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Association between physical activity, cardiometabolic risk factors and vitamin D in children and adolescents: a systematic review

Associação entre atividade física, fatores de risco cardiometabólico e vitamina D em crianças e adolescentes: uma revisão sistemática

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ABSTRACT

This systematic review aimed to synthesize evidence of cross-sectional studies on the associations between physical activity, cardiometabolic risk factors and vitamin D concentrations in children and adolescents. The search was performed in PubMed, SciELO, LILACS, Scopus, MEDLINE and SPORTDiscus. Cardiometabolic risk factors included obesity, insulin resistance, systemic arterial hypertension and unfavorable changes in the lipid profile (low levels of high-density lipoprotein, elevated low-density lipoprotein and triglycerides). Cross-sectional design studies published between 2007 and 2019 were included whether they evaluated the relationship between vitamin D and physical activity and/or vitamin D and cardiometabolic risk factors. Fourteen studies were selected, involving 8340 children and adolescents. The main results found were a significant inverse relationship between vitamin D levels and cardiometabolic risk factors. All studies (n = 8) that tested association between physical activity and 25-hydroxyvitamin D (25 (OH) D) concentrations showed a significant and direct relationship between them. In addition, nine out of eleven studies that tested the association between 25 (OH) D and body mass index reported an inverse and significant relationship between 25 (OH) D and obesity. In conclusion, sufficient concentrations of vitamin D are related to a more favorable cardiometabolic profile, and children and adolescents who are obese or insufficiently active have a higher risk of present hypovitaminosis D.

Keywords: Vitamin D; Exercise; Risk factors; Child; Adolescent; Review.

RESUMO

Esta revisão sistemática objetivou sintetizar evidências de estudos transversais sobre as associações entre atividade física, fatores de risco cardiometabólicos e concentrações de vitamina D em crianças e adolescentes. A busca foi realizada na PubMed, SciELO, LILACS, Scopus, MEDLINE e SPORTDiscus. No presente estudo, fatores de risco cardiometabólico incluíram obesidade, resistência à insulina, hipertensão arterial sistêmica e alterações desfavoráveis no perfil lipídico (high density lipoprotein baixo, low density lipoprotein e triglicerídeos elevados). Estudos originais com delineamento transversal, publicados entre 2007 e 2019, avaliando a relação entre vitamina D e atividade física e/ou vitamina D e fatores de risco cardiometabólico foram incluídos. No total, quatorze estudos foram selecionados, envolvendo 8340 crianças e adolescentes. Os principais resultados encontrados foram relação inversa significativa entre os níveis de vitamina D e os fatores de risco cardiometabólico. Todos os estudos (n = 8) que testaram a associação entre atividade física e concentrações de 25-hidroxivitamina D (25 (OH) D) mostraram uma relação direta e significativa entre eles. Além disso, nove dos onze estudos que testaram a associação entre 25 (OH) D e índice de massa corporal apresentaram uma relação inversa e significativa entre 25 (OH) D com obesidade. Conclui-se que concentrações suficientes de vitamina D estão relacionadas a um perfil cardiometabólico mais favorável. Crianças e adolescentes obesos ou insuficientemente ativos têm maior risco de apresentar hipovitaminose D.

Palavras-chave: *Vitamina D; Exercício; Fatores de risco; Criança; Adolescente; Revisão.*

Introduction

Low vitamin D concentration is identified as a global public health problem[1,2]. The main physiological implications of vitamin D deficiency are related primarily to problems in calcium absorption and consequently to bone health[3]. Furthermore, vitamin D also plays an important role in the metabolism and in the muscular, immunological and neurological functions, as well as in the regulation of the inflammation[4]. The vitamin D deficiency is associated with a higher risk of developing several diseases, such as rickets and osteomalacia[5], cancer[6,7], type 1 diabetes[8], type 2 diabetes[9], multiple sclerosis[10] and cardiometabolic diseases in adults[2,11,12]. However, the high frequency of low vitamin D levels has been a concern in all age groups[13,14] and it occurs in several countries[13,15], mainly due to changes in lifestyle during last decades, with longer stay in enclosure sedentary activities[16] leading to lower sun exposure, which is the main factor for absorption of vitamin D[17].

Besides that, researchers have found lower vitamin D concentrations in obese patients compared to healthy peers[18], which may be associated with lower vitamin D absorption due to increased body adiposity[19,20], as well as inadequate eating habits[21]. Another aspect is that vitamin D has an inverse relationship to the development of cardiovascular diseases, when present in sufficient levels[22].

However, despite of these evidences, there is a lack of systemic and compiled information about studies considering the associations between physical activity, cardiometabolic risk factors and vitamin D concentrations in children and adolescents. A synthesis of studies on this topic is justified by the fact that a better understanding of how these variables are related can contribute to improve of recommendations for vitamin D, such as the practice of physical activity with the intention of preventing obesity and cardiometabolic risk factors. Therefore, the objective of this systematic review was to analyze and synthesize evidence from cross-sectional studies on the associations between physical activity/physical fitness, cardiometabolic risk factors and vitamin D concentrations in children and adolescents.

Methods

The present study is a systematic review conducted according to the methodology of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[23]. Descriptors selection was based on the Health Sciences Descriptors (DeCs) and the Medical Subject Headings (MeSH), and the following descriptors were used in English, vitamin D; obesity; high density lipoprotein (HDL); low density lipoprotein (LDL); triglycerides; hypertension; insulin resistance; exercise; physical fitness and motor activity. In addition, the searches were performed using Boolean operators AND and OR, using the strategy ((“vitamin D”) AND (“obesity” OR “HDL” OR “LDL” OR “triglycerides” OR “hypertension” OR “insulin resistance”) AND (“exercise” OR “physical fitness” OR “motor activity”)). Moreover, additional research was done on the references of selected articles.

