

Prevalence and geographic distribution of vitamin A deficiency among preschool children in Ethiopia

Tadesse Mekonen¹, Dilnesaw Zerfu¹, Tefera Belachew², Yosef Beyene¹, Addisu Legesse¹, Nahome Tefera¹, Mesert W/Yohannes¹, Nigat Ashenafi¹ and Chera Tadesse¹

¹Ethiopian Public Health Institute (EPHI), Addis Ababa, Ethiopia

²Department of Nutrition, Jimma University, Jimma, Ethiopia

*Corresponding author: anguach257@gmail.com

Abstract

Introduction: Vitamin A deficiency (VAD) is the main cause of avoidable blindness in children, and significantly contributes to morbidity and mortality from common childhood infection, even at a sub-clinical level. There is limited evidence on the prevalence and distribution of VAD.

Objective: To assess the national prevalence and distribution of vitamin A deficiency among preschool children.

Method: Ethiopian national micronutrient survey (ENMS) is a nationally and regionally representative cross-sectional study. A multi-stage cluster sampling method was conducted and 1157 preschool children were selected. A structured and pre-tested questionnaire with Samsung tab S2 was used to collect data. Blood sample was also collected to analyzed biochemical indicators. Serum retinol concentrations were measured using high-performance liquid chromatography. Data were analyzed using Stata version 14.

Results: The national unadjusted prevalence of vitamin A deficiency among preschool children (serum retinol < 0.7 µmol/L) was 23.5% [95% CI: (21.16, 26.06%)] and adjusted prevalence was 14.5% [95% CI: (12.52, 16.61%)] thus representing 9% overestimation in the unadjusted prevalence of sub-clinical VAD. The lowest prevalence of subclinical VAD was among preschool children living in Addis Ababa (0.0 %), and the highest was among those living in Harari 20.97% [95% CI: (5.21, 32.97%)].

Conclusion: Vitamin A deficiency is a moderate public health problem in Ethiopia indicating the need for strengthening strategies' on vitamin A supplementation and food fortification.

Keywords: Preschool children, vitamin A deficiency, retinol, distribution, Ethiopia.

Introduction

World Health Organization (WHO) defines vitamin A deficiency (VAD) as tissue concentrations of vitamin A low enough to have adverse health consequences, even if there is no clinical deficiency (WHO 2009). VAD contributes significantly to morbidity and mortality from common childhood infection, even at a sub-clinical level (Chauhan et al. 2011). It is one of the main nutritional deprivations and cause of avoidable blindness in children (Pinkaw 2012). Preschool children, pregnant and lactating mothers are the most vulnerable groups to VAD and its adverse health consequences (Persson 2001). Globally, subclinical VAD (<=0.70 µmol/l) affects about 190 million (33.3%) preschool children and night blindness affects 5.2 million (0.9%) preschool children. According WHO estimate, as indicated by either night blindness or biochemical deficiency, VAD has a moderate and severe public significance in 45 and 122 countries, respectively. Africa and South-East Asia are the most affected regions by VAD, where 44 to 50% of affected preschool children live in South East Asia (WHO 2009). In Africa, VAD is endemic and is the leading cause of preventable childhood blindness (Haidar 2011), and is responsible for death of almost 6%

under-five children (WHO 2011). It is an underlying cause for nearly one-fourth of global child mortality from measles, diarrhea, and malaria (WHO 2004). VAD remains as one of the major public health problems, since more than 46. 1 % of under 5-years children are suffering from subclinical VAD, 4.9 % from night blindness, and 2.2 % from Bitot's Spots (WHO 2009). Serum retinol is the biomarker recommended by World Health Organization to assess Vitamin A status (WHO 1996). Circulating serum retinol is reduced during inflammation, which leads to overestimation of VAD prevalence (WHO 2011). C-reactive protein (CRP) and α-1-acid glycoprotein (AGP) are proteins synthesized by the liver in response to inflammatory stimuli (WHO 2014). Therefore, on a population of apparently healthy people, CRP and AGP will detect those who have acute and chronic inflammation, respectively (Thurnham and McCabe 2014). Even if different strategies have been initiated to reduce Vitamin A deficiency, it remains a public health concern in Ethiopia. There is no current data on the serum retinol level, which provides information on the prevalence and distribution of subclinical VAD at the national and regional level. Therefore, this study aimed to determine the prevalence and distribution of VAD among preschool children in Ethiopia.

