

# Effects of Vitamin A Supplementation during Pregnancy and Early Lactation on Body Weight of South African HIV-infected Women

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## ABSTRACT

Effects of vitamin A supplementation during pregnancy and early lactation on maternal weight among HIV-1-seropositive South African women were examined. Three hundred twelve HIV-seropositive pregnant women between 28 and 32 weeks gestation were studied as part of a randomized, double-blind, placebo-controlled trial at the King Edward VIII Hospital in Durban, South Africa. Patients were randomized to receive placebo or 5,000 IU of retinyl palmitate and 30 mg of beta-carotene daily during pregnancy. At delivery, patients received placebo or 200,000 IU of retinyl palmitate. The main outcome measures were prenatal and postnatal maternal weight and weight loss at three months after delivery as measured in body mass index (BMI). Supplementation of vitamin A was not associated with improvements in prepartum weight gain but was significantly associated with improved weight retention three to six months after delivery ( $p=0.02$ ). The benefit of vitamin A supplementation appeared to be confined to subgroups with baseline CD4+ count  $<200$  cells/ $\mu$ L and serum retinol 0-20  $\mu$ g/dL. Similar trends were observed in maintenance of postpartum BMI. However, no statistically significant associations were observed. Although there was no benefit of vitamin A supplementation on prepartum weight gain, a benefit on maintenance of postnatal weight was observed. The benefit was highest among those who were vitamin A-deficient or whose CD4+ count was  $<200$  cells/ $\mu$ L presupplementation. In populations for whom antiretroviral therapy is not readily available or accessible, the finding that vitamin A may improve postpartum weight lends some hope to a relatively inexpensive treatment which could be used for helping ameliorate some weight loss which is common during HIV infection.

**Key words:** Vitamin A; Vitamin A deficiency; Body weight; HIV; HIV infections; Pregnancy; Lactation; Weight gain; Nutrition; Randomized controlled trials; Double-blind method; South Africa

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## INTRODUCTION

During December 1998-December 1999, an estimated four million new HIV-infected cases were identified in sub-Saharan Africa. More than 50% were women of childbearing age, along with some infants (1,2). Since antiretroviral treatment is prohibitively expensive and inaccessible for most HIV-infected people living in developing countries, affordable alternative treatment

strategies need to be developed urgently. One such alternative is vitamin A.

Vitamin A, an important micronutrient, aids in modulating normal immune function through lymphopoiesis and cellular differentiation (3). Vitamin A deficiency may lead to alterations in immunity, including pathological changes in the mucosal surfaces, impaired antibody responses to challenge protein antigens, decreased CD4+ and CD28 cell populations, and altered T and B-cell function (3).

Vitamin A deficiency, common among HIV-infected individuals (4-7), is associated with the development of HIV-related disease sequelae and increased progression to AIDS and death (8-13). Vitamin A deficiency among HIV-infected pregnant women has also been associated with an increased risk of vertical transmission of HIV infection (5,6).

The relationship between HIV infection and vitamin A deficiency is not well-understood. Clinical evidence suggests that HIV infection may lead to nutritional deficiency through decreased food intake, malabsorption, or increased use and excretion of nutrients (10,11). HIV infection may increase use of vitamin A, depleting vitamin A stores in the liver.

Since HIV infection adversely affects nutrition, it is likely that, during HIV infection, the loss of vitamin A and other micronutrients may result in poor anthropometric status. Our understanding of the effect which HIV infection itself has on micronutrient status and the possible effect it may have on vitamin A stores have led many to question whether replacement of one such important micronutrient (vitamin A) may have an effect on nutrition status. This question is especially salient, given the observation that vitamin A deficiency is common among HIV-infected individuals, which may lead to clinical complications. We investigated whether supplementation of vitamin A to a cohort of HIV-infected pregnant women, given as part of a randomized, double-blind, placebo-controlled trial to prevent vertical transmission of HIV, improved maternal nutrition status, as judged by markers of maternal weight and weight gain.

