http://dx.doi.org/10.1590/1678-98652018000300004

ORIGINAL

The relationship between serum retinol concentrations and subclinical infection in rural Brazilian children

Relação entre as concentrações séricas de retinol e a infecção subclínica em crianças rurais brasileiras

Laísla França da Silva TELES[1] 0000-0002-2620-0989
Adriana de Azevedo PAIVA[1] 0000-0001-5089-4581
Liania Alves LUZIA[2] 0000-0001-8317-1398
Flávia Emília Leite de LIMA-FERREIRA[3] 0000-0002-2849-9902
Cecilia Maria Resende Gonçalves de CARVALHO[1] 0000-0002-8707-1447
Patrícia Helen de Carvalho RONDÓ[2] 0000-0002-8308-6393

ABSTRACT

Objective

To evaluate the relationship between serum retinol concentrations and subclinical infection in children from rural settlements.

---

[1] Universidade Federal do Piauí, Departamento de Nutrição, Programa de Pós-Graduação em Alimentos e Nutrição. *Campus* Universitário Ministro Petrônio Portela, s/n., 64049-550, Teresina, PI, Brasil. *Correspondência para*/Correspondence to: AA PAIVA. E-mail: <aapaiva@ufpi.edu.br>.

[2] Universidade de São Paulo. Departamento de Nutrição. Programa de Pós-Graduação em Nutrição em Saúde Pública. São Paulo, SP, Brasil.

[3] Universidade Federal da Paraíba. Departamento de Nutrição. Programa de Pós-Graduação em Modelo de Decisão em Saúde. João Pessoa, PB, Brasil.

Support: *Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES) (Edital CASADINHOPROCAD, grant 552239/2011-9) for financial support. L.F.S.

Article based on the master thesis of LFS TELES, entitled "*Deficiência de vitamina A e fatores relacionados à retinolemia em crianças de seis a cinquenta e nove meses de idade em assentamentos rurais de Teresina*". Universidade Federal do Piauí, 2015.

Como citar este artigo/How to cite this article

Teles LFS, Paiva AA, Luzia LA, Lima-Ferreira FEL, Carvalho CMRG, Rondó PHC. The relationship between serum retinol concentrations and subclinical infection in rural Brazilian children. Rev Nutr. 2018;31(3):299-310. http://dx.doi.org/10.1590/1678-98652018000300004

Methods

A cross-sectional population-based study was carried out in nine rural settlements in the northeastern region of Brazil, involving 118 children aged 6 to 59 months. The relationship between serum retinol and C-Reactive Protein levels, an important marker of infectious and inflammatory processes, was investigated by multiple linear regression, controlling for demographic, socioeconomic and nutritional variables. Serum retinol and C-Reactive Protein were measured, respectively, by High Performance Liquid Chromatography and immunoturbidimetric assay in automated equipment.

Results

Vitamin A deficiency (retinol <0.70µmol/L) was identified in 9.3% of the children. C-Reactive Protein was the only predictor of retinol concentrations in the final regression model, causing a 0.728µmol/L reduction in retinol concentrations in the studied children (*p*=0.008).

Conclusion

Vitamin A deficiency is a problem of mild/moderate severity and measures to control infectious diseases in this population are fundamental to prevent and/or combat this problem.

Keywords: Child, preschool. Infant. Infection. Rural area. Vitamin A.

RESUMO

Objetivo

Esta pesquisa teve por objetivo avaliar a relação entre concentrações séricas de retinol e infecção subclínica, em crianças de assentamentos rurais.

Métodos

Trata-se de estudo transversal, de base populacional, realizado em nove assentamentos rurais na região nordeste do Brasil, envolvendo 118 crianças de 6 a 59 meses de idade. A relação entre retinol sérico e níveis de proteína C-reativa, importante marcador de processos infecciosos e inflamatórios, foi investigada por análise de regressão linear múltipla, controlando-se variáveis demográficas, socioeconômicas e nutricionais. O retinol sérico e a proteína C-reativa foram medidos, respectivamente, por Cromatografia Líquida de Alta Performance e ensaio imunoturbidimétrico em equipamento automatizado.

