

HIV and nutrition: pregnant and lactating women

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*Consultation on Nutrition and HIV/AIDS in Africa:
Evidence, lessons and recommendations for action*

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1. Introduction

According to UNAIDS, approximately 17 million women worldwide between the ages of 15 and 49 years are HIV positive. Most (77%) live in sub-Saharan Africa. In some regions, such as Botswana and Swaziland, the HIV prevalence in women attending antenatal clinics is as high as 40% (1). Despite the many women of reproductive age who are HIV positive, few studies have investigated the relationship between HIV infection during pregnancy or lactation with a focus on maternal nutritional status and health. In most trials in HIV-positive pregnant women, the primary focus has been the effect on the infant rather than the HIV-positive mother. More detailed information on mother to child HIV transmission is reviewed elsewhere (2). In antiretroviral therapy trials to date, the intervention uses the woman to deliver prevention to the infant rather than being for her benefit.

Although the World Health Organization (WHO) recommends that HIV-positive mothers avoid breastfeeding “when replacement milk is acceptable, feasible, affordable, sustainable and safe” (3), breastfeeding is the social norm in many parts of the world for both HIV-positive and -negative mothers. Anecdotal reports suggest that considerable stigma is associated with not breastfeeding. Despite concerns about the HIV transmission risk to the infant from breastfeeding and the possible effect of breastfeeding on the health and nutrition of HIV-positive mothers (4), use of replacement milks is largely considered unacceptable, unaffordable or unsafe (5-8). Therefore, breastfeeding likely will remain the norm for HIV-positive mothers in most of Africa irrespective of the effect of lactation on the health of the HIV-positive mother.

This chapter briefly reviews general nutrient needs during pregnancy and lactation and the effect of HIV on nutritional status and it discusses reports on nutritional status of HIV-positive women during pregnancy and lactation. The Medline search strategy for the literature review included the search words HIV and lactation, HIV and mothers, HIV and women, HIV and breastfeeding, and HIV and nutrition. Additional searches were performed with the limits of AIDS, human and female, and included search words nutrition, micronutrients, lactation and nutrition, pregnancy and nutrition, lactation and weight or body composition, and pregnancy and weight or body composition. HIV-

related papers identified were focused primarily in women in Africa; none was focused on women in Asia.

2. Nutritional needs during pregnancy

Pregnancy is an anabolic condition that affects the metabolism of all nutrients in order to support maternal homeostasis, foetal growth and development and to prepare for lactation. In response to these new demands for nutrients, one or more of the following can occur: increased deposition of maternal stores and foetal tissue, redistribution of nutrients, and increase or decrease in nutrient absorption and rate of metabolism. For adequate energy support, the maternal response may be an increased appetite and food intake, a reduction in lipid synthesis and maternal fat storage, a reduction in basal metabolic rate and/or a reduction in physical activity (9). Although multiple potential mechanisms can adjust for nutrient metabolism, the capacity to make adjustments is limited. If nutrient intake falls below a threshold, foetal growth and development are compromised as is maternal health (9).

Similarly, adequate weight gain during pregnancy is important for optimal foetal growth and development and for maternal fat store deposits whereas inadequate weight gain is associated with intrauterine growth retardation and perinatal mortality. Improved maternal and infant outcomes are associated with the recommended weight gains, as shown in Table 1. It is generally recommended that women who begin pregnancy with a normal body mass index (BMI, expressed as kg/m^2 ; 19.8–26) gain 11–16 kg during pregnancy. Of this weight gain, approximately 4 kg will be deposited as maternal fat stores (10). Excessive gestational weight gain is a concern because of the increase in obesity across populations worldwide. A review of literature on North American pregnant women from a variety of subpopulations found that a weight gain of more than 16 kg was consistently associated with postpartum weight retention of more than 6 kg (11).

The pattern of weight gain during pregnancy is variable. In a study of approximately 400 pregnant women in Brazil, the mean gestational weight gain was 12.9 kg (95% confidence interval [CI] 12.2, 13.6; range –6.0 to 33.0 kg) (12); those with a greater gestational weight gain had higher postpartum weight retention. In a large study of multiracial American women receiving regular

prenatal care and who were well nourished during pregnancy, the average rate of weight gain was slowest in the first trimester and highest in the second trimester (13), consistent with other reports (10).

During pregnancy the maternal requirements for protein, folate, niacin, zinc, iron and iodine in particular are 30–50% higher than before pregnancy (14). During the first half of pregnancy, extra nutrients are primarily required for the increase in maternal tissues, such as expansion of blood and extracellular fluid volume, enlargement of the uterus and mammary tissue and fat deposition. During the third trimester the additional nutrients are mainly used by the foetus for rapid growth and storage.

The diversity of an individual's response to changes in nutrient metabolism makes nutritional assessment of the pregnant woman complex (15). Interpretation of micronutrient status during pregnancy is a challenge because nutrient levels may be influenced by hormone-induced metabolic changes as well as shifts in plasma volume. No pregnancy-specific nutrient laboratory reference values are available for comparison, thus assessment of micronutrient status during pregnancy is difficult (14). Although the total amount of a nutrient in the blood may be increased, its concentration may be decreased because of increased plasma volume. In general, concentrations of water-soluble vitamins are lower during pregnancy whereas concentrations of fat-soluble vitamins are unchanged or slightly higher (16).

2.1. Effect of maternal nutrition on infant and maternal health

Poor weight gain during pregnancy reflects maternal malnutrition (17). The effect of poor nutrition on maternal and infant morbidity and mortality in HIV-negative mothers is well documented. Poor nutritional status before and during pregnancy has been associated with intrauterine growth retardation, low birth weight and premature delivery conditions (11,18,19); these events are also associated with maternal HIV infection (20). Iron deficiency anaemia is associated with inadequate maternal weight gain, toxemia, and labor and delivery complications with increased risk of maternal mortality (21,22). Though little has been published on the effect of malnutrition on maternal health, Tomkins (23) review concluded that malnutrition contributes to the high rate of maternal morbidity and mortality in developing countries. For example, in Nepal where vitamin A

deficiency is relatively common among women, supplementation of vitamin A or β -carotene reduced maternal mortality by 44% compared with a placebo control group (24).

