Original Article

Limitations in vitamin A supplementation to optimise serum retinol in preschool children from two central Java districts

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Background and Objectives: Vitamin A deficiency is particularly common among children younger than 5 years. In 2011, a study conducted in West Java revealed that the prevalence of vitamin A deficiency in children aged 6–11 months, 12–23 months, and 24–59 months was 18.2%, 15.2%, and 9.9%, respectively. The present study analysed the differences in vitamin A intake and serum retinol in all the preschool children from Grobogan and Kudus, Central Java. **Methods and Study Design:** The baseline data of vitamin A efficacy were analysed. A total of 143 children aged 1-3 years participants (n=71 from Kudus and n=71 from Grobogan) were recruited and we used independent *t*-tests to analyse the data. **Results:** Among the study population, 50.7% and 48.6% were boys and 49.3% and 51.4% were girls from Kudus and Grobogan, respectively. The average intake of energy, carbohydrates, protein, fat, and vitamin A was 698±440 (Kcal), 89±60 (g), 25.9±18.5 (g), 26.1±18.5 (g), and 435.3±554.0 (μg) in Kudus and 868±493 (Kcal), 109±67 (g), 30.9±20.1 (g), 35.1±23.1 (g), and 538.1±622.9 (μg) in Grobogan, respectively. The average serum retinol in Kudus and Grobogan were 26.7±6.4 (μg/dL) and 29.6±5.9 (μg/dL), respectively. Significant differences in energy and fat intake (*p*<0.05) were also observed between the Kudus and Grobogan districts; however, no differences in protein, carbohydrates, and vitamin A intake (*p*≥0.05) were noted. A significant difference in serum retinol was observed between these two districts (*p*<0.05). **Conclusions:** An increase in vitamin A intake through various foods should improve the serum retinol in preschool children.

Key Words: vitamin A, serum retinol, children younger than 5 years

INTRODUCTION

Vitamin A deficiency (VAD) primarily occurs among high-risk groups; children younger than 5 years old are particularly vulnerable. A recent study of two districts in West Java revealed that the prevalence of VAD in children aged 6–11 months, 12–23 months, 24–59 months, and 6–9 years was 18.2%, 15.2%, 9.9%, and 10.9%, respectively; among lactating women and women who were of reproductive age, the prevalence of VAD were 10.0% and 5.3%, respectively.[1] In March 2015, Indonesia planed to implement the mandatory fortification of cooking oil with vitamin A[2], as regulated by the Ministry of Industry (decree No. 87, 2013) and the National Standardisation Board of National Red Palm Oil (standard No. 7709, 2012). However, it was postponed to March 2018. According to this policy, all cooking oil distributed for consumption must contain 45 IU/g of vitamin A (retinyl palmitate). This initiative of mandatory vitamin A fortification is based on numerous in-depth pilot studies that have been conducted by the Ministry of Health, Ministry of Trade and Industry, Board of Food and Drugs, various universities, and *Koalisi Fortifikasi Indonesia* (a nongovernment organisation actively supporting food fortification) since 2005. An improvement in the vitamin A status

of vulnerable groups is likely to impact many outcomes such as the prevalence of visual impairment, resistance to infection, prevalence of anaemia, and potentially the linear growth of children.[3-6] Vitamin A improves the mobilisation of iron stores for erythropoiesis, thereby increasing haemoglobin concentration without actually affecting iron stores.[7] In 2008, a *Lancet* series on nutrition and maternal and child health ranked VAD as the most critical micronutrient deficiency, which is responsible for more than 600,000 child deaths per year worldwide. However, as Black et al (2008) noted, high-dose vitamin A supplementation in children older than 6 months decreases mortality by approximately 23%.[8] Considering the high prevalence of VAD in preschool-aged children, campaigns to provide

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vitamin A capsules to young children have been implemented in many developing countries. In 1978, the government of Indonesia initiated a national vitamin A supplementation programme for children younger than 5 years and for postpartum mothers.[9] Vitamin A supplementation is provided twice annually, usually in February and August. Although this programme has been sustained for years and its coverage is relatively high, a large proportion of children cannot be reached through the programme; hence, they are at risk of developing VAD.[10]