Resultados

A deficiência de vitamina A (retinol <0,70µmll/L) foi identificada em 9,3% das crianças. A proteína C-reativa foi o único preditor de concentrações de retinol no modelo de regressão final, causando uma redução de 0,728µmol/L nas concentrações de retinol nas crianças estudadas (p=0,008).

Conclusão

A pesquisa concluiu que a deficiência de vitamina A é um problema de severidade leve/moderada, sendo fundamental a adoção de medidas para controlar doenças infecciosas nessa população, bem como para prevenir e/ou combater o problema.

Palavras-chave: *Pré-escolar. Lactantes. Infecção. Zona rural. Vitamina A.*

INTRODUCTION

The main manifestations of Vitamin A Deficiency (VAD), an essential micronutrient related to cell growth, immunity and vision, are associated with increased rates of infant morbidity and mortality [1]. It is estimated that 190 million children under the age of 5 years worldwide have low serum retinol concentrations (<0.70µmol/L). The prevalence of VAD in Brazil is high among children aged 6 to 59 months [2], with a predominance of the condition in the northeastern, where there have been rates around 20% [3].

Populations living in poor rural areas tend to be more vulnerable to nutritional deficiencies and infection. In Brazil, the latest form of rural organization, called "settlements", established by government policies has grown extensively over the past few years. However, most of these settlements still do not have the necessary infrastructure, predisposing the population to infections [4,5].

Within this context, the objective of the present study was to assess the relationship between serum retinol concentrations and subclinical infection in children aged 6 to 59 months living in the settlements of the northeastern region of Brazil.

METHODS

A cross-sectional, population-based study was conducted in the settlements of the *Instituto Nacional de Colonização e Reforma Agrária* (INCRA, National Institute for Colonization and Agrarian Reform), *Teresina, Piauí*, Brazil. *Teresina* is the capital of the state of *Piauí*, one of the poorest states in the country, located in the northeastern region of Brazil. In 2010, the mean per capita income was R$757.57 (approximately US$253.00) and the Human Development Index (HDI) was 0.751 [6]. According to INCRA data [7], *Teresina* has nine settlements created through the Federal Agrarian Reform between 2005 and 2008, which benefit 475 families within a total area of 6,746.97 hectares.

All children within the eligible age range from the nine settlements were invited to participate in the study, for a total of 132 children. There were 14 losses, including 3 (2.27%) due to refusal of the responsible person, 6 (4.54%) due to the absence of the legal guardian of the child at the residence, and 5 (3.78%) because of insufficient blood sample for biochemical analysis. Thus, the final sample consisted of 118 children who met the following inclusion criteria: living in the settlement, age 6 to 59 months, and free and formal consent of the parents who agreed to the child's participation by signing the free informed consent form.

Data collection

The data were collected from May to October 2013. The field team, which was trained by the supervisors of the project, consisted of nutritionists and nutrition students from the *Universidade Federal do Piauí* (UFPI, Federal University of *Piauí*).

Socioeconomic and demographic variables

Socioeconomic and demographic data of the families were collected using questionnaires during the home visits. The criteria of the Brazilian Association of Research Companies [8] were used for the classification of the socioeconomic status of the families. At the end of the interview, a date was scheduled for blood collection, anthropometry, and evaluation of food intake and health of the child.

Measurement of serum retinol and C-Reactive Protein (CRP)

Blood samples (3–5 mL) were collected by venipuncture into tubes without anticoagulant (Greiner Bio-One, *São Paulo*, Brazil) wrapped in aluminum foil for protection from light. Maintaining the cold chain, the samples were transported to the Laboratory of Experimental Nutrition, Department of Nutrition, UFPI, where they were centrifuged at 3,000rpm and divided into two serum aliquots. The two aliquots were stored in amber and transparent microtubes for the measurement of retinol and C-Reactive Protein, respectively, at 80ºC until the time of analysis.

Serum retinol was measured at the Laboratory of Micronutrients, School of Public Health, University of *São Paulo*, by High-Performance Liquid Chromatography (HLPC) in a Solvent Delivery Module LC-10Avp (Shimadzu® Corporation, Analytical Instruments Division, Kyoto, Japan) as described by Arnaud *et al*.

[9]. VAD was diagnosed when serum retinol concentrations were less than 0.70µmol/L. With respect to the level of epidemiological importance, the following prevalence classification was adopted: 2 to 10%, mild public health problem; 11 to 19%, moderate public health problem, or >20%, serious public health problem [10].