If a woman is poorly nourished before pregnancy, an inadequate supply of nutrients, whether from dietary intake or maternal stores, may cause a physiological competition for nutrients between the mother and the foetus, placing the well being of each at risk. King (25) suggested that nutrients are partitioned differently between mother and foetus depending on the mother's preconception nutrition status. In marginally depleted mothers, the nutrients are preferentially allocated to maternal tissues whereas in severely depleted mothers, foetal needs take priority.

2.2. Effect of HIV on nutritional status

HIV-positive women in developing countries are particularly vulnerable to nutrient deficiencies because of likely inadequate dietary intake and potentially increased nutrient requirements associated with HIV and other infections and the nutritional demands of pregnancy. HIV infection in adults has been associated with weight loss, progressive loss of fat-free mass (FFM) and fat mass (FM), and wasting, all associated with increased morbidity and mortality risks (26). More detailed information is reviewed elsewhere (27). Grinspoon et al. (28) found that resting energy expenditure in 33 HIV-positive women was higher ($119\% \pm 23\%$) than in 26 HIV-negative weight-matched control women. In a study of nonpregnant women in Zaire, Thea et al. (29) found that 51 HIV-positive asymptomatic women had significantly more subcutaneous fat as measured by skinfold thicknesses and more lean body mass as measured by bioimpedance than 48 women with AIDS but less subcutaneous fat and lean body mass than 11 HIV-negative women. Several studies in HIV-positive women showed that at least initially, weight loss is primarily in the form of FM (30,31). Loss of weight or body cell mass was associated with poorer clinical outcomes in HIV-positive men (32-35).

Lindan et al. (36) conducted a prospective study of predictors of mortality in 460 HIV-positive Rwandan women of childbearing age (mean age 28 years). The 2-year mortality for all women was 7% (95% CI 5%, 10%); for the 40 women with AIDS at entry, mortality was 21% (95% CI 8%, 34%). HIV accounted for 90% of deaths during the 2 years of follow-up; independent

predictors of mortality included a BMI less than 21 at enrolment (relative hazard 2.3; CI 1.1, 4.8) and low income (relative hazard 2.3; CI 1.1, 4.5).

A complex bidirectional relationship exists among HIV infection, nutrition and immune function (37). Several studies in industrialized countries found an association between low blood levels of vitamins (vitamin A, vitamin E, riboflavin, pyridoxine and cobalamin) and minerals (copper and zinc) and HIV disease progression (38-42). More detailed information on micronutrients is reviewed elsewhere (43). However, little is known about micronutrient intake and status and HIV disease progression in developing countries nor about the micronutrient profile of women infected with HIV. Baum et al. (44) found that deficiencies of zinc and vitamins A and E were widespread in HIV-positive drug-abusing women in the United States and were more severe than in a similar cohort of men. In HIV-negative adults, inadequate micronutrient intake is associated with altered immune function. Hence there is concern that similar inadequate diets may compound the susceptibility to infection with a further worsening of immune function in HIV-positive individuals.

2.3. Effect of pregnancy on HIV

For most mothers in early stages of the HIV disease, pregnancy does not appear to accelerate disease progression (45-47). In a study of 151 pregnant women in Tanzania, the median viral load (copies of HIV-1 RNA) was stable at 18 weeks gestation (20.4×10^6 copies/L), delivery (20.2×10^6 copies/L) and 7 months postpartum (19.1×10^6 copies/L) (48). This is somewhat similar to findings in the United States where RNA levels were stable during pregnancy but increased modestly after delivery to 18 months postpartum whether or not the mother received antiretroviral therapy (49). In the Tanzanian study noted above, women with more advanced disease (WHO stage 2) had higher HIV viral loads (median 59×10^6 copies RNA/L) than those in stage 1 (median 18.3×10^6 copies/L, $P=0.03$), though there were no differences at other stages (48). In addition, the study found that median CD4+ T cell count increased from 18 weeks gestation (381×10^6 cells/L) to 7 months postpartum (444×10^6 cells/L) with the peak at delivery (516×10^6 cells/L). A decline in absolute CD4+ T cell count during pregnancy is consistent with the hemodilution of pregnancy, and CD4+ and CD8+ percentages during pregnancy appear stable overall (45). In addition, other studies suggested that

pregnancy itself is not associated with increased infections, HIV disease progression or HIV viral load RNA (50-54).

Potential inexpensive markers for measures of HIV disease progression in HIV-positive pregnant or lactating women such as lymphocyte proliferation, delayed hypersensitivity skin testing and antibody formation have not been validated (55,56). Use of surrogate markers of HIV disease is further complicated by potential influence of independent factors such as pregnancy, tuberculosis infection and treatment, and opportunistic infections (57,58). Mid-upper-arm circumference (MUAC) was not correlated to HIV RNA viral load in pregnant women (48).

2.4. HIV and nutrition during pregnancy: weight gain

Because maternal body composition is an important determinant of maternal health and reproductive success, determining the influence of HIV on body composition is important. There is a small but growing body of evidence on the effect of HIV infection on body weight and composition during pregnancy.

Ladner et al. (59) conducted a prospective study to evaluate the effect of HIV-1 on weight gain in Kigali, Rwanda. Enrolment included 101 HIV-positive and 106 HIV-negative women between 24 and 28 weeks gestation. At enrolment the mean BMI was not different for HIV-positive (24.1, SD 2.8) and HIV-negative women (24.5, SD 4.1; $P= 0.89$). At the end of pregnancy the mean weight was not statistically different between groups (HIV-positive women: 60.7 kg, SD 6.7; HIV-negative women: 63.0 kg, SD 10.2; $P= 0.08$). Overall the HIV-positive women gained less weight than the HIV-negative women during pregnancy, but the slopes reflecting the rates of weight gain between groups were not significantly different ($P= 0.058$). Few women were underweight in either group (BMI <20: 4% in HIV-positive women, 6% in HIV-negative women; $P= 0.40$) but the authors noted that weight and BMI gains during pregnancy in both HIV-positive and -negative women were low and less than recommended.

