

Vitamin A deficiency in Brazilian Children younger than 5 years old: a systematic review

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Abstract

Objectives: to examine the nutritional status of vitamin A in Brazilian children under 5 years old, delimiting their deficiency and associated factors.

Methods: this is a systematic review of articles published between 2008 and 2018, using the SciELO, Bireme, and PubMed electronic databases. A validated instrument critically evaluated the studies. The summary measures were obtained by the random effect model, and their results are presented using the Forest Plot graph. The qualitative synthesis was based on the description of the main factors associated with Vitamin A Deficiency.

Results: we included 14 cross-sectional studies with observations in basic health units, daycare centers, and households. The summary measure indicated Vitamin A Deficiency of 20% (CI95%= 17% - 23%), with high homogeneity according to the source of the sample. Lower age of the child, low birth weight, poor iron nutritional status, diarrhea, subclinical infection, inadequate basic sanitation conditions, younger mothers and less maternal education represented the main exposures associated with the outcome.

Conclusion: the results show Vitamin A Deficiency as a public health problem in Brazilian children under 5 years old, especially when related to the development of infectious processes and maternal and child characteristics that show greater susceptibility.

Key words *Vitamin A, Vitamin A deficiency, Child*



Introduction

Vitamin A is an essential nutrient for a normal vision, maintaining the immune functions, growth, and development. The lack of this micronutrient can cause Vitamin A Deficiency (VAD), which is one of the main causes of preventable blindness in childhood and is related to the increase and severity of infections.¹⁻⁵ Due to the increased nutritional demands and the severity of the possible consequences for health associated with VAD, preschoolers and pregnant women are the most vulnerable segments to the disease.¹⁻³ Therefore, the fight against VAD is essential to the child's survival, well-being, and adequate growth and development.

The World Health Organization (WHO) estimates that approximately 33.3% of children under 5 years old (190 million) have VAD (serum retinol <0.70 μmol/L).¹ Analyzes conducted with 82 countries that implement supplementation programs for Vitamin A showed that in 34 of them, VAD is a serious public health problem, while in eight of them is moderate.⁴ In Latin America, 19 countries have interventions to combat the disease, and in 16 of them, VAD is a public health problem. Eight of these countries have classificatory proportions of severe or moderate intensity, according to a systematic review of the literature published between 1985 and 2014.⁶ In 2006, a shortage of 17.4% of children under 5 years old was identified in Brazil,⁷ the average prevalence estimated in a review study with children assisted in daycare centers was 12.5%.⁸

Despite the availability of such information, the existence of outdated data from diagnoses occurred mainly before 2006,^{4,9} including in Brazil.⁷ In Brazil, the lack of evaluation studies of the National Program of Vitamin A Supplementation impairs knowledge about its effectiveness.¹⁰ The Program aims to prevent and control VAD, focusing on children aged 6 to 59 months.¹¹

Thus, given the importance of the vitamin A nutritional status for child health and the updated statistics on VAD for the surveillance and implementation of public policies related to the problem in question, it was considered relevant to examine the nutritional status of vitamin A in Brazilian children under the age of five years old, delimiting their disability and associated factors.

Methods

The study is a systematic review of scientific articles on VAD in Brazilian children under 5 years old, complied with the PRISMA recommendation for

reporting systematic reviews and meta-analyses.

Eligibility criteria

We considered eligible observational studies on VAD developed with Brazilian children under 5 years old, published between 2008 and 2018. The choice of the year 2008 considered the characteristics of the last review of the wide-ranging theme, released that year, and included published articles between 1994 and 2007.¹² We considered records in English, Spanish and Portuguese analyzing the original articles with populations from Brazil that included children under five years old in their analysis.

Information sources

We identified the studies in SciELO (Scientific Electronic Library Online), Bireme (Virtual Health Library), and PubMed (National Library of Medicine) databases. The search was conducted on August 11, 2019.

Search strategy

All documents containing the combination of the descriptors "Child" OR "Pre-school" AND "Vitamin A deficiency" were considered. At SciELO, records before 2008 were deleted manually. At Bireme, the search considered Brazil with the filters of "country/region" as a subject the years of 2008 to 2018 as "year of publication". In PubMed, the descriptor "Brazil" was included and the personalized date range between 2008/01/01 and 2018/12/31 was used as a filter. The search was conducted in English and Portuguese. The complete electronic search strategy reproduced in English was as follows: i. Child [All indexes] or Child, Preschool [All indices] and Vitamin A Deficiency [All indexes], in SciELO; ii. (tw: (child)) OR (tw: (Child, Preschool)) AND (tw: (Vitamin A Deficiency)) and filters Brazil, in the country/region as a subject, and 2010 2014 2015 2016 2013 2012 2008 2009 2011 2017, in publication year, at Bireme; iii. (((child) OR Child, Preschool) AND Vitamin A Deficiency) AND Brazil and filter from 2008/01/01 to 2018/12/31, on publication dates, on PubMed.

