Brazilian Journal of Biology®

ISSN 1519-6984 (Print)
ISSN 1678-4375 (Online)

Original Article

Relationship between vitamin D and physical activity: systematic review and meta-analysis

Relação entre vitamina D e atividade física: revisão sistemática e meta análise

B. Mori[a*], J. F. M. Barcellos[a,b], L. E. R. Lima[c], V. Zaranza[d], R. G. Autran[a,e], E. B. Camargo[f] and C. S. M. Souza[g]

[a]Universidade Federal do Amazonas – UFAM, Instituto de Saúde e Biotecnologia, Programa de Pós-graduação em Imunologia Básica e Aplicada – PPGIBA, Coari, AM, Brasil
[b]Universidade Federal do Amazonas – UFAM, Laboratório de Histologia Funcional, Manaus, AM, Brasil
[c]Universidade Federal do Amazonas – UFAM, Manaus, AM, Brasil
[d]Universidade Federal do Amazonas – UFAM, Curso de Medicina, Manaus, AM, Brasil
[e]Universidade Federal do Amazonas – UFAM, Laboratório de Estudo do Desempenho Humano, Manaus, AM, Brasil
[f]Fundação Oswaldo Cruz, Brasília, DF, Brasil
[g]Universidade Federal do Amazonas – UFAM, Saúde Baseada em Evidências (Medicina Interna e Terapêutica), Manaus, AM, Brasil

Abstract

Vitamin D plays an important role in immune function and inflammation and the physical activity demonstrate relationship near to syntheses of vitamin D, considering to necessary to factors immunologics, environmental and physical. We searched five databases through February 20, 2021. Two reviewers screened the studies, collected data, assessed the risk of bias, and ranked the evidence for each outcome across the studies, independently and in duplicate. The prespecified endpoints of interest were Cardiorespiratory Fitness; Sunlight Exposure; Body Mass Index (BMI). We only included data from peer-reviewed articles in our primary analyses. In our primary analysis, there was a positive trend between serum 25(OH)D <20 ng/ml and body mass index, this result should be interpreted with caution, considering confidence intervals (RR 1.10 95% CI 0.37 to 1.83. We identified 4 high quality evidence that vitamin D levels and high physical activity required a direct relationship considering (four trials with 2,253) ; RR 0. (RR 0.0; 95% CI -0.15 to 0.15) (RR 0.59; 95% CI 0.43 to 0.75. Although the evidence available so far, from observational studies of medium quality, can be seen as showing a trend towards an association between sufficient serum levels of 25(OH)D and physical activity, this relationship has been shown. have a stimulating effect on vitamin D synthesis, the relationship of low body mass index with sufficient vitamin D levels is not based on solid evidence. We await results from ongoing studies to determine this effectiveness.

Keywords: vitamin D, physical activity, children, adolescent, body mass index.

Resumo

A vitamina D desempenha um papel importante na função imunológica e na inflamação e a atividade física demonstra relação próxima à síntese de vitamina D, sendo necessária a fatores imunológicos, ambientais e físicos. Pesquisamos cinco bancos de dados até 20 de fevereiro de 2021. Dois revisores examinaram os estudos, coletaram dados, avaliaram o risco de viés e classificaram as evidências para cada resultado nos estudos, de forma independente e em duplicata. Os endpoints de interesse pré-especificados foram aptidão cardiorrespiratória; Exposição à luz solar; Índice de Massa Corporal (IMC). Incluímos apenas dados de artigos revisados por pares em nossas análises primárias. Em nossa análise primária, houve uma tendência positiva entre 25(OH)D sérico <20 ng/ml e índice de massa corporal., esse resultado deve ser interpretado com cautela, considerando os intervalos de confiança (RR 1,10 IC 95% 0,37 a 1,83. Identificamos 4 evidências de alta qualidade de que níveis de vitamina D e atividade física alta exigiam uma relação direta considerando (quatro ensaios com 2.253) ; RR 0 . (RR 0,0; IC 95% -0,15 a 0,15) (RR 0,59; IC 95% 0,43 a 0,75. Embora as evidências disponíveis até agora, de estudos observacionais de qualidade média, possam ser vistas como uma tendência de associação entre níveis séricos suficientes de 25(OH) D e atividade física, essa relação foi demonstrada. têm um efeito estimulante na síntese de vitamina D, a relação de baixo índice de massa corporal com níveis suficientes de vitamina D não é baseada em evidências sólidas. Aguardamos resultados de estudos em andamento para determinar essa eficácia.

Palavras-chave: vitamina D, atividade física, crianças, adolescente, índice de massa corporal.

*e-mail: brunomori@ufam.edu.br
Received: May 10, 2022 – Accepted: September 20, 2022

1. Introduction

Recent observational data have suggested that approximately 40% of Europeans are vitamin D deficient and 13% are severely deficient. In the United States as well as in Brazil found reporting the prevalence of low vitamin D status in adolescents (Palacios and Gonzalez, 2014) Several studies have evaluated vitamin D status, body mass index and physical activity in childhood and together, they have shown widespread hypovitaminosis D worldwide, some studies have included large series targeting the pediatric age group from childhood to young adulthood (Bjarnadottir et al., 2015; Narchi et al. 2015; Blakeley et al., 2018).

However, it should be considered that comparing data from different studies is not always adequate. Different characteristics of enrolled patients (such as age, body mass index, sex, race/ethnicity, physical activity and prevalence of obesity) or other variables will affect vitamin D status, in particular latitude and season, as well as blood samples (Munns et al., 2016; Calvo and Lamberg-Allardt, 2017; Alghadir et al., 2018; Valtueña et al., 2013).