Villamor et al. (60) obtained monthly anthropometric measurements for 957 HIV-positive pregnant women in Tanzania. At baseline between 12 and 27 weeks gestation, 24% were asymptomatic and 12% had CD4+ cell counts less than 200×10^6 cells/L. Anaemia (hemoglobin <110

g/L) was found in 82% and malaria parasites were found in 19% of participants. The rate of weight gain decreased progressively during pregnancy as did MUAC. A lower baseline CD4+ T cell count ($<200 \times 10^6$ cells/L) was associated with a poorer rate of weight gain. In the second trimester, advanced HIV disease, low serum selenium and malarial disease contributed to decreased rates of weight gain; in the third trimester those with lower education level and helminthic infections at baseline had a decreased rate of weight gain. The rate of weight gain in these mothers was about 55–65% of that reported in pregnant women of undetermined HIV status in developed countries but similar to rates reported in developing countries.

The relationship between anthropometry and HIV status was examined in a cross-sectional study in Tanzanian women before week 23 of gestation (61). The mean BMI was no different between 1810 HIV-positive women (23.6, SD 3.4) and 11 950 HIV-negative women (23.5, SD 3.4) nor was the mean MUAC (HIV-positive women: 25.4 cm, SD 2.7; HIV-negative women: 25.5 cm, SD 2.7). Wasting, determined as MUAC less than 22 cm, was 34% (95% CI 3%, 73%) more prevalent among HIV-positive mothers after adjustment for height, age, weeks of gestation and socioeconomic status. The risk of wasting was highest in those with fewer than 4 years of education or unable to contribute to household income.

Friis et al. (62) conducted a cross-sectional study of body composition in HIV-positive and -negative pregnant women between 22 and 35 weeks gestation in Harare, Zimbabwe. Mean age was 24.4 years and 0.4% had malarial parasitaemia. No differences in anthropometric variables were found between the 526 HIV-positive and 1113 HIV-negative women (weight 65.2 versus 65.1 kg, triceps skinfold 15.9 versus 16.3 mm, respectively; BMI 25 in each group). However, women with HIV viral loads greater than $5 \log_{10}$ had a mean weight lower by 2.5 kg (CI $-0.1, 5.1$; $P= 0.058$) and a mean MUAC lower by 1.10 cm (CI 0.23, 1.97; $P= 0.01$) than values for HIV-negative women.

2.5. HIV and nutrition during pregnancy: micronutrients

The Women and Infants Transmission Study in North America is a large multicenter prospective cohort study that examined nutrition and clinical correlates during pregnancy in HIV-positive women (63). The 256 HIV-positive women received zidovudine during pregnancy either to

prevent mother-to-child transmission or for their own treatment. The study showed that the proportion of women with low serum albumin (<35 g/L) was greater in the third trimester than before the third trimester (45.6% vs 16.9%) and there was a significant decline with time (mean -2.3 g/L per week, $P= 0.0001$). Before the third trimester, lower CD4+ cell levels were associated with anaemia ($P= 0.01$) and higher viral loads were associated with anaemia and low BMI (<25; $P= 0.03$ for both). In the third trimester both lower CD4+ cell and higher viral loads were associated with decreased serum albumin. The mean change in BMI throughout pregnancy was 0.114 per week.

In their cross-sectional study mentioned previously, Friis et al. (64) examined folate, ferritin and hemoglobin concentrations of 1669 pregnant Zimbabwean women between 22 and 35 weeks gestation. The mean serum folate concentration of 1113 HIV-negative women was 11.6 nmol/L (95% CI 11.4, 11.9), with 75% having deficient (<6.7 nmol/L) or marginal (6.7–13.5 nmol/L) values. The 526 HIV-positive women had a lower mean serum folate concentration (11.0 nmol/L; 95% CI 10.6, 11.4; $P= 0.009$) with a larger proportion with deficient values (16% of HIV-positive women, 10% of HIV-negative women; $P= 0.001$). Similarly, the mean hemoglobin concentration was lower in HIV-positive (109 g/L; 95% CI 108, 110) than in HIV-negative women (118 g/L; 95% CI 117, 119; $P< 0.00001$), with significantly more HIV-positive women with hemoglobin lower than 110 g/L (54% HIV-positive versus 22% HIV-negative women; $P< 0.001$). The mean serum ferritin was no different between groups (116 μ g/L, 95% CI 112,121 in the HIV-positive group; 114 μ g/L, 95% CI 107, 120 in the HIV-negative group, $P=0.57$) as was the proportion of mothers with severely depleted ferritin stores defined as ≤ 12 μ g/L (63%, 95% CI 60, 66 HIV-positive mothers; 64%, 95% CI 59, 68 HIV-negative mothers, $P=0.82$). In multivariate analysis, when controlling for acute phase response as measured by α_1 -antichymotrypsin, HIV was slightly but significantly inversely related to serum ferritin. Friis et al. (65) also investigated vitamin A status in these women. When the acute phase response, as measured by α_1 -antichymotrypsin, was controlled for, HIV infection was associated with lower serum β -carotene and retinol.

Semba et al. (66) investigated correlations between iron status and markers of HIV disease progression in a cross-sectional study with 483 pregnant women in Malawi. They found a significant

correlation between increased viral load and decreased hemoglobin level ($r = -0.104$, $P < 0.03$). High plasma ferritin concentration was not related to more severe disease (viral load $r = 0.044$, $P = 0.34$; CD4+ count $r = 0.002$, $P = 0.95$) contrary to findings in some other studies (67-69). The prevalence of iron deficiency anaemia, however, was not different according to viral load or CD4+ cell count, and Semba et al. concluded that iron status is not related to markers of HIV disease severity as measured by viral load and CD4+ cell count.