Selection of studies

When calculating the total number of studies, we identified possible duplications in the databases in which we counted each record only once. The identi-

fied records were submitted to a screening process and, upon reading the titles and abstracts, we eliminated (i) the documents other than scientific articles, (ii) review articles, (iii) program evaluation studies, (iv) studies of experimental design, (v) studies on food consumption, (vi) studies focusing on chemical analysis of food, (vii) studies not carried out with samples of children under 5 years old, (viii) studies on individuals diagnosed with some disease. After the screening process, we submitted the chosen papers to the inclusion and exclusion criteria, with a thorough reading and analysis of the full text. For inclusion in this review, we considered studies that addressed hypovitaminosis A in children under 5 years old. We excluded studies (i) with a non-representative sample/no description of the sample calculation, (ii) with children submitted to specific supplementation, (iii) without VAD indicators for the age group of interest, (iv) addressing different themes. Also, for articles that used the same study sample, we included only one of them and in the quality assessment phase, the exclusion criterion adopted was to obtain a low-quality indicative score. The lists of bibliographic references of the included articles were analyzed to identify other possible studies of interest. The articles selected from the bibliographic references were submitted to the same previously described eligibility criteria.

Data collection process

To ensure the accuracy and reliability of results from the review, the articles identified in databases that met the selection criteria were grouped in folders. Two researchers (DFP and ESS) independently performed data collection during the screening, full reading, and extraction phases. For data extraction, a form was created with information on the methodological aspects and main findings of the studies. Another researcher participated in the discussion of doubts and/or disagreements.

The variables extracted from the articles for their characterization were: author, year of publication, objective, place of study, an age considered, sample size, investigation of subclinical infection, tests of hypotheses used, the prevalence of VAD (serum retinol $<0.70 \mu\text{mol/L}$)¹ and variables associated with VAD. Also, we verified the biochemical indicator and the analysis techniques used in all studies. The importance of considering the control or not of the subclinical infection by the researchers is because infectious processes can suppress the mobilization of vitamin A as a result of the low synthesis of the retinol transport protein during the acute phase,

resulting in the fall of the concentration in plasma retinol.¹³ The articles were also evaluated for their quality.

Quality evaluation of included articles

We evaluated the quality of studies using the critical evaluation instrument for prevalence studies developed and tested by Munn *et al.*¹⁴ This instrument has ten questions about the adequacy and accuracy of the study, related to validity of the methods, interpretation and applicability results. Thus, each article was checked against the representativeness of target population through the sample, recruitment of participants, sample size, description of the subjects and study scenario, data analysis, possibility of bias, reliability of the information on the outcome, ownership of statistical methods, identification of confounding factors and differences between groups, and use of objective criteria to identify subpopulations or subgroups. Each item was evaluated with one point when the answer was positive or “does not apply”, half a point when the answer was uncertain, and zero points when the answer was negative, generating a maximum score of 10 points. The score of each article classified them in three quality categories: high (8 to 10 points), medium (5 to 7 points), and low (0 to 4 points).

Summary of the results

To obtain summary measures, we used a meta-analysis with a random effect model, generating the forest plot graph. The heterogeneity between studies was analyzed using I^2 statistics. The analyzes were performed using the STATA 12.0 program. The number of times that a given factor was associated with VAD was also quantified, considering relevant those that appeared in more than one article. Both the average prevalence weighted by the sample size and the qualitative synthesis of the factors associated with VAD were generated for the set of studies included in the review and for subgroups according to their distribution in agreement with the source of the sample (basic health unit, daycare center, and household survey).

Results

Figure 1 shows the flowchart of the process of identification and selection of studies. After reading in full, 13 articles were eligible, in which, by reverse search, we identified two others that met the inclusion criteria. Only one article was excluded

