Prevalence of vitamin A deficiency in women of childbearing age in Brazil: a systematic review and meta-analysis

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Abstract

Vitamin A is an essential micronutrient, especially during pregnancy. We aimed to assess the prevalence of vitamin A deficiency in Brazilian women of childbearing age. We conducted a systematic review with meta-analysis of studies that assessed vitamin A deficiency in women of childbearing age following the registered protocol (CRD42020171856). Independent peer researchers selected the studies retrieved from MEDLINE, Embase, Scopus and other sources. Data from the eligible studies were extracted in pairs and assessed for methodological quality. The prevalence of vitamin A deficiency (< 0·70 µmol/l or <0·20 µg/dl) and 95 % CI was combined by meta-analysis, and heterogeneity was estimated by I^2. Out of 3610 screened records, thirty-two studies were included, which assessed 12 577 women from 1965 to 2017, mostly in maternity hospitals. Main limitations of the studies were in sample frame (30/32) and sampling method (29/32). Deficiency occurred in 13 % (95 % CI 9·4, 17·2 %; I^2 = 97 %) of all women and was higher in pregnant women (16·1 %; 95 % CI 5·6, 30·6 %; I^2 = 98 %) than non-pregnant women (12·3 %; 95 % CI 8·4, 16·8 %; I^2 = 96 %). The prevalence increased according to the decade, from 9·5 % (95 % CI 1·9–21·6 %; I^2 = 98 %) up to 1990, 10·8 % (95 % CI 7·9, 14·2 %; I^2 = 86 %) in the 2000s and 17·8 % (95 % CI 8·7, 29·0 %; I^2 = 98 %) in the 2010s. Over 10 % of Brazilian women in childbearing age were deficient in vitamin A. Higher prevalence was observed in pregnant women, and deficiency seemed to be increasing over the decades. Low representativeness of the studies, mainly based on convenience sampling that included pregnant, postpartum, lactating and non-pregnant women, as well as high heterogeneity, limits the findings.

Key words: Vitamin A deficiency: Prevalence: Women: Systematic review: Meta-analysis

Maternal and child malnutrition, which is generally caused by food insecurity that led to nutritional deficiencies, was the ninth leading cause of death worldwide in 2019[1]. Micronutrient deficiency has a negative impact on different aspects of human health, but major effects are observed during childbearing years in women and childhood[2]. Vitamin A deficiency is the most important cause of preventable blindness and a risk factor for morbidity and mortality during childhood and in reproductive period, especially in low- and middle-income countries[1–3]. Vitamin A deficiency is diagnosed mainly in surveys to estimate the prevalence of low serum retinol concentrations, a population biochemical indicator[4] and the presence of night blindness, a functional indicator[5].

In areas where vitamin A deficiency is considered a public health problem, the intervention measures that are commonly applied include supplementation, encouragement of consumption and the fortification of foods that are sources of vitamin A. Among the available strategies, vitamin A supplementation used to be recommended during pregnancy, the postpartum and childhood[6,7]. The current WHO guidelines do not

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recommend vitamin A supplementation for postpartum women due to the lack of benefits in the long term[8].

In Brazil – an emerging economy marked by high inequality – nationwide surveys are needed to assess the population's nutritional status and thus guide public policies, but their occurrence is infrequent. The last national survey carried out in Brazil on the population's food consumption was the Family Budget Survey in 2017–2018, which showed a prevalence of 89 % of inadequate vitamin A intake in the Brazilian population aged 19 to 59 years in both sexes, an increase compared with the 2008–2009 survey, which showed an intake deficiency of 85 % in the same group[9,10]. Nationally, vitamin A deficiency was assessed more than 15 years ago, and 12 % of Brazilian women of reproductive age presented vitamin A deficiency[11].

The lack of updated nationwide prevalence of vitamin A deficiency requires an effort to estimate the proportion of Brazilian women with this deficiency during their reproductive period. The aim of this research was to estimate the vitamin A deficiency prevalence in Brazilian women during their reproductive age.

Methods

The protocol containing the detailed methods of this systematic review was registered in the International Prospective Register of Systematic Reviews (CRD42020171856). This report followed the recommendations of the 2020 Preferred Reporting Items for Systematic Review and Meta-analysis[12].

Eligibility criteria

We considered eligible observational or experimental studies that assessed vitamin A deficiency in women of childbearing age (15–49 years of age) in Brazil[13], regardless of population representativeness. Case–control studies were excluded because reliable prevalence data cannot be derived from this study design due to the nature of the sample (i.e. one group previously known with the condition of interest and one group without). All vitamin A statuses were assessed at the serum retinol levels' cut-off points: normal (< 1·05 µmol/l or < 0·30 µg/dl), deficiency (< 0·70 µmol/l or < 0·20 µg/dl) and critical (< 0·35 µmol/l or < 0·10 µg/dl).

Information sources

The searches were carried out in MEDLINE, Embase, Scopus, LILACS, SciELO and Brazilian theses and dissertations databases (Brazilian Coordination for the Improvement of Higher Education Personnel and repositories of Brazilian universities with a postgraduate programme of collective health and nutrition). We screened the references of relevant publications to identify additional potentially eligible studies. No language or publication status restrictions were applied.

Search strategy

A pilot strategy was developed for MEDLINE database (via PubMed) and adapted for the other databases, following the recommendations of the Peer Review of Electronic Search Strategies guidance[14]. The final strategy for bibliographic databases is shown in online Supplementary Table S1. For theses and dissertations, the following keywords in Portuguese, in combination or separately, were used: 'deficiência', 'vitamina', 'hipovitaminose' and 'retinol'. The search results in compatible formats were imported into the Covidence platform (www.covidence. org) to remove duplications and further review steps. Searches in all databases were carried out on 2 June 2020 and fully updated on 31 March 2022.

Selection process

Six researchers (CMF, DAH, DFSA, JMO, MTS, TFG) in pairs independently selected the studies from title and abstracts and then in full-text assessment using the Covidence platform. Discrepancies were resolved in consensus meetings. Calibration of the selection process was carried out in meetings to assess discordances after the selection of 100 studies. For theses and dissertations, one reviewer (CMF) screened the search results, and eligibility was confirmed by a second researcher (DFSA), using an Excel spreadsheet.