More recently, studies conducted by Baseline Health Research in 2007, 2010, and 2013 have revealed that the coverage of high-dose vitamin A capsules among children was 71.5% (range across the province, 51.0%–84.7%), 69.8% (range, 49.3%–91.1%), and 75.5% (range, 52.3%–89.2%), respectively. By contrast, the coverage among postpartum women was only 52.2% (range, 33.2%–65.8%) in 2010.[11-13] These results demonstrate that large proportions of children younger than 5 years and postpartum mothers do not receive the capsules.

Indonesia is a world supplier of cooking oil. A pilot project study on unbranded vegetable oil fortification was conducted in Makassar. The study revealed that unbranded vegetable oil fortification led to significant improvement in the serum retinol concentrations of schoolchildren and low-income populations, who generally consume approximately 25 g/day of unbranded vegetable oil. Unbranded oil constitutes approximately 70% of the total oil traded in the country. Therefore, the fortification programme encourages Indonesian industries to perform oil fortification and export these oils, which in turn expands their market potential and directly reduces VAD in the.[14]

Food fortification is a strategy that enables nutrition interventions to reach almost all populations. Therefore, pilot studies on oil fortification were conducted to prepare for mandatory fortification. Other aspects, such as the types of food for vitamin A fortification, fortification technologies, fortification at the distribution and storage sites (rather than at the plant site), level of cooking oil consumption, lower vitamin A intake than the RDA, acceptability of oil fortification, stability of vitamin A (retinyl palmitate), and the results of efficacy and effectiveness studies on VAD in high-risk populations, were also studied.

An effectiveness study conducted in two districts of West Java (Tasikmalaya and Ciamis) demonstrated a significant correlation between the oil fortification programme and vitamin A status in children younger than 5 years, school-aged children, women of reproductive age, and lactating mothers. The overall prevalence of VAD decreased from 12.2% at baseline to 2.9% at 12 months after the fortification programme was implemented. Mean serum retinol increased by 0.7–8.1 μg/dL. The lowest improvement in mean serum retinol (0.7 μg/dL) was observed in children aged 12–23 months, which was the only nonsignificant improvement compared with that in the other groups.[1] The reasons for the limited improvement in young children aged 12–35 months remain unclear. However, the children participating in this group were assessed using a cross-sectional design, so considerable variation may have existed; by contrast, older age groups were assessed using a cohort design; additional

factors that may have influenced the results are low cooking oil consumption, high prevalence of infectious diseases, poor complementary food intake, and changes in food intake pattern. Because of these data, and for the aforementioned reasons, the present study analysed the differences in vitamin A intake and serum retinol among preschool children from two Central Java districts with low and high vitamin A capsule coverage.

MATERIALS AND METHODS

An efficacy cohort study design was applied to assess vitamin A fortification in cooking oil for 2 years (i.e., baseline and endline study). Baseline data were used for this analysis. The study site was selected from Riskesdas (2007), which identified the districts with high (Kudus) and low (Grobogan) coverage of vitamin A capsules. Another criterion for selecting the districts was that they were approachable for unbranded oil distributors. The ecthical approval was granted by Faculty of Health Sciences Esa Unggul University no.067/FIKES/XII/2014.

The sample population included children aged 12–35 months from poor households in two selected peri-urban villages (clusters) per district. The determination of poor households was made according to the availability of a valid family poverty card. Only households possessing this card were selected because these households were likely to be at increased risk for VAD, and they consumed unbranded cooking oil.

Serum retinol levels were the main indicator for determining sample size. Accordingly, a sample size in which a minimum difference of at least 10% in the mean serum retinol concentration could be detected, with a confidence interval of 95% (1.96) and a statistical power of 0.80 (1.28).