The available reviews illustrate the lack of data in most countries, particularly population representative data, with very limited information in children and adolescents. However, the number of recent publications in this area is escalating, with a broadening of the geographic diversity. Therefore, the aim of this systematic review was to evaluate what relationship between physical fitness and vitamin D.

2. Matherial and Methods

2.1. Eligibility criteria for inclusion and data extraction

Observational studies (case-control design) and intervention studies were evaluated, including randomized double-blind placebo control studies, non-randomized placebo control studies, clinical intervention, and audit studies. We included all published human studies without language restriction. Inclusion criteria were as follows: children and adolescents aged 6 to 9 years. The exclusion criteria were as follows: non-agreement to participate in the studies. Intervention studies were only included if they had an assessment of serum 25(OH)D levels at baseline. Search procedures were documented using the PRISMA protocol. The protocol of this systematic review and meta-analysis is available online on PROSPERO; registration number CRD42020159043.

2.1.1. Literature search

This study replicated the search strategy carried out from February 2021 to August 2020. We selected a total of 1,926 records from the following databases: Cochrane library (42), Sciense Direct (396), Scopus (1500), MEDLINE (3), EMBASE (7), we also searched for grey literature such as abstracts from conference presentations. Search terms used for all five databases included: "children OR adolescents" AND "physical activity" AND "Vitamin D". Our research included 1926 studies, in general, this review now has a total of 4 studies included, 1922 were the studies excluded for not answering the research question and 216 duplicates removed, this study based on the recommendations of the prefereed reporting items for systematic reviews and meta-analyzes (PRISMA).

2.2. Outcomes

Our Primary outcomes was Vitamin D. The secondary outcomes included: Cardiorespiratory Fitness; Sunligth Exposure; Body Mass Index (BMI).

2.3. Study selection and evidence abstraction

All relevant tasks listed below were implemented by 2 independent reviewers (BM, JFMB), and disagreements were resolved through discussions and/or with input from a content expert (CM).

2.3.1. Study selection

2.3.1.1. Risk of bias assessment

We assessed the quality of all included observational studies by outcomes. We used the Joanna Briggs - Check List for analytical Croos Seccional Studies (Higgins et al., 2021). We assessed the quality of the included clinical trials using the Cochrane Risk of bias tool, version 1 (Higgins et al., 2013).

2.4. Data synthesis and analysis

As a primary analysis, we conducted a random-effect meta-analysis, when at least two peer-reviewed studies were available for each predefined outcome using RevMan 5.4. (Higgins et al., 2021) For categorical outcomes, we calculated the relative risk (RR) and its 95% CI in patients with high serum 25(OH)D levels (<20 ng/ml as per the IOM), as compared to those with BMI (body mass index). Similarly, we calculated the mean difference (MD) and 95% CI of serum 25(OH)D level compared to physical activity levels. We assumed that serum 25(OH)D levels are normally distributed due to the low sample size. We therefore considered the mean as the median, and calculated the standard deviation by dividing the interquartile range by 1.35, when not provided (Jiménez-Pavón et al., 2014). We assessed statistical heterogeneity between studies using the I2, with significance at p value ≤0.05. We conducted sensitivity analyses using a higher 25 (OH)D cutoff (25(OH) D < 30 ng/ml), when such data was available. We did not conduct any subgroup analyses or publication bias assessment because of the limited number of available studies for every outcome of interest.

2.5. Selection of studies

The inclusion criteria used for the study were: (i) original articles; (ii) articles published in any language; (iii) studies to compose a systematic review and most of them are related to cardiorespiratory fitness or assessed vitamin D; (iv) studies that included children and adolescents, 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; (v) studies that evaluated the relationship between vitamin D and physical activity and/or vitamin D and cardiorespiratory fitness. 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). 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.

2.6. Assessment of risk of bias in included studies

Two review authors independently assessed the risk of bias for the two domains of randomisation sequence generation and allocation concealment, according to Joana Briggs Institute (JBI) - Check List for analytical Croos Seccional Studies.

2.7. Data analysis

Meta-analysis was performed using a random effects model with Revman 5.4 Software (Cochrane IMS), and sub group analysis was performed by location of the curve. If required, measures were corrected for diferences in the direction of the scales. Comparisons of Vitamin D vs BMI (Body Mass Index); Vitamin D vs Physical Activity. Care where the conservative management for the standard care group had similar intervention components were meta-analysed.

2.8. Assesment of heterogeneity

We assessed heterogeneity by visually inspecting the forest plots to determine closeness of point estimates with each other and overlap of CIs. We used the Chi2 test with a P value of 0.10 to indicate statistical significance, and the I2 statistic to measure heterogeneity. We used the following ranges outlined in the Cochrane Handbook for Systematic Reviews of Interventions to interpret the I2 statistic.

2.9. Quality of the evidence

Two review authors independently assessed the risk of bias for the two domains of randomisation sequence generation and allocation concealment, according to Joana Briggs Institute (JBI) - Check List for analytical Croos Seccional Studies (Moola et al., 2020).

This review included a body of evidence from 4 trials with 2,253 participants. Our bias risk assessments and quality assessments are shown in Figure 1. The evidence base from studies that examined vitamin D alone versus Body Mass Index and vitamin D versus Physical activity was high ("It is very unlikely that further research will change our confidence in estimating the effect") or moderate quality ("It is likely that additional research has an important impact on our confidence in estimating the effect and may change the estimate").