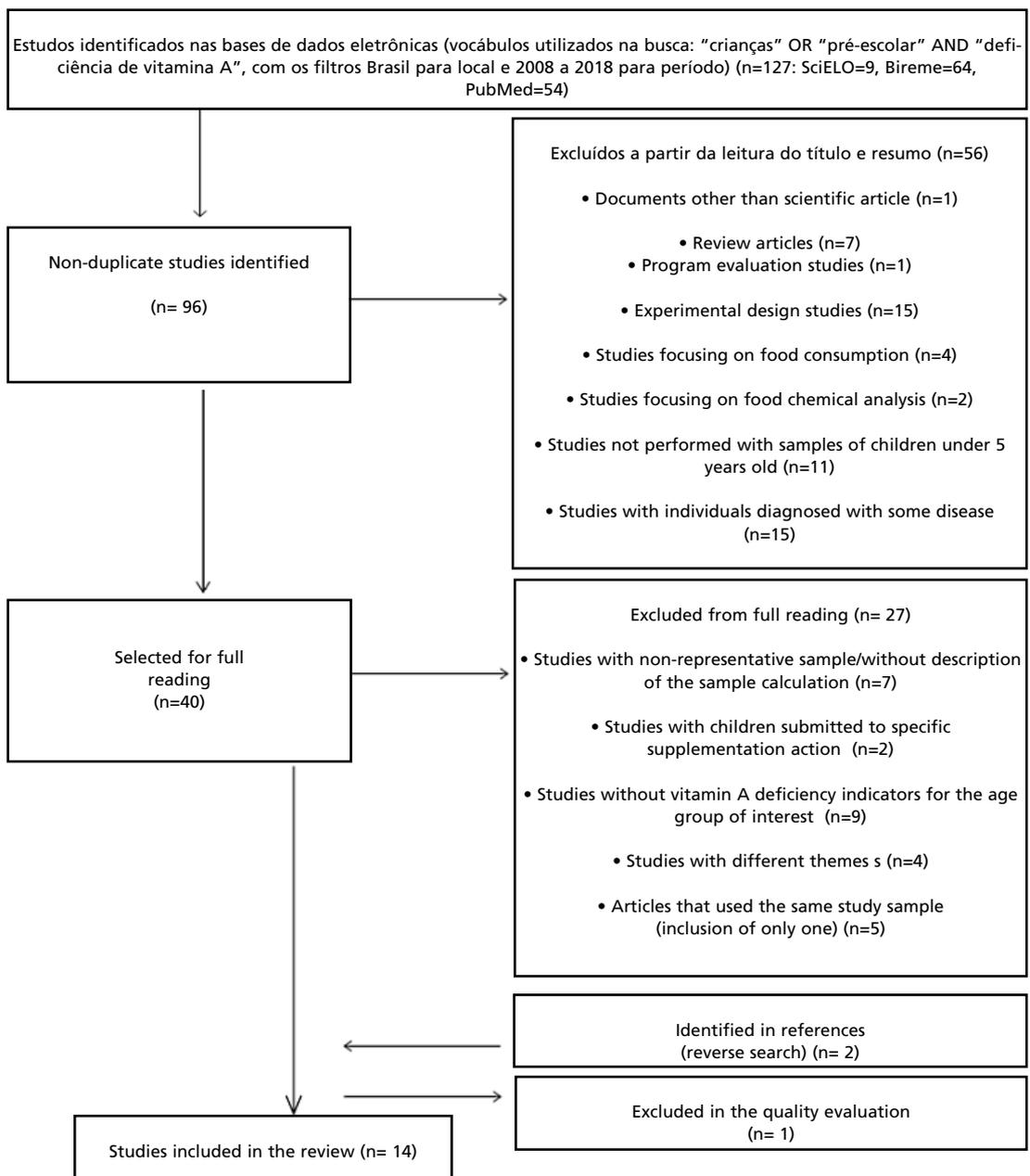
according to the quality evaluation, totaling 14 articles eligible for review.

Table 1 shows the general characterization of the studies and their quality evaluation. We included 14 articles with cross-sectional designs.¹⁵⁻²⁸ One of the studies was focused on in the whole country,¹⁶ 10 were focused on cities in the Northeast,^{15,17,19,21,22,24-28} one was in a city in the North region²³ and the other two were in the capitals of Goiás¹⁸ and Espírito Santo.²⁰ Nine observations were based on household data,^{15,16,22-28} while the

other studies had samples obtained from daycare centers^{17,19,21} and basic health units.^{18,20} Most articles reported analyzes of inflammatory processes that interfere with serum retinol levels.^{15,17-19,21,23,25,26} Latex agglutination,^{21,25,26} chemiluminescence^{18,23} and immunoturbidimetric assay^{15,19} were the most used methods for measuring C-reactive protein, while the values $>5\text{mg/dL}$ ^{15,18,23} and $>6\text{mg/dL}$ ^{19,21,25} were the main cutoff points used as the indicatives of the presence of subclinical infection. Most studies were classified as high quality,¹⁵⁻

Figure 1

Fluxograma das fases de identificação, triagem e seleção de artigos publicados entre 2008 e 2018 sobre deficiência de vitamina A em crianças brasileiras menores de cinco anos.