## MATERIALS AND METHODS

The detailed methods of this study have been reported earlier (14). Briefly, the trial was conducted in the context of a larger trial at the King Edward VIII Hospital in

Durban, South Africa. Women who attend the antenatal clinic are referred by local community healthcare providers unable to provide care for women with complicated pregnancies. The hospital is situated in KwaZulu-Natal, the province at the epicentre of the HIV epidemic in South Africa. The current estimate of the HIV prevalence at the clinic is 27%. Women, recruited during July 1995-September 1997, were randomized to receive vitamin A or placebo. Vitamin A treatment comprised a daily vitamin A capsule containing 5,000 IU of retinyl palmitate and 30 mg beta-carotene. The women started to receive the treatment between 28 and 32 weeks gestation. Women in the vitamin A group received a megadose of 200,000 IU of retinyl palmitate at delivery given in liquid form. Women in the placebo group received an identical-looking placebo on the same schedule. No study women received any antiretroviral therapy.

All women attending the antenatal clinic were screened for HIV-1 with their consent by ELISA (Wellcozyme, Wellcome Diagnostics, Dartford, UK). For women whose tests were positive on ELISA, a confirmatory test was performed using the western blot (Bio-Rad Laboratories, Hemel Hempstead, UK). Women who were HIV-positive and who were in their third trimester of pregnancy were informed of the study and were asked for their consent to participate. At registration, baseline demographic and clinical information, weight using a calibrated digital scale, and height using a stadiometer were collected. After registration, the women were asked to attend a follow-up clinic four weeks after registration, and at one week, three months, and six months postpartum. At delivery and at each follow-up visit, the women were weighed on a calibrated digital scale.

Venous blood was collected from mothers on entry to the study for baseline differential count and lymphocyte subset analysis. The CD4 T-cell subset was enumerated by flow cytometry on a Coulter EPICS Profile 2 Flow Cytometer (Coulter Electronics, Miami, FL, USA) using specific monoclonal antibodies. Baseline serum vitamin A concentrations were determined by reverse-phase high-pressure liquid chromatography (15).

The study was approved by the Ethics Committee of the University of Natal and the Institutional Review Board of Columbia University. Written informed consents were obtained from all women who participated in the trial.

### Statistical methods

Analyses of data were based on intent-to-treat comparisons of the two groups as randomized. To determine the comparability between the treatment groups in baseline clinical and demographic information, means and proportions were calculated to present continuous and categorical baseline data. Student's *t*-test for continuous variables and  $\chi^2$  statistics for categorical variables were calculated to determine whether any statistically significant differences existed in means or proportions between the treatment groups.

Two parameters were used for assessing maternal weight gain and weight retention: (1) prepartum weight gain (weight at delivery or four weeks before delivery minus weight at registration) and (2) postpartum weight retention (weight three to six months postpartum minus weight one week postpartum). Each parameter was divided by the time interval between the weight measures to correct for the effect of length of time on weight measures.

Calculations were also done using weight alone and with maternal weight converted to body mass index (BMI)–weight/height (2). To determine whether treatment had an effect on the primary endpoints (weight, weight gain, and weight retention), means and standard deviations were calculated for the treatment groups. Hypothesis was tested using Student's *t*-test to determine whether any statistically significant differences existed in mean weight or BMI between the treatment groups.

To control for the possible differences between the treatment and the placebo groups at baseline, a multivariate model using linear regression was used. Effects of possible interaction between treatment and baseline clinical information were also modelled using linear regression. All statistical analyses were completed using the SAS 6.12 software.

The original sample size calculated for this analysis estimated that 400 women would be required. This sample size was designed to detect a significant difference in weight gain as small as 0.73 kg per week with a standard deviation of 0.37 based on an average weekly weight gain of 0.43 kg, set by the Institute of Medicine's Subcommittee on Nutritional Status and Weight Gain During Pregnancy assuming power of 80% and an alpha level of 0.05 (16).

## RESULTS

### Study sample

Three hundred twelve HIV-seropositive women were recruited for the study. One hundred fifty-nine women were randomized to receive vitamin A treatment and 153 to receive placebo (Table 1). Of the 312 women enrolled, 217, 221, 160, 173, and 153 had information on weight four weeks before delivery, at delivery, and one week, three months, or six months postpartum respectively. The baseline and clinical characteristics of participants missing at each follow-up visit did not differ from the characteristics of those seen at that visit (Table 2).

