# VITAMIN A STATUS OF FILIPINO PRESCHOOL CHILDREN GIVEN A MASSIVE ORAL DOSE

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**Abstract.** The protection period of a 200,000 IU of vitamin A on Filipino children was determined. Subjects were 105 children aged 1-5 years given a single massive dose during the "Araw ng Sangkap Pinoy" (ASAP) in March 1995. Serum retinol was measured by HPLC at baseline, one, two, four and six months after the administration of the dose. Results showed that baseline serum retinol levels were significantly lower than all follow-up values. Serum retinol values were maintained at levels higher than pre-supplementation values although the values decreased on the second month after supplementation. The proportions of deficient and low (< 20 μg/dl) levels were significantly lower one and six months after supplementation. All follow-up serum retinol levels of children with deficient and low values at baseline were significantly lower ($p < 0.001$) than those with normal values. The WHO recommendation of 200,000 IU was effective in increasing serum retinol concentrations and maintaining it above pre-supplementation levels up to 6 months after administration of the dose. It also replenished organic vitamin A reserves as shown by the dose response (S30DR) approach. Incidence of infection also decreased among the children. Supplementation with vitamin A has likewise resulted in an increase in hemoglobin values and a decrease in the proportion of anemics (Hb < 11.0 g/dl) among the children.

## INTRODUCTION

Micronutrient malnutrition refers to a deficiency in any of the micronutrients and in the Philippines as in other developing countries it refers principally to deficiencies in vitamin A, iron and iodine. Also called hidden hunger because its effects are not readily seen, micronutrient malnutrition is deemed of public health importance in the Philippines. Results of national nutrition surveys conducted in 1986, 1987 and 1993 have shown that less than 10 μg/dl vitamin A levels are present in more than 5% (IVACG, 1982) of 6 months to 6 year old children in several regions of the country indicating that vitamin A deficiency is a significant public health problem (Kuizon *et al*, 1994 a, b, 1995). The 1993 national nutrition survey (Kuizon *et al*, for publication) has likewise shown that iron deficiency anemia among preschoolers is high. The same survey also showed that goiter prevalence was high among 7 year old and over but was was highest among pregnant and lactating women (Velandria, 1994).

In 1993, an Advocacy Meeting on Ending Hidden Hunger in the Philippines was held where it was decided to conduct a three-year program from 1993 to 1995 to end micronutrient malnutrition. High dose vitamin A supplements were then distributed nationwide twice a year (May and October 1993, April and September 1994 and March and October 1995) during the "National Micronutrient Day" which was also known as "Araw ng Sangkap Pinoy" or ASAP (DOH, 1993). During the ASAP days 200,000 IU of vitamin A is administered to preschoolers aged 1-5 years. In 1993 coverage for the distribution of the vitamin A capsules was more than 100% of target while in 1994, coverage was reported to be 100% also (DOH, 1994). Reported adverse reactions like vomiting and diarrhea were very minimal, mild and of short duration (DOH, 1993).

Administration of 200,000 IU of vitamin A to a child is supposed to give them protection for a period of 3 to 6 months depending on the vitamin A content of the diet and the rate at which the body utilizes it (WHO, 1988). The first ASAP was

conducted in May 1993 during the fourth national nutrition survey where serum vitamin A levels were determined among preschoolers. Results have indicated that prevalence of deficient and low levels of children in areas where the survey was conducted within two months after ASAP were lower than in areas where the survey was conducted before ASAP (Kuizon *et al*, 1995). The survey, however, could not determine the levels of protection given by ASAP beyond two months. Such information would be important for planning the future of ASAP program.

This study therefore was conducted to evaluate the protection period of a single massive dose of the vitamin to 1-5 year old Filipino children followed up to 6 months after administration. The effects of vitamin A supplementation on the hemoglobin levels and infection were also determined.