Anaemia was also investigated using baseline data from 1064 HIV-positive pregnant women enrolled in the Tanzanian supplementation study (70). Eighty-three percent of the women were anaemic (hemoglobin < 110 g/L), with mean CD4+ cell count and serum retinol levels independently associated and significantly positively correlated with hemoglobin. Women with BMI less than 19 were at least three times more likely to have severe anaemia than were those with BMI greater than 24. Folate deficiency, assessed by the presence of macrocytic cells, was found in only 5% of the women.

In a randomized trial of high-dose vitamin supplementation (vitamin A and β -carotene alone; multivitamins containing thiamin, riboflavin, vitamins B₆ and B₁₂, niacin, folic acid and vitamins C and E, with or without vitamin A; or placebo) in 1075 pregnant HIV-positive women in Tanzania, Fawzi et al. (71) found that CD4+ cell count increased between 18 weeks gestation and 6 weeks postpartum, consistent with other studies (45,53). CD4+ cell count and percentage, however, increased more in the women receiving supplementation than in those without supplementation. In addition, the women taking the multivitamins improved their iron status, with hemoglobin increasing by a mean of 13 g/L (SD 21) by 6 weeks postpartum compared with a mean of 6 g/L (SD 22) in those who had not taken supplements. Vitamin A supplementation alone did not affect CD4+ T cell count nor hemoglobin status.

In the same cohort, Villamor et al. (72) reported that women gained an average of 4.0 ± 3.2 kg between study enrolment and the last visit before delivery, with a mean gain of 306 g/week during the second trimester and 247 g/week in the third trimester. During the third trimester there was a small but significant increased mean weight gain (304 g; 95% CI 17,590; $P = 0.04$) in women who received multivitamin supplement compared with those who did not, with a lower risk of low total weight gain

(relative risk [RR] 0.70; 95% CI 0.55, 0.90; $P= 0.005$) or weight loss (RR 0.69; 95% CI 0.50, 0.95; $P= 0.02$). Vitamin A supplementation alone did not significantly affect overall weight gain. The authors of both reports suggest that the positive effect of multiple vitamins on maternal immunity may decrease the risk of secondary maternal infections during pregnancy and result in improved weight gain. Lower levels of anaemia in the multivitamin group may contribute to decreased maternal birth complications. In addition, T cell improvement could result from provision of folic acid and vitamin B₁₂, which have roles in development and proliferation of cells.

In a study of 357 HIV-positive Kenyan women of reproductive age, high dose multiple vitamins with selenium versus placebo were used to determine the effect of micronutrient supplementation on cervical and vaginal shedding of HIV-infected cells. After 6 weeks of supplementation, vaginal HIV shedding was significantly higher in those supplemented than in those receiving placebo, suggesting that high dose multiple vitamins with selenium may increase HIV infectivity in women. Supplementation resulted in higher CD4+ and CD8 lymphocyte counts, however, with no difference in plasma HIV viral load. These results raise questions about the risks versus benefits of high dose multiple vitamin with selenium supplementation to women during pregnancy (73).

3. Nutritional needs during lactation

Requirements for many nutrients such as energy, vitamins A, C, B₁₂ and E, riboflavin, and minerals iodine, selenium and zinc are considerably higher during lactation than during pregnancy (74,75) and are proportional to the intensity and duration of breastfeeding. Ideally, some of the nutrients stored during pregnancy, including energy stored as fat, will be available during lactation. To support the mother and infant during the first 6 months of lactation, breastfeeding mothers need to consume approximately 500 kcal/day in addition to usual energy intake before pregnancy. This assumes that approximately 170 kcal/day will be used from stores accumulated during pregnancy (76). If the mother has not gained adequate weight during pregnancy, additional energy will need to be consumed during lactation to make up for the lack of additional stores. As with pregnancy, several

metabolic adaptations meet the metabolic needs of lactation. These include increased appetite and food intake, mobilization of tissue stores and reduced physical activity.

Little is known about the effect of lactation on maternal micronutrient status. The mammary gland exerts metabolic priority for many vitamins, even at the expense of maternal stores (77). During lactation the maternal requirements for protein, vitamins A, B₆, and C, riboflavin, pantothenic acid, zinc and iodine are 40–90% higher than before pregnancy depending on the nutrient whereas the requirements for thiamin, niacin, folate, vitamin E and selenium are about 25% higher (14). There is a decrease in the maternal requirement for iron and no change in the need for calcium, magnesium and phosphorus. Dewey (78) suggests that because lactation exerts the highest increase in requirement for vitamins A, B₆ and C and for minerals iodine and zinc that the micronutrient status of these nutrients would most likely differ between lactating and nonlactating mothers. The effect of low maternal intake of various nutrients on the success of lactation or maternal and infant health remains largely unknown except when a nutritional deficiency is so severe that it is evident in the infant, as has been seen with vitamin B₁₂ and vitamin D deficiencies.

Several maternal micronutrient deficiencies are likely to affect breast-milk composition, as summarized in the review by Allen (79). In general, inadequate maternal intake of water-soluble vitamins affects breast-milk concentration whereas the breast-milk is affected to a lesser extent by maternal intake of fat-soluble vitamins or minerals. Allen has classified micronutrients during lactation into 2 groups. Group 1 includes nutrients in which breast-milk concentrations are affected by maternal nutrient status, and include: thiamine; riboflavin; vitamins A, B₆ and B₁₂; iodine; and selenium. Group 2 includes nutrients not affected by maternal nutrient status: folic acid, vitamin D, calcium, iron, copper and zinc. In endemically deficient populations, an adequate intake of group 1 nutrients are top priorities because maternal deficiencies of these results in lower concentration in breast milk and documented adverse effects in infants. The concentrations of these nutrients in breast milk can be improved with maternal intake, and breast milk is the primary source of most of these nutrients for infants.