^{17,19,21-27} with the sample selection process being the item with the highest number of negative evaluations.^{15,18,20,28}

As for the biochemical indicator and analysis techniques (data not shown in the table), serum retinol was used as a marker of the vitamin A nutritional status and values $<0.70\mu\text{mol/L}$ to define its inadequacy in all studies.¹ All researchers used high-performance liquid chromatography to measure serum retinol concentrations, except in one of the studies that opted for spectrophotometry.²⁰ The venous blood sample was reported in all studies in which this information was available,^{15,18-23,25-28} while only four articles reported whether the collection had happened or not, in the child's fasting,^{17-19,25} a condition that was considered in two of the cases.^{17,18}

Table 2 shows the synthesis of the main results of studies. VAD varied from 9.3%¹⁵ to 45.4%.²⁶ Statistical associations were not reported in two articles.^{21,23} The presence of subclinical infection was identified as an associated factor to VAD in two^{15,25} of the four articles^{15,18,23,25} in which there were analyzes with values adjusted for the concentration of C-reactive protein.

Figure 2 shows the result of the summary of the effect of meta-analysis, which was 0.20 (CI95%=0.17 - 0.23). According to the origin of the sample, the values were similar, from 0.21 (CI95%=0.18 - 0.24) in basic health units, 0.20 (CI95% = 0.12 - 0.28) in daycare centers and 0.20 (CI95% = 0.16 - 0.24) in household surveys. The heterogeneity (I^2) of 94.53% ($p = 0.00$) is considered high.

Analyzes of the factors associated with VAD highlight that younger children,^{17,26} who were born with low weight,^{24,26} with iron-deficient nutritional status,^{18-20,27} with episodes of diarrhea in the last 15 days,^{22,24} with subclinical infection,^{15,22,25} living in households with inadequate basic sanitation conditions,^{22,25,28} of younger mothers^{17,24} and in cases of lower maternal education^{18,26} represented the main explanatory conditions for the occurrence of the lack of VAD. Of these factors, the nutritional status of iron deficiency was common, in the subgroup of studies developed in basic health units,^{18,20} and low birth weight,^{24,26} the presence of subclinical infection,^{15,22,25} and the inadequate conditions of basic sanitation,^{22,25,28} in the subgroup of studies carried out as household surveys. Table 3 shows the synthesis of these results.

Discussion

This work synthesizes cross-sectional studies with Brazilian children under 5 years old that addressed the biochemical diagnosis of the nutritional status of vitamin A. We included articles based on studies that used representative random samples, guaranteeing the applicability of the results obtained. In all studies, the diagnosis of prevalence of VAD used as a cutoff point the analyzed serum retinol values of $<0.70\mu\text{mol/L}$,¹ using the high-performance liquid chromatography method, except for one study that guarantees methodological similarities in aspects of the systematization process. The control of the negative effect of subclinical infection in the serum retinol biomarker reported in eight articles guarantees in these studies an accurate evaluation of the nutritional status of vitamin A, while in the other studies, the possibility of over estimated prevalence should be considered in case of corrections have not been made and inflammatory processes are present in the observed children.²⁹ Despite this, the results show the existence of isolated experiences related to the biochemical evaluation of the nutritional status of vitamin A, similar to findings in a previous review, specific for children assisted in daycare centers. This explains this situation based on the difficulties of blood collection in children, the high costs and the technical problems of the analyzes.⁸

The average prevalence weighted by the sample size of VAD estimated for the set of children in the studies in this review was 20% (CI95% = 17% - 23%) and it is within the WHO epidemiological classification as a public health problem of severe degree ($\geq 20\%$).¹ This proportion is higher than in children assisted in daycare centers⁸ and that diagnosed in Brazilian children.⁷ According to a review that used population-based data, considering populations of children from developing countries, the prevalence found in this study is only lower than that of regions where the problem is also a serious public health one (Sub-Saharan Africa: 48%; 25 - 75 and South Asia: 44%; 13 - 79) and higher than estimated for Latin America and the Caribbean (11%; 4 - 23).⁹

The high prevalence found is inserted in a reality that can be considered positive considering the priority given to the reduction and control of VAD in Brazilian children from 6 to 59 months old through the National Vitamin A Supplementation Program.¹¹

However, evaluative results on the Program point out deficiencies that include a fragmented work process, irregularity in supplementation, lack of standardization, and failure to carry out food and

Table 1

General characteristics and quality evaluation of studies on vitamin A deficiency in Brazilian children less than five years old, according to articles published in the period 2008-2018.