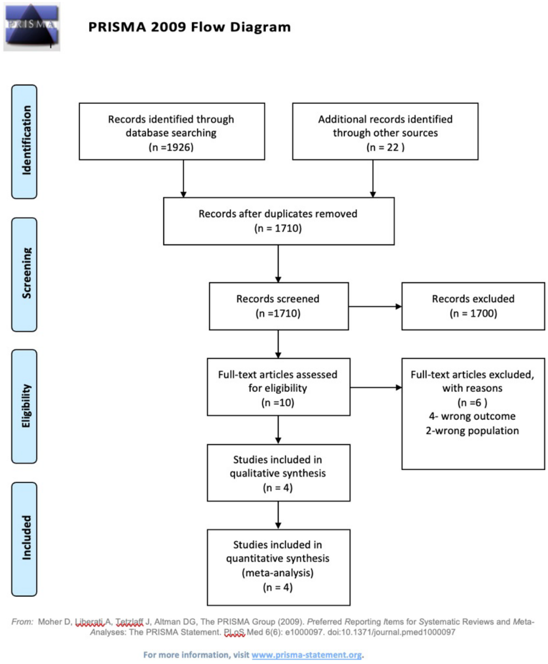

Figure 1. Prisma Flow.

3. Results

The search strategy identified 1926 citations. Following duplicate removal, we screened a total of 1710 citations. We also screened 19 citations from the grey literature and three articles based on the opinion of experts and senior authors, of which 10 were potentially eligible (Figure 1 Prisma Flow).

3.1. Description of included studies

Four randomized controlled trials were included in this review (Narchi et al., 2015; Al-Othman et al., 2012; Dong et al., 2010; Sallis et al., 2000) with design crossectional, totaling 2,253 participants. In general terms, the included trials fall into three main groups. Trials with cholecalciferol, ergocalciferol or 25-hydroxy vitamin D. In this first group, 4 studies were allocated, totaling 2,253 participants, aged 9 to 12 years (10.64), these studies were carried out in: Spain, Saudi Arabia, United States, Republic of Korea, they stratified vitamin levels D, with other outcomes (Table 1). These studies recruited children and adolescents in schools in such a way that all participants were regularly enrolled (Narchi et al., 2015; Al-Othman et al., 2012; Dong et al., 2010; Sallis et al., 2000). Tests with BMI Body Mass Index. The second group included 2 studies, with 1053 participants, aged 12.5 to 17.5 years (15.5), (Sallis et al., 2000; Pagels et al., 2016; Jiménez-Pavón et al., 2014) the first study was carried out on the European continent in 9 countries, respectively the second in the United States of America, both recruiting children and adolescents from their schools. For the definition of the body mass index (BMI) (Jiménez-Pavón et al., 2014), made use of the calculation (kg/Height 2), in the studies

Table 1. Summary of results of the included studies in the primary analysis per outcome.

Authors (Year) - Country (reference)	Study Design	Sample	BMI Mean ± SD	25(OH)D Levels	Physical Activity	25(OH) D Assay Timing of 25(OH)D Meansurement
Al-Othman et al. (2012) **- Saudi Arabia**	Cross seccional	331	23.1 ± 7.9	12.5 ± 24.9 nmol/l	22.1 ± 1.5 min/d	Vitamin D was measured using enzyme linked immunosorbent assay (ELISA)
Ha et al. (2013) **- Republic of Korea**	Cross seccional	310	19.8 ± 3.7	31.0 ± 7.1 nmol/L	24 ± 30 min/d	competitive chemiluminescence immunoassay for human serum or plasma
Jiménez-Pavón et al. (2014) **- Spain**	Cross seccional	1053	21.4 ± 3.58	58.9 ± 23.1 nmol/L	9.0 ± 14.1 min.d	enzyme-linked immunosorbent assay (ELISA)
Dong et al. (2010) **- United States**	Cross seccional	559	7.7 ± 11.3	73.3 ± 38.0 nmol/L	4.6 ± 6.8 min/d	Liquid chromatography-tandem mass spectroscopy

of Dong et al. (2010) the body mass index was calculated with the aid of: Total-body scans were assessed by using dual-energy x-ray absorptiometry (DXA).

3.1.1. Physical activity tests

This third group included 2 studies, with 1612 participants, aged 7 to 18 (10.23) (Sallis et al., 2000; Narchi et al., 2015). The studies were carried out respectively on the following continents: North America (United States) and Europe. In the study by Dong et al. (2010), was used to calculate physical activity and, minutes per day spent on moderate and vigorous physical activities was assessed using MTI Actigraph monitors (model 7164 [MTI Health Services, Fort Walton Beach, FL]). Describing an average of 38.6 (24.2) minutes per day of moderate physical activity and 4.6 (6.8) of vigorous physical activity. In studies by Jiménez-Pavón et al. (2014), validated Fitnessgran tests were applied to the European population, on the practice of physical activity, registering an average of 19.0 (14.01) of vigorous physical activity.

3.1.2. Quality of assessment

The results of the assessment of the methodological quality of each included trial are in Figure 2.

Four studies were considered to be at high risk of bias, primarily due to failure to report adequate methods of random sequence generation, concealment of allocation and failure to blind assessors (Narchi et al., 2015; Al-Othman et al., 2012; Dong et al., 2010; Sallis et al. 2000).