## MATERIALS AND METHODS

The study was conducted in Barangay Landayan, San Pedro, Laguna during the March 1995 ASAP. Subjects were 1-5 year old preschools who were given a massive oral dose of 200,000 IU of vitamin A together with 40 IU of vitamin E. The parents or guardians of the prospective subjects were informed of the importance and design of the study before baseline blood collection was made. Consent for participation was given by them. At the start of the study there were 121 children but only 105 had the one-month follow-up and only 67 were able to finish the six-month study. Drop outs were mainly due to transfer of residence and parents not allowing subsequent blood collection.

Finger prick blood collection was done at baseline, 1, 2, 4 and 6 months after administration of the dose. Blood samples were collected in non-heparinized tubes, centrifuged, serum separated and stored frozen at -20°C till analysis was done. Serum retinol was analyzed at baseline and at all follow-ups by HPLC (Furr, 1992). Analysis for serum retinol was done after the last collection day of the sixth month. Baseline and all subsequent follow-up serum for each child was analyzed on the same day. Hemoglobin was determined by the cyanmethemoglobin method (ICSH, 1978).

Height and weight were measured at baseline using the procedures prescribed by Jellife (1966). Weight for age, height for age and weight for height were evaluated using the Anthropometric Standards for Filipinos (Florentino et al, 1992). A one month history of episodes of infection (measles, chicken pox, diarrhea and upper respiratory tract infection) which could affect vitamin A status was asked from the parent of each child at each period of blood collection. They were also asked to report any illness experienced by the child during the 6 month study. Vitamin and mineral supplements, as well as previous intake of a massive dose of vitamin A during the September 1994 ASAP were also recorded.

All statistical analysis was done using the Statistical Package for the Social Sciences (SPSS). Means and standard deviations were computed. Mean difference was tested using ANOVA and difference between two proportions was tested using the Z-test. The S30DR approach was also applied to estimate the prevalence of primary vitamin A deficiency.

## RESULTS

Table 1 shows the characteristics of the children at the start of the study. Baseline characteristics of the subjects as to age, height, weight, serum retinol and hemoglobin levels for the males and females were similar. Mean age was 32.8 ± 14.7 months. Mean hemoglobin was 11.0 ± 1.2 g/dl, and 48 out of 105 children or 45.7% were anemic. Mean plasma retinol was 27 ± 9 μg/dl and 18 of the children or 17.1% had deficient and low retinol values. It was apparent that vitamin A deficiency was a significant public health problem in this barangay since deficient and low levels exceeded the WHO criteria of 15% (IVACG, 1982). Most of the children (92.4%) had normal nutritional status based on the anthropometric standard for Filipinos.

At baseline, mean serum retinol of all the subjects was 27 ± 9 μg/dl, increasing to 35 ± 12 μg/dl one month after supplementation (Fig 1). This corresponds to an increase of 8 μg/dl. After the second and fourth month mean serum retinol slightly decreased (NS) to 33 ± 11 μg/dl, and 31 ± 10 μg/dl (Table 2). The slight increase in mean serum retinol levels from the 4th to the 6th month was not significant. The baseline level was significantly lower than all the follow-up values ($p < 0.001$). The

Table 1

Baseline characteristics of the subjects.

| | Male | Female | Total |
|---|---|---|---|
| Number | 55 | 50 | 105 |
| Age (mos) | 32.7 ± 15.1 | 32.8 ± 14.3 | 32.8 ± 14.7 |
| Height (cm) | 87.5 ± 10.0 | 87.1 ± 10.1 | 87.3 ± 10.0 |
| Weight (kg) | 12.0 ± 2.5 | 15.5 ± 17.6 | 13.7 ± 12.4 |
| Nutritional Status | | | |
| Normal Only[1] | 90.9 | 94.0 | 92.4 |
| Stunted Only[2] | 5.5 | 2.0 | 3.8 |
| Wasted Only[3] | 1.8 | 0 | 1.0 |
| Wasted and Stunted[4] | 1.8 | 0 | 1.0 |
| Hemoglobin (g/dl) | 10.9 ± 1.2 | 11.0 ± 1.3 | 11.0 ± 1.2 |
| %Anemic[5] | 45.5 | 46.0 | 45.7 |
| Retinol (μg/dl) | 26 ± 7 | 28 ± 11 | 27 ± 9 |
| %Def and Low[6] | 14.5 | 20.2 | 17.1 |