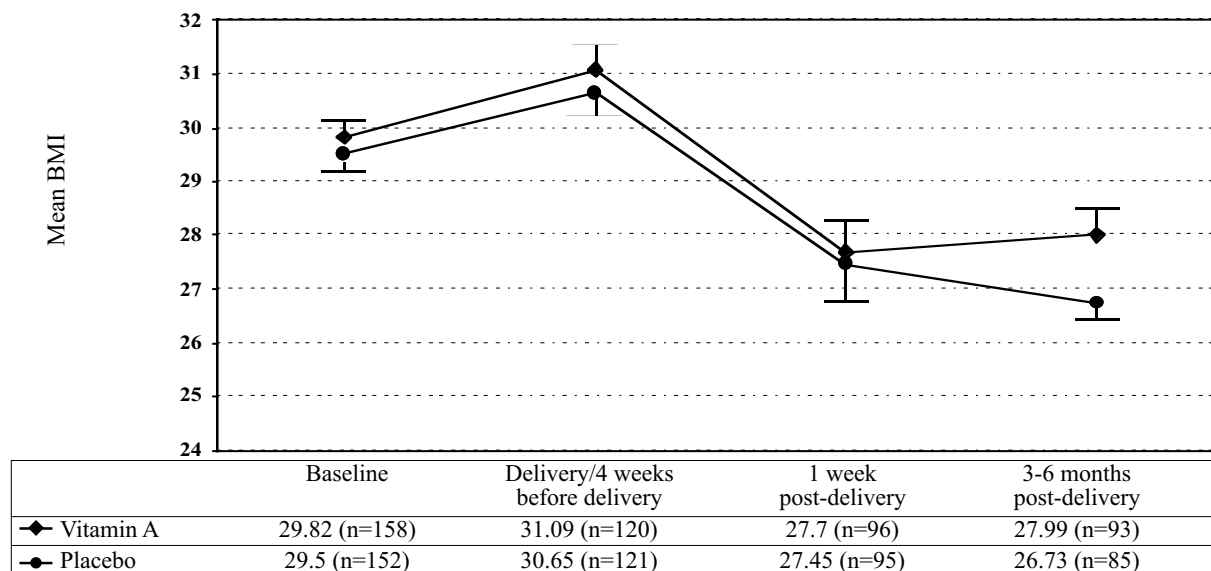
**Table 1.** Baseline demographic and clinical characteristics of 312 HIV-seropositive pregnant women at a mean gestational age of 29 weeks assigned to vitamin A and placebo

| Characteristic                       | Vitamin A group* | Placebo group* | p value† |
|--------------------------------------|------------------|----------------|----------|
| Number of women                      | 159              | 153            |          |
| Age (years)                          | 26.3±4.6         | 25.4±5.2       | 0.12     |
| Body weight (kg)                     | 73.1±13.2        | 72.6±14.9      | 0.77     |
| Height (m)                           | 1.56±0.06        | 1.56±0.06      | 0.95     |
| Body mass index (kg/m <sup>2</sup> ) | 29.7±5.0         | 29.5±5.7       | 0.65     |
| Gestational age at baseline          | 29.3±2.5         | 29.4±2.5       | 0.74     |
| Mean number of weeks of treatment    | 6.77±3.3         | 6.77±3.2       | 0.98     |
| Serum retinol level (µg/dL)          | 26.75±13.21      | 26.89±13.40    | 0.95     |
| CD4+ counts (cells/µL)               | 454.0±206.2      | 501.9±212.8    | 0.054    |
| CD8+ counts (cells/µL)               | 879.2±403.9      | 831.6±323.2    | 0.27     |
| Ratio of CD4+/CD8+                   | 0.57±0.34        | 0.64±0.29      | 0.053    |
| Haemoglobin (g/dL)                   | 10.5±1.2         | 10.5±1.3       | 0.73     |

\* The results are presented as the mean±standard deviation (SD)  
† p value using Student's *t*-test