Measurement of CRP

C-Reactive Protein was measured in the samples at the Laboratory of Clinical Analyses, University Hospital, UFPI, by an immunoturbidimetric assay in an automated Cobas Integra Plus 400 biochemical analyzer (Roche® Diagnostics, Mannheim, Germany) using the CRP kit (Cassete C-Reactive Protein Roche®). A level of CRP>5mg/L was defined to indicate the presence of infection or of an inflammatory process.

Anthropometry

The weight of the children was measured with a digital scale (Plena®, *São Paulo*, Brazil; capacity of 150kg) to the nearest 100g. Children younger than 2 years were weighed on the arms of the responsible person whose weight was deduced from the total weight. Height was measured with a fabricated infantometer (measuring range of 100cm and subdivisions in millimeter) in children younger than 2 years and with a stadiometer (Seca®, Hamburg, 206, Germany) containing a 2.2 measuring tape and subdivisions in millimeter in children older than 2 years. Nutritional status was evaluated based on height/age, weight/age, weight/height, and Body Mass Index (BMI)/age indices [11].

Food intake

Food intake was evaluated using a 24-hour diet recall by interview with the mother or responsible person of the child. If the children attended daycare centers or nursery schools, the employees responsible for the preparation and distribution of the child's meal at the institutions were also interviewed. Photographic records of the utensils and portions [12] were used to help the interviewed subjects identify the amounts of foods ingested and conversion tables [13,14] were applied to transform the home measures into gram (g) or milliliter (mL).

For the estimation of intrapersonal variability, a second 24-hour recall was applied to 40% of the sample selected randomly after an interval of 2 months, repeating the same procedure as used in the first interview. Habitual nutrient intake was estimated using the Multiple Source Method (version 1.0.1) [15].

The amounts of nutrients were calculated using the Nutwin 1.5 software [16]. The foods not found in the database of the program were inserted based on chemical composition tables of the foods [17-19]. For processed foods not included in these tables, the nutritional information on the labels of the products was considered. Regional preparations were included in the program according to the ingredients and home quantities described in the form.

The intake of vitamin A (µg), proteins (g), lipids (g), iron (mg), and zinc (mg) was evaluated, the last four because they are involved in the bioavailability of vitamin A [20-22]. The reference values proposed by the Institute of Medicine were used for the evaluation of nutrient intake [23]. The Estimated Average Requirement (EAR) was adopted as the cut-off for calculation of the prevalence of inadequacy. In the case of nutrients for which no EAR was available, the Adequate Intake (AI) was used. In these cases, it was not possible to estimate the prevalence of inadequacy. The volume of milk consumed by breast-fed children was estimated according to the Brazilian Food Guide for children under the age of 2 years [24].

Data of the child

A questionnaire was applied to the person responsible for the child to obtain data regarding breast-feeding practices, presence of morbidities in the last 15 days, and use of vitamin complexes. The date of birth of the child and information about vitamin A supplementation in the last 6 months were collected from the Child's Health Card.

Statistical analysis

The data were processed and analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, United States) 20.0. The Kolmogorov-Smirnov test was used to evaluate the normality of the dependent variable (serum retinol concentrations). Natural logarithmic transformation was necessary to obtain normality of the data. Levene's test was used to verify the homogeneity of variances. In bivariate analysis, the Student *t*-test and analysis of variance were used for comparison between serum retinol concentrations and variables with two or more categories, respectively. Numerical variables were compared using Pearson's correlation coefficient. A level of significance of 5% was adopted. The variables showing $p<0.20$ in bivariate analysis were included in the multiple linear regression model (backward stepwise method). In this case, significance was assumed when $p<0.05$.

RESULTS

Among the 118 children studied, 59.3% were girls, with a mean age of 30.37 (16.68) months (Table 1). The mean serum retinol level was 1.33 (0.57) μmol/L and the prevalence of VAD was 9.3%.

As can be seen in Table 2, vitamin A intake was inadequate in almost 100.00% of children aged 48 to 59 months (99.98%). Another finding that calls attention is the high percentage of inadequate iron intake, especially among children aged 7 to 11 months (99.66%). Mean zinc intake was higher than the EAR in children older than 12 months, with low percentages of inadequacy. With respect to macronutrients, mean protein intake was above the EAR and AI for the corresponding age groups. Mean fat intake was lower than the AI in children under the age of 1 year.