3.1. Weight change postpartum

Butte and Hopkinson (80) summarized results of many longitudinal studies of weight changes postpartum in women worldwide. They concluded that most women have a mild, gradual weight loss during the first 6 months postpartum but that the changes in weight are highly variable within and across populations. Women in more affluent countries tend to lose more weight (-0.8 kg/month) than those in developing countries (-0.1 kg/month). Several studies reported that women from the Gambia, Egypt and Taiwan gained weight postpartum. Differences were likely attributable to gestational weight gain, prepregnancy weight, cultural practice, physical activity and seasonal food availability, with gestational weight gain being the strongest and most consistent predictor. Few studies on changes in body composition during lactation have been conducted in developed countries. Butte and Hopkinson (80) used skinfold thickness measurements to measure adiposity changes during lactation in 45 well-nourished presumed HIV-negative women in the first 4 months of breastfeeding. They reported that fat was mobilized from the trunk and thighs and was redistributed to the upper body. Suprailiac and subscapular skinfold thicknesses decreased significantly whereas the triceps and biceps skinfold thicknesses did not. In addition, percent body fat determined by anthropometry decreased from 28% to 26–27%.

Brewer et al. (81) measured anthropometric changes postpartum in 56 presumed HIV-negative American mothers during the first 6 months of lactation. Mothers who exclusively breastfed lost a mean of 8.3 kg (SD 0.74) whereas those who exclusively formula fed lost a mean of 7.2 kg (SD 0.74, $P < 0.01$), with the largest loss of weight between 3 and 6 months in the exclusively breastfeeding mothers. Consistent with Butte and Hopkinson (80), suprailiac and subscapular skinfold thickness measurements decreased and the triceps skinfold thickness increased at 3 months, suggesting mobilization of fat stored during pregnancy.

Dugdale and Eaton-Evans (82) measured weight and skinfold thickness changes in 174 Australian, presumed HIV-negative, breastfeeding mothers for 12 months postpartum. Mothers lost weight between months 1 and 6 of breastfeeding and had stable weight thereafter; women with higher BMI initially lost more weight than those with a lower BMI. Similar to the findings of Brewer et al.

(81), triceps skinfold thickness increased until 5 months postpartum, when it began to decline.

Breastfeeding duration did not affect changes in weight or skinfold thickness measurements.

Motil et al. (83) measured 10 exclusively breastfeeding, well-nourished, presumed HIV-negative women at 4 times between 6 and 24 weeks postpartum. Whole-body potassium counting was used to determine body composition. Women maintained a mean lean body mass of 46 kg (SD 3.7–4.8 depending on time point). Mean weight loss (0.27 kg/month) was in the form of body fat (1.4 kg, SD 1.8) during follow-up.

A meta-analysis using 41 databases and 1726 measurements was conducted to determine whether low BMI is a useful predictor of impaired lactational performance (84). No relationship was found between BMI and the volume of milk produced by mothers, even for BMIs lower than 18.5, and the authors concluded that BMI was not a sensitive predictor of functional lactation capacity. The BMIs from the studies included in this meta-analysis were between a low of 16.8 in Myanmar and a high of 24.4 in Zaire.

3.2. Effect of lactation on HIV

Zimmer and Garza (85) commented in an editorial that we have limited understanding of the effect of lactation on the immune system of healthy women and none on that of HIV-positive women. No evidence supports the hypothesis of Mbori-Ngacha et al. (86) in Kenya, who suggested the possibility that breast milk from HIV-positive mothers may lack immunoprotective factors. Labbok (87) reviewed the maternal benefits of breastfeeding and concluded that little is known about the effects of breastfeeding on maternal health (both short and long term) because most research focused narrowly on human milk as a nutrient source for infants. Recently, however, several studies found that lactation is associated with a reduced risk of breast cancer (88–90).

As part of a randomized trial of abrupt breastfeeding cessation at 4 months compared with mothers' choice of longer breastfeeding in Lusaka, Zambia, Kuhn et al. (unpublished, 2004) investigated whether prolonged breastfeeding was associated with rapid disease progression. They followed 695 mothers for 2 years postpartum. The study found that CD4+ counts at 12 months were lower in the mothers who weaned abruptly at 4 months (median CD4+ 336) compared with those

breastfeeding for longer (median CD4+ 427, $P= 0.02$). The authors suggested that prolonged breastfeeding may provide immunological benefits to the mother.

In the previously mentioned Tanzanian micronutrient supplementation trial, breastfeeding status and duration were not associated with HIV disease progression (death, CD4+ $<200 \times 10^6$ cells/L, anemia defined as hemoglobin <85 g/L or excessive weight loss defined as $>10\%$ loss of body weight) (91). In the 600 HIV-positive women with known breastfeeding duration, the mean duration of breastfeeding was 18 months and the mean duration of exclusive breastfeeding was 2.9 months.

3.3. HIV and nutrition during lactation

Little is known about the effect of breastfeeding on the health and nutrition of HIV-positive women; reports on the nutritional status and changes over time are even fewer than those on HIV-positive pregnant women.

3.3.1. Weight change postpartum

In their Rwandan study of HIV-positive and -negative women, Ladner et al. (59) reported weight changes through 5 months postpartum. Between 10 days and 5 months postpartum, both HIV-positive and -negative mothers gained weight, but the HIV-negative mothers gained more (HIV-positive mothers: 0.7 kg, SD 3.8; HIV-negative mothers: 1.9 kg, SD 4.7; $P= 0.03$). BMI increased in both groups (HIV-positive mothers: 0.3, SD 1.5; HIV-negative mothers: 0.80, SD 1.9; $P= 0.03$). Ladner et al. do not report whether women were breastfeeding, exclusively or otherwise. In a smaller sample at 9 months postpartum, weight change was not different between the two groups (HIV-positive mothers: 1.1 kg, SD 4.6; HIV-negative mothers: 1.8 kg, SD 4.8; $P= 0.28$). Though reports on lactating women of unreported HIV-status worldwide indicate that most lose some weight postpartum and with breastfeeding, the authors suggest that HIV infection impairs weight gain postpartum.

In a randomized clinical trial of formula feeding versus breastfeeding in Kenyan HIV-positive mothers, weight measured between 0.5 and 3 months postpartum was compared with weight measured between 5 and 9 months postpartum (4). Formula-feeding mothers lost no weight whereas breastfeeding mothers lost 0.17 kg/month ($P= 0.03$). The wide time span for each measurement makes interpretation of this finding difficult. A limitation of both these studies is that the first weight

measurement, if taken before 6 weeks postpartum, may still include the increased fluid from pregnancy and thus may not represent a true baseline weight.