Materials and Methods

Data for this study was taken from the national micronutrient survey, which was conducted by the Ethiopian Public Health Institute. The Ethiopian National Micronutrient Survey employed a multi-stage sampling which covered all the nine regions and two city administrations to produce a national and regional representative estimate of micronutrient status. A population-based cross-sectional study design was conducted. Only children aged 6 to 59 months were extracted from the National micronutrient survey dataset. Preschool children found in randomly selected households were the study population. The sample size was calculated using single population proportion formula by taking the following assumptions: highest prevalence of micronutrient deficiencies (50% prevalence, since there was no recent national/regional prevalence data), 5% desired precision at national level and 10% precision at regional level for different micronutrient indicators with an assumed participation rate of 90% at household and 85% at individual level. To account for heterogeneity among regions in specific micronutrient deficiency (MND), the design effect of two was applied. Hence, nationally 4026 households (HH) were randomly selected and 11 HHs per EA were assigned to determine the number of EAs drawn from the CSA enumeration area pool. As the first stage of sampling, 366 EAs were selected and distributed based on probability proportional to population size to the regions and adjusted for the fourth root because of the huge variability of population size between regions. As the second stage, the selected 366 EAs were visited by the team of data collectors to conduct a quick listing of all the households (HH) within the boundary before the actual survey. Name, age, sex of individuals living in the household and GPS coordinates of the household were registered. The quick HH listing data had been used to draw 11 HHs from each EA. Systematic random sampling technique was applied to generate random number. Then HH identifiers (i.e region, zone, woreda, kebele, enumeration area code, GPS coordinate, and household head name) were loaded in the electronic tablet. Finally, all preschool children aged 6 to 59 months within the household were eligible. If eligible occupants were not present, two continuative return visits with written appointments were made. If the eligible respondents were not available during the appointments, then it was recorded as refusal or any reason given for the unavailability of eligible respondent without any replacement.

Data were collected using a structured interview questionnaire administered by trained health professional enumerators using electronic tablet with Open data kit (ODK). The data collection tools were pretested before the survey training. Three-week training was given to the data collectors, supervisors,

and regional coordinators. The weight of each preschool child was taken in duplicate using Seca 874 U electronic scale (Germany). Calibration of the scale was done regularly. Venous blood sample was collected by trained Phlebotomists. The blood was drawn into different evacuated BD Vacutainer tubes per blood collection protocol. The first trace metal free Vacutainer tube (blue top) contained a clot activator used for retinol. The second Vacutainer (red top) was used to draw blood for AGP and CRP analysis. Samples were transported promptly after collection in cold boxes containing frozen gel packs (<8 oC). Each team vehicle maintained field laboratory setup that included a portable centrifuge to allow for immediate centrifugation and aliquoting serum in cryovials, -20 oC freezer powered either by car battery or electric power and backup generator for fast freezing of serum samples in the field.

Laboratory analyses

Serum retinol determination: Vitamin A status was assessed using serum retinol concentration. Analysis of serum retinol level was performed by isocratic phase HPLC using retinol acetate internal standard (Kane et al. 2008). Serum (200µL), retinol acetate (200µL) and ethanol (200µL) were added to a test tube gently shaken and vortexed for 45 seconds. Serum retinol concentration of ≤ 0.70 µmol/L and ≤ 0.35 µmol/L indicates sub-clinical and severe VAD respectively (WHO, 1996). To exclude the depression of serum retinol concentration from children who have elevated AGP and/or CRP due to inflammation, retinol value was adjusted to AGP and/or CRP. Finally, the adjusted serum retinol concentration was subjected to the estimation of the prevalence of VAD (Thurnham and McCabe 2014). The retinol values were adjusted with the following equation for those with inflammation:

Retinol adjusted = original retinol value + (beta coefficient of AGP or CRP * AGP or CRP value) (Suchdev et al. 2016).

CRP, AGP, and hemoglobin determination: AGP and CRP concentrations were determined by the immune-turbidimetry method using Hitachi Cobas Integra 600 clinical analyzer with Roche commercial insert kit (Cobas, 2015). The lower limit of detection for AGP and CRP was 0.1g/l and 0.15mg/l respectively. AGP values < 1 g/L were considered normal and elevated concentrations were categorized as ≥ 1 g/L whereas CRP values <5 mg/l were considered normal and elevated concentrations were categorized as ≥ 5 mg/l (Thurnham et al. 2003). Hemoglobin was measured from venous blood using a Hemocue® photometer (Hb201+, Hemocue AB, Angelholm, Sweden). Values of hemoglobin were corrected for altitude and cut-off value was made as per recommendation based on age and sex (but smoking was very rare in the study population).