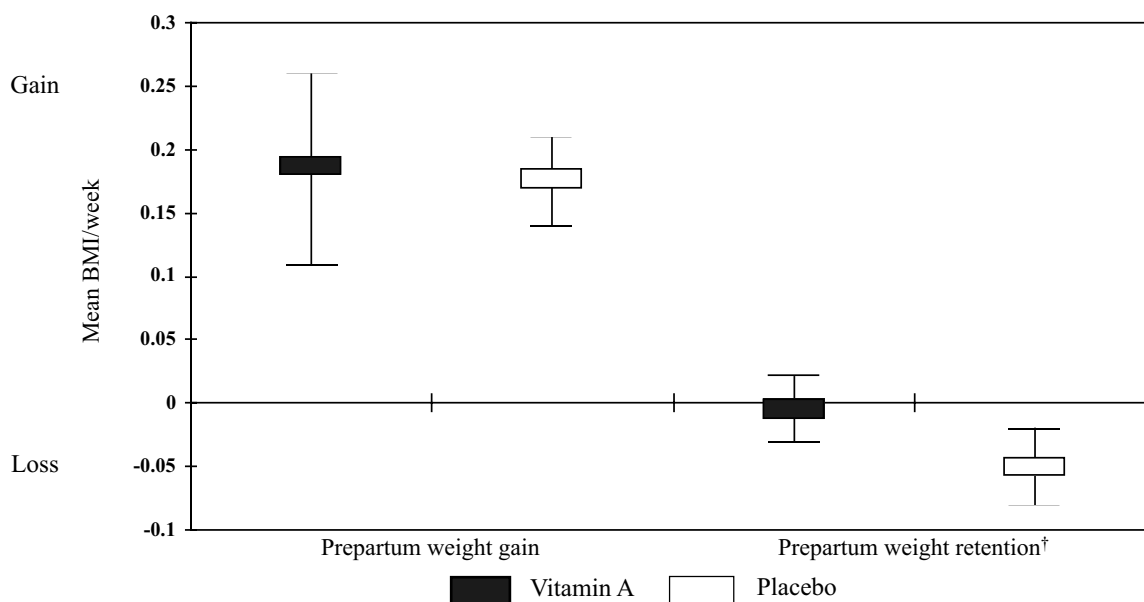
**Fig. 1.** Mean BMI (kg/m<sup>2</sup>) of HIV-seropositive women at baseline (29 weeks gestation), at delivery or four weeks before delivery, one week after-delivery and at three to six months post-delivery assigned to receive vitamin A supplementation or placebo



Standard error bars represented

Follow-up time

**Fig. 2.** Mean weight gain in BMI\*, at delivery four weeks before delivery, and weight retention three to six months post-delivery among HIV-seropositive women recruited 29 weeks gestation assigned to receive vitamin A supplementation or placebo



\* Mean gain in BMI: kg/m<sup>2</sup>/week ( $\pm$ 95% CI); † p=0.02 using Student's *t*-test; Prepartum weight gain: Weight at delivery or four weeks before delivery minus weight at registration/time interval between delivery or four weeks before delivery and registration; Postpartum weight retention: Weight three to six months after delivery minus weight one week after delivery/time interval between postpartum visit and one week visit