Data collection process

Six researchers (CMF, DAH, DFSA, JMO, MTS, WWGS) in pairs independently extracted the data from the studies using an extraction form customised in Covidence. Calibration of the collection process was carried out in meetings to assess discordances after the extraction of two studies to standardise the process and adapt the extraction form as needed. One author (TFG) compared the independent extraction and resolved discrepancies to define the final extracted data to be included. To harmonise the data from studies with multiple publications, the main study information was compared in an Excel spreadsheet by one author (WWGS), and the report with the most complete data was defined by another author (TFG). The study's authors were contacted to obtain additional data in case of absence in the reports or to clarify conflicting information included in different reports of the same study.

Data items

We extracted data about the study (author, year of data collection, research location, sample source, study design), characteristics of the population (age, number of women, reproductive status) and outcome (biological matrix, technique for analysis, cut-off point adopted, number of women with deficiency of vitamin A and total of women assessed).

Study risk of bias assessment

Paired and independent researchers (CMF, DAH, DFSA, JMO, MTS, WWGS) assessed the methodological quality of the included studies using the Joanna Briggs Institute's checklist for prevalence data[15], loaded in the extraction form in Covidence consisting of the items: (i) sample frame, (ii) sampling method, (iii) sample size, (iv) setting and participants description, (v) coverage of data analysis, (vi) methods for outcome measurement, (vii) the condition measured in a standard and
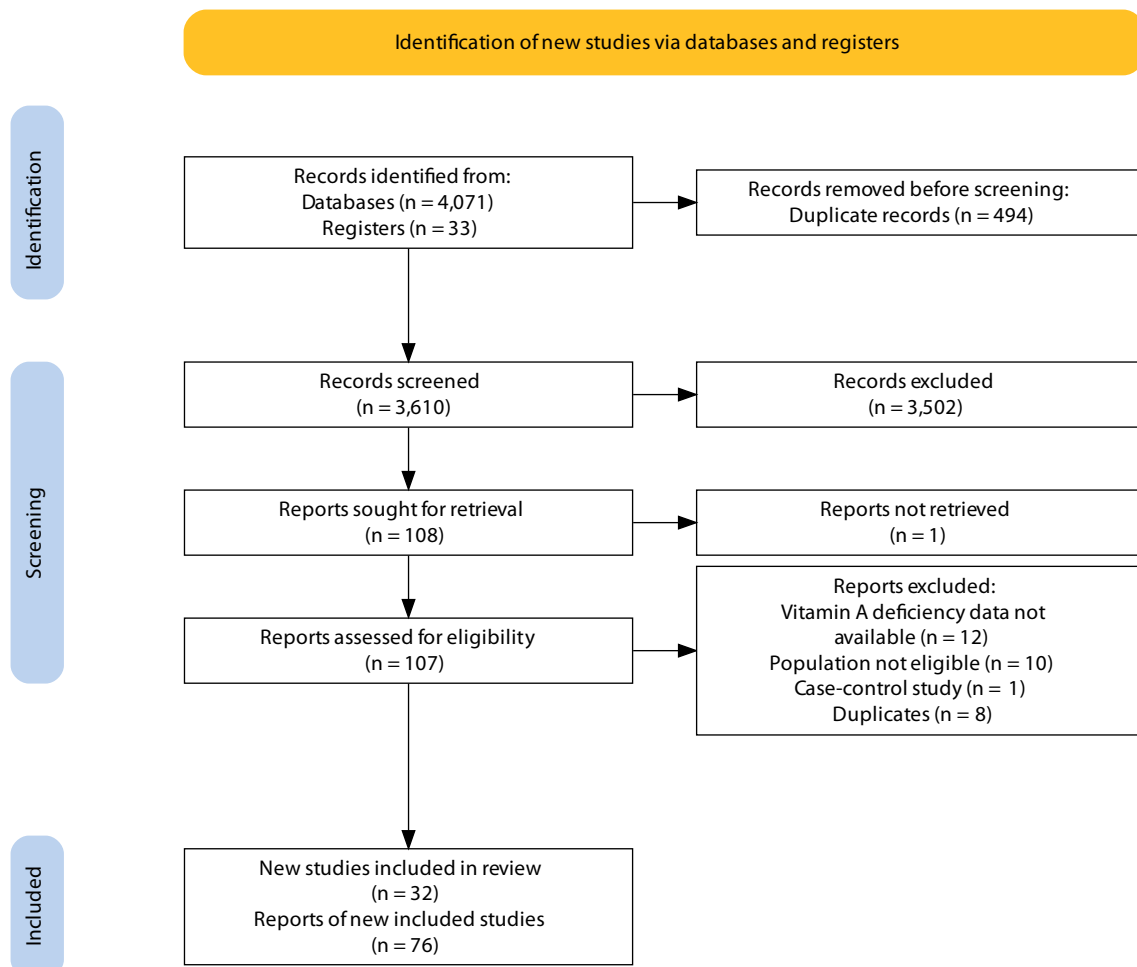
Fig. 1. Process of selection and inclusion of studies in the review.

reliable, (viii) statistical analysis and (ix) response rate (online Supplementary Table S2). Reviewers assigned one point for each item properly addressed by the studies, with a maximum score of nine per study. One author (TFG) checked the independent ratings of the risk of bias and assigned the final assessment, resolving discrepancies.

Effect measures

The primary outcome was the prevalence of vitamin A deficiency (serum retinol < 0·70 μmol/l or < 0·20 μg/dl) and 95 % CI. Secondary outcomes included the prevalence of normal (serum retinol < 0·30 μg/dl or < 1·05 μmol/l) and critical (serum retinol < 0·10 μg/dl or < 0·35 μmol/ l) levels, prevalence of deficiency by reproductive status (pregnant, postpartum, breast-feeding and not pregnant women), Brazilian geographic regions (North, Northeast, Midwest, Southeast and South) and decade of research (≤ 1990s, 2000s and 2010s).

Synthesis methods

Meta-analysis of proportions was calculated with Freeman–Tukey double arcsine transformation (*metaprop* command, *ftt* option in Stata software v. 14.2)[16,17]. Heterogeneity was estimated by the assessment of inconsistency between studies (I^2) and χ^2 tests, with a significance level of $P < 0·10$[18].

Meta-regressions were calculated using the modified Knapp–Hartung method to investigate the effects of independent variables (year of research, decade, quality score, Brazilian region) on the variability of the prevalence of vitamin between studies[19]. Sensitivity analysis to assess the robustness of the results against the removal of studies with discrepant results was performed.

Reporting bias assessment

Publication bias was assessed by visual inspection of funnel plots of the log odds of vitamin A deficiency against standard error of the estimate and of the log odds of vitamin A deficiency against the study size[20] and Egger's test at the significance level of $P < 0·05$[21].