Individual hemoglobin was adjusted for altitude as follows:

$Hb\ adjustment = (Hb\ measured - 0.032 \times [altitude\ (m) \times 0.0032808] + 0.022 \times [(altitude\ (m) \times 0.0032808)]^2)$ for all persons living at an altitude of 1,000 meters above sea level or higher (Sullivan et al. 2008).

Data were sent to the EPHI server every night upon completion of each household and after reviewed by supervisors. The data (questionnaires, anthropometry, and laboratory) were taken from the server with CSV data file and then exported to Stata version 14, where the data were cleaned and analyzed. Anthro was used to analyze anthropometric data. Descriptive analysis such as frequencies, proportion, mean and summary values were determined. The study was conducted after getting ethical clearance from the Ethiopian Public Health Institute scientific and ethical review office. Written informed consent was obtained from all mothers before data collection. Preschool children with xerophthalmia or anemia were referred to the nearest health institution.

Results

Socio-demographic characteristics of the preschool children: Of the total 1157 preschool children involved in the study, 52.6% were females, 36.3% were in the age group of 48 to 59 months and 84.6% were from rural area. Regarding parental educational status, more than half of the parents (53.8%) were illiterate and more than three fourth of the participants (86.3%) lived in an altitude above 1000 meters (Table 1).

Table 1: Background characteristics of children 6 to 59 months, ENMNS, March to July, 2015.

Variables	No. (%) (n = 1157)
Sex	
Male	609 (52.6)
Female	548 (47.4)
Age group	
6-11	45 (3.9)
12-23	134 (11.5)
24-35	246 (21.3)
36-47	312 (27.0)
48-59	420 (36.3)
Parental educational level	
None	622 (53.8)
Elementary	384 (33.3)
Secondary	101 (8.7)
Higher	48 (4.2)
Religion	
Orthodox	470 (40.6)
Muslim	446 (38.6)
Protestant	223 (19.3)
Others	18 (1.6)
Altitude (meter)	
Less than 1000	158 (13.7)
1000 to 1500	282 (24.4)
1500 to 2000	367 (31.7)
2000 to 2500	239 (20.7)
Greater than 2500	111 (9.6)

¹Educational level refers to the highest completed parental educational level

Note: Numbers may not sum up due to missing data

Prevalence of vitamin A deficiency, inflammatory markers and hemoglobin values: Nationally, the unadjusted prevalence of subclinical vitamin A deficiency was 23.5% [95% CI: (21.16, 26.06%)] and after adjusting for markers of inflammation, the prevalence of subclinical VAD decreases to 14.5% [95% CI: (12.52, 16.61%)], thus representing a 9% overestimation. One hundred forty-nine (12.8%) of those tested had acute inflammation and 490 (42.4%) had chronic inflammation. More than one-third of the children [358 (31%)] had anemia whereas 20 of them (1.7%) had severe anemia (Table 2).

Table 2: Markers of Retinol, anemia and inflammatory status of children 6 to 59 months ENMNS, March to July, 2015.

Variables	Children 6 to 59 month no(%)
Serum retinol level (μmol/L) ⁴	
< 0.7	165 (14.5)
≥7 to 1.05	515 (45.1)
>1.05	462 (40.4)
Serum C-reactive protein level (mg/L)	
≤ 5	1008 (87.1)
>5 to 10	100 (8.6)
>10	49 (4.2)
Serum α1-Acid Glycoprotein level (g/L)	
≤1	671 (58.0)
>1-1.5	345 (29.8)
>1.5	141 (12.2)
Hemoglobin level (g/L) ⁴	
Severe anaemia ¹	20 (1.7)
Moderate anaemia ²	121 (10.5)
Mild anaemia ³	217 (18.8)

¹Serum retinol values are corrected for elevated serum α1-Acid Glycoprotein and serum C - reactive protein and hemoglobin was adjusted for altitude.² severe anemia: Hemoglobin <70g/L; ³Moderate anemia: Hemoglobin 70-99g/L; and ⁴Mild anemia: Hemoglobin 100-114g/L.

Note: Numbers may not sum up due to missing data

Distribution of sub-clinical vitamin A deficiency among preschool children: Overall, about 165 (14.5%) preschool children [95% CI: (12.52, 16.61%)] suffered from subclinical vitamin A deficiency. The lowest prevalence of subclinical vitamin A deficiency was among preschool children living in Addis Ababa (0.0 %) followed by Amhara (10.27%) [95% CI: (2.52, 16.38%)] the highest (20.97%) was among those living in Harari [95% CI: (5.21, 32.97%)] followed by Afar (17.44%) [95% CI: (4.12, 27.02%)] (Table 3).