**Table 3.** Relation between baseline indices and mean BMI at specific follow-up interval

| Characteristic           | BMI baseline          |                  |          | BMI delivery <sup>†</sup> /Mean BMI (kg/m <sup>2</sup> ) |                  |          | BMI 3 months post-delivery <sup>‡</sup> |                  |          |
|--------------------------|-----------------------|------------------|----------|--|------------------|----------|---|------------------|----------|
|                          | Vitamin A             | Placebo          | p value* | Vitamin A  | Placebo          | p value* | Vitamin A                               | Placebo          | p value* |
|                          | CD4+ (cells/ $\mu$ L) |                  |          |  |                  |          |   |                  |          |
| <200                     | 30.90 $\pm$ 7.05      | 26.84 $\pm$ 4.14 | 0.08     | 31.22 $\pm$ 6.73   | 27.75 $\pm$ 3.99 | 0.20     | 30.08 $\pm$ 6.14                        | 22.28 $\pm$ 4.29 | 0.01     |
| 200-499                  | 29.55 $\pm$ 4.89      | 29.51 $\pm$ 5.56 | 0.96     | 30.30 $\pm$ 5.33   | 30.62 $\pm$ 5.78 | 0.75     | 27.74 $\pm$ 5.38                        | 27.17 $\pm$ 5.55 | 0.64     |
| $\geq$ 500               | 30.06 $\pm$ 5.50      | 30.25 $\pm$ 6.30 | 0.86     | 31.21 $\pm$ 6.64   | 31.43 $\pm$ 8.09 | 0.87     | 28.14 $\pm$ 5.37                        | 27.64 $\pm$ 5.58 | 0.70     |
| Haemoglobin (g/dL)       |                       |                  |          |  |                  |          |   |                  |          |
| 0-10                     | 28.08 $\pm$ 3.61      | 28.61 $\pm$ 5.24 | 0.58     | 28.33 $\pm$ 3.68   | 29.31 $\pm$ 5.86 | 0.38     | 25.83 $\pm$ 5.39                        | 26.67 $\pm$ 6.92 | 0.64     |
| >10                      | 30.72 $\pm$ 5.97      | 30.02 $\pm$ 5.59 | 0.41     | 31.71 $\pm$ 6.56   | 31.14 $\pm$ 5.34 | 0.56     | 28.95 $\pm$ 5.94                        | 26.94 $\pm$ 5.63 | 0.04     |
| Retinol ( $\mu$ g/dL)    |                       |                  |          |  |                  |          |   |                  |          |
| 0-19                     | 29.94 $\pm$ 5.35      | 28.29 $\pm$ 4.86 | 0.10     | 30.89 $\pm$ 6.42   | 29.27 $\pm$ 7.75 | 0.21     | 28.44 $\pm$ 5.67                        | 25.67 $\pm$ 3.99 | 0.03     |
| 20-29                    | 29.51 $\pm$ 5.82      | 29.23 $\pm$ 6.23 | 0.82     | 30.16 $\pm$ 5.76   | 30.12 $\pm$ 6.70 | 0.98     | 26.55 $\pm$ 6.19                        | 27.32 $\pm$ 7.42 | 0.71     |
| $\geq$ 30                | 29.92 $\pm$ 6.14      | 29.17 $\pm$ 5.77 | 0.58     | 30.75 $\pm$ 6.31   | 30.04 $\pm$ 6.18 | 0.62     | 28.07 $\pm$ 6.34                        | 26.09 $\pm$ 4.41 | 0.12     |
| Supplement given (weeks) |                       |                  |          |  |                  |          |   |                  |          |
| 0-7                      | 29.78 $\pm$ 4.87      | 28.94 $\pm$ 5.20 | 0.30     | 31.07 $\pm$ 5.66   | 29.28 $\pm$ 7.06 | 0.18     | 27.90 $\pm$ 5.33                        | 25.35 $\pm$ 4.41 | 0.01     |
| >7                       | 29.75 $\pm$ 6.01      | 29.92 $\pm$ 6.16 | 0.87     | 30.50 $\pm$ 6.13   | 31.02 $\pm$ 6.26 | 0.65     | 28.07 $\pm$ 5.52                        | 27.74 $\pm$ 6.45 | 0.79     |

\* p value derived from Student's *t*-test within stratum; <sup>†</sup> BMI at delivery or four weeks before delivery; <sup>‡</sup> BMI three to six months after delivery

maternal BMI and parameters of prepartum weight gain and retention of postpartum weight within subgroups stratified by CD4+ T-lymphocyte count, haemoglobin, serum retinol level at baseline, and by weeks on treatment. Maternal BMI three to six months after delivery was higher among the vitamin A-supplemented group whose CD4+ T-lymphocyte count was <200 cells/ $\mu$ L at baseline ( $p=0.01$ ). Likewise, the vitamin A-supplemented group also experienced higher BMI three to six months after delivery among those whose serum retinol level was between 0 and 20  $\mu$ g/dL (Table 3) at baseline ( $p=0.03$ ). In addition, the vitamin A-supplemented group also experienced higher BMI three to six months after delivery among those whose haemoglobin level was >10 g/dL ( $p=0.04$ ). Retention of postpartum weight was calculated using weight unadjusted for height, and the results were similar.