The inclusion criteria used for the study were: (i) original articles published between 2007 and 2019; (ii) articles published in English, Portuguese and Spanish; (iii) studies with cross-sectional design, because of the number reduced of studies with a longitudinal design to compose a systematic review[24-27] and most of them are related to sports performance[25-27] or assessed vitamin D supplementation[27]; (iv) studies that included children and adolescents, because this phase is crucial for the choice of habits, such as habits of sun exposure and practice of physical exercise, which tends to be maintained at other stages of life, making this phase of life important to be studied[28-31]; (v) studies that evaluated the relationship between vitamin D and physical activity and/or vitamin D and cardiometabolic risk factors. For this, the cardiometabolic risk factors considered in the present review were obesity, insulin resistance, systemic arterial hypertension, unfavorable changes in lipid profile (low HDL and elevated LDL and TG)[32-34]. Measurement of physical activity levels were considered both with objective (accelerometer) and subjective (questionnaire) measurements and physical fitness (strength, cardiorespiratory fitness, flexibility and muscular endurance) and (vi) studies that used blood analysis of 25-hidroxivitamina D (25 (OH) D) concentrations, which is the most abundant metabolite and the best indicator for evaluation of vitamin status[35].

The exclusion criteria applied were: (i) studies carried out with animals; (ii) books, book chapters, monographs, dissertations, theses, review articles, case studies or abstracts; (iii) studies in which vitamin D was not the dependent variable (outcome); and (iv) studies with vitamin D supplementation.

The search was conducted in peer-reviewed journals indexed in the website databases PubMed, SciELO, LILACS, Scopus, MEDLINE and SPORTDiscus. The time interval comprised the period from January 2007 to April 2018 and updated in April 2019.The search in the databases and the selection of titles, abstracts and articles were carried out by two researchers independently, considering the inclusion and exclusion criteria. In cases of disagreement among researchers a third researcher was consulted at consensus meetings.

Studies selected in this systematic review were analyzed for their methodological quality by of the criteria proposed by Downs and Black[36]. A checklist of 27 questions, evaluating the domains of communication, external validity, internal validity (bias), confounding variables/selection bias, and statistical power. However, some questions are not applicable to observational studies, so we considered just 18 questions, excluding questions 4,8,9, 13-15, 19, 23 and 24. Responses are scored with score 1 (when the criterion that characterizes quality is present) and 0 (when the criterion that characterizes quality is absent), except a question (5) in which three answers are allowed (scores from 0 to 2). Therefore, the maximum points that studies can obtain is 19. Thus, studies of better methodological quality reach higher scores. Two researchers performed the analysis of the methodological quality of the articles, when there was disagreement between them a third researcher was required. The Kappa statistical test (K = 0.95) was applied to verify the level of agreement between the two researchers.

For the data collection, a table was elaborated, in which detailed information about each study included in the review was inserted: a) author, year of publication and country of study; b) sample size and age; c) main variables analyzed; d) main results and; e) methodological quality score. For this, we used aggregated data from the participants of each study and was performed a descriptive synthesis of the selected studies. We provide summaries of the correlations for each variable of interest in the study. Due to the great heterogeneity between the studies, it was not possible performing a meta-analysis.

The consistency of results was established as the proportion of studies that showed a direct association between measures of physical activity/physical fitness and 25 (OH) D and an inverse association between measures of cardiometabolic risk factors and 25 (OH) D; the exception is the HDL, it is expected a direct relationship with 25 (OH) D. This strategy derived a classification of associations in consistent (≥ 60%); moderate (30-59%); and inconsistent (< 30%) and has been used previously in other studies[37,38]. The direction of the association between vitamin D, physical activity and cardiometabolic risk was classified as direct (+), null (0), or inverse (-).

Results

Characteristics and selection of studies

Initially, 1685 articles were found in the databases. A total of 455 references were excluded because they were duplicated.

The next stage comprised the reading of all titles (1230 selected articles) and 986 articles were excluded, which titles had no relation with the subject approached. Thus, 244 studies were analyzed by reading the abstracts, of which 223 articles were excluded. In the next stage, the 21 selected articles were read in full and the pre-established inclusion and exclusion criteria were applied. After the application of these criteria were designated for the present review 14 articles. The steps performed for the selection of studies are illustrated in Figure 1.

From the seven articles that were not considered eligible for the review two studies were excluded because vitamin D was not considered the dependent variable in the statistical analysis, one study presented a longitudinal design and four studies did not exclude individuals who were supplementing vitamin D at the time of data collection.

Methodological quality

Quality evaluation of the articles included showed that the highest score was 18 points and two articles scored this value[39,40]. One article scored 17 points[41] and two articles were quantified with 16 points[42,43]. Six articles reached 15 points in the evaluation of methodological quality[44-49]. One article reached 14 points[50], one article presented 13 points[51] and one study scored 12 points[52].

Regarding the location of the studies: three[40,47,51] studies were performed in South Korea, two studies were conducted in the United States[42,48] two other studies in Italy[44,45], a study from England[39], a study conducted in different countries from Europe[41], other studies were conducted in Iran[43], Saudi Arabia[49], Brazil[52], Spain[46] and Denmark[50].