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

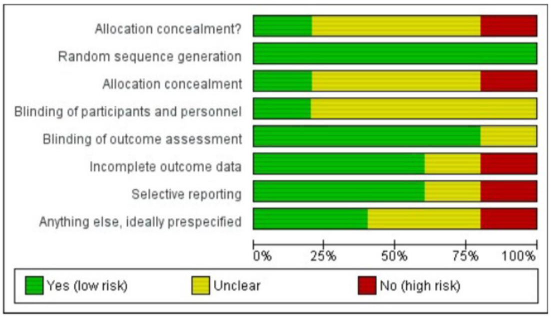

Figure 2. The results of the assessment of the methodological quality of each included trial.

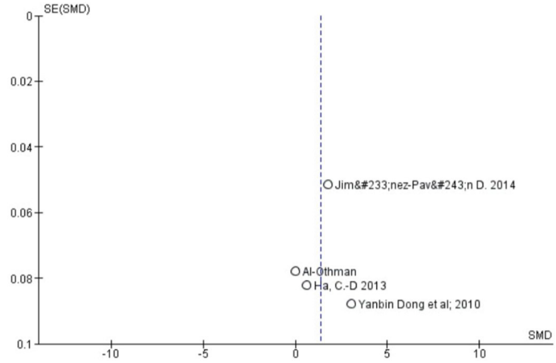

Figure 3. Funnel Plot of comparison 1,25 (OH) D, outcome versus physical activity (PA).

4. Discussion

This systematic review and meta-analysis reveals robust evidence for a negative association between serum 25(OH)D levels <20 ng/ml and increased body mass index (obese) and physical fitness levels (Narchi et al., 2015; Al-Othman et al., 2012; Dong et al., 2010; Sallis et al., 2000) .Physical activity is any movement of the body produced by skeletal muscles that results in greater energy expenditure than resting levels. Practicing physical activity outdoors, with sun exposure, would provide benefits both from the physical work itself and from the synthesis and action of vitamin D in the body.

The supposed protective effects of vitamin D on health outcomes related to physical activity are stipulated to be mediated by several mechanisms: vitamin D receptor (VDR), phosphorus, serum calcium. These include the modulation of immunoprotective maintenance. In the study by Pagels et al. (2016) and Jiménez-Pavón et al. (2014), which compared physical activity indoors and outdoors among 179 school children aged 7 to 14 years in Sweden, they found that outdoor physical activity led to a moderate increase and vigorous physical activity, during all seasons of the year, this mechanism can lead to the protective role of vitamin D.

In our meta-analysis, there was a trend that we presented with 25 (OH) D levels being more expressive when associated with physical activity (Roth et al., 2018). Vitamin D sufficiency related to physical activity provides better neuromuscular performance, including increased type II muscle fibers, and also improves the regulatory role of the immune system (Bouillon and Carmeliet, 2018).

This strong correlation between moderate/vigorous physical activity and outdoor environment variables was also found in studies by Cooper et al. (2010), Al-Othman et al. (2012), Dong et al. (2010) and Sallis et al. (2000).

In a cross-sectional study, they found an association between vitamin D levels, body mass index, and outdoor physical activity in white and non-Hispanic Hispanics. In Hispanics, there was a high prevalence of hypovitaminosis D among the obese compared to the non-obese. The practice of outdoor physical activity decreased the prevalence of hypovitaminosis D, with individuals 47% less likely to have this condition (Muscogiuri et al., 2017).

We are not aware of any other systematic review and meta-analysis aimed at assessing the relationship between serum 25(OH)D levels and physical fitness in children and adolescents. Furthermore, the strengths of our study lie in its extensive and rigorous search, reach to investigators for missing data, use of accepted instruments to assess the quality of studies and the strength of reported evidence, as well as scrutiny of the type of vitamin trial. D used and serum 25(OH)D levels in relation to outcomes. We also excluded non-peer-reviewed articles to improve the quality of evidence. This systematic review and meta-analysis presents a complete and reliable review and analysis of the available evidence and a comprehensive overview of the clinical trials included, based on a systematic search of major trial registries.

The strength of the evidence available to date is sufficient to recommend that children and adolescents who have sufficient vitamin D levels have greater physical fitness (Narchi et al., 2015; Al-Othman et al., 2012; Dong et al., 2010; Sallis et al., 2000).

4.1. Vitamin D versus BMI (Body Mass Index)

Few studies have examined the comparison of vitamin D with the body mass index, and the results are dominated by those of studies by Ha et al. (2013) and Dong et al. (2010) with 331 participants. Although the lowest level of vitamin D seems to be associated with lower levels of body mass index, this result should be interpreted with caution, considering confidence intervals (RR 1.10 95% CI 0.37a 1.83), however (Ha et al., 2013; Dong et al., 2010) in, their studies found higher levels of Vitamin D related to lower body mass indexes, reflected in the wide confidence intervals (RR 42.80, 95% CI 41.36 to 44.24), where the results are described by only 310 participants Figure 4.

4.2. Vitamin D versus physical activity

There was high quality evidence that vitamin D levels and high physical activity resulted in a direct relationship considering (four trials with 2,253) participants; (RR 0.0; 95% CI -0.15 to 0.15) (RR 0.59; 95% CI 0.43 to 0.75), respectively (Ha et al., 2013; Al-Othman et al., 2012; Dong et al., 2010) the first with adolescent population in Saudi Arabia and the second with adolescent population in South Korea. However, the findings of Dong et al. (2010) and Sallis et al. (2000) estimated that high levels of vitamin D associated with low levels of physical activity were found in the American population; without statistically significant effect (RR 1.76; 95% CI 1.66-1.87) (Figure 5).