### Interactions

Linear regression models were used for testing whether the apparent interaction between presupplementation CD4+ T-lymphocyte count <200 cells/ $\mu$ L and vitamin A treatment on predicting BMI retention three to six months postpartum was statistically significant. A statistically significant interaction between CD4+ T-lymphocyte <200 cells/ $\mu$ L and treatment was observed in predicting at BMI retention three to six months postpartum ( $\beta=7.23$ ,  $p=0.01$ ). Interactions between serum retinol levels and treatments were not statistically significant.

### Analyses for placebo group

Stratified analyses were conducted among the placebo group only to investigate whether associations between indicators of the severity of HIV infection (CD4+ count, haemoglobin levels, and serum retinol levels at baseline) and maternal BMI pre- and postpartum were clinically relevant (Table 4). Women whose CD4+ T-lymphocyte count was  $\geq$ 500 cells/ $\mu$ L had statistically significant greater mean BMI during the prepartum (at baseline,  $p=0.04$ , at delivery or four weeks before delivery,  $p=0.04$  and postpartum (three to six months after delivery,  $p=0.02$  periods compared to those whose CD4+ T-lymphocyte count was <200 cells/ $\mu$ L (Table 3). Mean weekly BMI gain during the prepartum period was also greater in

**Table 4.** Risk factors for weight and weight gain (BMI) among placebo group

| Characteristic        | Baseline         |                   |                | Weight at delivery <sup>†</sup> |                   |                | Prepartum weight gain <sup>§</sup> |                   |                | Weight 3-6 months post delivery |                   |                | Postpartum weight retention <sup>**</sup> |                   |                |
|-----------------------|------------------|-------------------|----------------|---------------------------------|-------------------|----------------|------------------------------------|-------------------|----------------|---------------------------------|-------------------|----------------|---|-------------------|----------------|
|                       | Mean             | $\beta^{\dagger}$ | p <sup>‡</sup> | Mean                            | $\beta^{\dagger}$ | p <sup>‡</sup> | Mean                               | $\beta^{\dagger}$ | p <sup>‡</sup> | Mean                            | $\beta^{\dagger}$ | p <sup>‡</sup> | Mean                                      | $\beta^{\dagger}$ | p <sup>‡</sup> |
| CD4+ (cells/ $\mu$ L) |                  |                   |                |                                 |                   |                |                                    |                   |                |                                 |                   |                |   |                   |                |
| <200*                 | 26.84 $\pm$ 4.14 |                   |                | 27.75 $\pm$ 3.99                |                   |                | 0.05 $\pm$ 0.13                    |                   |                | 22.29 $\pm$ 4.29                |                   |                | -0.07 $\pm$ 0.03                          |                   |                |
| 200-499               | 29.52 $\pm$ 5.56 | 2.67              | 0.13           | 30.62 $\pm$ 5.78                | 2.87              | 0.12           | 0.12 $\pm$ 0.17                    | 0.07              | 0.15           | 27.18 $\pm$ 5.55                | 4.88              | 0.03           | -0.07 $\pm$ 0.06                          | 0.008             | 0.88           |
| $\geq$ 500            | 30.25 $\pm$ 6.30 | 3.41              | 0.04           | 31.43 $\pm$ 8.09                | 3.68              | 0.04           | 0.14 $\pm$ 0.14                    | 0.08              | 0.08           | 27.64 $\pm$ 5.58                | 5.35              | 0.02           | -0.05 $\pm$ 0.05                          | 0.01              | 0.72           |
| Haemoglobin (g/dL)    |                  |                   |                |                                 |                   |                |                                    |                   |                |                                 |                   |                |   |                   |                |
| 0-10*                 | 28.61 $\pm$ 5.24 |                   |                | 29.31 $\pm$ 5.86                |                   |                | 0.10 $\pm$ 0.15                    |                   |                | 26.67 $\pm$ 6.92                |                   |                | -0.07 $\pm$ 0.04                          |                   |                |
| >10                   | 30.03 $\pm$ 5.59 | 1.41              | 0.19           | 31.14 $\pm$ 5.34                | 1.83              | 0.17           | 0.13 $\pm$ 0.13                    | 0.02              | 0.39           | 26.95 $\pm$ 5.63                | 0.27              | 0.85           | -0.06 $\pm$ 0.06                          | 0.01              | 0.74           |
| Retinol ( $\mu$ g/dL) |                  |                   |                |                                 |                   |                |                                    |                   |                |                                 |                   |                |   |                   |                |
| 0-19*                 | 28.30 $\pm$ 4.86 |                   |                | 29.27 $\pm$ 7.58                |                   |                | 0.09 $\pm$ 0.16                    |                   |                | 25.67 $\pm$ 3.99                |                   |                | -0.01 $\pm$ 0.03                          |                   |                |
| 20-29                 | 29.23 $\pm$ 6.23 | 0.93              | 0.46           | 30.12 $\pm$ 6.70                | 0.85              | 0.65           | 0.11 $\pm$ 0.12                    | 0.02              | 0.63           | 27.32 $\pm$ 7.42                | 1.65              | 0.27           | -0.05 $\pm$ 0.03                          | -0.03             | 0.31           |
| $\geq$ 30             | 29.19 $\pm$ 5.77 | 0.88              | 0.47           | 30.04 $\pm$ 6.18                | 0.77              | 0.54           | 0.12 $\pm$ 0.18                    | 0.03              | 0.47           | 26.09 $\pm$ 4.41                | 0.41              | 0.78           | -0.09 $\pm$ 0.06                          | -0.08             | 0.02           |