In relation to the age group of individuals analyzed two studies included only children[49,50] five studies only adolescents[41-43,47,48] and seven studies included both age groups[40,44-46,51,52] and one article evaluated only girls[43]. In addition, the number of individuals evaluated included varies from 33 Brazilians children and adolescents[52] to 1466 Korean children and adolescents[40].

Table 1 shows the direction and consistency of the association between 25 (OH) D with physical activity and cardiometabolic risk factors.

The main characteristics of the selected articles are presented in Tables 2 and 3. Table 2 shows the description of the studies that analyzed the relation between physical activity/physical fitness and 25 (OH) D and Table 3 description of the included studies regarding the relationship of 25 (OH) D concentrations and cardiometabolic risk factors.

Characteristics of vitamin D

In the initial analysis, we observed a variety of methods

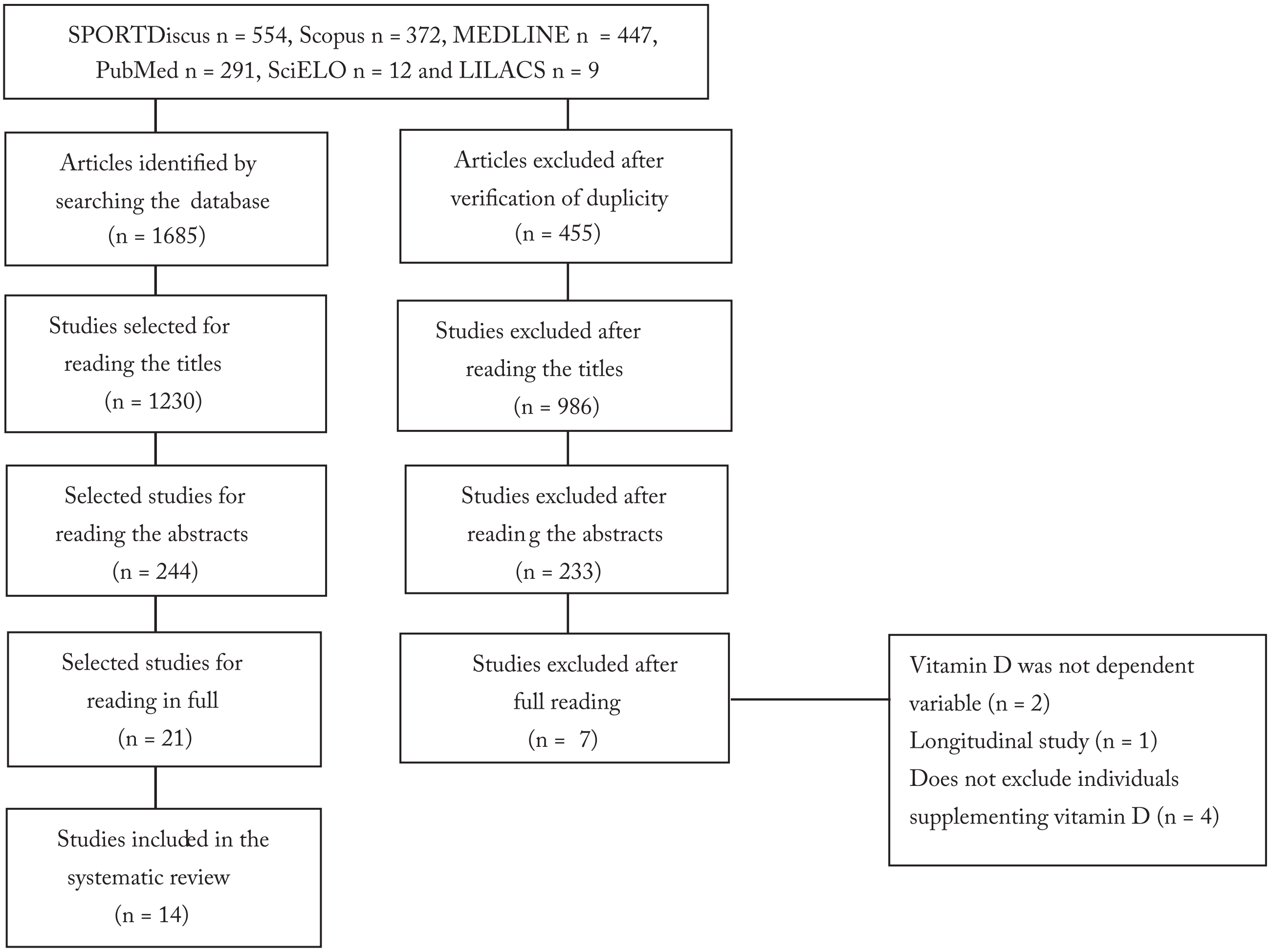

Figure 1 – Flowchart of the selection process of the present review.

Table 1 – Summary of the association between 25 (OH) D, physical activity / physical fitness and cardiometabolic risk factors.