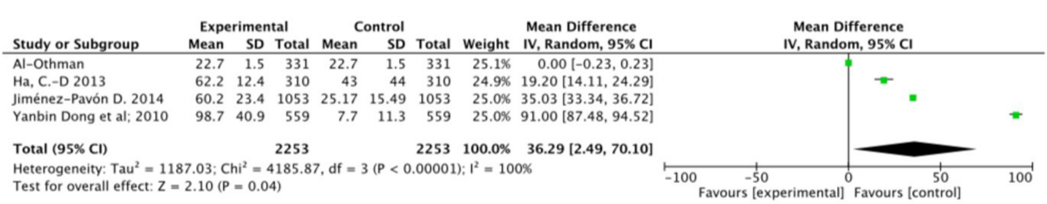

Figure 4. Forest Plot for the Man Difference in 25(OH)D versus BMI (body mass index).

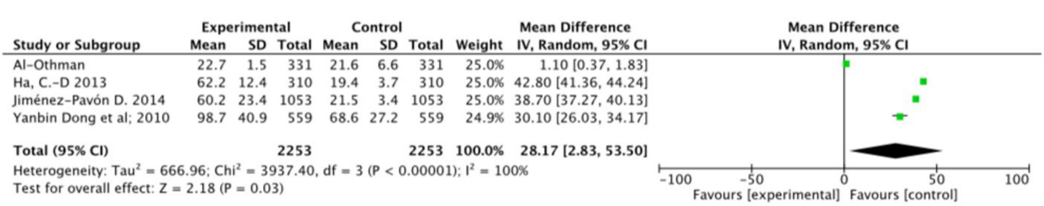

Figure 5. Forest Plot for the Man Difference in 25(OH)D versus Physical Activity (PA).

Considerable epidemiological evidence supports that there is a direct relationship between vitamin D levels and cardiorespiratory fitness in children and adolescents who regularly practice physical activity (Florez et al. 2007). Although the social, economic and geographic characteristics of the participants are different, the inclusion criteria were followed in such a way as to portray the outcomes chosen by our research team.

4.3. Overall completeness and applicability of evidence

This review included an evidence base from 04 studies that examined vitamin D (including 25-hydroxyvitamin D) and its relationship between physical activity, especially in the school setting, children's homes or sports clubs. In the studies analyzed, participants had an average age between 7 and 17 years. It is not clear whether the effectiveness of the relationship between the practice of physical activity and vitamin D is transferable to other populations of children and adolescents in other countries.

Additional studies in similar environments in other countries would be valuable, although the adoption of physical activity is related to the most adequate levels of vitamin D given the evidence provided by Muscogiuri et al. (2017) and Florez et al. (2007). In addition, physical activity that is known to reduce body weight by increasing the rate of lipolysis can increase the mobilization of adipose tissue, thereby increasing your serum vitamin D level. Serum vitamin D levels were inversely related to body fat and several metabolic risk factors and positively related to levels of physical activity based on an accelerometer. Low levels of vitamin D, along with decreased physical activity, were independent predictors of the cluster of metabolic risk factors in this study sample (Bezrati et al., 2016; Zhang et al., 2014; Saggese et al., 2015; Arnson et al., 2007; Aranow, 2011).

These findings suggest that an increase in the intake of a balanced diet and physical activity should be the main targets of lifestyle interventions against the increase in metabolic risk factors in Korean children. In the observations of (Narchi et al., 2015; Jiménez-Pavón et al., 2014; Abu Shady et al., 2015, 2016; Amr et al., 2012; Kolokotroni et al., 2015; Petersen et al., 2016; Saki et al., 2017; Alghadir et al., 2018; Bouillon and Carmeliet, 2018) with European adolescents, a gender dimorphism is suggested in the identification of risk factors for the association between vitamin D levels and physical activity. To guarantee vitamin D sufficiency, increase levels of Physical Activity.

Despite the modulating physiological capacity of the practice of physical activity on vitamin D synthesis, being widely debated to reduce the decline in winter in serum vitamin D concentrations (Sallis et al., 2000), the apparently positive results incur robust evidence that the practice of the activity exercise at moderate and high levels is effective for maintaining serum vitamin D levels throughout the year.

4.4. Agreements and disagreements with other studies or reviews

There has been a large number of recent trial level data for individual vitamin D patients, with or without the practice of physical activity. Although this systematic review with meta-analysis includes cross-sectional studies. Most reported that the practice of physical activity is necessary in addition to vitamin D for the effectiveness of serum levels (Narchi et al., 2015; Sallis et al., 2000; Bezrati et al., 2016). However, no meta-analysis of trials with vitamin D treatment arms and cardiorespiratory fitness compared to body mass index was performed, as in our comparison.

The main finding of this study was the identification of the relationship between vitamin D levels and cardiorespiratory fitness as the strongest risk factors for insulin resistance in female adolescents in Europe, regardless of confounding factors, including body fat markers, while in men, only leptin remained significant after the same adjustments. Body fat markers were also confirmed as relevant risk factors after basic adjustments (Narchi et al., 2015).