\* Reference group; <sup>†</sup>  $\beta$  coefficient obtained from linear regression models; <sup>‡</sup> p value using linear regression; <sup>§</sup> Weight at delivery or four weeks before delivery; <sup>\*\*</sup> Weight at delivery or four weeks before delivery minus weight at baseline; <sup>§§</sup> Weight three to six months post-delivery minus weight one week after delivery

those whose CD4+ T-lymphocyte count was  $\geq$ 500 cells/ $\mu$ L compared to those whose CD4+ T-lymphocyte count was <200 cells/ $\mu$ L (Table 4). Those whose haemoglobin level were >10 g/dL had statistically significant greater mean weekly BMI gain during the prepartum period compared to those whose haemoglobin level was between 0 and 10 g/dL. No relation was found between BMI within serum retinol level (Table 4). Analyses were conducted using weight alone, and the results were similar.

## DISCUSSION

This is the first study to examine the effects of vitamin A supplementation on macro-nutritional parameters of HIV-1-infected adults. Evidence from this study suggests that there is an association between vitamin A supplementation prenatally and retention of postpartum weight, the benefit being greater among those who were vitamin A-deficient or whose CD4+ T-lymphocyte count was <200 cells/ $\mu$ L at baseline.

Vitamin A supplementation did not have any effect on weight and weight gain prenatally. Reasons for this are unclear but may be related to any increase in serum retinol which would have been used by the foetus to help sustain foetal growth. There is evidence to suggest that 'during pregnancy' extra vitamin A is needed for the growth and maintenance of the foetus, building vitamin A reserves in the foetal liver and for maternal tissue growth (17). Evidence also suggests that increase in serum retinol is often used by the foetus, implying that the needs of the foetus take pre-eminence (18). In this cohort of pregnant women, 66% were vitamin A-deficient (serum retinol level <29  $\mu$ g/dL), and 37% were severely vitamin A-deficient (serum retinol level <20  $\mu$ g/dL) at entry into the study. Since extra vitamin A, above the recommended levels, is needed to sustain foetal growth and development, it is possible that the added benefit of supplementation prepartum would have been used by the foetus and may not have conferred any benefits in anthropometric status of the mothers.

The apparent improvement in weight retention postnatally might have occurred, because foetal needs are no longer competing for vitamin A reserves or this may be related to the large dose given at delivery. Given the observations that, during pregnancy, extra vitamin A is needed for the growth, development, and maintenance of foetal organs, the added benefit of supplementation prenatally may not have been realized, since foetal requirements would compete for vitamin A stores among

supplemented individuals, thereby limiting the amount used by the body to sustain the growth of maternal tissue. However, once the foetal needs no longer compete for vitamin A, one may surmise that supplementation may have helped confer some benefit, one being the improvement in anthropometric status. The large-dose supplementation given at delivery may have conferred the greatest benefit.