[1] Normal - > P5 of standard weigh-for-height and > P5 standard height for age
[2] Stunted only - > P5 of standard weight-for-height and ≤ P5 of standard height-for-age
[3] Stunted only - ≤ P5 of standard weight-for-height and > P5 of standard height-for-age
[4] Both wasted and stunted - ≤ P5 of standard weight-for-height and ≤ P5 standard height-for-age
[5] Hb < 11.0 g/dl
[6] Retinol < 20 μg/dl

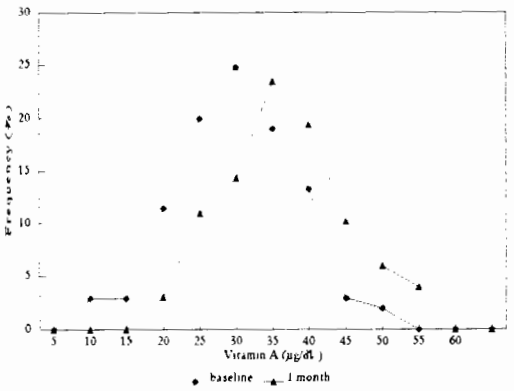


Fig 1–Frequency distribution of serum vitamin A at baseline and after supplementation.

increase in the serum retinol concentration one month after supplemention can also be seen from Fig 1. Results as a whole have shown that 200,000 IU of retinol, although decreasing after the second month of supplementation, was able to maintain blood levels of the vitamin higher than the pre-supplementation values.

Deficient and low serum retinol levels were present in 17.1% of the subjects at baseline (Table 2). This proportion f subjects decreased significantly to 5.1% ($p < .01$) a month after the administration of the dose, increasing to 10.1% and 13.7% after 2 and 4 months respectively and decreasing again to 6.0% ($p < 0.05$) after 6 months. The decrease in the proportion of children with deficient and low levels from the fourth to the sixth month was not significant.

Serum retinol values of all the children with deficient and low levels increased to acceptable or high values one month after the dose (data not shown). However, the mean values for these children were consistently lower at all times compared with the children who were already normal at baseline ($p < 0.001$).

Results of the S30DR shows that the percentage difference in serum levels of vitamin A after a month was 36%. This value is greater than the 20% cut-off (Flores, 1993) for the percentage increase in serum vitamin A that reflects replenishment of organic reserves.

Table 2

Mean serum retinol and prevalence of deficient and lowlevels at baseline and after the dose.

| Time of collection | No. | Male | | Female | | Total | |
|---|---|---|---|---|---|---|---|
| | | $\bar{X} \pm SD$ | % Def & low | $\bar{X} \pm SD$ | % Def & low | $\bar{X} \pm SD$ | % Def & low |
| Baseline | 105 | 26 ± 7 | 14.5 | 29 ± 11 | 20.0 | 27 ± 9 | 17.1 |
| 1 Month | 105 | 33 ± 10 | 6.0 | 36 ± 13 | 4.2 | 35 ± 12*** | 5.1** |
| 2 Months | 88 | 32 ± 11 | 13.3 | 34 ± 12 | 7.0 | 33 ± 11*** | 10.1 |
| 4 Months | 81 | 31 ± 9 | 13.5 | 31 ± 11 | 13.9 | 31 ± 10*** | 13.7 |
| 6 Months | 67 | 31 ± 6 | 3.2 | 34 ± 10 | 8.3 | 32 ± 9*** | 6.0* |

*** significantly higher compared to baseline $p < 0.001$
** significantly lower compared to baseline $p < 0.01$
* significantly lower compared to baseline $p < 0.05$

At baseline, 5.7% of the children had measles, 2.9% had chicken pox, 87.6% had upper respiratory tract infection (URTI) and 16.2% had diarrhea (Table 3). The proportion of children with infection significantly decreased one month after. However, the proportion of children with upper respiratory tract infections was still high but considerably lower than baseline. The decrease in the proportion of children with URTI and diarrhea from the baseline to the succeeding follow-ups was significant ($p < 0.01$). The decrease in proportion of children with measles from the baseline up to one month after the dose was likewise significant ($p < 0.01$). None of the children had chicken pox, 1% had measles and 2.9% had diarrhea after one month. Episodes of URTI were observed from the second to the sixth month while that of diarrhea was observed up to the fifth month only.