Author, Year	Objective	Place of study	Age (months old)	Sample	Investigation of subclinical infection	Hypothesis testing used	Study quality
Teles <i>et al.</i> ¹⁵ 2018	To evaluate the relationship between serum retinol concentrations and subclinical infection in children from rural settlements	Teresina (PI) (household survey in rural settlements)	6-59	118	Reactive protein C measured by an immunoturbidimetric assay, defining values > 5mg/L as the indicative of the presence of infection (analyzes with values adjusted for protein concentration)	Pearson's Correlation Coefficient T-student ANOVA Multiple Linear Regression	High
Lima <i>et al.</i> , ¹⁶ 2018	To analyze variables associated with VAD in Brazilian children aged 6 to 59 months old	Brazil (household population survey)	6-59	3.417	Not considered	Poisson Regression	High
Novaes <i>et al.</i> , ¹⁷ 2016	To determine the prevalence of VAD and associated factors in children attending daycare centers	Vitória da Conquista (BA) (full-time public daycare centers)	24-60	259	Reactive Protein C measured by nephelometry, defining values > 10 mg/dL as the indicative of the presence of infection (analyzes excluding the cases of altered protein)	Chi-square Fisher's exact test Logistic Regression	High
Silva <i>et al.</i> , ¹⁸ 2015	To evaluate the nutritional status of vitamin A and associated factors in children treated at basic health units	Goiânia (GO) (basic health units)	12-16	228	Reactive protein C measured by chemiluminescence, defining values > 5mg/L as the indicative of the presence of infection (analyzes with values adjusted by the concentration of CRP)	Chi-square Multiple Linear Regression	Average
Figuerola Pedraza <i>et al.</i> , ¹⁹ 2014	To estimate the isolated and combined prevalence of anemia, VAD and zinc deficiency in preschool children	Daycare centers of the State Secretariat for Human Development of the Government of Paraíba (public daycare centers)	12-72	240	Reactive protein C measured by immunoturbidimetric assay, defining values >6mg/L as the indicative of the presence of infection (analyzes excluding the cases of altered protein)	T-student Chi-square Gross and adjusted Odds Ratio calculation	High

continue

VAD = vitamin A deficiency.

Table 1

continuation

General characteristics and quality evaluation of studies on vitamin A deficiency in Brazilian children less than five years old, according to articles published in the period 2008-2018.

Author, Year	Objective	Place of study	Age (months old)	Sample	Investigation of subclinical infection	Hypothesis testing used	Study quality
Saraiva <i>et al.</i> ²⁰ 2014	To analyze the occurrence of anemia and iron deficiency in children aged 1 to 5 years old and the association of these outcomes with retinol deficiency	Vitória (ES) (basic health units)	12-60	692	Not considered	Spearman's Correlation Coefficient Poisson regression with robust adjustment of variance	Average
Pedraza <i>et al.</i> , ²¹ 2014	To analyze the association between food (in) security and the nutritional status of children assisted in daycare centers	Cities with public daycare centers of the government of Paraíba (public daycare centers)	<60	193	Reactive Protein C measured by Latex Agglutination, defining values > 6mg/L as the indicative of the presence of infection (analyzes excluding the cases of altered protein)	T student Chi-square Multiple Linear Regression	High
Silva de Paula <i>et al.</i> , ²² 2014	To describe the prevalence and factors associated with anemia and VAD in children under 5 years old assisted by the Family Health Strategy	Pernambuco (household population survey)	6-59	563	Not considered	Probability ratio test Simple Poisson regression Multiple Poisson regression	High
Cobayashi <i>et al.</i> , ²³ 2014	To examine the prevalence of stunting and overweight in children and adolescents and identify associated biochemical indicators	Acrelândia (AC) (household survey)	<60	557	Reactive protein C measured by chemiluminescence, defining values > 5mg/L as the indicative of the presence of infection (analyzes with values adjusted by the concentration of CRP)	Chi-square Simple Poisson regression Multiple Poisson regression	High
Miglioli <i>et al.</i> , ²⁴ 2013	To analyze the prevalence and factors associated with VAD in mothers and their children under 5 years old	Pernambuco (household survey)	6-59	790	Not considered	Complementary log-log model as a link function	High

continue

VAD = vitamin A deficiency.

Table 1

conclusion

General characteristics and quality evaluation of studies on vitamin A deficiency in Brazilian children less than five years old, according to articles published in the period 2008-2018.