In subgroup analyses, the benefits on postpartum weight were greatest among those who were vitamin A-deficient or whose CD4+ T-lymphocyte count was <200 cells/ $\mu$ L. These findings suggest that supplementation may only benefit those with more advanced HIV infection or below a certain threshold level of micronutrient deficiency. Of those who were vitamin A-deficient at baseline, the benefit of supplementation may have helped improve retinol stores to a level at which the growth of maternal tissue was sustainable. This same benefit may not have been conferred to those who were not vitamin A-deficient, since any added supplementation would not have raised the serum retinol levels to a point in which the growth of maternal tissue would be better than that experienced before supplementation.

Evidence from this study also suggests that retention of postpartum weight was greatest among those whose baseline haemoglobin level was >10 g/dL. Although there is evidence clearly suggesting that vitamin A deficiency can result in iron-deficiency anaemia (19) and may interfere with iron metabolism (20,21), most women in this population received iron supplementation at baseline as part of their antenatal care. Therefore, baseline iron levels may not reflect levels subsequent to registration in the study. It is possible that those who showed signs of iron-deficiency at baseline may not have been deficient during subsequent follow-up periods.

Results of analyses done among the placebo group suggest that individuals with CD4+ T-lymphocyte count  $\geq$ 500 cells/ $\mu$ L have greater weight during pre- and postpartum follow-up periods compared to those with CD4+ T-lymphocyte count <200 cells/ $\mu$ L at baseline. Similar results were obtained among those with haemoglobin level >10 g/dL. Pre- and postpartum weight tended to be greater in this group compared to those with haemoglobin level <10 g/dL at baseline. These results are plausible, given the prevailing knowledge regarding the interrelation between HIV infection and CD4+ T-lymphocyte count and haemoglobin levels, in that HIV infection leads to decreased CD4+ T-lymphocyte count

and malabsorption of micronutrients, both of which may have an impact on weight (22-24). It also suggests that weight parameters considered here may be clinically meaningful.

Very little is known about the association between vitamin A and indices of weight among HIV-infected pregnant women. No other studies, either observational or experimental, have investigated the association between vitamin A and indices of weight among HIV-infected pregnant women. Thus, the suggestion that vitamin A may offer some clinical benefits to HIV-infected adults should be further investigated.

An important finding of this study is that the randomization process seems to have accomplished its desired aims of attaining *ceteris paribus*, all else being equal. External factors which may have confounded the association between weight and weight gain/retention and treatment were more or less distributed evenly between both the treatment groups. Thus, the associations found between basal weight, weight gain/retention and vitamin A treatment are not likely to be confounded by extraneous factors. Consistent with the strengths of a clinical trial, selection into a particular exposure group, i.e. treatment group, was determined by the investigators and not by nature. In addition, the temporal order of the association between treatment and weight and weight gain/retention is known.

However, the study has several limitations. The first limitation is that the dose used during the prepartum period (5,000 IU daily) was directed to reduce perinatal transmission and may not have been optimal for the treatment of maternal disease. The second limitation is that mostly asymptomatic HIV-infected women were recruited for the study. The participants may not have been ill enough to benefit from treatment with vitamin A. The third limitation was loss-to-follow-up. Although we observed no differences between those who were lost to follow up and those retained in the study, we cannot rule out possible selection bias. In addition, the sample size was relatively small and had low power to detect mere subtle associations. Lastly, the findings of this study were limited to a cohort of HIV-infected pregnant women recruited during their third trimester of pregnancy. The complexity of pregnancy may have had a bearing on the association found between vitamin A supplementation and weight and weight gain/retention.

In populations for whom antiretroviral therapy is readily available and accessible, the findings of the study

may not add knowledge to alternative treatment modalities. However, in populations for whom antiretroviral therapy is not readily available or accessible, the finding that vitamin A may improve postpartum weight lends some hope to a relatively inexpensive treatment which could be used for helping ameliorate some weight loss which is common during HIV infection. Additional research is urgently needed to help better understand these effects.

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