Variables	Nº of articles	Direction of association with 25 (OH) D (numbers are the study reference number)			Consistency of the association with 25 (OH) D	
		+	0	-	% studies	Classification*
PA	8	39,42,44,45,49,50,51,52	--	--	100	Consistent
CF	3	41,42,52	--	--	100	Consistent
BMI	11	--	40,43	39,41,42,44,45,47,49,50,51	81.8	Consistent
FM	6	--	--	40,41,42,50,51,52	100	Consistent
WC	5	--	43,50	42,47,51	60	Consistent
Glucose	4	--	--	40,43,48,51	100	Consistent
Insulin	3	--	--	40,48,51	100	Consistent
HDL	5	46,48	43,50,51	--	40	Moderate
LDL	3	--	46,48	50	33.33	Moderate
TG	5	--	43,48	46,50,51	60	Consistent
SBP	4	--	43,50,51	48	25	Inconsistent
DBP	4	--	43,51	48,50	50	Moderate

25 (OH) D = 25-hydroxyvitamin D; PA = physical activity; CF = cardiorespiratory fitness; BMI = body mass index; FM = fat mass; WC = waist circumference; HDL =high density lipoprotein; LDL = low density lipoprotein; TG = triglycerides; SBP = systolic blood pressure; DBP = diastolic blood pressure; (+) direct, (0) null or (-) inverse.

used to classify individuals regarding vitamin D levels, four cutoff points were found. Among them, the most frequently cutoff point used considered vitamin D deficiency values below 20.00 ng/mL (50.00 nmol/L), vitamin D insufficiency between 20.00 and 30.00 ng/mL (50.00-75.00 nmol/L) and sufficiency, equal or above 30.00 ng/mL (75.00 nmol/L)[42,44,45,52].

Another cutoff point, which was present in three articles, was considered as subjects with vitamin D deficiency values below 20.00 ng/mL (50.00 nmol/L) and sufficiency in vitamin D, values equal or above of 20.00 ng/mL (50.00 nmol/L)[39,43,46]. The cut-off point used by Chung et al.[40] considered individuals with deficiencies with values lower than 15.00 ng/mL (37.50 nmol/L); vitamin D insufficiency values between 15.00 ng/mL and 20.00 ng/mL (37.50 to 50.00 nmol/L) and vitamin D sufficiency those with values above 20.00 ng/mL (50.00 nmol/L). Finally, Petersen et al.[50], considered values of 25 (OH) D deficiency < 10.00 ng/mL (25.00 nmol/l) and 25 (OH) D sufficiency > 20.00 ng/mL (50.00 nmol/l).

In addition, in some studies, vitamin D levels were divided into terciles[47,48] and quartiles[46,51]. In view of the uncertainty regarding cutoff points for vitamin D deficiency, insufficiency and sufficiency, those researchers decided to analyze the means of the group itself[41,49].

An important factor to be mentioned is the period of the year in which the blood collection was performed. Several studies use this as a factor to be adjusted and considered in the interpretation of the results [40,42,48]. Of the studies that are part of this review, thirteen[39-51] described when the blood collection was performed.

Among the five studies that were carried out in Asia, three were performed in South Korea[40,47,51] and the highest prevalence of vitamin D insufficiency found in studies with Korean children and adolescents was 71%[47]. In addition, a study was conducted in Iran[43] and the prevalence of vitamin D deficiency was 96%

Table 2 – Description of the included studies that analyzed the relation between physical activity/physical fitness and 25 (OH) D.

Author	Sample / age (years)	Variables analyzed	Main results	#
Chung et al.[40] South Korea	1466 children and adolescents 10-19 years	25 (OH) D and PA (Questionnaire)	Regular PA (n (no/yes)) 37.50 nmol/l = 242/311; 37.50 to <50.00 nmol/l = 188/355 and >50.00 nmol/l = 85/285 (p = 0.001)	18
Valtueña et al.[41] Europe	1006 adolescents 12-17 years	25 (OH) D, CF and strength	Boys = direct relationship with vitamin D = VO_{2max} ($p < 0.050$) Girls = direct relationship with vitamin D = strength ($p < 0.010$)	17
Rafraf et al.[43] Iran	216 adolescents girls 14-17 years	25 (OH) D and PA (Questionnaire)	Used physical activity as adjustment in the statistical analysis	16
Absoud et al.[39] England	1102 children and adolescents 4 -18 years	25 (OH) D, PA (Questionnaire*) and SB	Inverse relationship with vitamin D: Overweight (p = 0.010) Direct relationship: Exercise (≥ 30min/d) and watch TV (< 2.5 h/d) ($p < 0.001$)	16
Dong et al.[42] United States	559 adolescents 14 -18 years	25 (OH) D, CF and PA (Accelerometry and CF)	Direct relationship with vitamin D = VPA ($p < 0.010$) e CF (p = 0.025)	16
Kensarah et al.[49] Saudi Arabia	503 children 1-6 years	25 (OH) D and PA (Questionnaire)	Direct relationship with vitamin D PA outdoors (p = 0.011) Outdoor physical inactivity is a predictor of hypovitaminosis D	15
Vierucci et al.[45] Italy	427 children and adolescents 10-21 years	25 (OH) D and PA (Interview)	< 3 hours/week of outdoor exercise greater prevalence of hypovitaminosis D	15
Colao et al.[44] Italy	373 children and adolescents 11-20 years	25 (OH) D and PA (Interview)	Direct relationship with vitamin D: practice of exercise ($p < 0.001$)	15
Nam et al.[47] South Korea	713 adolescents 12 -19 years	25 (OH) D, and PA (LPA and VPA) (Questionnaire)	The mean serum 25 (OH) D level was significantly higher for those who exercise regularly than those do not (p = 0.010)	15
Rodríguez et al.[46] Spain	149 children and adolescents 8-13 years	25 (OH) D and PA (Questionnaire)	The lack of physical activity predisposes 25 (OH) D deficiency (p = 0.009)	15
Parikh et al.[48] United States	701 adolescents 14-18 years	25 (OH) D and PA (Accelerometry)	Used physical activity as adjustment in the statistical analysis	15
Petersen et al.[50] Denmark	782 children 8-11years	25 (OH) D and PA (Accelerometry)	Positively associated with MVPA (p = 0.010)	14
Ha et al.[51] South Korea	310 children and adolescents 10-12 years	25 (OH) D and PA (Accelerometry)	Direct relationship with vitamin D = VPA, MPA and LPA ($p < 0.001$)	13
Corazza et al.[52] Brazil	33 children and adolescents 11-13 years	25 (OH) D, CF and PA (Questionnaire)	Direct correlation between 25 (OH) D and VO_{2max} (p = 0.01), MVPA (p = 0.010)	12

25 (OH) D = 25-hydroxyvitamin D; PA = physical activity; SB = sedentary behavior; CF = cardiorespiratory fitness; VPA = vigorous physical activity; MPA = moderate physical activity; LPA = light physical activity; MVPA = moderate to vigorous physical activity; VO2max = maximum oxygen volume; *for the sub-group of the sample the physical activity information collected in a subjective assessment was validated by directly measuring the activity level using a motion sensor (accelerometer).