Analysis of the categorical variables showed that serum retinol concentrations were significantly lower in children living in dwellings made of mud and unfinished masonry ($p=0.025$) and in those diagnosed with subclinical infection ($p=0.008$). With respect to the numerical variables studied, vitamin A intake and retinol concentrations showed a weak and positive, but significant association ($r=0.118$; $p=0.049$) (Table 3).

The final multiple linear regression model (Table 4) showed that the presence of subclinical infection caused a reduction of 0.728μmol/L in retinol concentrations ($p=0.008$), explaining 51.1% of the variability in serum retinol in the population studied.

DISCUSSION

The mean serum retinol concentrations of the children studied were within the normal range; however, regarding the concentrations identified as low, the percentage found (9.3%) classifies VAD as a mild public health problem.

Low vitamin A intake, as well as infectious processes, can cause a reduction in blood retinol concentrations. In the first case, there is a decrease in liver stores. In the second case, vitamin A concentrations stored in the liver may be normal, but mobilization of the vitamin is suppressed as a result of the low synthesis of the retinol transport protein, also as a consequence of infectious processes [25].

Table 1. Characteristics of the population (n=118).

1 of 2

Variables	n	%	Mean	SD
Child age (months)			30.37	16.68
Child's gender				
Female	70	59.3	-	
Male	48	40.7	-	
Socioeconomic class				
C and D	10	8.5	-	
E	108	91.5	-	
Government assistance				
Yes	86	72.8	-	
No	32	27.2	-	
Access to health services				
Local health center	3	2.5	-	
Municipal health center	98	83.1	-	
Municipal hospital	15	12.7	-	
Other	2	1.7	-	
Type of dwelling				
Mud/unfinished masonry	58	49.2	-	
Finished masonry	60	50.8	-	
Presence of piped water				
Yes	100	84.7	-	
No	18	15.3	-	
Waste destination				
Septic tank	90	76.3	-	
Open sky	28	23.7	-	
Public garbage collection				
Yes	53	44.9	-	
No	65	55.1	-	
Use of vitamin complexes (last 3 months)				
Yes	18	15.3	-	
No	100	84.7	-	
Vitamin A supplementation (last 6 months)[*]				
Yes	70	61.9	-	
No	43	38.1	-	
Exclusive breast-feeing[†]				
<1 month or never	23	20.0	-	
1 to 5 months	38	33.0	-	
6 months	37	32.2	-	
>6 months	17	14.8	-	
Health complications (in the last 15 days)				
Diarrhea	7	5.7	-	
Vomiting	5	4.1	-	
Parasitosis	5	4.1	-	
Respiratory diseases	65	52.8	-	

Table 1. Characteristics of the population (n=118).

2 of 2

Variables	n	%	Mean	SD
Presence of subclinical infection‡				
Yes	14	11.9	-	
No	104	88.1	-	
Maternal age (years)	-		26.30	5.62
Maternal education level (years of schooling)	-		6.81	3.10
Paternal education level (years of schooling)	-		6.57	3.60
Number of household members	-		4.83	1.79
Household income (R$)	-		859.36	437.00
Per capita *household income (R$)*	-		190.95	109.66
Number of rooms	-		5.00	1.37
Number of persons per room	-		1.04	0.43
Anthropometry (Z-score)				
Weight for height	-		0.20	0.93
Weight for age	-		-0.10	0.99
Height for age	-		-0.44	1.15
BMI for age	-		0.24	0.94
Nutrient intake				
Proteins (g)	-		57.1	25.2
Lipids (g)	-		35.8	9.7
Vitamin A (µg)	-		286.8	99.9
Iron (mg)	-		8.0	2.5
Zinc (mg)	-		5.5	2.2

Note: *Interviewee could not answer. †The child had not health booklet. ‡Assessed by C-Reactive Protein concentrations >5mg/L. BMI: Body Mass Index; SD: Standard Deviation.