Author, Year	Objective	Place of study	Age (months old)	Sample	Investigation of subclinical infection	Hypothesis testing used	Study quality
Queiroz <i>et al.</i> , ²⁵ 2013	To estimate the prevalence of VAD and its associated factors in children	Paraíba cities representing the regions of the outback, the wild and forest zone (household survey)	6-59	1.211	Reactive Protein C measured by Latex Agglutination, defining values > 6mg/L as the indicative of the presence of infection (analyzes with values adjusted for the concentration of CRP)	Chi-square Fisher's exact test Logistic Regression	High
Ferreira <i>et al.</i> , ²⁶ 2013	To identify the factors associated with VAD in children	Semi-arid region of Alagoas (household population survey)	<60	551	Reactive Protein C measured by Latex Agglutination, defining the presence of agglutination of visible particles on the test plate as the indicative of the presence of infection (analyzes excluding cases of altered protein)	Poisson regression with robust adjustment of variance	High
Gondim <i>et al.</i> , ²⁷ 2012	To analyze the relationship between hemoglobin levels, serum retinol concentration and nutritional status in children aged 6 to 59 months old	Estado da Paraíba (population survey)	6-59	1.108	Not considered	Chi-square Fisher's exact test Poisson regression	High
Oliveira <i>et al.</i> , ²⁸ 2010	To determine the prevalence of anemia and VAD and analyze the association of food (in) security with levels of hemoglobin and serum retinol in children under 5 years old	Gameleira (PE) e São João do Tigre (PB) (household survey)	<60	959	Not considered	Pearson's Correlation Coefficient T-student ANOVA Multiple Linear Regression	Average

VAD = vitamin A deficiency.

Table 2

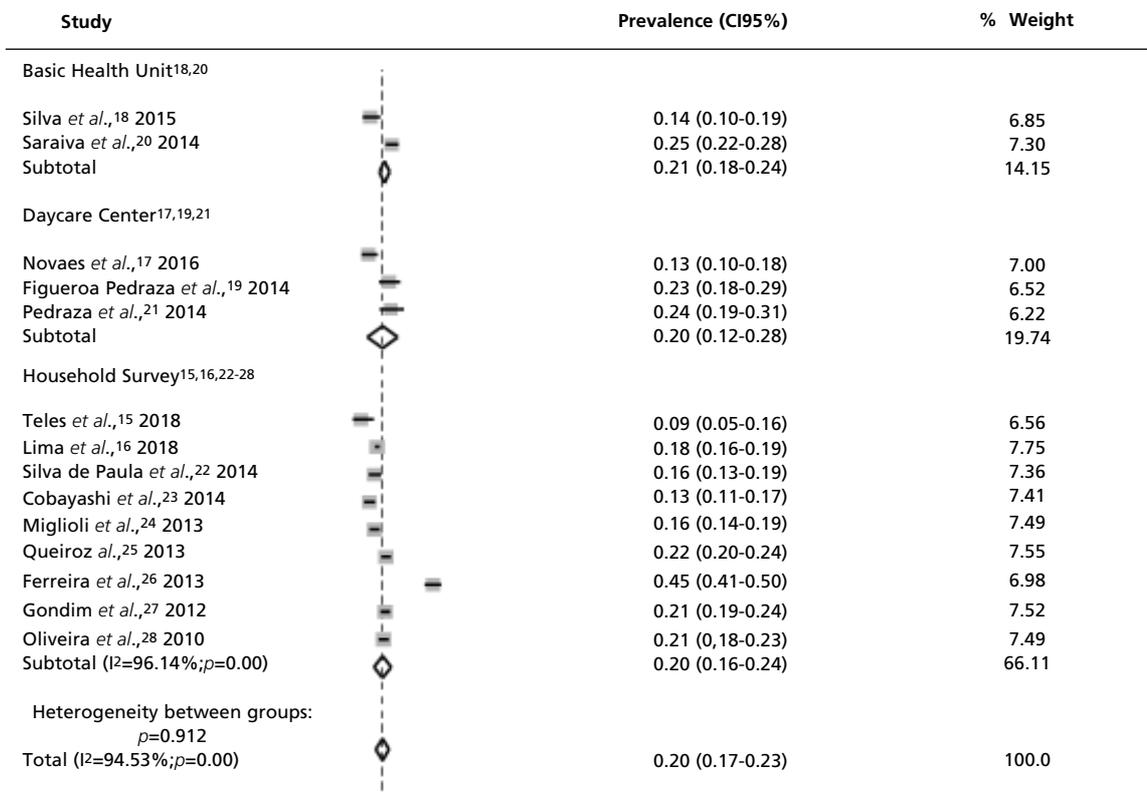
Prevalence of vitamin A deficiency and associated variables in Brazilian children less than five years old, according to articles published in the period 2008-2018.