Table 3 – Description of the included studies regarding the relationship of 25 (OH) D concentrations and some factors related to cardiometabolic risk.

Author / year / location	Sample / age	Main variables analysed	Main results	#
Chung et al.[40] 2014, South Korea	1466 children and adolescents 10-19 yrs	25 (OH) D, BMI, % fat, FM, insulin, glucose, QUICKI	Inverse relationship with vitamin D = glucose (p = 0.039), insulin, HOMA-IR (p < 0.001), FM (p = 0.016), %FM (p = 0.023), direct relationship with vitamin D = QUICKI (p < 0.001)	18
Valtueña et al.[41] 2013, Europe	1006 adolescents 12-17 yrs	25 (OH) D and BMI	Inverse relationship with vitamin D = BMI (p < 0.050)	17
Rafraf et al.[43] 2014, Iran	216 a dolescents girls 14-17 years	25 (OH) D, BMI, WC, BP, blood glucose, HDL	Inverse relationship with vitamin D = fasting blood glucose (p < 0.040)	16
Absoud et al.[39] 2011, England	1102 children and adolescents 4-18 yrs	25 (OH) D and BMI	Inverse relationship with vitamin D = overweight (p = 0.010) and watch TV > 2.5 h/d (p < 0.001)	16
Dong et al.[42] 2010, United States	559 adolescents 14-18 yrs	25 (OH) D, BMI, WC, lean mass, FM, % fat, VAT, SAT	Inverse relationship with vitamin D = BMI (p = 0.020), WC; FM, % fat (p < 0.010), visceral adipose tissue (p = 0.015) and subcutaneous adipose tissue (p = 0.039)	16
Kensarah et al.[49] 2015, Saudi Arabia	503 children 1-6 yrs	25 (OH) D and BMI	Inverse relationship with vitamin D = BMI (p < 0.001)	15
Vierucci et al.[45] 2014, Italy	427 children and adolescents 10-21 yrs	25 (OH) D and BMI	Increased hypovitaminosis D = overweight, low sun exposure, regular use of sunscreens < 3 hours/week of outdoor exercise	15
Colao et al.[44] 2014, Italy	373 children and adolescents 11-20 yrs	25 (OH) D and BMI	Inverse relationship with vitamin D = BMI (p < 0.001)	15
Nam et al.[47] 2012, South Korea	713 adolescents 12-19 yrs	25 (OH) D, BMI, WC, Glucose, insulin, TC, HDL, TG	Inverse relationship with vitamin D = WC (p = 0.020) and BMI (p = 0.010)	15
Rodríguez et al.[46] 2011, Spain	149 children and adolescents 8-13 yrs	25 (OH) D, BMI, TG, HDL, LDL	Compared to children with serum 25 (OH) D concentrations in the fourth quartile (higher values), those in the first had higher triglyceride (p < 0.050), 25 (OH) D inversely to the TG (p = 0.010)	15
Parikh et al.[48] 2012, United States	701 adolescents 14-18 yrs	25 (OH) D, BMI, BP, HOMA-IR, lipid profile, adiponectin, glucose	Inverse relationship with vitamin D = HOMA-IR (p < 0.010), leptin (p < 0.01), glucose (p = 0.02), SBP (p = 0.02), DBP (p < 0.01), direct relationship with vitamin D = adiponectin (p = 0.050) and HDL-C (p = 0.020)	15
Petersen et al.[50] 2015, Denmark	782 children 8-11 yrs	25 (OH) DBP, glucose, HOMA-IR, plasma lipids, FM	25 (OH) D status was negatively associated with BMI Z-scores (p = 0.030), FM (p = 0.001), BP and plasma lipids	14
Ha et al.[51] 2013, South Korea	310 children and adolescents 10-12 yrs	25 (OH) D, BMI, WC, HOMA-IR, % fat, glucose, insulin, HDL, TG	Inverse relationship with vitamin D = BMI (p = 0.001), % fat e WC (p < 0.001), glucose (p = 0.011), TG, insulin and HOMA-IR (p < 0.001)	13
Corazza et al.[52] 2018, Brazil	33 children and adolescents 11-13 yrs	25 (OH) D, BP, TC, LDL, HDL, lean mass, %FM, TG, FM	Direct correlations between 25 (OH) D and % of lean mass (p = 0.010), lean mass (p = 0.030), and an inverse relationship between 25 (OH) D and % fat (p = 0.010)	12

Methodological quality score; 25 (OH) D = 25-hydroxyvitamin D; BMI = body mass index; FM = fat mass; WC = waist circumference; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; TC = total cholesterol; HDL = high density lipoprotein; LDL = low density lipoprotein; TG = triglycerides; HOMA-IR = Momeostasis Model Assessment, Yrs = years, SAT = subcutaneous adipose tissue; VAT= visceral adipose tissue.

and the mean hypovitaminosis D was extremely low (7.26 ng/mL or 18.00 nmol/L). The study in Saudi Arabia found a vitamin D deficiency of 63% in the early childhood[49].