In a cross-sectional body composition study in 44 HIV-negative and 17 HIV-positive South African women measured at a mean of 10 weeks postpartum, no difference was detected between HIV-positive and -negative women in height (159.8, SD 4.5, versus 158.2, SD 5.3 cm, respectively; $P=0.73$), weight (66.7 kg, SD 9.2, versus 62.9 kg, SD 11.9, respectively; $P=0.23$), BMI (26.2, SD 3.7, versus 25.1, SD 4.6, respectively; $P=0.40$), MUAC (29.6 cm, SD 3.5, versus 28.4 cm, SD 3.9, respectively; $P=0.30$), triceps skinfold thickness (19.0 mm, SD 7.9 mm, versus 18.8 mm, SD 7.6, respectively; $P=0.92$) (92). In the HIV-positive women, median CD4⁺ count was 631×10^6 cells/L and viral load was 25×10^6 RNA copies/L (\log_{10} 4.4). Fat free mass (FFM) as determined by multifrequency bioimpedance spectrometry was higher in the HIV-positive mothers (HIV-positive mothers: 41.7 kg, SD 4.2; HIV-negative mothers: 38.8 kg, SD 5.2; $P=0.05$) and was consistent that of well-nourished HIV-positive nonpregnant white and black American women (93,94) and HIV-negative breastfeeding North American women (83,95). The fat mass (FM) (HIV-positive women: 25.9 kg, SD 7.6; HIV-negative women: 24.4 kg, SD 8.7; $P=0.53$) and percent body fat appeared the same or higher than in reports in presumed HIV-negative breastfeeding mothers in the United States.

In a longitudinal study of 73 HIV-positive and 47 HIV-negative South African breastfeeding women, the HIV-positive mothers lost more weight between 8 and 24 weeks postpartum than did the HIV-negative mothers (-1.41 kg, SD 3.1, versus $+0.27$ kg, SD 3.33; $P=0.006$, respectively), or approximately 0.35 kg/month loss in HIV-positive and 0.08 kg/month gain in HIV-negative mothers (Papathakis et al., unpublished, 2004). As measured by bioimpedance spectrometry, 92% of the weight loss was fat loss. At both 8 and 24 weeks postpartum the two groups did not differ in any anthropometric and body composition measurement (height, weight, BMI, skinfold thicknesses, MUAC, FFM, FM and percent body fat). At 8 weeks none of the women was considered mildly underweight (BMI <18.5). Conversely, one third of women in each group were classified as mildly to moderately overweight (BMI 25–33.9) at 8 and 24 weeks postpartum.

3.3.2. Micronutrient supplementation

The previously mentioned Tanzanian vitamin supplementation trial examined the effect of the supplement on the risk of clinical HIV disease progression (96). Compared with placebo, high-dose vitamin B complex with vitamins C and E significantly delayed progression of HIV disease (RR of WHO stage 4 or death from AIDS-related causes 0.71; 95% CI, 0.51,0.98, $P= 0.04$) whereas vitamin A alone was not significantly different from the placebo. Multivitamin supplementation also decreased the incidence of other illnesses, such as oral thrush and ulcers, and vomiting and diarrhoea. The effect of the supplement was strongest in the first 2 of the 4 years of follow-up.

3.3.3. Mortality

Several studies reported the mortality risk for HIV-positive women who breastfeed. In the Kenyan formula feeding trial above, maternal mortality in the 2 years after delivery was 11% among those who breastfed compared with 4% in those who did not (RR 3.2, 95% CI 1.3, 8.1; $P= 0.01$) (4). An RR of 3.4 (CI 2.0, 5.8) was found for weight loss of each 1 kg/month, with a median weight loss of 0.7 kg/month in those who died compared with a weight loss of 0.05 kg/month in those who lived. The authors suggested that the nutritional demands of breastfeeding together with the HIV infection may impair nutritional status and result in increased death. Note that although women were randomly assigned to the method of infant feeding, the median HIV viral load was higher in the breastfeeding mothers than in the formula-feeding mothers, as was the rate of intrauterine HIV transmission. These factors suggest that there may have been more advanced disease in the breastfeeding mothers than in the formula-feeding mothers (97).

In a randomized clinical trial of maternal vitamin A supplementation in South Africa in which HIV-positive women chose to breastfeed or replacement-milk-feed their infants, the mortality rate was not different between groups (98). In addition, the mortality rate was much lower than in the Kenyan study—0.5% in women who ever breastfed compared with 1.9% who never breastfed.

In the randomized clinical trial conducted in Zambia, Kuhn et al. (unpublished data, 2004) tested whether mortality among HIV-positive women was associated with prolonged breastfeeding. No difference was found in the Kaplan-Meier estimates of mortality between 347 HIV-positive

women who abruptly ceased breastfeeding at 4 months (mortality at 12 months 4.6% [95% CI 1.79,7.31]) compared with 348 HIV-positive women who were encouraged to exclusively breastfeed to 6 months with weaning foods introduced thereafter (4.9% [95% CI 1.91,,7.86]), $P=0.954$.

The Breastfeeding and HIV International Transmission Study analyzed individual patient data from clinical trials to estimate mortality risk during 18 months postpartum by breastfeeding status. Mortality was 28.7/1000 person years follow-up at 12 months and 32.3/1000 person years at 18 months. Breastfeeding was not associated with mortality ($P> 0.11$). Independent mortality risk factors included low maternal CD4+ count and breastfeeding status (ever breastfed had lower risk of mortality at 12 months than never breastfed, $P= 0.03$ (99)).

The World Health Organization concluded that there was no scientific evidence to indicate that breastfeeding increases mortality among HIV-positive women. It stated that further study and analysis are warranted before the current recommendations on feeding infants of HIV-positive mothers can be changed (100).