In this study, the presence of subclinical infection was inversely associated with serum retinol concentrations. Similar results have been reported in other studies. Rohner *et al*. [26] showed a significant increase in the risk of VAD in children diagnosed with inflammation, demonstrated by elevated concentrations of CRP and alpha-1-acid glycoprotein.

The prevalence of VAD was 9.3%, but the prevalence of subclinical infection, assessed by CRP concentrations, was 11.9%. It is important to emphasize that retinol-binding protein is a negative acute phase protein, and that the occurrence of a subclinical infection can interfere with its serum concentrations [27]. Excluding from the final sample (n=118) the children with subclinical infection (n=14), the prevalence of VAD is reduced to 7.7%. This reduction may reflect an overestimation of 1.6% of the overall prevalence of low serum retinol concentrations, in agreement with the study of Silva *et al*. [28] who reported an overestimation of 4.1%.

With respect to the variables related to food intake, vitamin A intake was significantly associated with serum retinol concentrations, although this association was no longer observed in the final Multiple Linear Regression (MLR) model. The perception of the influence of vitamin A intake on serum retinol concentrations has been shared by some authors [29-31].

One of the limitations of the present study, in addition to those inherent to dietary

Table 2. Habitual nutrient intake in the population (n=118).

Nutrients	EAR/ IA	Mean	SD	Percentiles of nutrient intake			Prevalence of inadequacy %
				25th	50th	75th	
6 months							
Proteins (g)*	9.10	13.5	1.5	12.3	13.3	14.7	-
Lipids (g)*	31	27.6	6.6	23.7	30.0	31.5	-
Vitamin A (µg)*	400	671.9	97.9	609.7	701.9	734.1	-
Iron (mg)*	0.27	4.4	0.8	3.9	4.1	5.0	-
Zinc (mg)*	2	1.6	0.1	1.5	1.5	1.7	-
7-11 months							
Proteins (g)	9	25.9	7.4	19.8	23.7	29.4	1.13
Lipids (g)*	30.0	26.2	8.8	22.0	26.3	32.8	-
Vitamin A (µg)*	500	381.5	56.7	322.2	404.8	430.4	-
Iron (mg)	6.9	3.1	1.4	1.9	2.6	4.3	99.66
Zinc (mg)	2.5	2.5	0.8	2.1	2.3	3.0	0
12-47 months							
Proteins (g)	11	58.9	19.9	42.9	56.4	69.6	0.80
Lipids (g)†	-	36.0	5.0	32.6	36.2	38.6	-
Vitamin A (µg)	210	280.4	75.7	218.2	274.9	330.4	17.62
Iron (mg)	3.0	8.1	2.0	6.6	7.9	9.3	0.54
Zinc (mg)	2.5	5.7	1.2	4.9	5.5	6.4	0.40
48-59 months							
Proteins (g)	13	71.0	27.8	55.9	71.0	84.8	1.88
Lipids (g)†	-	42.3	14.5	31.7	41.2	49.7	-
Vitamin A (µg)	275	213.3	16.2	201.3	211.6	224.3	99.98
Iron (mg)	4.1	9.8	2.5	8.1	9.6	10.9	1.13
Zinc (mg)	4	7.0	2.7	5.4	6.5	8.4	13.35

Note: *IA: Inadequate intake as reference value. †Dietary reference intake not determined. Other nutrients = EAR: Estimated Average Requirement. BMI: Body Mass Index; SD: Standard Deviation.

surveys, was the fact that two persons were interviewed (the mother or responsible person of the child and employees of daycare centers or nursery schools). Additional limitations include the lack of control of seasonality, since some foods such as fruits are generally influenced by this factor [32], and the existence of different food composition tables, which often do not contain adequate information about the content of regional foods. Despite these limitations, care was taken in this study to minimize potential measurement errors resulting from the use of the data collection instrument.

CONCLUSION

The variables associated with serum retinol concentrations in this population were the presence of subclinical infection. Vitamin A deficiency is a mild public health problem in the children studied. These results indicate the need to implement public policies designed to control infectious diseases and nutritional interventions that stimulate the consumption of foods containing vitamin A in order to prevent and/or combat not only VAD, but also other nutritional deficiencies that are common in this age group.

Table 3. Characteristics of the population according to serum retinol concentrations (µmol/L) (n=118).