Nutritional status of preschool children: The study revealed that 397 (34.7%) [95% CI: (31.99, 37.51%)] preschool children were stunted, whereas 14.8% [95% CI: (12.83, 16.95%)] were severely stunted. The lowest prevalence of stunting was among preschool children living in Addis Ababa (10.0 %) followed by Gambella (21.84%); and the highest was among those living in Tigray (45.96%) followed by Amhara (38.36%). The study further showed that 120 preschool children were affected by wasting nationally, (10.5%) [95% CI: (8.85, 12.42%)] where 3.2% [95% CI: (2.35, 4.44%)] severely wasted. The lowest prevalence of wasting was among preschool children living in Addis Ababa (0.0%) followed by

Amhara (6.16%), and the highest was among those living in Benishangul-Gumuz (17.78%), followed by Somali (17.07%). Nationally 257 (22.47%), [95% CI: (20.14, 24.98%)] of pre-school children were underweight and 7.5%, [95% CI: (6.1, 9.2%)] were severely underweight. The lowest prevalence of

underweight was among pre-school children living in Addis Ababa (0.0%) followed by SNNP (16.1%), and the highest was among those pre-school children living in Amhara (29.45%), followed by Somali (28.05%) (Table 4).

Table 3: Prevalence and distribution of sub-clinical vitamin A deficiency (serum retinol < 0.7) among children 6 to 59 months by region, ENMNS, March to July, 2015.

Region	Total	At risk no. (%)	No. deficient (%; 95% CI)
Tigray	152	54 (35.5)	18 (11.8, 2.63-18.05)
Afar	86	37 (43.0)	15 (17.4, 4.12-27.02)
Amhara	146	59 (40.4)	15 (10.3, 2.52-16.38)
Oromia	207	105 (50.7)	34 (16.4, 2.58-22.13)
Somali	85	40 (47.1)	12 (14.1, 3.79-23.31)
Benishangul-Gumuz	90	33 (36.7)	12 (13.3, 3.60-22.10)
SNNP	165	81 (49.1)	24 (14.6, 2.75-20.18)
Gambella	88	48 (54.6)	14 (15.9, 3.92-25.16)
Harari	62	26 (41.9)	13 (21.0, 5.21-32.97)
Addis Ababa	10	5 (50.0)	0
Dire Dawa	51	27 (52.9)	8 (15.7, 7.98 – 28.52)
National	1142	515 (45.1)	165 (14.5, 121.52 – 16.61)

Table 4: Nutritional status among children 6 to 59 months by region, ENMNS, March to July, 2015.

Region	Stunting	Wasting	Underweight
	Overall no. (%)	Overall no. (%)	Overall no. (%)
Tigray	74 (46.0,)	12 (7.5)	45 (27.8)
Afar	25 (28.4)	10(11.4)	18 (20.5)
Amhara	56 (38.4)	9 (6.2)	43 (29.5)
Oromiya	72 (35.3)	19 (9.3)	39 (19.1)
Somali	28 (34.2)	14 (17.1)	23 (28.1)
Benishangul-Gumuz	32 (35.6)	16 (17.8)	25 (27.8)
SNNP	55 (33.7)	12 (7.4)	26 (16.1)
Gambella	19 (21.8)	12 (13.8)	15 (17.2)
Harari	22 (35.5)	10 (16.1)	14 (22.6)
Addis Ababa	1 (10.0)	0 (0.0)	0 (0.0)
Dire Dawa	13 (25.5)	6 (11.7)	9 (17.7)
Sex	Boys 223 (19.5)	69 (6.0)	141 (12.3)
	Girls 174 (15.2)	51 (4.5)	116 (10.1)
National	397 (34.7)	120 (10.5)	257 (22.5)

Discussion

It is crucial to realize that many children who are vitamin A deficient will not have the eye signs. This means that children with eye signs are only the “tip of the iceberg”? (Gilbert, 2013). The unadjusted prevalence of subclinical vitamin A deficiency was - 23.5%. However due to the effect of inflammation on serum retinol value; it is adjusted for markers of inflammation. The adjusted prevalence was 14.5%, this prevalence was overestimated by 9%. It is therefore important to measure biomarkers of inflammation as well as of nutrition in prevalence surveys of nutritional status in apparently healthy people. In this study, nearly half of the preschool children had inflammation, as indicated by elevated AGP and/or CRP. These findings suggest that the prevalence of subclinical infection is high in those populations who had high prevalence of vitamin A deficiency. Higher prevalence of inflammation (67%) was reported in Cote d'Ivoire (Rohner et al. 2012) and 49.6% of the children had inflammation (Maqsood et al. 2004).