The WHO formula (WHO, 1990), which indicates a minimum sample size of 58, was applied herein to determine the correct sample size. Considering a design effect of 2 and assuming a 20% drop-out rate, 140 participants were required: 70 aged 12–23 months and 70 aged 24–35 months. In the baseline, the number of samples who available to follow this study were 143 samples: 71 from Kudus and 72 from Grobogan. Data analysis was then performed to evaluate the nutrient intake (energy, carbohydrates, fat, protein, and vitamin A) in preschoolers stratified by serum retinol, gender, and age, and independent student t-tests were used to prove the research hypothesis. The participants' weight and height were measured by trained enumerators, with weight measured to the nearest 0.1 kg using a weighing scale, and height measured to the nearest 0.1 cm using a metre line. Dietary intake information was collected through a 24-h dietary recall of 2 days, by trained enumerators with a nutrition background. Finally, serum retinol were evaluated using blood drawn from the cubital vein by trained phlebotomists in the study areas, and measured through HPLC.

RESULTS

Table 1 shows the characteristics of the participants. The proportions of examined boys and girls were comparable between the two districts. Specifically, a total of 50.7% and 48.6% of the boys and 49.3% and 51.4% of the girls from Kudus and Grobogan, respectively, were assessed

Table 1. Characteristics of respondent

Variable	Kudus (n=71)	Grobogan (n=72)	Total (n=143)
Gender			
Boys	36 (50.7)	35 (48.6)	71 (49.7)
Girls	35 (49.3)	37 (51.4)	72 (50.4)
Age (y)	23.6±6.9	25.1±7.6	24.4±7.3
Weight (kg)	10.3±1.8	10.4±1.9	10.3±1.9
Height (cm)	81.6±7.2	81.3±7.9	81.5±7.6
Z-score W/H (WHZ)	-0.4±1.5	-0.6±1.2	-0.5±1.4
Z-score W/A (WAZ)	-1.2±1.3	-1.0±1.1	-1.1±1.2
Z-score H/A (HAZ)	-1.7±1.1	-1.1±1.2	-1.4±1.2
Z-Score BMI/A (BAZ)	-0.1±1.6	-0.5±1.2	-0.3±1.4

WHZ: weight for height z-score; WAZ: weight for age z-score; HAZ: height for age z-score; BAZ: body mass index for age z-score.

Table 2. The difference intake of nutrient in two districts

Variable	Areas	n	Mean±SD	% RDA	SEM	T-test	p-value
Energy, Kcal[*]	Kudus	71	698±440	1125	52.2	-2.17	0.031
	Grobogan	72	868±493		58.0		
Carbohydrate, g	Kudus	71	89±60	155	7.1	-1.83	0.069
	Grobogan	72	109±67		7.9		
Protein, g	Kudus	71	25.9±18.5	26	2.2	-1.56	0.120
	Grobogan	72	30.9±20.1		2.4		
Fat, g[*]	Kudus	71	26.1±18.5	44	2.2	-2.57	0.011
	Grobogan	72	35.1±23.1		2.7		
Vitamin A, mcg	Kudus	71	435±554	400	65.7	-1.04	0.298
	Grobogan	72	538±623		73.3		

[*]$p<0.05$.

(Table 1).

The data indicates that the proportions stratified by sex, age, weight, height, and mean z-scores of weight for height z-score (WHZ), weight for age z-scor (WAZ), height for age z-score (HAZ), and body mass index for age z-score (BAZ) did not differ significantly. The total average of the z-scores for WHZ, WAZ, HAZ, and BAZ were −0.53±1.40, −1.12±1.25, −1.43±1.19, and −0.35±1.42, respectively. As per the average of all indicators, the Z-score for the nutritional status of children younger than 5 years was normal.

Differences in the dietary intake of energy, carbohydrates, fat, protein, and vitamin A between the two districts

According to our data (Table 2), significant differences were observed in the intake of energy and fat ($p<0.05$). The range of SEM values was not much larger (or smaller), implying that the participants who contributed to the study were representative of the total population in the study area.