1 of 2

Variables	Mean*	SD	r†	*p*
Child age (months)	-		-0.125	0.178
Child's gender				
Female	1.31	0.61	-	0.511
Male	1.35	0.52		
Socioeconomic class				
C and D	1.47	0.71	-	0.622
E	1.32	0.56		
Government assistance				
Yes	1.32	0.57	-	0.778
No	1.36	0.57		
Access to health services				
Local health center	2.09	0.53	-	0.140
Municipal health center	1.32	0.54		
Municipal hospital	1.32	0.68		
Other	1.08	0.75		
Type of dwelling				
Mud/unfinished masonry	1.21	0.52	-	0.025
Finished masonry	1.44	0.60		
Presence of piped water				
Yes	1.34	0.56	-	0.614
No	1.29	0.61		
Waste destination				
Septic tank	1.39	0.59	-	0.063
Open sky	1.16	0.48		
Public garbage collection				
Yes	1.33	0.58	-	0.794
No	1.34	0.56		
Use of vitamin complexes (last 3 months)				
Yes	1.27	0.35	-	0.955
No	1.34	0.60		
Vitamin A supplementation (last 6 months)				
Yes	1.02	0.55	-	0.189
No	1.38	0.56		
Exclusive breast-feeing				
< 1 month or never	1.30	0.46	-	0.170
1 to 5 months	1.40	0.60		
6 months	1.37	0.62		
> 6 months	1.06	0.45		
Health complications				
Diarrhea	1.50	0.81	-	0.503
Vomiting	1.52	0.77		
Parasitosis	1.52	0.50		
Respiratory diseases	1.29	0.54		

Table 3. Characteristics of the population according to serum retinol concentrations (µmol/L) (n=118).

2 of 2

Variables	Mean*	SD	r†	*p*
Presence of subclinical infection				
Yes	1.02	0.55	-	0.008
No	1.38	0.56		
Maternal age (years)	-		0.009	0.921
Maternal education level (years of schooling)	-		0.053	0.574
Paternal education level (years of schooling)	-		-0.002	0.987
Number of household members	-		-0.062	0.508
Household income (R$)	-		0.070	0.450
Per capita *household income (R$)*	-		0.098	0.290
Number of rooms	-		0.088	0.345
Number of persons per room	-		-0.111	0.232
Anthropometry (Z-score)	-			
Weight for height	-		0.117	0.206
Weight for age	-		0.064	0.490
Height for age	-		-0.018	0.851
BMI for age	-		0.116	0.211
Nutrients				
Proteins (g)	-		0.044	0.667
Lipids (g)	-		0.005	0.960
Vitamin A (µg)	-		0.118	0.049
Iron (mg)	-		-0.064	0.488
Zinc (mg)	-		-0.008	0.934

Note: *Student *t*-test and analysis of variance for comparison between serum retinol concentrations and variables with two or more categories, respectively. †Pearson's correlation coefficient. ‡Assessed by C-Reactive Protein concentrations >5mg/L. BMI: Body Mass Index; SD: Standard Deviation.

Table 4. Final multiple linear regression model considering serum retinol concentration as the dependent variable (outcome).

Variables	Coefficients		T	*p*	Exp(B)*	95%CI for Exp(B)	
	B	Standard error				Lower limit	Upper limit
(Constant)	0.238	0.040	5.906	0.000	1.269	1.171	1.374
Presence of subclinical infection†	-0.317	0.117	-2.708	0.008	0.728	0.578	0.919

Note: *Data converted to their original values by exponential transformation. †Assessed by C-Reactive Protein concentrations >5mg/L. ANOVA (*p*=0.008), normality (*p*=0.946), homogeneity (*p*=0.723), R^2=51.1%.

CONTRIBUTORS

LFS TELES participated in the development of the study protocol, data collection and analysis, interpretation of the results, and writing of the manuscript. AA PAIVA was responsible for the design of the study and coordination of the research, and participated in the interpretation of the results and writing and revision of the manuscript. LA LUZIA performed the retinol analysis and participated in the revision of the manuscript. FEL LIMA-FERREIRA participated in the analysis of food intake and revision of the manuscript. CMRG CARVALHO participated in the data analysis and the revision of the manuscript. PHC RONDÓ participated in the revision of the manuscript and retinol analysis.