Intake of vitamin (vitamin A, $B_1$, $B_2$ and C) and mineral (iron) supplements and previous massive dose of vitamin A administered during the September 1994 ASAP had apparently no effect on the plasma retinol values (Table 4). The mean serum retinol values were similar in the subjects with and without supplements (data shown). However, intake of supplements were rather irregular. Forty-two of the children with supplements received a previous high dose of vitamin A during the September 1994 ASAP. The baseline mean serum retinol values of the children who received the massive dose vitamin A (28 ± 8 µg/dl) was similar compared to those who did not receive tha dose (27 ± 10 µg/dl). The proportion of children with deficient and

Table 3

Incedence of infection within one month before each blood collection period.

| | Measles | Chicken pox | URTI | Diarrhea |
|---|---|---|---|---|
| Baseline | 5.7 | 2.9 | 87.6 | 16.2 |
| 1 Month | 1.0* | 0 | 16.2* | 2.9* |
| 2 Months | 0 | 0 | 41.9* | 4.8* |
| 4 Months | 0 | 0 | 28.6* | 1.0* |
| 6 Months | 0 | 0 | 7.6* | 0 |

* significantly lower compared to baseline

Table 4

Mean serum retinol and prevalence of deficient and low levels among children with and without previous massive dose of vitamin A.

| | With dose | | Without dose | |
|---|---|---|---|---|
| | $\bar{X} \pm SD$ | % Def & low | $\bar{X} \pm SD$ | % Def & low |
| Baseline | 28 ± 8 | 11.9 | 27 ± 10 | 20.6 |
| 1 Month | 36 ± 12 | 5.3 | 34 ± 11 | 5.0 |
| 2 Months | 32 ± 9 | 8.8 | 33 ± 13 | 11.1 |
| 4 Months | 31 ± 9 | 12.5 | 31 ± 11 | 14.6 |
| 6 Months | 31 ± 9 | 10.7 | 34 ± 9 | 2.6 |

Table 5

Mean hemoglobin levels and prevalence of anemia at baseline and after the dose.

| Time of collection | Male | | Female | | Total | |
|---|---|---|---|---|---|---|
| | $\bar{X}$ ± SD | % Anemic | $\bar{X}$ ± SD | % Anemic | $\bar{X}$ ± SD | % Anemic |
| Baseline | 10.9 ± 1.2 | 45.5 | 11.0 ± 1.3 | 46.0 | 11.0 ± 1.2 | 45.7 |
| 1 Month | 10.9 ± 1.3 | 47.3 | 11.0 ± 1.5 | 42.0 | 10.9 ± 1.4 | 44.8 |
| 2 Months | 10.9 ± 1.1 | 38.2 | 11.4 ± 1.2 | 30.0 | 11.2 ± 1.2 | 34.3 |
| 4 Months | 11.2 ± 1.2 | 29.1 | 11.6 ± 1.2 | 28.0 | 11.4 ± 1.2 | 28.6 |
| 6 Months | 11.7 ± 1.2 | 21.8 | 11.6 ± 1.3 | 28.0 | 11.6 ± 1.3 | 24.8 |

low levels at baseline among those with the high dose was likewise not significantly lower than those without the dose (11.9% and 20.6% for those with and without the massive dose respectively). All follow-up mean serum retinol levels and proportion of deficient to low values in children with and without previous massive dose were likewise similar.