5. Limitations

Although this review used a sensitive search strategy, assessed quality using the Cochrane guidelines, and summarised levels of evidence according to the Joanna Brigs, there were inherent limitations. The authors were reliant on data from significantly heterogeneous studies that have been found to be at high risk of bias. Secondly, the grey literature was not explored, and the small number of studies included meant that the authors were unable to explore potential publication biases. Furthermore, most studies had small sample sizes, which could have masked variation due to systematic error or poor precision. In addition, when rating indirectness as a factor for quality of evidence, the authors took a broad approach.

6. Conclusion

6.1. Implications for systematic reviews and evaluations of healthcare

The practice of physical activity has a direct and proportional relationship with vitamin D levels. The benefits have been printed by several studies vitamin D and vigorous physical activity have been recommended in the control of body mass index, systemic arterial hypertension, hypercholesterolemia, obesity, and finally, metabolic syndrome. Vitamin D alone is one of the health indicators it modulates the innate immune system by reducing the release of pro-inflammatory cytokines from Th1 cells.

Acknowledgements

This work was funded by Fundação de Amparo à Pesquisa do Estado do Amazonas (FAPEAM) (POSGRAD Program [#006/2020 and #008/2021]).

References

ABU SHADY, M.M., YOUSSEF, M.M., SALAH EL-DIN, E.M., ABDEL SAMIE, O.M., MEGAHED, H.S., SALEM, S.M., MOHSEN, M.A., ABDEL AZIZ, A. and EL-TOUKHY, S., 2016. Predictors of serum 25-hydroxyvitamin D concentrations among a sample of Egyptian schoolchildren. *The Scientific World Journal*, vol. 2016, pp. 8175768. http://dx.doi.org/10.1155/2016/8175768. PMid:26942211.

ABU SHADY, M.M., YOUSSEF, M.M., SHEHATA, M.A., EL-DIN, E.M. and ELMALT, H.A., 2015. Association of serum 25-hydroxyvitamin D with life style and dietary factors in egyptian prepubescent children. *Open Access Macedonian Journal of Medical Sciences*, vol. 3, no. 1, pp. 80-84. http://dx.doi.org/10.3889/oamjms.2015.006. PMid:27275201.

ALGHADIR, A.H., GABR, S.A. and RIZK, A.A., 2018. Physical fitness, adiposity, and diets as surrogate measures of bone health in schoolchildren: a biochemical and cross-sectional survey analysis. *Journal of Clinical Densitometry*, vol. 21, no. 3, pp. 406-419. http://dx.doi.org/10.1016/j.jocd.2017.12.006. PMid:29657025.

AL-OTHMAN, A., AL-MUSHARAF, S., AL-DAGHRI, N.M., KRISHNASWAMY, S., YUSUF, D.S., ALKHARFY, K.M., AL-SALEH, Y., AL-ATTAS, O.S., ALOKAIL, M.S., MOHARRAM, O., SABICO, S. and CHROUSOS, G.P., 2012. Effect of physical activity and sun exposure on vitamin D status of Saudi children and adolescents. *BMC Pediatrics*, vol. 12, no. 1, pp. 92. http://dx.doi.org/10.1186/1471-2431-12-92. PMid:22759399.

AMR, N., HAMID, A., SHETA, M. and ELSEDFY, H., 2012. Vitamin D status in healthy Egyptian adolescent girls. *Georgian Medical News*, vol. 210, no. 210, pp. 65-71. PMid:23045423.

ARANOW, C., 2011. Vitamin D and the immune system. *Journal of Investigative Medicine*, vol. 59, no. 6, pp. 881-886. http://dx.doi.org/10.2310/JIM.0b013e31821b8755. PMid:21527855.

ARNSON, Y., AMITAL, H. and SHOENFELD, Y., 2007. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. *Annals of the Rheumatic Diseases*, vol. 66, no. 9, pp. 1137-1142. http://dx.doi.org/10.1136/ard.2007.069831. PMid:17557889.

BEZRATI, I., HAMMAMI, R., BEN FRADJ, M.K., MARTONE, D., PADULO, J., FEKI, M., CHAOUACHI, A. and KAABACHI, N., 2016. Association of plasma 25-hydroxyvitamin D with physical performance in physically active children. *Applied Physiology, Nutrition, and Metabolism*, vol. 41, no. 11, pp. 1124-1128. http://dx.doi.org/10.1139/apnm-2016-0097. PMid:27764544.

BJARNADOTTIR, A., KRISTJANSDOTTIR, A.G., HRAFNKELSSON, H., JOHANNSSON, E., MAGNUSSON, K.T. and THORSDOTTIR, I., 2015. Insufficient autumn vitamin D intake and low vitamin D status in 7-year-old Icelandic children. *Public Health Nutrition*, vol. 18, no. 2, pp. 208-217. http://dx.doi.org/10.1017/S1368980013003558. PMid:24476995.

BLAKELEY, C.E., VAN ROMPAY, M.I., SCHULTZ, N.S. and SACHECK, J.M., 2018. Relationship between muscle strength and dyslipidemia, serum 25(OH)D, and weight status among diverse schoolchildren: a cross-sectional analysis. *BMC Pediatrics*, vol. 18, no. 1, pp. 23. http://dx.doi.org/10.1186/s12887-018-0998-x. PMid:29394922.

BOUILLON, R. and CARMELIET, G., 2018. Vitamin D insufficiency: definition, diagnosis and management. *Best Practice & Research. Clinical Endocrinology & Metabolism*, vol. 32, no. 5, pp. 669-684. http://dx.doi.org/10.1016/j.beem.2018.09.014. PMid:30449548.