The articles evaluated from the European continent totalized six articles. In Italy, the prevalence of vitamin D deficiency was 49.9%[44] and 1.7%[45], insufficiency was 32.3%[44] and 79.3%[45], and sufficient was 17.8%[44] and 19%[45]. In England, vitamin D insufficiency was found in 35% of the children studied[39]. In Denmark vitamin D insufficiency were observed in 28.4% of the children[50]. In Spain 37.6% of the children had vitamin D deficiency[46]. In addition, a study conducted in differents European countries with 1006 European adolescents, the average of vitamin D concentration was 18.49 ng/mL (58.80 nmol/L)[41].

Among the 14 studies found in the analysis, three were performed in the American continent. The study by Dong et al.[42] found that vitamin D insufficiency was 56.4% and deficiency in 28.8% of U.S. adolescents. In the study by Parikh et al.[48] the average concentration of vitamin D found among U.S. adolescents was 22.80 ng/mL (72.50 nmol/L). Finally, a study conducted with Brazilian children and adolescents showed that the average of vitamin D for the insufficiently active group was 23.94 ng/mL (59.85 nmol/L) and for the active group was 31.45 ng/mL (78.62 nmol/L)[52].

Characteristics of assessment of physical activity and physical fitness

From the 14 articles included in the review, four articles have evaluated the objectively measured physical activity levels[42,48,50,51] and nine articles by subjective-measures[39,40,43-47,49,52]. Furthermore, three articles evaluated the physical fitness assessing the levels of cardiorespiratory fitness[41,42,52] and one article assessed the strength[41].

For the evaluation of objectively measured physical activity, the Actigraph MTI accelerometer was used in two studies[42,48], the study conducted by Ha et al.[51] used the Kenz Lifecorder EX accelerometer and Petersen et al.[50] used the Accelerometry (ActiGraph GT3X+ Tri-Axis Accelerometer Monitor). In addition, all study participants were instructed to use accelerometers for seven consecutive days.

Concerning the studies that used accelerometry in the evaluation of physical activity, a significant direct relationship between vitamin D and vigorous physical activity ($r = 0.13$; $p < 0.001$) was found by Dong[42]. In addition, a direct relationship between vitamin D and levels of low, moderate and vigorous physical activity ($r = 0.40$; $p < 0.001$) was found in the study conducted by Ha et al.[51] in Korean children. However, this relationship was not significant in the study by Parikh et al.[48] with 701 US adolescents.

In relation to physical activity levels evaluation through subjective measures, seven studies applied questionnaires[39,40,43,46,47,49,52] and two studies used interviews[44,45]. Only the study conducted by Rafraf et al.[43] used a validated Iranian version of the International Physical Activity Questionnaire (IPAQ). The study presented by Absoud et al.[39] used a seven-day physical activity diary. In addition, Chung et al.[40] used a questionnaire to assess the physical activity level and two other studies only used questions in the general questionnaire to quantify physical activity[47,49]. Corazza et al.[52] used a questionnaire self-administered physical activity checklist. Rodríguez et al.[46] applied a questionnaire of physical activity that recorded the length of time spent sleeping, eating, and playing sport. For the interviews, the two studies also only used questions to quantify the levels of physical activity of those evaluated[44,45].

In studies that assess physical activity levels through questionnaires and interviews and tested the association with 25 (OH) D, the results are consistent. In the UK population-based study conducted by Absoud et al.[39] it was found that children and adolescents with a level of physical activity less than 30 minutes a day and those who had spent more than 2.5 hours per day watching TV had lower levels of vitamin D (odds ratio, OR = 1.5; 95%CI: 1.0–2.3). In addition, six studies found direct and significant relationships between vitamin D levels and physical activity[39,44,45,49,52]. Three studies[40,46,47] performed comparisons with physical activity. The individuals with lower vitamin D concentrations had lower coefficients of physical activity. ($p = 0.010$)[46]. Among the 25 (OH) D categories, the highest 25 (OH) D group participants were more physically active than those in the lower 25 (OH) D group ($p < 0.001$)[40]. The mean 25 (OH) D level was significantly higher for those who exercise regularly than those do not ($p = 0.010$)[47].

For the evaluation of cardiorespiratory fitness, the study conducted by Dong et al.[42] and Corazza et al.[52] used the treadmill test and showed a direct relationship between vitamin D and cardiorespiratory fitness ($r = 0.10$; $p = 0.025$), ($r = 0.60$; $p = 0.010$), respectively. In the study proposed by Valtueña et al.[41], a 20 m shuttle run test was used to evaluate the cardiorespiratory fitness a direct relationship between vitamin D and VO_{2max} in boys ($r = 0.18$; $p < 0.005$) and strength evaluated by dynamometer showed a direct relationship between vitamin D and strength was found in girls ($r = 0.12$; $p < 0.001$).

When the studied variable is vitamin D, it is necessary to have information about where the physical activity was performed (external or internal environment), because this may interfere with the vitamin D concentration value. Of the eight[39,42,44,45,49, 50,51,52] studies that tested the association between physical activity and 25 (OH) D, four [39,45,49,52] evaluated issues such as sun exposure and physical exercise practiced outdoors. In addition, of these eight studies, only one evaluated the use of sunscreen[45].