The average intake of energy and fat in the two districts were significantly different, but no differences were observed in the intake of protein, carbohydrates, and vitamin A. However, the average intake of vitamin A in the two districts was still within the normal range (i.e., above 400 μg, as per the RDA): 435±554 μg in Kudus and 538±623 μg in Grobogan. In addition, significant differences were observed in the serum retinol between Kudus

Table 3. The differences of serum retinol in two districts

Serum retinol	n	Mean±SD	SEM	T-test	p-value
Kudus	71	26.7±6.4	0.7	-2.67	0.008
Grobogan	70	29.6±5.9	0.7		

(26.7±6.4 μg/dL) and Grobogan (29.6±5.9 μg/dL). However, the total serum retinol (28.1±6.3 μg/dL) were within normal limits (i.e., between 20 and 30 μg/dL).

Unlike the intake of energy and fat, no differences were observed in the intake of protein, carbohydrates, and vitamin A ($p≥0.05$). The sources of vitamin A were primarily vegetable and animal proteins, which was reflected in the average protein intake of the participants, which met the RDA levels. Nevertheless, a varied diet is highly recommended to achieve RDA levels of intake.

Differences in the serum retinol levels among preschool children

In this study, differences in the serum retinol were observed between the two districts ($p<0.05$), depending on the characteristics of the region (i.e., according to whether the area under assessment had a high coverage [Kudus] or low coverage [Grobogan] of high-dose vitamin A capsules). Despite these differences, serum retinol in both districts were still at an acceptable level (≥20 μg/dL).

Serum retinol ≥20 µg/dL were considered to be within the normal range because of subclinical vitamin A. However, this was inadequate because the values were still ≤30 µg/dL, indicating a lack of serum retinol storage in the blood.

This study also provides key information about the concerns of the vitamin A capsule programme. Some parents admitted that they received vitamin A capsules from the village health care but did not visit the village healthcare centre.

A review of Table 4 indicates that a larger number of participants living in Kudus received vitamin A capsules and had serum retinol <20 µg/dL (17.4%) compared with those living in Grobogan (4.7%).

Differences in the vitamin A intake according to serum retinol levels among preschool children

We verified our hypothesis regarding the differences in vitamin A intake according to serum retinol categorised as follows: <20 µg/dL and ≥20 µg/dL. Independent student t-test results revealed no significant differences in vitamin A intake according to serum retinol ($p≥0.05$; $t=−1447$). Given the sample size calculation, this means that a difference of 20 µg/dL was not in evidence with vitamin A supplement in this study (Figure 1).

DISCUSSION

Indonesia still has districts with low coverage of the vitamin A capsule programme, which indicates that the management and socialisation of the programme is not optimally performed at the regency or city level. Vitamin A is an essential nutrient required in small amounts.[15] Vitamin A is critical for normal functioning of the visual system; growth and development, especially in children younger than 5 years; the maintenance of epithelial cellular integrity; immune response; and reproduction in girls and women.[16,17]

This study identified differences in the serum retinol levels between Kudus and Grobogan. Serum retinol ≥20 µg/dL indicated that the participant was within the normal range, according to the serum retinol in subclinical VAD. Notably, our findings are similar to those of another study, which stated that 43.2% of participants had inadequate serum retinol (≤30 µg/dL).[18]

Compared with the nutrition intake, as per the Indonesian RDA 2014, the average intake of energy and fat remained considerably below the average RDA rate, specifically for energy (RDA, 1125 Kcal) and fat (RDA, 44 g). However, the intake of carbohydrates, protein, and vitamin A has been widely addressed and sufficient intake as per the RDA has been achieved.[19] This implies that the variety in food sources was defined to meet the dietary intake as per the 2014 RDA.

