendations of the Brazilian Society of Endocrinology and Metabolism (SBE) for the diagnosis and treatment of hypovitaminosis D. Arq Bras Endocrinol Metabol. 2014;58:411–33.

7. Yao Y, Zhu L, He L, Duan Y, Liang W, Nie Z, et al. A meta-analysis of the relationship between vitamin D deficiency and obesity. Int J Clin Exp Med. 2015;8:14977–84.

8. Zakharova I, Klimov L, Kuryaninova V, Nikitina I, Malayavskaya S, Dobnya S, et al. Vitamin D insufficiency in overweight and obese children and adolescents. Front Endocrinol (Lausanne). 2019;10:103.

9. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr. 2000;72:690–3.

10. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chem Biol. 2014;21:319–29.

11. Vimaleswaran KS, Cavadino A, Berry DJ, Genetic Investigation of Anthropometric Traits (GIANT) Consortium, Whitaker JC, Power C, et al. Genetic association analysis of vitamin D pathway with obesity traits. Int J Obes (Lond). 2013;37:1399–406.

12. Zhang HQ, Teng JH, Li Y, Li XX, He YH, He X, et al. Vitamin D status and its association with adiposity and oxidative stress in schoolchildren. Nutrition. 2014;30:1040–4.

13. Wakaya T, Whitling SJ, Belachew T. Vitamin D deficiency is associated with overweight and/or obesity among schoolchildren in Central Ethiopia: a cross-sectional study. Nutrients. 2016;8:190.

14. Huang K, Jiang YJ, Fu JF, Liang JF, Zhu H, Zhu ZW, et al. The relationship between serum 25-hydroxyvitamin D and glucose homeostasis in obese children and adolescents in Zhejiang, China. Endocr Pract. 2015;21:1117–24.

15. Jari M, Qorbani M, Moafi M, Motlagh ME, Keikha M, Ardalan G, et al. Association of 25-hydroxy vitamin D levels with indexes of general and abdominal obesity in Iranian adolescents: the CASPIAN-III study. J Res Med Sci. 2015;20:122–6.

16. Al-Sadat N, Majid HA, Sim PY, Su TT, Dahlui M, Abu Bakar MF, et al. Vitamin D deficiency in Malaysian adolescents aged 13 years: findings from the Malaysian Health and Adolescents Longitudinal Research Team study (MyHeARTs). BMJ Open. 2016;6:e010689.

17. Wang L, Wang H, Wen H, Tao H, Zhao X. Relationship between HOMA-IR and serum vitamin D in Chinese children and adolescents. J Pediatr Endocrinol Metab. 2016;29:777–81.

18. Dyłań H, Rowicka G, Strucińska M, Riahi A. Assessment of vitamin D status in children aged 1–5 with simple obesity. Rocz Panstw Zakl Hig. 2014;65:325–30.

19. Durá-Travé T, Gallinas-Victoriano F, Chueca-Guindulain MJ, Berrade-Zubiri S, Moreno-González P, Malumbres-Chacón M. Prevalence of hypovitaminosis D and associated factors in Spanish population of school children and adolescents. Atten Primaria. 2018;50:422–9.

20. Rajakumar K, Fernstrom JD, Holick MF, Janosky JE, Greenspan SL. Vitamin D status and response to Vitamin D(3) in obese vs. non-obese African American children. Obesity (Silver Spring). 2008;16:90–5.

21. Elizondo-Montemayor L, Ugaide-Casas PA, Serrano-González M, Cuello-García CA, Borbolla-Escobosa JR. Serum 25-hydroxyvitamin D concentration, life factors and obesity in Mexican children. Obesity (Silver Spring). 2010;18:1805–11.

22. Khor GL, Chee WS, Sheriff ZM, Poh BK, Arumugam M, Rahman JA, et al. High prevalence of vitamin D insufficiency and its association with BMI-for-age among primary school children in Kuala Lumpur, Malaysia. BMC Public Health. 2011;11:95.