Evaluation of cardiometabolic risk factors

- **Obesity**

Concerning the total of 14 articles selected for analysis, all studies used body mass index (BMI) as an evaluation of the body composition.[39-52]. About the methodology to evaluate BMI the cut-offs were derived from sex specific and BMI age curves in twelve[39-45,47-49,52,50] and two[46,51] used the BMI formula = weight (kilograms) ÷ height (metres^2) to access the values.

Eleven studies correlated vitamin D to BMI[39-47,49-51] and nine[39,41,42,44,45,47,49-51] reported an significant and inverse relationship between these two variables ((r = -0.10; p < 0.010)[42], (r = -0.43; p <0.001)[44], (r = - 0.14; p = 0.007)[45],(OR 1.6; 95%CI: 1.0–2.5)[39], (p = 0.030)[50], (r = -0.10; p = 0.010)[47], (r = -0.23; p < 0.001)[51], (r = - 0.08; p = 0.013)[41], (r = - 0.42; p < 0.001)[49]). Waist circumference was also used to predict visceral adipose tissue in five articles[42,43,47,50,51], an inverse and significant relationship between waist circumference and vitamin D levels was observed in three[42,47,51] studies. Besides that, only one article used the waist-to-hip ratio as an evaluation of obesity[51], however, it did not find any significant relation. In addition, among the 25 (OH) D categories, the highest 25 (OH) D group participants had lower BMI values than those in the lower 25 (OH) D group (p < 0.001).

Regarding to the methods used to evaluate body fat, the most commonly used dual energy X-ray densitometry (DXA) in three articles[40,42,50] and bioelectrical impedance, evaluated, also in three articles[41,51,52].In this systematic review, it was found that of the six studies that tested the relationship between vitamin D and body composition[40-42,50-52] all showed that fat mass has an inverse relationship with vitamin D.

- **Insulin resistance**

Regarding other cardiometabolic risk factors, four studies verified the association between vitamin D levels and insulin resistance[40,43,48,51]. In the study by Ha et al.[51]in 310 Korean children, vitamin D was inversely associated with glucose (r = - 0.22; p < 0.001), insulin (r = -0.23; p < 0.001), and the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) (r = -0.26; p < 0.001). Similar results were found by Chung et al.[40] who found inverse relationships between vitamin D and markers of insulin resistance (p < 0.001), fasting blood glucose (p = 0.039), HOMA-IR index (p < 0.001) and direct relation with the QUICKI index (p < 0.001) after adjusting for possible confounding factors (age, sex, physical activity and adiposity) in 1466 Korean children and adolescents. Similarly, Parikh et al.[48] found a significant inverse relationship between vitamin D levels and the HOMA-IR index (r = -0.17; p < 0.010) and glucose (r = -0.16; p = 0.020) in 701 US adolescents. Rafraf, Hasanabad and Jafarabadi[43] identified an inverse relationship between vitamin D and fasting glycemia (r = -0.13; p = 0.034) in Iranian girls. In the study that performed the comparison between the different tertile of serum 25 (OH) D[47], no significant values were found for glucose.

- **Systemic arterial hypertension**

About the protocols used to measure blood pressure, Rafraf, Hasanabad and Jafarabadi[43] measured in the morning by a mercury sphygmomanometer, on the upper right arm. Participants were resting in the sitting position for 5 minutes. Two readings were recorded (interval of one–two min). The mean of the two was calculated for analysis. Petersen et al.[50] measured the blood pressure using an automated device after 10 min of rest. Measurements were performed three times whereof the mean of the last two measurements was used. Ha et al.[51] blood pressure was measured using an automated instrument. The participants lay for twenty minutes and then sat for five minutes. Two blood pressure assessments were taken at 3-min intervals. Means of the two were calculated for this variable. Finally, Parikh et al.[48] does not describe in the methods the protocol used to measure blood pressure.

Four articles analyzed the relationship between vitamin D with high blood pressure[43,48,50,51]. The study conducted by Parikh et al.[48] found a significant inverse relationship between vitamin D levels and systolic blood pressure (r = -0.10; p = 0.020) and diastolic blood pressure (r = -0.21; p < 0.010) in U.S. adolescents. Petersen et al.[50] found a significant inverse association between vitamin D and diastolic blood pressure (p = 0.020). However, two studies found no relationship between blood pressure with vitamin D[43,51]. In the comparison between the terciles, in the study performed by Nam[47], for the systolic blood pressure were not found differences (p = 0.868) and for the diastolic blood pressure, those with the highest values of this variable also had lower concentrations of vitamin D (p = 0.029).

- **Lipid profile (HDL, LDL and TG)**

Five articles had the objective to verify the levels of vitamin D and its association with HDL and triglycerides[43,46,48,50,51], and of these, three articles also verified LDL[46,48,50]. Thus, Parikh et al.[48] observed a direct and significant a correlation between vitamin D and HDL levels (r = 0.14; p = 0.020) and did not correlate with LDL and triglycerides. Rodríguez et al.[46] compared children with serum 25 (OH) D concentrations in the fourth quartile (higher values), those in the first had higher triglycerides (p < 0.050), the same was found by HA et al.[51] (r = -0.15; p = 0.010). Therefore, 25 (OH)

D level was found to be inversely proportional to the triglycerides (r = -0.86; p = 0.010)[46]. Petersen et al.[50] presented in his study an inverse relationship between 25 (OH) D and LDL (p < 0.001). Moreover, this association with vitamin D levels and HDL and TG levels were not found in the other studies[43,47,48].