REFERENCES

1. Wirth JP, Petry N, Tanumihardjo SA, Rogers LM, McLean E, Greig A, *et al*. Vitamin A supplementation programs and country-level evidence of vitamin A deficiency. Nutrients. 2017;9(3):190. http://dx.doi.org/10.3390/nu9030190
2. Pedraza DF, Queiroz D, Paiva AA, Cunha MAL, Lima ZN. Seguridad alimentaria, crecimiento y niveles de vitamina A, hemoglobina y zinc en ninos preescolares del nordeste de Brasil. Ciênc Saúde Coletiva. 2014;19(2):641-50. http://dx.doi.org/10.1590/1413-81232014192.22612012
3. Queiroz D, Paiva AA, Pedraza DF, Cunha MAL, Esteves GH, Luna JG, *et al*. Deficiência de vitamina A e fatores associados em crianças de áreas urbanas. Rev Saúde Pública. 2013;47(2):248-56. http://dx.doi.org/10.1590/S0034-8910.2013047002906
4. Fietz VR, Salay E, Watanabe EAMT. Condições socioeconômicas, demográficas e estado nutricional de adultos e idosos moradores em assentamento rural em Mato Grosso do Sul, MS. Segur Aliment Nutr. 2010;17(1):73-82. http://dx.doi.org/10.20396/san.v17i1.8634801
5. Oliveira EC, Santos ES, Zeilhofer P, Souza-Santos R, Atanaka-Santos M. Spatial patterns of malaria in a land reform colonization project, Juruena municipality, Mato Grosso, Brazil. Malar J. 2011;10:177. http://dx.doi.org/10.1186/1475-2875-10-177
6. Programa das Nações Unidas para o Desenvolvimento. Atlas do desenvolvimento humano no Brasil, 2013 [acesso 2016 set 30]. Disponível em: http://atlasbrasil.org.br/2013/pt/perfil/teresina_pi
7. Instituto Nacional de Colonização e Reforma Agrária. Sistema de Informações de Projetos de Reforma Agrária: relação de projetos de reforma agrária, 2012 [acesso 2016 set 30]. Disponível em: http://www.incra.gov.br/index.php/reforma-agraria-2/projetos-eprogramas-do-incra/relacao-de-projetos-de-reforma-agraria
8. Associação Brasileira de Empresas de Pesquisa. Critério de Classificação Econômica Brasil. São Paulo: Abep; 2013. [acesso 2016 set 30]. Disponível em: http://www.abep.org/new/
9. Arnaud J, Fortis I, Blachier S, Kia D, Favier A. Simultaneous determination of retinol, alfa-tocopherol, and beta-carotene in serum by isocratic high-performance liquid chromatography. J Chromatogr. 1991;572(1-2):103-16.
10. World Health Organization. Indicators for assessing Vitamin A Deficiency and their application in monitoring and evaluating intervention programmes: Report of a joint. Geneva: WHO; 1996 [cited 2016 Sept 30]. Available from: http://www.who.int/nutrition/publications/micronutrients/vitamin_a_deficiency/WHONUT96.10.pdf
11. World Health Organization. Multicentre Growth Reference Study Group. WHO child growth standards based on length/height, weight and age. Acta Paediatric. 2006;450:76-85.
12. Zabotto CB. Registro fotográfico para inquéritos dietéticos. Campinas: Unicamp; 1996.
13. Alencar MAPM, Alvarenga ESL, Melo MTSM. Alimentos: medidas caseiras: correspondência peso-volume. Teresina: EDUFPI; 2005.
14. Pinheiro ABV, Lacerda EMA, Benzecry EH, Gomes MCS, Costa VM. Tabela para avaliação de consumo alimentar em medidas caseiras. São Paulo: Atheneu; 2005.
15. European Food Consumption Validation Project. Multiple Source Method (MSM) for estimating usual dietary intake from short-term measurement data. Nuthetal: Dife; 2011 [cited 2016 Sept 30]. Available from: http://msm.dife.de
16. Anção MS, Cuppari L, Draibe SA, Sigulem D. Programa de apoio à nutrição Nutwin: versão 1.5 [CD-ROM]. São Paulo: Unifesp,EPM. 2002.
17. Núcleo de Estudos e Pesquisa em Alimentação. Tabela Brasileira de Composição de Alimentos. Campinas: Unicamp; 2011.
18. Instituto Brasileiro de Geografia e Estatística. Pesquisa de Orçamentos Familiares 2008-2009: tabelas de composição nutricional dos alimentos consumidos no Brasil. Rio de Janeiro: IBGE; 2011.
19. Philippi ST. Tabela de composição de alimentos: suporte para decisão nutricional. Barueri: Manole; 2011.
20. Reboul E. Absorption of vitamin A and carotenoids by the enterocyte: Focus on transport proteins. Nutrients. 2013;5(9):3563-81. http://dx.doi.org/10.3390/nu5093563
21. Kopec RE, Cooperstone JL, Schweiggert RM, Young GS, Harrison EH, Francis DM, *et al*. Avocado consumption enhances human postprandial provitamin A absorption and conversion from a Novel high-β-carotene tomato sauce and from carrots. J Nutr. 2014;144(8):1158-66. http://dx.doi.org/10.3945/JN.113.187674
22. Kana-Sop MM, Gouado I, Achu MB, Van Camp J, Amvam Zolo PH, Schweigert FJ, *et al.* The influence of iron and zinc supplementation on the bioavailability of provitamin A carotenoids from papaya following consumption of a vitamin A-deficient diet. J Nutr Sci Vitaminol. 2015;61(3):205-14.