Results

Study selection

Out of 3529 retrieved records, 108 were selected for full-text assessment and seventy-six reports from thirty-two studies were included in the review (Fig. 1). We contacted fourteen authors

Table 1. Characteristics of included studies

Study	Year	City, state	Source	Study design	Age group (years)	Characteristics	Biological matrix, analysis technique	Sample size	Quality score
Andreto 2011[22]	2007–2009	Recife, PE	Maternity hospital	Randomised controlled trial	13–45	Puerperal pregnant women of single fetus	Serum, HPLC	325	7
Azeredo 2008[23]	2004	Rio de Janeiro, RJ	Outpatient clinic	Cross-sectional	14–19	Healthy adolescent women, single healthy term baby and lactating women	Plasma, HPLC	72	6
Batista Filho 1973[24]	1969–1970	Água Preta e Gameleira, PE	Basic health unit	Cross-sectional	15–40	Pregnant women	Serum, spectrophotometric	159	5
Bezerra 2020[25]	2011–2014	Santa Cruz, RN	Hospital	Cross-sectional	18–40	Pregnant women low obstetric risk, delivery at term and single concept	Serum, HPLC	84	5
Costa 2013[26]	2006	Recife and 18 cities, PE	Household	Cross-sectional	16–49	Healthy non-pregnant women	Serum, HPLC	761	8
Dantas 2011[27]	2009–2010	Natal, RN	Maternity hospital	Cross-sectional	23·3*	Healthy voluntary parturient	Serum, HPLC	190	5
Deminice 2018[28]	2012	Ribeirão Preto, SP	Maternity hospital	Cross-sectional	18–39	Healthy women from pregnancy to term and single pregnancy	Serum, HPLC	180	7
Desai 1980[29]	1978	Riberão Preto, SP	Household	Cross-sectional	20–56	Cold buoy's men and women	Plasma, spectrophotometric	85	2
Dimenstein 2006[30]	2002	Natal, RN	Maternity hospital	Cross-sectional	≥18 years	Healthy voluntary parturient, 37 weeks minimum, normal birth and single concept	Serum, HPLC	53	4
Figueiredo 2013[31]	2012	Santo Antônio de Jesus, Juazeiro, BA	Basic health unit	Cross-sectional	15–38	Pregnant women of a single conception (not twinning), without evident pathologies or dysmorphia	Serum, HPLC	210	6
Garcêz 2016[32]	2011–2013	Teresina, PI	Maternity hospital	Cross-sectional	10–19	Teenage pregnancies started prenatal care at 20 weeks or less of gestation	Serum, HPLC	126	6
Garcia 2010[33]	2008	Natal, RN	Maternity hospital	Cross-sectional	13–31	Puerperal pregnant women (parturient)	Serum, HPLC	73	5
Gurgel 2016[34]	2013–2015	Natal, RN	Maternity hospital	Cross-sectional	13–40	Single pregnancy, delivery at term, without malformations, chronic diseases	Serum, HPLC	795	5
Kelner 1969[35]	1965–1966	Recife, PE	Maternity hospital	Cross-sectional	14–41	Puerperal pregnant women	Serum, spectrophotometric	265	4
Lopes 2006[36]	2005	Recife, PE	Outpatient clinic	Cross-sectional	12–41	Healthy pregnant women evaluated postpartum (regardless of the type of delivery)	Serum, HPLC	72	6
Machado 2019[37]	2012–2013	Rio de Janeiro, RJ	Outpatient clinic	Cross-sectional	20–40	Healthy, lactating mothers and a fetus	Serum, HPLC	22	4
Maia 2018[38]	2011–2012	Recife, Vitória de Santo Antão, Caruaru, PE	Outpatient clinic	Cross-sectional	15–45	Pregnant women	Serum, HPLC	676	6
Martins 2010[39]	2006–2007	Ribeirão Preto, SP	Basic health unit	Randomised controlled trial	18–42	Pregnant women, single newborn, healthy	Serum, HPLC	66	5
Mello-Neto 2009[40]	2003–2004	Marília, SP	Human milk bank	Cross-sectional	16–41	Lactating mothers, 20–60 d postpartum	Serum, HPLC	136	5

Table 1. (*Continued*)

Study	Year	City, state	Source	Study design	Age group (years)	Characteristics	Biological matrix, analysis technique	Sample size	Quality score
Meneses 2004[41]	2002–2003	Rio de Janeiro, RJ	Outpatient clinic	Cross-sectional	26·6*	Healthy breast-feeding babies born at term	Plasma, HPLC	49	5
Neves 2018[42]	2015–2016	Cruzeiro do Sul, AC	Basic health unit	Cohort	24·7*	Pregnant women up to 20 weeks of gestation	Serum, HPLC	587	6
Paes-Silva 2018[43]	2013	Recife, PE	School	Cross-sectional	12–19	Teenagers in general	Serum, HPLC	251	8
PNDS 2006[11]	2006	Brazil	Household	Cross-sectional	15–49	Non-pregnant women of reproductive age	Single blood sample	5698	9
Ramalho 1999[44]	1995–1996	Rio de Janeiro, RJ	Maternity hospital	Cross-sectional	69 % > 20 years old†	Voluntary puerperal women	Serum, spectrophotometric	220	6
Ramalho 2006[45]	1999–2001	Rio de Janeiro, RJ	Maternity hospital	Cross-sectional	24·5*	Puerperal women low obstetric risk and single fetus	Serum, spectrophotometric	291	7
Resende 2013[46]	2010–2012	Natal, RN	Maternity hospital	Cross-sectional	14–41	Healthy women with unique concept	Serum, HPLC	109	4
Ribeiro 2009[47]	2006	Natal, RN	Maternity hospital	Cross-sectional	18–40	Healthy pregnant women up to 16 h postpartum, single pregnancy, term (37 weeks), without pathologies and exclusive breast-feeding	Serum, HPLC	91	4
Roncada 1975[48]	1970	Vale do Ribeira, Apiaí, Ribeira, SP	Household	Cross-sectional	17–48	All pregnant women	Serum, spectrophotometric	140	2
Roncada 1975[49]	1972	São Paulo, SP	Migrant reception centre	Cross-sectional	15–60	Migrants in general	Serum, spectrophotometric	332	5
Rondo 1995[50]	1991–1992	Campinas, SP	Maternity hospital	Cross-sectional	14–42	Postpartum women	Plasma, HPLC	712	5
Silva 2018[51]	2016–2017	Natal, RN	Maternity hospital	Cross-sectional	18–40	Puerperal women low obstetric risk and delivery at term	Serum, HPLC	116	4
Vítolo 2004[52]	1997–1998	São Paulo, SP	School	Cross-sectional	10–19	Teenagers in general	Serum, spectrophotometric	91	3

PNDS, *Pesquisa Nacional de Demografia e Saúde* (National Demographic and Health Survey).
*Mean age.
† Frequency of age for most of the sample.