Discussion

This review found evidence from cross-sectional studies that supported a relationship between sufficient concentrations of vitamin D and a more favorable cardiometabolic profile in children and adolescents. Also, evidence indicated that children and adolescents who were obese or insufficiently active have a higher risk of present hypovitaminosis D.

Cross-sectional studies supported the hypothesis that obese individuals are more likely to have vitamin D deficiency than normal weight individuals because of several important factors, including increased vitamin D sequestration in adipose tissue, low vitamin D dietary intake due to poor nutritional habits and minimal sun exposure due to sedentary lifestyle[53,54].

However, some authors affirm in their findings that the association between vitamin D levels and obesity rates is complex. The methodological problems in the studies that tested this relationship were the non-use of the BMI Z score in two studies[46,51]. When the population studied involves children and adolescents, it is important to consider sex and age for the classification of nutritional status. Even so, the results are consistent for the BMI variable, proving the tendency of individuals with excess weight to present hypovitaminosis D.

The data presented in the different studies assessed questions related to insulin resistance were considered consistent. The mechanisms of association between 25-hydroxyvitamin D (25 (OH) D) and insulin resistance are not fully understood, however one hypothesis is that 25 (OH) D promotes insulin sensitivity by insulin receptor expression and regulation of intracellular calcium[55].

Evidence on the relationship between blood pressure and vitamin D concentration were moderate or inconsistent. The authors recognize that the mechanisms by which low levels of vitamin D lead to high blood pressure are not known. However, vitamin D deficiency is believed to affect blood pressure through various mechanisms, such as the regulation of the renin-angiotensin system[56,57] suppression of parathyroid hormone activity[58], and hypertrophy of left ventricular and vascular smooth muscle[59]. One problem was the heterogeneity regarding the protocol used for this variable. The rest time ranged from five minutes[43,51] to ten minutes[50], and before that in the study conducted by Ha et al.[51] individuals were lying down for twenty minutes. One study have reported that three measurements were done[50], two others measured twice[43,51]. The way to arrive at a final value was through the calculation of the average of the different measures[43,50,51]. In addition, one of the limitations was that Parikh et al.[48] did not present the procedure for blood pressure measurement.

In this review, the consistency of the data regarding HDL was considered moderate and in relation to the LDL and triglyceride levels, consistent. Another variable that may influence the profile is the stage of maturational development, mainly in relation to HDL. It is known that girls tend to have increased HDL concentrations in adolescence, and menarche is probably of great importance in this mechanism [60]. Perhaps, these differences may influence the concentrations of 25 (OH) D.

All included studies confirmed an association between vitamin D concentrations and physical activity/physical fitness in children and adolescents (see Table 1). It is suggests that skeletal muscle can serve as a 25 (OH) D hijacker, protecting this metabolite from liver degradation, which may explain why individuals who practice physical activity in indoor settings may have sufficient vitamin D[61]. The practice of physical activity regularly provides higher lean mass and lower fat mass values. This increases considerably the possibility of this active individual presenting a sufficiency of 25 (OH) D, considering that there is a decrease of a potential barrier (fat), and the aid of the skeletal muscle[62]. Probably greater benefits regarding vitamin D status will be obtained if physical activity is performed outdoors. Otherwise, sedentary activities lead to a decrease in the level of physical activity and decrease the chances of sun exposure, predisposing to obesity and possibly to hypovitaminosis D[51].

The most common methodological problems in studies that tested this relationship were the control of some variables that may influence the relationship between vitamin D and physical activity[63], such as the use of sunscreen, if the environment chosen for exercise is outdoor environment or internal environment and what are the habits of sun exposure[42,43,48,50].

The present study has some limitations that should be mentioned; first, the study was related only to cross-sectional design, as mentioned in the inclusion criteria. This makes impossible to establish causal relations between the analyzed variables. In addition, most of the studies evaluated the level of physical activity through subjective assessment (questionnaire and interview), consequently, this type of evaluation is very dependent on the memory of the evaluated and their self-perception regarding the topic. Finally, the lack of consensus regarding the cutoff point to determine vitamin D deficiency, insufficiency, and sufficiency as well variations in vitamin D concentrations according to the season of collection, may influence the interpretation of the data.

Therefore, there is a need for more scientific studies on the role of vitamin D, when associated with cardiometabolic risk factors and physical activity levels in the world population, and especially with children and adolescents, because little is known about these processes since childhood, so that there is a better understanding and, if necessary, later intervention, aiming at the prevention of cardiovascular diseases in adulthood.

It is suggested that better-quality studies should be conducted with objective measures of physical activity and vitamin D. Practical recommendations for future studies are controlling of possible confounding factors, such as the season of the year, sun exposure and sunscreen habits and outdoor or indoor exercise habits. Consequently, providing more higher quality information about these relevant issues.

The main conclusion of the present review is that higher concentrations of vitamin D are related to a more favorable cardiometabolic profile. In this sense, vitamin D showed a consistent and direct association with physical activity and cardiorespiratory fitness, and inverse and consistent relationship related to BMI, waist circumference, glucose, insulin and triglycerides. Thus, children and adolescents obese and insufficiently active have a higher risk of present hypovitaminosis D.

Conflict of interest declaration

The authors declare no conflict of interest.

Authors contributions

Corazza PRP, elaboration of the idea; selection of databases; development and interpretation of the results; drafting of the manuscript and translation. Tadiotto MC, identification; selection of databases, assessment and data extraction of original studies; interpretation of the results; drafting of the manuscript. Michel DA, data extraction of original studies; interpretation of the results. Mota J, interpretation of the results; critical review of the text. Leite N elaborated the idea, assessment of original studies, interpretation of the results; critical review of the text.

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