This adjusted prevalence of VAD (14.5%) was lower than that of previous Ethiopian national studies

conducted among preschool children which showed a prevalence of 34.4% (Demissie et al. 2009) and another national study in preschool children, found prevalence of 37.7% (Demissie et al. 2010). This difference can be attributed to the fact that both studies did not adjust their retinol values with a marker of inflammation. Similarly, this study found a lower prevalence of subclinical VAD as compared to other studies, 76.6% in Bungoma district of western Kenya (Nabakwe and Ngare 2004), and 47% in Marshal Islands (Maqsood et al. 2004).

As we compare with the findings of the previous national study, both the national and regional prevalence of subclinical vitamin A deficiency has been decreased, except SNNPR where it showed a slight increment (Demissie et al. 2010). The present study confirmed that highest prevalence of subclinical vitamin A deficiency was reported in the Harari (21.0%) [95% CI: (5.21-32.97%)] and Afar regions (17.4%) [95% CI: (4.12-27.02%)], whereas the lowest rates were observed in Addis Ababa (0.0%) followed by Amhara (10.3%) [95% CI: (2.52-16.38%)].

Based on these findings, Vitamin A deficiency has severe public health importance only in Harari region, and all the other regions showed moderate public health importance as set by World Health Organization standard (WHO 1996). The lower prevalence observed in the current study may be attributable to multiple factors, such as better availability and higher consumption of fruits and vegetables, relatively high vitamin A supplementation coverage, and low level of morbidity.

In this study, 0.61% of the preschool children developed Bitot's spot which was higher than the cut of point of public health importance of WHO (WHO 1996). This is similar to what Arlappa found in West Bengal in India, a prevalence of Bitot's spot of 0.6% (Arlappa et al. 2010) and a bit higher with the finding from Jimma, Ethiopia (0.48%) (Getaneh et al. 2000). Likewise, 0.52% of the preschool children were affected by night blindness. These findings were lower with the study findings conducted in Ethiopia (1.7% Bitot's spot and 0.8 Night blindness) (Demissie et al. 2010), Asgede-tsimbla, Ethiopia (1.46% Bitot's spot and 1.22 night blindness) (Abrha, 2016), and Uttar Pradesh, India (9.1% Xerophthalmia) (Sachdeva et al. 2011).

Although several strategies have been followed to prevent and control vitamin A deficiency, the findings of this study implied that vitamin A deficiency is still at the level where WHO declares it to be a problem of moderate public health importance in Ethiopia. VAD has a strong negative repercussion on health, survival, growth, and wellbeing of preschool children. This poses arguments on the need for the programs aiming at achieving the sustainable development goals and the health transformation plan of Ethiopia should look into innovative strategies of addressing this problem.

Acknowledgments

We would like to acknowledge Ethiopian public health institute for granting access to data.

Conflict of Interest: The authors declare that they have no competing interests.