4. Nutrition assessment

4.1. Pregnancy

Body weight measured several times throughout pregnancy is most commonly used to assess nutritional status, and gestational weight change is routinely monitored worldwide (17). BMI, which takes maternal height into account, may be useful, especially in identifying those at risk, by indicating wasting of both fat and lean tissue. MUAC reflects past and current nutritional status but is not as sensitive to short-term changes in nutritional status during pregnancy (17). Skinfold thicknesses measured at several body sites have been shown to detect changes in subcutaneous fat distribution. In a study of presumed HIV-negative, mainly white American pregnant women at 30 weeks gestation, Huston Presley et al. (101) found that maternal weight and triceps, subscapular and suprailiac skinfold measurements explained 91% of the variance in FM compared with that estimated from density determined by underwater weighing and total body water determined by isotope dilution methods. They argued that because of increased plasma volume and amniotic fluid during pregnancy, weight

alone may not be a good indicator of nutritional status. They also noted that in late gestation, most body composition estimation models cannot differentiate between maternal and fetal tissues.

Because total body water increases during pregnancy, measuring FFM accurately presents a challenge, especially in developing countries. Expensive and complex research methods, such as isotope dilution and dual-energy X-ray absorptiometry, are available but are not readily available to many investigators and are not practical for the field setting. Generally, height, weight, BMI, MUAC and skinfold thickness measurements are used to measure adiposity during pregnancy.

When determining the best measurement to obtain during pregnancy, it is important to consider the purpose of the indicator. For example, if the goal is to screen and identify women at risk, then BMI or MUAC can identify women who are malnourished and in need of intervention (17). If the goal is to measure responsiveness to an intervention, then repeated weight measurements and change in weight between measurements may be used (17). Change in weight between times can also be used to screen for those at risk. Obviously, selection of the best measurement will also depend on practical considerations such as equipment, facilities, training and human resources. For HIV-positive pregnant women, cutoff points have not yet been developed for any anthropometric indexes in relation to improved maternal and infant outcomes.

4.2. Lactation

When women face food shortages during lactation, they mobilize fat or lose body weight to support milk production at the expense of nutritional status (81,101,102). Whether HIV poses a similar burden in marginally nourished women is not known.

In his review of weight and fat store changes during lactation, Dorea (103) suggested that changes in maternal body weight and FM postpartum vary considerably depending on the mother's nutritional status, reproductive history and stage of lactation. Most of the maternal physiological and body composition changes occur during the first 3 months postpartum, with weight loss being the norm internationally regardless of socioeconomic status. Changes in fat are highly variable. In developing countries, mothers lose subcutaneous fat from all sites, and triceps skinfold thickness appears to be a sensitive measure in marginally nourished mothers. Affluent mothers, however, show

more variable results: triceps skinfold measurements generally increase but the sum of skinfold thicknesses measured at several sites either increases or decreases. Therefore, it is recommended that the triceps skinfold measurement be used as an indication of fat mobilization but not necessarily of total body fat. Similarly, Butte and Hopkinson (80) suggested that triceps skinfold thickness measurements may reflect fat stores or redistribution during the first 4 months of lactation and should not be used alone to reliably predict total body fat. They found that the biceps and triceps skinfold measurements did not change significantly but that the supriliac and subscapular skinfold measurements did.

In the previously mentioned body composition study in South Africa, all skinfold thickness measurements (triceps, biceps, subscapular and supriliac), BMI and MUAC were strongly correlated with FM in HIV-positive and -negative breastfeeding mothers and were useful in measuring changes in FM (92). For HIV-positive breastfeeding mothers, however, none of the anthropometric measurements was correlated with FFM, suggesting that other measurements such as bioimpedance should be used to accurately assess FFM. This finding is similar to that of Grinspoon et al. (28), who found that BMI was not correlated with FFM in non-breastfeeding HIV-positive women.

Reference data for assessing nutritional status and identifying individuals at risk during lactation are not available, but it has been suggested that a cutoff value for BMI of 20.3 at 1 month postpartum should be used rather than the usual 18.5; by 6 months postpartum, however, the cutoff of 18.5 can be used to identify women at risk (17). This compares with a study conducted in the Gambia, where BMI < 18 in HIV-positive men and women was a predictor of mortality (104). As with HIV-positive pregnant women, when determining the best measurement to assess nutritional status during lactation, it is important to consider the purpose of the indicator. BMI, MUAC or change in weight can be used to identify women who are malnourished and in need of intervention (17). Cutoff values for anthropometric indexes related to improved maternal outcome or delay of disease progression during lactation in HIV-positive women have not yet been developed.

5. Programmatic considerations and obstacles

The scientific data regarding HIV-positive women who become pregnant and choose to breastfeed their infants do not exist in a vacuum but in the context of communities, health systems, government policies and international recommendations. The latter, however, are constrained because of lack of empirical data on which to base clear and explicit guidelines. Common perceptions are that HIV-positive women rapidly deteriorate when pregnant or while breastfeeding. Although these perceptions likely reflect the course of women with more advanced disease, they prejudice the attitudes of health care workers in their daily clinical practice. In most studies investigating mother-to-child transmission, 12–15% of HIV-positive pregnant women have CD4+ counts less than 200×10^6 cells/L. It is not clear whether the effect of pregnancy and lactation is the same for women with advanced disease as for those who are still immunologically competent. This information would affect some or all aspects of antenatal, delivery and postnatal care.

Clinic and hospital staffs reflect their own views and those of their communities on what is the best way to feed young infants irrespective of the HIV status of women. Breastfeeding is more than just providing nutrition to a young infant; in many communities it also represents an important symbol of care. Hence a mother may feel obliged to breastfeed even when she feels unwell or when food is not readily available for herself. Clarification of the nutritional and health consequences of breastfeeding on the health of HIV-positive women would help nurses and counsellors to give the most appropriate counselling and support. Clarification would also provide information about whether breast pathology, such as mastitis, should be managed differently for HIV-positive and -negative women.

6. Research gaps

Maternal survival is of obvious importance to the mother but also for the survival of her children. Preliminary evidence, though scanty, suggests that an HIV-positive mother who is well nourished in both macro- and micronutrients is likely to have adequate health and immune function as

determined by CD4+ cell count and viral load. Therefore, determining the best way to optimize the nutritional status of HIV-positive women is essential.