23. Rajakumar K, de las Heras J, Chen TC, Lee S, Holick MF, Arslanian SA. Vitamin D status, adiposity, and lipids in Black American and Caucasian children. J Clin Endocrinol Metab. 2011;96:1560–7.

24. Sacheck J, Goodman E, Chui K, Chomitz V, Must A, Economos C. Vitamin D deficiency, adiposity, and cardiometabolic risk in urban schoolchildren. J Pediatr. 2011;159:945–50.

25. Abdous M, Cummins C, Lim MJ, Wassmer E, Shaw N. Prevalence and predictors of vitamin D insufficiency in children: a Great Britain population based study. PLoS One. 2011;6:e22179.

26. Olson ML, Maalouf NM, Oden JD, White PC, Hutchison MR. Vitamin D deficiency in obese children and its relationship to glucose homeostasis. J Clin Endocrinol Metab. 2012;97:279–85.

27. Turer CB, Lin H, Flores G. Prevalence of vitamin D deficiency among overweight and obese US children. Pediatrics. 2013;131:e152–61.

28. Bellone S, Esposito S, Giglione E, Genoni G, Fiorito C, Petri A, et al. Vitamin D levels in a paediatric population of normal weight and obese subjects. J Endocrinol Invest. 2014;37:805–9.

29. Moore CE, Liu Y. Low serum 25-hydroxyvitamin D concentrations are associated with total adiposity of children in the United States: National Health and Examination Survey 2005 to 2006. Nutr Res. 2016;36:72–9.

30. Barja-Fernández S, Aguilar CM, Martínez-Silva I, Vazquez R, Gil-Campos M, Olza J, et al. 25-Hydroxyvitamin D levels of children are inversely related to adiposity assessed by body mass index. J Physiol Biochem. 2018;74:111–8.

31. Shulhaj AM, Pavlyshyn H, Shulhaj O. Peculiarities of the prevalence and risk factors for vitamin D deficiency in overweight and obese adolescents in Ukraine. Arch Balk Med Union. 2019;54:57–63.

32. Peters BS, dos Santos LC, Fisberg M, Wood RJ, Martini LA. Prevalence of vitamin D insufficiency in Brazilian adolescents. Ann Nutr Metab. 2009;54:15–21.

33. Almeida AC, de Paula FJ, Monteiro JR, Nogueira-de-Almeida AC, Del Campo LA, Aragon DC, et al. Do all infants need vitamin D supplementation? PLoS One. 2018;13:e0195368.

34. Sociedade Brasileira de Pedriatria (SBP), Departamento Científico de Endocrinologia. Hipovitaminose D em pediatria: recomendações para o diagnóstico, tratamento e prevenção. Rio de Janeiro: SBP; Guia Prático de Atualização; 2016. p. 1–11.

35. Zakharova I, Klimov L, Kuryaninova V, Nikitina I, Malayavskaya S, Dobnya S, et al. Vitamin D insufficiency in overweight and...
obese children and adolescents. Front Endocrinol (Lausanne). 2019;10:103.

36. Aguirre Castaneda R, Nader N, Weaver A, Singh R, Kumar S. Response to vitamin D3 supplementation in obese and non-obese Caucasian adolescents. Horm Res Paediatr. 2012;78:226–31.

37. Harel Z, Flanagan P, Forcier M, Harel D. Low vitamin D status among obese adolescents: prevalence and response to treatment. J Adolesc Health. 2011;48:448–52.

38. Vidalhêt M, Mallet E, Bocquet A, Bresson JL, Briend A, Chouraqui JP, et al. Vitamin D: still a topical matter in children and adolescents. A position paper by the Committee on Nutrition of the French Society of Paediatrics. Arch Pediatr. 2012;19:316–28.

39. Kumar S, Kelly AS. Review of childhood obesity: from epidemiology, etiology, and comorbidities to clinical assessment and treatment. Mayo Clin Proc. 2017;92:251–65.