Vitamin A deficiency in Brazilian women

(regarding twenty studies), and eleven (regarding seventeen studies) provided clarification or additional data based on our request. The reasons for exclusions of the studies sought for full-text assessment are shown in online Supplementary Table S3, and the list of reports of included studies is available in online Supplementary Table S4.

Study characteristics

In total, 12 577 women were assessed in all included studies conducted from 1965 to 2017. Most of the studies were cross-sectional, held at institutions such as hospitals, conducted in the Northeast and Southeast regions, and included women aged 10–60 years (Table 1). The methodological quality score ranged from 2 to 9 with a median of 6, with high risk being more frequent in the sample frame (30/32) and sampling method (29/32), while all studies met the requirements of valid methods to diagnose vitamin A deficiency and measurement of the outcome in a standard, reliable way for all participants (online Supplementary Table S5).

Results of syntheses

The prevalence of vitamin A deficiency in women was 13·1 % (95 % CI 9·4, 17·2; 29 studies; $I^2 = 96.6$ %). The Midwest region had higher prevalence of vitamin A deficiency (12·8 %; 95 % CI 11·0, 14·9; 1 study), similar to the Southeast region (11·7 %; 95 % CI 10·6, 12·8; 13 studies; $I^2 = 97.4$ %), while lower prevalence was noted in the South region (8·0 %; 95 % CI 6·6, 9·7; 1 study) (Fig. 2). After removal of a discrepant study with highest prevalence rate (Deminice 2018[28]), prevalence and heterogeneity did not significantly change. Since no reason for exclusion was identified, the study was kept in the final result.

A higher prevalence of vitamin A deficiency was noted in subgroups of studies held in schools, with cross-sectional design, assessments based on serum samples and by HPLC, in the 2010s and in pregnant women (Table 2). Homogeneous results were observed in cohort studies, clinical trials and studies held in schools, while no homogeneity was observed in subgroups of high or low risk of bias in the methodological quality domains (online Supplementary Table S6).

The variability in the prevalence of vitamin A deficiency was not significantly affected by the year of research ($P = 0.114$; residual $I^2 = 99.6$ %), the methodological quality score of the studies ($P = 0.180$; residual $I^2 = 99.6$ %), women's ages ($P = 0.711$; residual $I^2 = 99.7$ %) and Brazilian region ($P = 0.407$; residual $I^2 = 99.6$ %) (online Supplementary Fig. S1). A symmetric distribution was noted in the funnel plots (online Supplementary Fig. S2), and a small studies effect was discarded ($P = 0.217$).

Discussion

More than one in ten Brazilian women of reproductive age were estimated to have vitamin A deficiency according to the available evidence at all time periods. Pregnant women had a higher prevalence of deficiency than non-pregnant or breast-feeding women. Prevalence seems to be increasing over time. In the 2010s, nearly 20 % of Brazilian women of reproductive age had deficient vitamin A levels. This estimate of almost one in five

women of childbearing age presenting vitamin A deficiency in the more recent studies is regarded as a moderate public health problem and requires proper nutritional public policies to avoid the related disease burden[4].

Our findings are based on over thirty different studies conducted over a wide range of times that mainly employed convenience sampling to recruit women from highly selected sources, such as hospitals, which impact the representativeness of the sample. The estimates were highly heterogeneous, and attempts to identify the sources of heterogeneity did not elucidate the causes, which may be inherent to prevalence studies held in different settings[17]. Assessing only more recent studies with better methodological quality, for example, was not feasible due to the low number of studies meeting these criteria. Publication bias was not suspected and improves the confidence in the completeness of our results.

The overall prevalence of vitamin A deficiency in women of childbearing age is higher in low- and middle-income countries. While 2 % of vitamin A deficiency was estimated for women in North America, in the Caribbean (9 %) and Latin America (10 %) nearly five-fold of women had this deficiency, with a higher burden for maternal and childhood health[1]. A Pakistani national survey conducted in 2017–2018 observed a prevalence of vitamin A deficiency of 27 % in women aged 15–49 years, with 22 % experiencing moderate deficiency and 5 % severe deficiency[53].

Vitamin A deficiency was shown to increase over the decades in the present study. The global prevalence of vision loss associated with vitamin A deficiency increased by 9 % from 1990 to 2017, rising from 69 to 75 % in this period[54]. In Ethiopia, although dietary vitamin A deficiency has reduced from 1990 to 2017, the age-standardised incidence rate of vitamin A deficiency increased by 9 %, and the proportion of disability-adjusted life years due to this deficiency increased from 0·6 % in 1990 to over 1 % in 2017[55].