References

- Abbrha T, Girma Y, Haile K, Hailu M & Hailemariam M (2016). Prevalence and associated factors of clinical manifestations of vitamin A deficiency among preschool children in asgede-tsimbla rural district, north Ethiopia. *Archives of Public Health*, 74(4):1–8.
- Arlappa N, Balakrishna N, Laxmaiah A, Nair K & Brahman G (2011). Prevalence of Clinical and Sub-Clinical Vitamin A Deficiency Among Rural Preschool Children of West Bengal, India. *Indian Pediatrics*, 48(1):47–49.
- Chauhan N, Atul T, Iqbal K & Niti T (2011). Prevalence of Clinical Vitamin A Deficiency Among Primary School Children in Urban Slums of Ahmedabad. *Journal of Clinical and Diagnostic Research*, 5(8):1627–1630.
- Demissie T, Ali A, Mekonen Y, Haider J & Umata M (2010). Magnitude and distribution of vitamin A deficiency in Ethiopia. *Food and Nutrition Bulletin*, 31(2):234–41.
- Demissie T, Ali A, Mekonnen Y, Haider J & Umata M (2009). Demographic and Health-related Risk Factors of Subclinical Vitamin A Deficiency in Ethiopia. *Journal of Health Population and Nutrition*, 27(5):666–73.
- Fabian R, Christine N, Andres B, Patrice E, Valérie K & Juergen G (2013). Prevalence and public health relevance of micronutrient deficiencies and under nutrition in pre-school children and women of reproductive age in cote d'ivoire, West Africa. *Public health nutrition*, 17(9):2016–28.
- Getaneh T, Assefa A & Tadesse Z (2000). Dietary practices and xerophthalmia in under-fives in Jimma town, southwest Ethiopia. *East African medical journal*, 77(6):313–5.
- Gilbert C (2013). The eye signs of vitamin A deficiency. *Community eye Health Journal*, 26(84): 66–67.
- Haider J (2011). Common micronutrient deficiencies among food beneficiaries : Evidence from refugees in Ethiopia. *Ethiopian journal of Health Development*, 25(3):222–229.
- Kevin MS, Zuguo M, Laurence G & Ibrahim P (2008). Hemoglobin adjustments to define anemia. *Tropical Medicine and International Health*, 13(10):1267 – 1271.
- Maqsood M, Dancheck B, Gamble MV, Palafox NA, Ricks MO, Briand K, et al (2004). Vitamin A deficiency and inflammatory markers among preschool children in the Republic of the Marshall Islands. *Nutrition Journal*, 3:21–21.
- Maureen K, Alexandra E & Joseph N (2008). HPLC quantitation of retinal, retinol, and retinyl esters in serum and tissues. *Analytical Biochemistry Journal*, 378 (1): 71–9.
- Nabakwe E & Ngare D (2004). Health and nutritional status of children in western kenya in relation to vitamin a deficiency. *East African Journal of Public Health*, 1(1):1–5.
- Parminder S, Sorrel M, Grant J, Daniel J, Kenneth H & Rafael F (2016). Overview of the biomarkers reflecting inflammation and nutritional determinants of anemia (brinda) project. *Advances in Nutrition*, 7(2):349–56.

- Pinkaew S (2012) Vitamin A and zinc efficacy in triple fortified extruded rice. ETH Zurich. doi: 10.3929/ETHZ-A-7356130.
- Rice A, West K, Black R, Ezzati M, Lopez A, Rodgers A, et al. (2004). Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors, vol. 1. Geneva: World Health Organization *World Health Organization Geneva?*
- Roche Diagnostic (2015). CRPHS. Cardiac C-Reactive Protein (Latex) High Sensitive Order information. Cardiac C - reactive protein (latex) high sensitive. *Cobas*, 7(10):1-4.
- Roche Diagnostics GmbH (2015). AAGP2. Tina-quant α 1-acid glycoprotein gen.2. *Cobas Specific protiens*, 7:1-4. Available at: *Sandhofer Strasse 116, D-68305 Mannheim www. roche.com*
- Sachdeva S, Alam S, Beig F, Khan Z & Khaliq N (2011). Determinants of Vitamin A Deficiency amongst Children in Aligarh District, Uttar Pradesh. *Indian Pediatrics*, 48(11):861-6.
- Thurnham D & McCabe G (2014). Influence of infection and inflammation on biomarkers of nutritional status with an emphasis on vitamin A and iron. World Health Organization, Geneva.
- Thurnham DI, McCabe GP & Nestel P (2003). Effects of subclinical infection on plasma retinol concentrations and assessment of prevalence of vitamin A deficiency. *The Lancet*, 362 (9401):2052-58.
- Viveka P (2004). Vitamin A intake, status and improvement using the dietary approach Studies of vulnerable groups in three Asian countries. *Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine*.
- World Health Organization (1996). Indicators for assessing Vitamin A Deficiency and their application in monitoring and evaluating interventions programmes. World Health Organization Geneva.
- World Health Organization (2011). Vitamin A supplementation in infants and children 6 – 59 months of age. World Health Organization Geneva.
- World Health Organization (2014). C-reactive protein concentrations as a marker of inflammation or infection for interpreting biomarkers of micronutrient status. World Health Organization. <https://apps.who.int/iris/handle/10665/133708>
- World Health Organization. (2009). Global prevalence of vitamin A deficiency in populations at risk 1995-2005: WHO global database on vitamin A deficiency. *World Health Organization*. <https://apps.who.int/iris/handle/10665/44110>.
- World Health Organization. (2011). Serum retinol concentrations for determining the prevalence of vitamin A deficiency in populations. World Health Organization. <https://apps.who.int/iris/handle/10665/85859>.