CALVO, M.S. and LAMBERG-ALLARDT, C.J., 2017. Vitamin D research and public health nutrition: a current perspective. *Public Health Nutrition*, vol. 20, no. 10, pp. 1713-1717. http://dx.doi.org/10.1017/S1368980017001835. PMid:29125453.

COOPER, A.R., PAGE, A.S., WHEELER, B.W., HILLSDON, M., GRIEW, P. and JAGO, R., 2010. Patterns of GPS measured time outdoors after school and objective physical activity in English children: the PEACH project. *The International Journal of Behavioral Nutrition and Physical Activity*, vol. 7, no. 1, pp. 31. http://dx.doi.org/10.1186/1479-5868-7-31. PMid:20412582.

DONG, Y., POLLOCK, N., STALLMANN-JORGENSEN, I.S., GUTIN, B., LAN, L., CHEN, T.C., KEETON, D., PETTY, K., HOLICK, M.F. and ZHU, H., 2010. Low 25-hydroxyvitamin D levels in adolescents: Race, season, adiposity, physical activity, and fitness. *Pediatrics*, vol. 125, no. 6, pp. 1104-1111. http://dx.doi.org/10.1542/peds.2009-2055. PMid:20439594.

FLOREZ, H., MARTINEZ, R., CHACRA, W., STRICKMAN-STEIN, N. and LEVIS, S., 2007. Outdoor exercise reduces the risk of hypovitaminosis D in the obese. *The Journal of Steroid Biochemistry and Molecular Biology*, vol. 103, no. 3-5, pp. 679-681. http://dx.doi.org/10.1016/j.jsbmb.2006.12.032. PMid:17267209.

HA, C.-D., CHO, J.-K., LEE, S.-H. and KANG, H.-S., 2013. Serum vitamin D, physical activity, and metabolic risk factors in Korean children. *Medicine and Science in Sports and Exercise*, vol. 45, no. 1, pp. 102-108. http://dx.doi.org/10.1249/MSS.0b013e31826c6956. PMid:22895369.

HIGGINS, J.P.T., LANE, P.W., ANAGNOSTELIS, B., ANZURES-CABRERA, J., BAKER, N.F., CAPPELLERI, J.C., HAUGHIE, S., HOLLIS, S., LEWIS, S.C., MONEUSE, P. and WHITEHEAD, A., 2013. A tool to assess the quality of a meta-analysis. *Research Synthesis Methods*, vol. 4, no. 4, pp. 351-366. http://dx.doi.org/10.1002/jrsm.1092. PMid:26053948.

HIGGINS, J.P.T., THOMAS, J., CHANDLER, J., CUMPSTON, M., LI, T., PAGE, M.J. and WELCH, V.A., eds., 2021 [viewed 10 May 2022]. *Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021)* [online]. Cochrane. Available from www.training.cochrane.org/handbook

JIMÉNEZ-PAVÓN, D., SESÉ, M.A., VALTUEÑA, J., CUENCA-GARCÍA, M., GONZÁLEZ-GROSS, M., GOTTRAND, F., KAFATOS, A., MANIOS, Y., WIDHALM, K., DE HENAUW, S., POLITO, A., PÉREZ-LÓPEZ, F.R. and MORENO, L.A., 2014. Leptin, vitamin D, and cardiorespiratory fitness as risk factors for insulin resistance in European adolescents: gender differences in the HELENA Study. *Applied Physiology, Nutrition, and Metabolism*, vol. 39, no. 5, pp. 530-537. http://dx.doi.org/10.1139/apnm-2013-0250. PMid:24766234.

KOLOKOTRONI, O., PAPADOPOULOU, A., YIALLOUROS, P.K., RAFTOPOULOS, V., KOUTA, C., LAMNISOS, D., NICOLAIDOU, P. and MIDDLETON, N., 2015. Association of vitamin D with adiposity measures and other determinants in a cross-sectional study of Cypriot adolescents. *Public Health Nutrition*, vol. 18, no. 1, pp. 112-121. http://dx.doi.org/10.1017/S1368980013003480. PMid:24476931.

MOOLA, S., MUNN, Z., TUFANARU, C., AROMATARIS, E., SEARS, K., SFETCU, R., CURRIE, M., QURESHI, R., MATTIS, P., LISY, K. and MU, P.-F., 2020. Chapter 7: Systematic reviews of etiology and risk. In: E. AROMATARIS and Z. MUNN, ed. JBI Manual for Evidence Synthesis. Adelaide: JBI. Available from https://synthesismanual.jbi.global.

MUNNS, C.F., SHAW, N., KIELY, M., SPECKER, B.L., THACHER, T.D., OZONO, K., MICHIGAMI, T., TIOSANO, D., MUGHAL, M.Z., MÄKITIE, O., RAMOS-ABAD, L., WARD, L., DIMEGLIO, L.A., ATAPATTU, N., CASSINELLI, H., BRAEGGER, C., PETTIFOR, J.M., SETH, A., IDRIS, H.W., BHATIA, V., FU, J., GOLDBERG, G., SÄVENDAHL, L., KHADGAWAT, R., PLUDOWSKI, P., MADDOCK, J., HYPPÖNEN, E., ODUWOLE, A., FREW, E., AGUIAR, M., TULCHINSKY, T., BUTLER, G. and HÖGLER, W., 2016. Recommendation on Prevention and management of nutricional rickets. *The Journal of Clinical Endocrinology and Metabolism*, vol. 101, no. 2, pp. 394-415. http://dx.doi.org/10.1210/jc.2015-2175. PMid:26745253.