Pregnant women had a higher prevalence of vitamin A deficiency than non-pregnant or lactating women. During pregnancy, physiological adaptations include an increase in plasma volume with haemodilution and higher demands of vitamin A due to fetal needs, mainly during the third trimester[56–59]. The placental barrier is highly selective for vitamin A transfers to the conceptus to avoid teratogenic effects[60]. These modifications could lead to lower plasmatic levels of vitamin A[56]. After birth, retinol-binding protein transports most of the serum retinol to breast reaching the breast milk[61], and breast-feeding provides vitamin A during the first 6 months of life at a rate of sixty-fold more amount than placental levels during the whole pregnancy[62]. Pregnancy itself is an inflammatory period due to the immunological conditions for proper development of the conceptus. The conventional cut-off points may underestimate vitamin A status, especially in the last trimester and in populations with a high prevalence of infections[56,63–65]. Our findings could also be affected by these factors, and the higher deficiency observed in pregnant women could be due to overestimation of deficiency as a result of not considering these physiological changes that may artificially increase the prevalence. Despite this possible limitation, no official recommendation of different cut-offs for vitamin A deficiency during pregnancy is available.
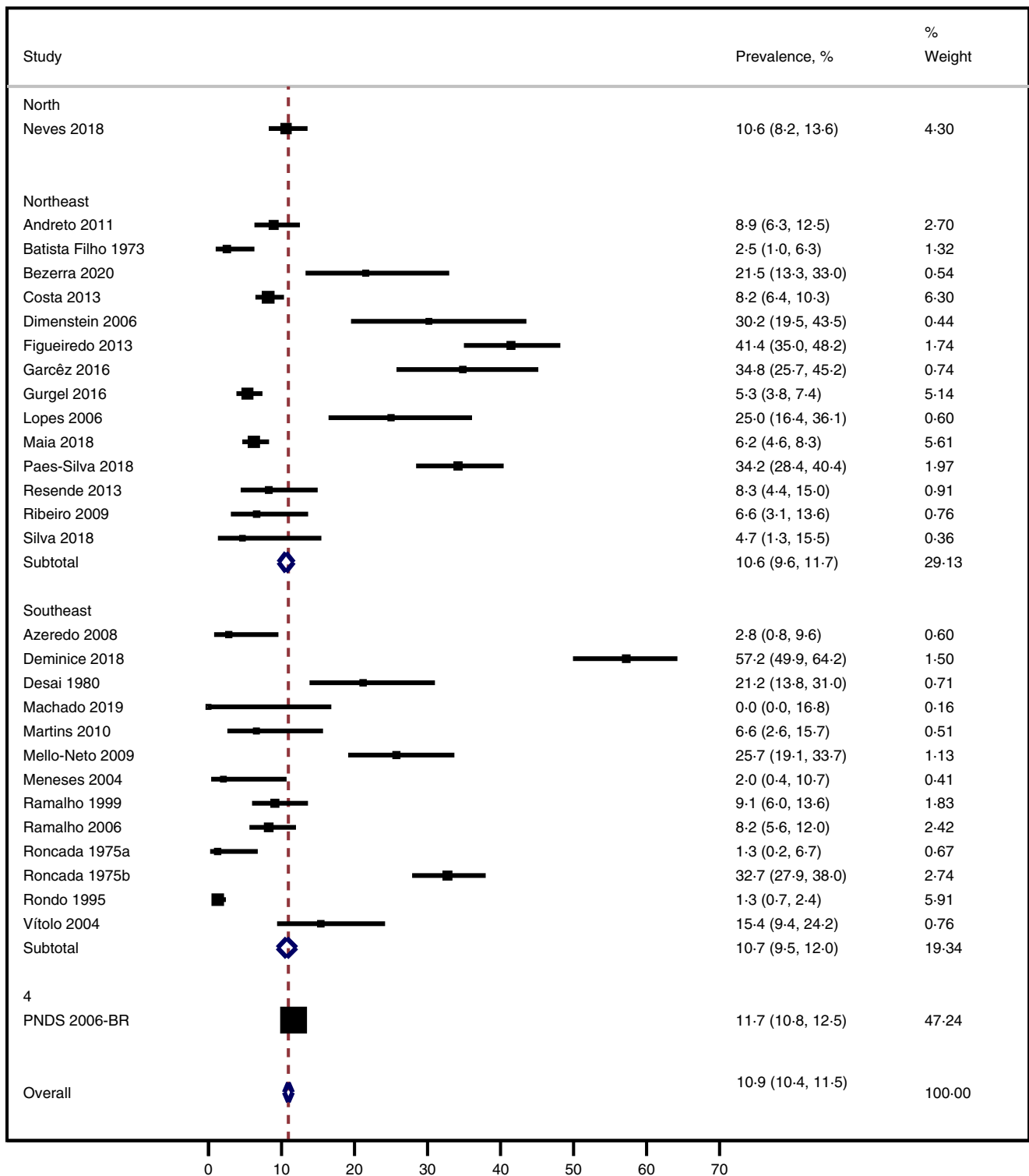
Fig. 2. Prevalence of vitamin A deficiency in women by Brazilian region.

Study	Prevalence, %	% Weight
North		
Neves 2018	10·6 (8·2, 13·6)	4·30
Northeast		
Andreto 2011	8·9 (6·3, 12·5)	2·70
Batista Filho 1973	2·5 (1·0, 6·3)	1·32
Bezerra 2020	21·5 (13·3, 33·0)	0·54
Costa 2013	8·2 (6·4, 10·3)	6·30
Dimenstein 2006	30·2 (19·5, 43·5)	0·44
Figueiredo 2013	41·4 (35·0, 48·2)	1·74
Garcêz 2016	34·8 (25·7, 45·2)	0·74
Gurgel 2016	5·3 (3·8, 7·4)	5·14
Lopes 2006	25·0 (16·4, 36·1)	0·60
Maia 2018	6·2 (4·6, 8·3)	5·61
Paes-Silva 2018	34·2 (28·4, 40·4)	1·97
Resende 2013	8·3 (4·4, 15·0)	0·91
Ribeiro 2009	6·6 (3·1, 13·6)	0·76
Silva 2018	4·7 (1·3, 15·5)	0·36
Subtotal	10·6 (9·6, 11·7)	29·13
Southeast		
Azeredo 2008	2·8 (0·8, 9·6)	0·60
Deminice 2018	57·2 (49·9, 64·2)	1·50
Desai 1980	21·2 (13·8, 31·0)	0·71
Machado 2019	0·0 (0·0, 16·8)	0·16
Martins 2010	6·6 (2·6, 15·7)	0·51
Mello-Neto 2009	25·7 (19·1, 33·7)	1·13
Meneses 2004	2·0 (0·4, 10·7)	0·41
Ramalho 1999	9·1 (6·0, 13·6)	1·83
Ramalho 2006	8·2 (5·6, 12·0)	2·42
Roncada 1975a	1·3 (0·2, 6·7)	0·67
Roncada 1975b	32·7 (27·9, 38·0)	2·74
Rondo 1995	1·3 (0·7, 2·4)	5·91
Vítolo 2004	15·4 (9·4, 24·2)	0·76
Subtotal	10·7 (9·5, 12·0)	19·34
4		
PNDS 2006-BR	11·7 (10·8, 12·5)	47·24
Overall	10·9 (10·4, 11·5)	100·00

Within the Brazilian territory, a heterogeneous distribution of deficiency was observed, and the lowest prevalence was observed in the South and more developed region of Brazil, which was assessed in the nationwide survey – no local study to assess hypovitaminosis A has been performed in this region. This may indicate that most investigations on vitamin A deficiency in Brazil may focus on more vulnerable regions, and this research interest may impact the findings. Another hypothesis is

Table 2. Prevalence of vitamin A deficiency in women, 95 % confidence interval (CI) and heterogeneity (*I*²) according to the study design, sample source and geographic region of the studies