In an animal study, plasma vitamin A concentrations did not provide a linear indication of liver or body vitamin A status, and both topical and oral supplementation with an oil-based vitamin A formulation increased liver stores in amphibians.[2,20-22] Laillou et al (2013) stated that the fortification of edible oils is gaining recognition as an effective, low-cost technology to improve the consumption of nutritious foods and reduce the burden of VAD in developing countries.[23-27] Large-scale fortification of vegetable oil in Malaysia, Indonesia, Bangladesh, and Cambodia can reach millions of people globally, including children younger than 5 years.[28-32] The levels of fortification used are far from reaching the tolerable upper intake level. Nevertheless, vegetable oil fortification has the potential to become a global public health intervention strategy.[2,23,33-35]

VAD can occur at any age; however, the shortcomings accompanied with abnormalities in the eye are generally observed in children aged 6 months to 4 years.[21,36] It is a condition resulting from decreases in the storage of vitamin A in the body. The initial stage is characterised by symptoms of night blindness or a reduced ability to see in the dark,[2,37] known as *hemeralopia* (night blindness),[17,37] which is accompanied by decreased serum retinol levels (<20 µg/dL).[36] In later stages, epithelial tissue abnormalities in organs such as the lungs, intestines, skin, and eyes are observed.[38]

Our findings are inconsistent with those of another study on 37 participants, aged 6–59 months, who were randomly selected from 2260 children younger than 5 years and living in a subdistrict in Indonesia. In that study, thyroid-stimulating hormone (TSH) and serum retinol measurements were performed through ELISA and HPLC, respectively. The results revealed that 43.2% of participants had higher levels of inadequate serum retinol (≤30 µg/dL) and 10.8% had subclinical VAD levels of serum retinol (<20 µg/dL).[17,39] However, the study did not confirm the relationship between serum retinol and (log) elevated serum TSH levels.[18]

Another study found that 50.2% of children younger than 5 years had serum vitamin A levels <20 µg/dL, which is higher than the threshold of 15% according to the International Vitamin A Consultative Group. Helen Keller International (1995) reported that the incidence of blindness in women of childbearing age in the province of Central Java was 1%–3.5%.[39]

Vitamin A is vital, fat-soluble vitamin found in fish oil,[15] cheese, egg yolks, green vegetables, and reddish vegetables such as tomatoes and carrots.[21,40-41] Generally, vitamin A is a generic name that indicates all the retinoids and precursors, provitamin A, and carotenoids that have biological activity as retinol.[18] Vitamin A is stored in the liver and cannot be made by the body, so it must be obtained externally. Moreover, vitamin A contributes to vision, growth, and the increased resistance of the immune system to disease.[17,38]

VAD is a systemic disease that can damage body cells and organs, and then induce metaplasia of epithelial keratinocytes in the respiratory, urinary, and gastrointestinal tracts. The third stage is severe form that cause permanent lose of vision.[2] However, because only the eyes are easily observed and inspected, clinical diagnosis of VAD is often made on the basis of the eye examination.[21,42] The national survey in 1978 reported that the prevalence of X1b xerophthalmia (bitot spots) among children under five year was 1.34%, which decreased to 0.35% in 1992.[37,43]

The effects of vitamin A supplementation are as follows. High doses of vitamin A for children older than 6 months reduces mortality by approximately 23%. Thus, the region's prevalence indicated that despite the relative-

ly normal serum retinol, only approximately 70% of the population receives vitamin A supplementation. The present study demonstrated that the proportion of participants who received the vitamin A capsules and had serum retinol <20 μg/dL were higher in Kudus (17.4%) than in Grobogan (4.7%); notably, whether the participants consumed the vitamin A capsules after accepting them could not be confirmed. Single micronutrient supplementations with vitamin A does not have the value of synergy with other through factors. For example zinc adequacy is requisite for several vitamin A functions as with retinol dehydrogenase.[44-46]

Conclusions

Differences were observed in the intake of energy and fat between the participants of Kudus and Grobogan, but no differences were noted in their intake of protein, carbohydrates, and vitamin A. Furthermore, the serum retinol differed between the two districts with high and low coverage of vitamin A, although no differences were observed in the vitamin A intake assessed according to the serum retinol levels. The participants were all normal, according to their retinol (>20 μg/dL) in subclinical VAD; however, these values were inadequate because they were ≤30 μg/dL, which is indicative of absent serum retinol stores in the blood. Therefore, the effects of vitamin A intake through a variety of foodstuffs and supplements on serum retinol in preschool children can be observed in a long-term study.

AUTHOR DISCLOSURES
These authors have no conflict of interest to declare in this study.

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