Author, Year	VAD (%)	Variables associated with VAD
Teles <i>et al.</i> ¹⁵ 2018	9.3	Presence of subclinical infection ($p = 0.008$)
Lima <i>et al.</i> , ¹⁶ 2018	17.5	-Live in the Southeast (PR = 1.59; CI95%= 1.19-2.17) and in the Northeast (PR=1.56; CI95%= 1.16-2.15) -Live in an urban area (PR = 1.31; CI95%= 1.02-1.72) - Maternal age ≥ 36 years old (PR = 2.28; CI95%= 1.37-3.98) -Eat meat every day (protection factor) (PR = 0.61; CI95%= 1.37-3.98)
Novaes <i>et al.</i> , ¹⁷ 2016	13.1	-Child's age ≤ 34 months old (OR = 2.66; CI95% = 1.23-5.74) -Lower maternal age (OR = 2.39; CI95%= 1.11 - 5.17)
Silva <i>et al.</i> , ¹⁸ 2015	14.0	-Low maternal education ($p = 0.017$) -Low hemoglobin concentration ($p = 0.022$)
Figueroa Pedraza <i>et al.</i> , ¹⁹ 2014	23.3	-No vitamin A supplementation ($p < 0.05$) - Anemia (OR = 2.21; CI95%=1.03-4.84)
Saraiva <i>et al.</i> , ²⁰ 2014	24.7	Anemia (OR= 3,96; CI95%= 2.62-6.00) and iron deficiency (OR = 3.96; CI95%=2.62-6.00)
Pedraza <i>et al.</i> , ²¹ 2014	24.4	No statistical associations were found
Silva de Paula <i>et al.</i> , ²² 2014	16.0	-Inappropriate waste destination (PR= 1.6; CI95%= 1.1-2.3) - Diarrhea in the last fifteen days (PR= 1.6; CI95%= 1.0-2.4)
Cobayashi <i>et al.</i> , ²³ 2014	13.4	No statistical associations were found
Miglioli <i>et al.</i> , ²⁴ 2013	16.1	-Lower maternal age (PR = 3.00; CI95%= 1.43-6.31) -Fewer number of prenatal consultations (PR = 3.99; CI95%= 1.41-11.30) -Low birth weight (PR = 2.80; CI95%= 1.22-6.42) - Maternal VAD (PR = 3.99; CI95%= 1.73-9.19) -Diarrhea in the last 15 days (PR = 1.88; CI95%= 1.04-3.41)
Queiroz <i>al.</i> , ²⁵ 2013	21.8	-Presence of subclinical infection (OR = 2.55; CI95%= 1.74-3.75) -Presence of water at home (protection factor) (OR = 0.65; CI95%= 0.45-0.96)
Ferreira <i>et al.</i> , ²⁶ 2013	45.4	-Age of the child from 12.1 to 24 months old (PR = 1.45; CI95%= 1.04-2.02) -Low birth weight (PR = 1.41; CI95%= 1.07-1.86) -Low maternal education (PR = 1.66; CI95%= 1.12-2.44)
Gondim <i>et al.</i> , ²⁷ 2012	21.4	Anemia (PR= 1.38; CI95%= 1.10-1.74)
Oliveira <i>et al.</i> , ²⁸ 2010	20.6	-Male ($p = 0.03$) -Lower <i>per capita</i> income ($p < 0.01$) -Absence of cell phone ($p = 0.04$) - Absence of sanitary sewage ($p = 0.05$)

VAD = vitamin A deficiency.

Figure 2

Forest Plot of the prevalence of vitamin A deficiency in Brazilian children less than five years old, according to articles published between 2008-2018.



The values of the articles were obtained through random effects.

Table 3

Synthesis of the variables associated with vitamin A deficiency in Brazilian children less than five years old, according to articles published between 2008-2018.

Studies according to sample origin	Variables associated with vitamin A deficiency in more than one article
Basic Health Unit ^{18,20}	Deficient nutritional status of iron
Daycare center ^{17,19,21}	-
Household survey ^{15,16,22-28}	Low weight at birth Presence of subclinical infection Inadequate basic sanitation conditions
Total ¹⁵⁻²⁸	Child's lower age Low weight at birth Deficient nutritional status of iron Diarrhea in the last fifteen days Presence of subclinical infection Inadequate basic sanitation conditions Lower maternal age Lower maternal education

nutrition education actions, suggesting the need for training of health professionals.^{30,31} Also, such programs face great challenges in their coverage and sustainability, and for not being able to address the underlying problem of inadequate vitamin A food intake and chronic deficiency in isolation.¹⁰ In this sense, according to a literature review,³² supplementations with a megadose of vitamin A should be analyzed since the effects of the intervention may still be compromised as a consequence of the change in disease patterns (notably, reductions in measles and diarrhea). Thus, the authors reinforce the importance of daily vitamin A intake and food fortification and regular supplementation with low doses.³² As an example, there are the results achieved in Central American countries, in which there was a significant reduction of VAD in children under 6 years old, probably due to the adoption of multiple strategies to control this deficiency, mainly the universal sugar fortification.²⁹