Subgroup	No. of studies	No. of women	Prevalence, %	95 % CI	*I*² (%)
Study design					
Cross-sectional	26	11 145	13·6	9·5, 18·3	97·0
Cohort and clinical trial	3	904	9·6	7·7, 11·6	0·0
Sample source					
Health services*	23	5099	12·8	7·8, 18·8	96·9
Household	4	6622	9·5	5·6, 14·1	89·8
School	2	328	28·5	23·7, 33·5	0·0
Biological matrix for analysis					
Serum	24	5433	14·7	9·8, 20·3	96·4
Dried blood spot	1	5698	11·7	10·8, 12·5	–
Plasma	4	918	5·0	0·1, 15·3	92·7
Analysis technique					
HPLC	22	10 793	13·7	9·4, 18·5	96·9
Spectrophotometric	7	1256	11·1	4·0, 21·1	95·5
Decade					
≤ 1990	7	1677	9·5	1·9, 21·6	97·7
2000	11	7607	10·8	7·9, 14·2	86·1
2010	11	2765	17·8	8·7, 29·0	97·8
Reproductive status					
Not pregnant	22	9987	12·3	8·4, 16·8	96·1
Pregnant†	5	1652	16·1	5·6, 30·6	97·8
Postpartum and breast-feeding	17	3117	10·9	5·5, 17·6	96·1
Total	29	12 049	13·1	9·4, 17·2	96·6

*One study[49] was carried out in a migrant reception centre.
† Includes postpartum and lactating women in some studies.

publication bias (which was discarded in our overall assessment): studies of low prevalence could refrain from being published or end up testing associations with a higher threshold to indicate sub-optimal levels of vitamin A, instead of the recommended cut-off point for deficiency.

Women of childbearing age, especially pregnant and lactating women, should practise a healthy diet that includes natural vitamin A food sources, which in turn requires proper economic conditions of the individual and communities. In Brazil, in 2009, 72% of women aged 19–59 years had inadequate intake of vitamin A. In the following decade, this percentage increased to 80%; higher frequencies were observed in the North region (87%) and lower in the Southeast region (76 %), while the average intake of vitamins – equivalent to the activity of retinol – decreased from 410 to 342 in this period[66].Contrary to the healthy eating needs of Brazilians, costs of healthy diet increased from 2009 to 2018, mainly for the poorer individuals, and acquisition of expensive foods richer in vitamin A was low in Brazil[67]. Hunger, once a solved problem in Brazil, is on the rise due to dismantling of major social programmes that affect food security such as family agriculture incentives[68]. The conditional cash transfer *Bolsa Família* – which led to reduction of poverty and reaching sustainable development goals, such as maternal mortality – was terminated in 2021 after 18 years of existence[69]. Vitamin A supplementation during pregnancy had no impact on maternal and child outcomes in low- and middle-income countries[70], as well as in the postpartum[6], which led to the discontinuation of the former Brazilian recommendation of vitamin A megadose (200 000 IU) supplementation in the immediate postpartum period for women living in risk areas[71]. Food security policies and nutrition education strategies targeted to priority groups – especially during pregnancy and lactation – should be a priority in Brazil in order to improve vitamin A food sources availability and ingestion and reduce the burden of vitamin A deficiency in the country.

Conclusion

Over one in ten women of reproductive age were estimated to suffer from vitamin A deficiency in Brazil, and this prevalence seemed to be increasing over the decades. Pregnant women had a higher prevalence of deficiency than non-pregnant or postpartum women. The results are limited by the low representativeness of the studies, mainly based on convenience sampling, and would be better addressed by future representative research that assesses this deficiency. Food and nutrition security policies should be prioritised to avoid the burden of vitamin A deficiency in women of childbearing age in Brazil.

C. M. F., M. T. S., J. M. O., D. A. H., D. F. S. A. and T. F. G. conceived the work, formulated the research question and designed the study (Conceptualisation), C. M. F., M. T. S. and T. F. G. analysed the data (Data curation and Formal Analysis), T. F. G. conceived the funding acquisition, supervision and project administration, C. M. F., M. T. S., J. M. O., D. A. H., D. F. S. A., W. W. G. S. and T. F. G. collected the data, interpreted the findings, drafted and revised the work (Investigation, Methodology, Resources and Software). C. M. F. and T. F. G. concieved the validation and visualization this project. All authors approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved (Writing – original draft, review and editing).

There are no conflicts of interest.

Supplementary material

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The full dataset of this research is available at https://osf.io/4fjq7.