23. Institute of Medicine. Food and nutrition board: Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. New York: National Academy Press, 2001 [cited 2018 Aug 15]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK222310/

24. Ministério da Saúde (Brasil). Guia alimentar para crianças menores de 2 anos. Distrito Federal: Ministério da Saúde; 2013.

25. Rubin LP, Ross AC, Stephensen CB, Bohn T, Tanumihardjo SA. Metabolic effects of inflammation on vitamin A and carotenoids in humans and animal models. Adv Nutr. 2017;8(2):197-212. http://dx.doi.org/10.3945/an.116.014167

26. Rohner F, Woodruff BA, Aaron GJ, Yakes EA, Lebanan MA, Rayco-Solon P, *et al*. Infant and young child feeding practices in urban Philippines and their associations with stunting, anemia, and deficiencies of iron and vitamin A. Food Nutr Bull. 2013;34(2Suppl):S17-34.

27. Garcêz LS, Lima GSP, Paiva AA, Paz SMRS, Gomes EIL, Nunes VS, *et al*. Serum retinol levels in pregnant adolescents and their relationship with habitual food intake, infection and obstetric, nutritional and socioeconomic variables. Nutrients. 2016;8(1):669. http://dx.doi.org/10.3390/nu8110669

28. Silva LLS, Peixoto MRG, Hadler MCCM, Silva SA, Cobayashi F, Cardoso MA. Vitamin A status and associated factors in infants attending at Primary Health Care in Goiânia, Goiás, Brazil. Rev Bras Epidemiol. 2015;18(2):490-502. http://dx.doi.org/10.1590/1980-5497201500020016

29. Hotz C, Chileshe J, Siamusantu W, Palaniappan U, Kafwembe E. Vitamin A intake and infection are associated with plasma retinol among pre-school children in rural Zambia. Public Health Nutr. 2012;15(9):1688-96. http://dx.doi.org/10.1017/S1368980012000924

30. Ribeiro-Silva RC, Nunes IL, Assis AMO. Prevalence and factors associated with vitamin A deficiency in children and adolescents. J Pediatr. 2014;90(5):486-92. http://dx.doi.org/10.1016/j.jped.2014.01.014

31. Faber M, Van Jaarsveld PJ, Kunneke E, Kruger HS, Schoeman SE, Van Stuijvenberg ME. Vitamin A and anthropometric status of South African preschool children from four areas with known distinct eating patterns. Nutrition. 2014;31(1):64-71. http://dx.doi.org/10.1016/j.nut.2014.04.024

32. Arsenault JE, Nikiema L, Allemand P, Ayassou KA, Moursi M, Moura FF, *et al*. Season differences in food and nutrient intakes among young children and their mothers in rural Burkina Faso. J Nutr Sci. 2014;3:e55. http://dx.doi.org/10.1017/jns.2014.53

Received: April 4, 2018
Final version: July 12, 2018
Approved: August 2, 2018