According to the arguments of other researchers, the persistence of high prevalence of deficiency may be related to the inaccessibility to foods rich in vitamin A, insufficient dietary diversity, fractional food fortification, frequent exposure to infectious processes, and the restricted effect of supplementation for short periods.^{9,33} In the previous context of the factors associated with VAD, this study mainly allowed to verify the influence of exposures related to the development of infectious processes, which is similar to the result of a specific review focusing on children assisted in daycare centers.⁸ Frequent infections, especially diarrhea and respiratory problems, can affect serum retinol levels due to low food intake, malabsorption, and increased vitamin A catabolism. Furthermore, VAD once installed can reduce immune resistance to these diseases, generating a vicious cycle of nutritional deficiency and infections in children.^{8,18}

The effects of infectious processes on retinol concentrations can be observed in the first 24 hours after the onset of infection, even in the so-called subclinical phase.²⁵ This phenomenon is particularly important in the child population given its susceptibility to infectious diseases,^{17,34} which can explain the associations found.

The deficiency of vitamin A and iron finds reasons linked to the presence of common etiological factors that comprise characteristics of the context of social vulnerability related to food security, environmental health, health services, and care practices.¹⁹ The reduction in serum levels retinol may be also a consequence of the metabolic interactions between vitamin A and iron. Iron deficiency

can affect the use of vitamin A by the human body and feedback loops are generated between the two deficiencies.^{19,34} In a review study focusing on Sri Lanka, with similar results, instead of isolated emphases, the authors emphasized the importance of worry about the simultaneous deficiency of several micronutrients and their interactions during the screening and treatment of these problems.³⁵

In the context of a previous causality with a focus on the influence of infectious processes on the nutritional status of vitamin A, inadequate environmental sanitation and hygiene conditions stand out for having direct impacts on the development of infectious diseases, particularly diarrhea, which explains the associations found of VAD with inappropriate waste disposal and water supply.³⁶ Similar national studies results have been reported not only among Brazilian children.³⁷

For the other factors that have been systematized with importance in VAD, the influence of maternal and child characteristics is highlighted. Differences in prevalence may be associated with the age of the children, as seen in the semi-arid region of Alagoas that infants were more vulnerable than preschoolers.²⁶ The decrease in the prevalence of VAD with the child's age suggests that it is because of the greater susceptibility of younger children to diseases such as intestinal and respiratory infections that can cause anorexia, malabsorption and greater catabolism, impairing the nutritional status of the nutrient.^{17,26} Children born with low birth weight may have deficient levels of vitamin A as a consequence of the nutrient's deficient nutritional status also in the mother, which influences the child's cell stocks, reinforcing the need for preventive measures even in the gestational period.²⁶ Worse maternal nutrition, lower socioeconomic level and the lower capacity for care at this age may be an explanation of the VAD in children of younger mothers, a fact that can interfere with the food offered to the child.^{17,24} The association of maternal education with hypovitaminosis A occurs similarly to age, highlighting the relevance of education in preventive care, in the management of diseases and in the understanding of guidelines provided by health professionals. Greater instruction enables the mothers to achieve better socioeconomic status and sanitary housing conditions.¹⁸

When interpreting the results, we can consider some limitations. First, the inclusion of articles identified in only three bibliographic bases, which was minimized by consulting the lists of bibliographic references of the articles previously included in the review. Also, the limited number of articles on VAD

that have been systematized. Yet, it is important to highlight the evaluation of the quality of the articles showed restrictions in the selection of the sample in some of them, admitting the possibility of bias in this sense. Despite this, the relevance of the results obtained should be highlighted considering the difficulty of studies related to the diagnosis of the nutritional status of vitamin A, especially at the national and multicentric level.

Conclusions

VAD is still poorly studied in Brazilian children under the age of five. The average prevalence weighted by the sample size identified in this review suggests a serious public health problem, highlighting the susceptibility of children conditioned to

the nutritional status of deficient iron, the presence of diarrhea, the diagnosis of subclinical infection, the low birth weight and younger age risk factors. Furthermore, younger age and lower maternal education, as well as inadequate environmental sanitation conditions also seem to be important predictors of deficiency. Further studies are needed on VAD in Brazilian children under the age of five.

Author's contribution

Figueroa Pedraza D participated in the design of the article, bibliographic review, analysis, and interpretation of data, writing, and approval of the article.

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