MUSCOGIURI, G., ALTIERI, B., ANNWEILER, C., BALERCIA, G., PAL, H.B., BOUCHER, B.J., CANNELL, J.J., FORESTA, C., GRÜBLER, M.R., KOTSA, K., MASCITELLI, L., MÄRZ, W., ORIO, F., PILZ, S., TIRABASSI, G. and COLAO, A., 2017. Vitamin Dand chronic diseasses: the current state of the art. *Archives of Toxicology*, vol. 91, no. 1, pp. 97-107. http://dx.doi.org/10.1007/s00204-016-1804-x. PMid:27425218.

NARCHI, H., KOCHIYIL, J., HAMAD, S.A., YASIN, J., LALEYE, L. and DHAHERI, A.A., 2015. Hypovitaminosis D in adolescent females--an analytical cohort study in the United Arab Emirates. *Paediatrics and International Child Health*, vol. 35, no. 1, pp. 36-43. http://dx.doi.org/10.1179/2046905514Y.0000000144. PMid:25547176.

PAGELS, P., RAUSTORP, A., GUBAN, P., FRÖBERG, A. and BOLDEMANN, C., 2016. Compulsory school in- and outdoors-implications for school children's physical activity and health during one academic year. *International Journal of Environmental Research and Public Health*, vol. 13, no. 7, pp. 699. http://dx.doi.org/10.3390/ijerph13070699. PMid:27420079.

PALACIOS, C. and GONZALEZ, L., 2014. Is vitamin D deficiency a major global public health problem? *The Journal of Steroid Biochemistry and Molecular Biology*, vol. 144, no. Pt A, pp. 138-145. http://dx.doi.org/10.1016/j.jsbmb.2013.11.003. PMid:24239505.

PETERSEN, R.A., DAMSGAARD, C.T., DALSKOV, S.M., SØRENSEN, L.B., HJORTH, M.F., RITZ, C., KJØLBÆK, L., ANDERSEN, R., TETENS, I., KRARUP, H., ASTRUP, A., MICHAELSEN, K.F. and MØLGAARD, C., 2016. Vitamin D status and its determinants during autumn in children at northern latitudes: a cross-sectional analysis from the optimal well-being, development and health for Danish children through a healthy New Nordic Diet (OPUS) School Meal Study. *British Journal of Nutrition*, vol. 115, no. 2, pp. 239-250. http://dx.doi.org/10.1017/S000711451500433X. PMid:26563915.

ROTH, D.E., ABRAMS, S.A., ALOIA, J., BERGERON, G., BOURASSA, M.W., BROWN, K.H., CALVO, M.S., CASHMAN, K.D., COMBS, G., DE-REGIL, L.M., JEFFERDS, M.E., JONES, K.S., KAPNER, H., MARTINEAU, A.R., NEUFELD, L.M., SCHLEICHER, R.L., THACHER, T.D. and WHITING, S.J., 2018. Global prevalence and disease burden of vitamin D deficiency: a roadmap for action in low- and middle-income countries. *Annals of the New York Academy of Sciences*, vol. 1430, no. 1, pp. 44-79. http://dx.doi.org/10.1111/nyas.13968. PMid:30225965.

SAGGESE, G., VIERUCCI, F., BOOT, A.M., CZECH-KOWALSKA, J., WEBER, G., CAMARGO JUNIOR, C.A., MALLET, E., FANOS, M., SHAW, N.J. and HOLICK, M.F., 2015. Michael F. Vitamin D in childhood and adolescence: an expert position statement Holick. *European Journal of Pediatrics*, vol. 174, no. 5, pp. 565-576. http://dx.doi.org/10.1007/s00431-015-2524-6. PMid:25833762.

SAKI, F., DABBAGHMANESH, M.H., OMRANI, G.R. and BAKHSHAYESHKARAM, M., 2017. Vitamin D deficiency and its associated risk factors in children and adolescents in southern Iran. *Public Health Nutrition*, vol. 20, no. 10, pp. 1851-1856.

SALLIS, J.F., PROCHASKA, J.J. and TAYLOR, W.C., 2000. A review of correlates of physical activity of children and adolescents. *Medicine and Science in Sports and Exercise*, vol. 32, no. 5, pp. 963. http://dx.doi.org/10.1097/00005768-200005000-00014. PMid:10795788.

VALTUEÑA, J., GRACIA-MARCO, L., HUYBRECHTS, I., BREIDENASSEL, C., FERRARI, M., GOTTRAND, F., DALLONGEVILLE, J., SIOEN, I., GUTIERREZ, A., KERSTING, M., KAFATOS, A., MANIOS, Y., WIDHALM, K., MORENO, L.A. and GONZÁLEZ-GROSS, M., 2013. Cardiorespiratory fitness in males, and upper limbs muscular strength in females, are positively related with 25-hydroxyvitamin D plasma concentrations in European adolescents: the HELENA study. *QJM*, vol. 106, no. 9, pp. 809-821. http://dx.doi.org/10.1093/qjmed/hct089. PMid:23657707.

ZHANG, H.Q., TENG, J.H., LI, Y., LI, X.X., HE, Y.H., HE, X. and SUN, C.H., 2014. Vitamin D status and its association with adiposity and oxidative stress in schoolchildren. *Nutrition*, vol. 30, no. 9, pp. 1040-1044. http://dx.doi.org/10.1016/j.nut.2014.02.024. PMid:25102819.