References

1. Murray CJ, Aravkin AY, Zheng P, et al. (2020) Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* **396**, 1223–1249.
2. Carazo A, Macáková K, Matoušová K, et al. (2021) Vitamin A update: forms, sources, kinetics, detection, function, deficiency, therapeutic use and toxicity. *Nutrients* **13**, 1703.
3. World Health Organization (2009) *Global Prevalence of Vitamin A Deficiency in Populations at Risk 1995–2005: WHO Global Database on Vitamin A Deficiency*. Geneva: World Health Organization.
4. World Health Organization (2011) *Serum Retinol Concentrations for Determining the Prevalence of Vitamin A Deficiency in Populations*. pp. 5. Geneva: World Health Organization.
5. World Health Organization (2014) *Xerophthalmia and Night Blindness for the Assessment of Clinical Vitamin A Deficiency in Individuals and Populations. Vitamin and Mineral Nutrition Information System*. pp. 6. Geneva: World Health Organization.
6. Oliveira JM, Allert R & East CE (2016) Vitamin A supplementation for postpartum women. *Cochrane Database Syst Rev* **3**, CD005944.
7. World Health Organization (1994) *Indicators for Assessing Vitamin A Deficiency and their Application in Monitoring and Evaluating Intervention Programmes. Report of a WHO/UNICEF Consultation*. Geneva: WHO.
8. World Health Organization (2011) *Guideline: Vitamin A Supplementation in Postpartum Women*. Geneva: World Health Organization.
9. IBGE (2009) *Household Budget Survey 2008–2009: Analysis of Personal Food Consumption in Brazil*. Brasilia: Ministry of Health.
10. IBGE (2018) *Household Budget Survey 2017–2018: Analysis of Personal Food Consumption in Brazil*. Brasilia: Ministry of Health.
11. IBGE (2006) *National Survey of Demographics and Health of Children and Women-PNDS 2006: Dimensions of the Reproductive Process and Children's Health*. Brasilia: Ministry of Health.
12. Page MJ, McKenzie JE, Bossuyt PM, et al. (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* **372**, n71.
13. Estatística IBGE (2012) Synthesis of Social Indicators: an analysis of living conditions. Studies & Research – Demographic and Socioeconomic Information, n 29, Brazilian Institute of Geography and Statistics. https://biblioteca.ibge.gov.br/index.php/biblioteca-catalogo?view=detalhes&id=262715 (accessed June 2022).
14. McGowan J, Sampson M, Salzwedel DM, et al. (2016) PRESS Peer review of electronic search strategies: 2015 guideline statement. *J Clin Epidemiol* **75**, 40–46.
15. Munn Z, Moola S, Lisy K, et al. (2015) Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int journal Evidence-Based Healthcare* **13**, 147–153.
16. Newcombe RG (1998) Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med* **17**, 857–872.
17. Barendregt JJ, Doi SA, Lee YY, et al. (2013) Meta-analysis of prevalence. *J Epidemiol Community Health* **67**, 974–978.
18. Higgins JPT & Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. *Stat Med* **21**, 1539–1558.
19. Knapp G & Hartung J (2003) Improved tests for a random effects meta-regression with a single covariate. *Stat Med* **22**, 2693–2710.
20. Hunter JP, Saratzis A, Sutton AJ, et al. (2014) In meta-analyses of proportion studies, funnel plots were found to be an inaccurate method of assessing publication bias. *J Clin Epidemiol* **67**, 897–903.
21. Egger M, Smith GD, Schneider M, et al. (1997) Bias in meta-analysis detected by a simple, graphical test. *BMJ* **315**, 629–634.
22. Andreto ML (2011) Impact of double megadose vitamin A supplementation on serum retinol concentrations in postpartum women during the first six months postpartum. Universidade Federal de Pernambuco. https://repositorio.ufpe.br/handle/123456789/8142 (accessed June 2022).
23. de Azeredo VB & Trugo NM (2008) Retinol, carotenoids, and tocopherols in the milk of lactating adolescents and relationships with plasma concentrations. *Nutrition* **24**, 133–139.
24. Batista Filho M, Teixeira S & Linhares E (1973) Serum retinol of pregnant women assisted in Public Health services. *Rev Bras Pesq Med e Biol* **6**, 215–221.
25. Bezerra DS (2015) Effect of maternal supplementation with megadoses of vitamin A given at different intervals on retinol concentrations in breast milk. Federal University of Pernambuco. Universidade Federal do Pernambuco. https://repositorio.ufpe.br/handle/123456789/13989 (accessed June 2022).
26. Miglioli TC, Fonseca VM, Gomes Junior SC, et al. (2013) Vitamin A deficiency in mothers and children in the state of Pernambuco. *Ciência Saúde Coletiva* **18**, 1427–1440.
27. de Oliveira Dantas JC, Medeiros ACP, Rodrigues KD, et al. (2011) Serum retinol concentration and prevalence of vitamin A deficiency in postpartum women. *Rev Bras em Promoção da Saúde* **24**, 40–45.
28. Deminice TMM, Ferraz IS, Monteiro JP, et al. (2018) Vitamin A intake of Brazilian mothers and retinol concentrations in maternal blood, human milk, and the umbilical cord. *J Int Med Res* **46**, 1555–1569.

29. Desai I, Garcia Tavares M, Dutra de Oliveira B, *et al.* (1980) Food habits and nutritional status of agricultural migrant workers in Southern Brazil. *Am J Clin Nutr* **33**, 702–714.

30. Dimenstein R, Nascimento T, Melo IL, *et al.* (2006) Evaluation of retinol levels in human colostrum and its relationship with maternal nutritional status in vitamin A. *Rev Bras Med* **65**, 206–210.

31. Figueiredo ACMG (2013) Nutritional status and oral condition of pregnant women using public health services. http://tede2.uefs.br:8080/handle/tede/176 (accessed June 2022).

32. Spíndola Garcêz L, De Sousa Paz Lima G, de Azevedo Paiva A, *et al.* (2016) Serum retinol levels in pregnant adolescents and their relationship with habitual food intake, infection and obstetric, nutritional and socioeconomic variables. *Nutrients* **8**, 669.

33. Garcia L, Ribeiro K, Araújo K, *et al.* (2010) Alpha-tocopherol concentration in the colostrum of nursing women supplemented with retinyl palmitate and alpha-tocopherol. *J Hum Nutr Diet* **23**, 529–534.

34. Gurgel CSS, de Araújo Pereira LA, de Assis Costa A, *et al.* (2017) Effect of routine prenatal supplementation on vitamin concentrations in maternal serum and breast milk. *Nutr* **33**, 261–265.

35. Kelner M (1966) Vitamin A and carotene in the pregnant-puerperal cycle: study of some aspects in poor patients in Recife: Universidade Federal de Pernambuco Press. Recife: Imprensa Universitária da Universidade Federal de Pernambuco. https://viaf.org/viaf/138362573/ (accessed June 2022).

36. Lopes RÉ, Ramos KD, Bressani CC, *et al.* (2006) Prevalence of anemia and hypovitaminosis A in postpartum women at the Women's Care Center at Instituto Materno Infantil Prof. Fernando Figueira, IMIP: a pilot study. *Rev Bras de Saude Matern Infant* **6**, S63–S68.

37. Machado MR, Kamp F, Nunes JC, *et al.* (2019) Breast milk content of vitamin A and E from early-to mid-lactation is affected by inadequate dietary intake in Brazilian adult women. *Nutrients* **11**, 2025.

38. Bastos Maia S, Costa Caminha MDF, Lins da Silva S, *et al.* (2018) The prevalence of vitamin A deficiency and associated factors in pregnant women receiving prenatal care at a reference maternity hospital in Northeastern Brazil. *Nutrients* **10**, 1271.

39. Martins T, Ferraz I, Daneluzzi J, *et al.* (2010) Impact of maternal vitamin A supplementation on the mother–infant pair in Brazil. *Eur J Clin Nutr* **64**, 1302–1307.

40. Mello-Neto J, Rondó PH, Oshiiwa M, *et al.* (2009) The influence of maternal factors on the concentration of vitamin A in mature breast milk. *Clin Nutr* **28**, 178–181.

41. Meneses F, Torres AG & Trugo NM (2004) Influence of recent dietary intake on plasma and human milk levels of carotenoids and retinol in Brazilian nursing women. *Adv Exp Med Boil* **554**, 351–354.

42. Neves PA, Castro MC, Oliveira CV, *et al.* (2020) Effect of vitamin A status during pregnancy on maternal anemia and newborn birth weight: results from a cohort study in the Western Brazilian Amazon. *Eur J Nutr* **59**, 45–56.