There was an increase in hemoglobin level from 11.0 ± 1.2 g/dl at baseline to 11.6 ± g/dl after 6 months (Table 5). Likewise the proportion of children with Hb < 11.0 g/dl steadily declined from 45.7% at baseline to 24.8% after 6 months.

## DISCUSSION AND RECOMMENDATIONS

There are different intervention strategies in the control of vitamin A deficiency. Long term measures are designed to increase the availability and consumption of foods rich in vitamin A. Medium term measures include the fortification of food. The administration of a hihg dose vitamin A supplements to at risk groups constitutes the short term measure (WHO, 1988). Periodic supplementation with large doses of vitamin A is intended to protect the individual against deficiency and its severe consequences over a certain period of time by building up a buffer stock of the vitamin in the liver (WHO, 1988). This is done when urgent and immediate action is needed in areas where vitamin A deficiency is a public health problem.

A measure of the extent to which an intervention program has succeeded is when a shift to the right in the lower portion of the frequency distribution curve of serum vitamin A levels in a population is observed (IVACG, 1989). A shift to the right from the baseline curve of this study is clearly seen in Fig 1 indicating a general increase in the serum retinol levels of the children. The maximum rise in serum retinol was achieved one month after the dose, decreasing up to the fourth month and slightly increasing again on the sixth month. Although no apparent effect on the intake of supplement on vitamin A levels was observed, the irregular intake of supplements by the subjects could have helped maintain the retinol levels. A study by Humphrey *et al* (1993) has shown that priming with a small dose vitamin A improved the apparent retention of a dose delivered a week later and he has suggested that a large dose may be better retained during the seasons when vitamin A intake is adequate. This study was conducted during summer when fruits rich in vitamin A like mango were abundant and the intake of such could be considered as the priming dose.

The organic reserves of vitamin A was also replenished by the dose administered as shown by results of the S30DR approach. This measures the dose response of a supplementation trial 30 days after administration of the vitamin. The dose response test has also showed that vitamin A deficiency in this group of subjects is caused by an absolute or relative deficit of vitamin A intake (Flores, 1992). This can be corrected by an improved diet or the administration of supplements as shown in this study.

The interaction between vitamin A nutriture and infection is bidirectional whereby marginal vitamin A status leads to increased susceptibility to infection (Sommer *et al*, 1984) and serum retinol may decrease as a result of an increased vitamin A requirement during infection which could precipitate deficiency in individuals of previously marginal status (Filteau, 1993). The observed trend in serum retinol values in the children with infection is consistent with other studies. A study in Brazil

by Barreto *et al* (1994) showed that overall incidence of diarrhea episodes was significantly lower in the group supplemented with high dose vitamin A than in the placebo group. Vitamin A supplementation also significantly reduced the overall incidence of severe illnesses (especially diarrhea with dehydration) (Ross, 1995).

During vitamin A deficiency, the transport of iron from the liver to the erythropoietic tissues is possibly blocked (West *et al*, 1993). Supplementation with vitamin A then results in the mobilization of available stored iron and of increased iron utilization for hemoglobin formation (Bloem *et al*, 1990). A high dose of vitamin A to preschool children has resulted in an increase in hemoglobin and other iron parameters (Bloem *et al*, 1990). In another study by Mejia and Chew (1988), iron parameters also increased after supplementation with vitamin A. Results of this study has likewise shown the same trend. The increase in hemoglobin levels and the proportion of anemic children was observed up to 6 months after supplementation.

Results of this study have shown that the WHO recommendation of administering a high dose of 200,000 IU of vitamin A to preschool children, 1-5 years of age is enough to maintain serum retinol concentrations higher than the presupplementation levels up to 6 months after the administration of the dose and reduce the proportion of children with deficient to low levels. Values however were highest one month after the dose. Increased intake of foods high in vitamin A and intake of supplement can help maintain the serum vitamin A levels. Incidence of infection also decreased among the children. Vitamin A supplementation can likewise increase hemoglobin levels and decrease the proportion of anemic children.

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