43. Paes-Silva RP, Tomiya MTO, Maio R, *et al.* (2018) Prevalence and factors associated with fat-soluble vitamin deficiency in adolescents. *Nutrición Hospitalaria: Organo oficial de la Sociedad española de nutrición parenteral y enteral* **35**, 1153–1162.

44. Ramalho RA, Anjos LA & Flores H (1999) Nutritional status of vitamin A in the mother/newborn binomial in two maternity hospitals in Rio de Janeiro, Brazil. *Arch Latinoam Nutr* **49**, 318–321.

45. Ramalho RA, Flores H, Accioly E, *et al.* (2006) Association between maternal and newborn vitamin A status and economic stratum in Rio de Janeiro, Brazil. *Rev da Associação Médica Bras* **52**, 170–175.

46. Resende F, Lira LQ, Grilo EC, *et al.* (2015) Gestational diabetes: a risk of puerperal hypovitaminosis A? *An Acad Bras Cienc* **87**, 463–470.

47. Ribeiro KD, Araújo KF & Dimenstein R (2009) The effect of vitamin A supplementation upon retinol concentration in the colostrum of women in a public maternity hospital. *Rev da Associação Médica Bras* **55**, 452–457.

48. Roncada MJ & Szarfarc SC (1975) Hypovitaminosis A and iron deficiency anemia in pregnant women from two communities in Vale do Ribeira (São Paulo State, Brazil). *Rev Saude Publica* **9**, 99–106.

49. Roncada MJ (1975) Survey among migrants assisted by the Triage and Forwarding Center, in the capital of the State of São Paulo, Brazil: II. Biochemical aspects of hypovitaminosis A. *Rev Saúde Pública* **9**, 313–329.

50. de Carvalho Rondó PH, Villar BS & Tomkins AM (1999) Vitamin A status of pregnant women assessed by a biochemical indicator and a simplified food frequency questionnaire. *Arch Latinoam Nutr* **49**, 322–325.

51. da Silva AGCL, de Sousa Rebouças A, Mendonça BMA, *et al.* (2019) Relationship between the dietary intake, serum, and breast milk concentrations of vitamin A and vitamin E in a cohort of women over the course of lactation. *Matern Child Nutr* **15**, e12772.

52. Vítolo MR, Gama CM, Queiroz SD, *et al.* (2004) Retinol blood levels in high school students of São Paulo, Brazil. *Rev Nutrição* **17**, 291–299.

53. UNICEF (2019) *National Nutrition Survey 2018. Key Findings Report. Nutrition Wing Ministry of Health Services, Regulation and Coordination*. Pakistan: Government of Pakistan.

54. Xu Y, Shan Y, Lin X, *et al.* (2021) Global patterns in vision loss burden due to vitamin A deficiency from 1990 to 2017. *Public Health Nutr* **24**, 5786–5794.

55. Hassen HY, Ali JH, Gebreyesus SH, *et al.* (2020) National incidence, prevalence and disability-adjusted life years (DALYs) of common micronutrient deficiencies in Ethiopia from 1990 to 2017: estimates from the global burden of diseases study. *Global Health Action* **13**, 1776507.

56. Bastos Maia S, Rolland Souza AS, Costa Caminha MD, *et al.* (2019) Vitamin A and pregnancy: a narrative review. *Nutrients* **11**, 681.

57. Yang C, Chen J, Liu Z, *et al.* (2015) Prevalence and influence factors of vitamin A deficiency of Chinese pregnant women. *Nutr J* **15**, 1–7.

58. Gao F, Guo F, Zhang Y, *et al.* (2021) Vitamin A, D, and E levels and reference ranges for pregnant women: a cross-sectional study 2017–2019. *Front Nutr* **8**, 628902.

59. West KP, Christian P, Labrique AB, *et al.* (2011) Effects of vitamin A or beta carotene supplementation on pregnancy-related mortality and infant mortality in rural Bangladesh: a cluster randomized trial. *JAMA* **305**, 1986–1995.

60. Azaïs-Braesco V & Pascal G (2000) Vitamin A in pregnancy: requirements and safety limits. *Am J Clin Nutr* **71**, 1325S–1333S.

61. Green MH, Green JB, Akohoue SA, *et al.* (2001) Vitamin A intake affects the contribution of chylomicrons *v.* retinol-binding protein to milk vitamin A in lactating rats. *J Nutr* **131**, 1279–1282.

62. Stoltzfus R & Underwood BA (1995) Breast-milk vitamin A as an indicator of the vitamin A status of women and infants. *Bull World Health Organ* **73**, 703.

63. Kæstel P, Martinussen T, Aaby P, *et al.* (2012) Serum retinol is associated with stage of pregnancy and the acute phase response in pregnant women in Guinea-Bissau. *J Nutr* **142**, 942–947.

64. Larson LM, Namaste SM, Williams AM, *et al.* (2017) Adjusting retinol-binding protein concentrations for inflammation: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr* **106**, 390S–401S.

65. Larson LM, Guo J, Williams AM, *et al.* (2018) Approaches to assess vitamin A status in settings of inflammation: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Nutrients* **10**, 1100.

66. Verly Junior E, Marchioni DM, Araujo MC, *et al.* (2021) Evolution of energy and nutrient intake in Brazil between 2008–2009 and 2017–2018. *Rev Saúde Pública* **55**, 5s.

67. Verly Junior E, Oliveira DC & Sichieri R (2021) Cost of healthy and culturally acceptable diets in Brazil in 2009 and 2018. *Rev Saude Publica* **55**, 7s.

68. Ferreira Costa CG (2021) Increased vulnerability of family farming in the context of a weakened FNS agenda due to austerity measures in Brazil. *Economía Agraria Recursos Nat-Agricult Resour Econ* **21**, 103–134.

69. Rasella D, Alves FJO, Rebouças P, *et al.* (2021) Long-term impact of a conditional cash transfer programme on maternal mortality: a nationwide analysis of Brazilian longitudinal data. *BMC Med* **19**, 127.

70. Keats EC, Oh C, Chau T, *et al.* (2021) Effects of vitamin and mineral supplementation during pregnancy on maternal, birth, child health and development outcomes in low- and middle-income countries: a systematic review. *Campbell Syst Rev* **17**, e1127.

71. Brasil B (2005) Portaria nº. 729, de 13 de maio de 2005. Establishes the National Vitamin A Supplementation Program and makes other provisions. Diário oficial da União. https:// bvsms.saude.gov.br/bvs/saudelegis/gm/2005/prt0729_13_05_ 2005.html (accessed June 2022).