Operational research is needed on the delivery of comprehensive nutrition and health services to HIV-positive women to support maintenance and improvement of body composition and micronutrient status. Body composition assessment methods need to be investigated and validated in HIV-positive pregnant and lactating women.

6.1. Pregnancy

6.1.1. *Biological research gaps*

6.1.1.1. *Gestational weight gain pattern and body composition changes*

- Anthropometric cutoffs regarding risk of maternal health and disease progression
- Practical and reliable field methods to measure body composition
- Means to improve weight gain rate
- For all of the above, comparison between HIV-positive women by CD4+ count, disease stage and viral load
- For HIV-positive women, nutritional modifiers of maternal CD4+ count

6.1.1.2. *Appropriate micronutrient supplementation*

- Appropriate levels of micronutrient intake throughout pregnancy
- Methods to achieve optimal intake of micronutrients
- Dietary intake indicators of micronutrient status
- For all of the above, comparison between HIV-positive women by CD4+ count, disease stage and viral load
- For HIV-positive women, nutritional modifiers of maternal CD4+ count
- For HIV-positive women, appropriate treatment of anaemia

6.1.1.3. *Effect of parity and birth spacing on nutritional status and disease progression*

- Effect of HIV on lactational amenorrhea.

6.1.2. Operational research gaps

6.1.2.1. *Means to deliver appropriate level of energy and micronutrients (pill versus food versus fortified food product)*

- System for monitoring supply, use and need
- Methodology to accurately assess food security and dietary diversity
- Barriers to adequate intake
- Efficacy, including consideration of nutritional status, quality of life, ability to work and care for family, disease progression and frequency of illness, immune function

6.1.2.2. *Appropriate recommendations for frequency and amounts of locally available foods to optimize maternal nutritional status*

6.1.2.3. *Means to monitor BMI, change in weight and MUAC in health care facilities and other community settings*

6.1.2.4. *Algorithm (evidence based) to trigger nutrition intervention; may include identification of at-risk individual, weight change, food insecurity).*

6.2. Lactation

6.2.1. Biological research gaps

6.2.1.1. *Effect of breastfeeding duration and intensity*

- Micronutrient status and changes
- Body composition changes postpartum (including a comparison of HIV-positive women who are and are not breastfeeding)
- Identification of anthropometric cutoffs regarding risk of maternal health and disease progression
- Maternal body composition changes in relation to breast milk composition (proteins, immune factors, micronutrients)
- Maternal morbidity and mortality during breastfeeding and 1–2 years afterward

- Maternal health and breast health
- Breast milk nutrients and immunity factors
- For all of the above, comparison between HIV-positive women by CD4+ count, disease stage and viral load
- For HIV-positive women, effect on maternal HIV disease progression and immune function
- For HIV-positive women, effect of nutritional modifiers on maternal CD4+ counts and clinical HIV disease progression

6.2.1.2. *Appropriate micronutrient supplementation*

- Appropriate levels of micronutrient intake throughout lactation
- Methods to achieve optimal intake of micronutrients
- Nutritional modifiers of maternal CD4+ count
- For all of the above, comparison between HIV-positive women by CD4+ count, disease stage and viral load
- Appropriate level of iron supplementation in iron-deficient postpartum HIV-infected women

6.2.1.3. *Appropriate weight loss postpartum with consideration to disease progression and maternal health*

6.2.1.4. *Effect of antiretroviral therapy on maternal body composition and micronutrient status and breast milk nutrient composition (including proteins and micronutrients) and immunity factors.*

6.2.2. *Operational research gaps*

6.2.2.1. *Means to deliver appropriate level of energy and micronutrients (pill versus food versus fortified food product)*

- System for monitoring supply, use and need
- Methodology to accurately assess food security and dietary diversity

- Barriers to adequate intake
- Efficacy, including consideration of nutritional status, quality of life, ability to work and care for family, disease progression and frequency of illness, immune function

6.2.2.2. *Appropriate recommendations for frequency and amounts of locally available foods to optimize maternal nutritional status*

6.2.2.3. *Means to monitor BMI, change in weight and MUAC in health care facilities and other community settings*

6.2.2.4. *Development of algorithm (evidence based) to trigger nutrition intervention; may include identification of at-risk individual, weight change, food insecurity).*

7. Summary

When comparing HIV-positive and HIV-negative pregnant women, studies found little difference between groups in terms of weight, BMI, MUAC and triceps skinfold thickness measurements. Most likely, the women are at early stages of HIV infection (though ~12% had CD4+ counts $<200 \times 10^6$ cell/L). Most studies, however, found that anthropometric measures decline with increasing viral load and decreasing CD4+ cell count. One study reported that HIV-positive pregnant women gained less weight in each trimester than HIV-negative women and generally less than the average weight gain reported in presumed HIV-negative women in developed countries. The rates of weight gain reported in HIV-positive mothers, however, are consistent with the weight gains in undernourished pregnant women in developing countries. A high proportion of women were found with low or deficient folate or vitamin A status and with anaemia, suggesting that many HIV-positive mothers in developing countries may not be consuming a varied diet rich in micronutrients nor prenatal vitamin and mineral supplements. Some evidence shows that a higher proportion of HIV-positive pregnant women had low or deficient levels of folate, albumin and vitamin A and that these are associated with increased viral load and decreased CD4+ cell count.

The few studies comparing HIV-positive and -negative breastfeeding women found no difference between groups in terms of anthropometry and body composition. Though the observed

weight loss of HIV-positive women during lactation appears to be more than that observed in HIV-negative women, the loss of weight is similar to that seen in breastfeeding women throughout the world. Breastfeeding does not appear to increase maternal mortality, but increased rate of weight loss (>1.0 kg/month) was associated with increased risk in one study.

To determine appropriate nutrition interventions, estimating body composition is important for all HIV-positive individuals. Although advanced and sophisticated methods of measuring body composition are available and useful for research purposes, simple anthropometric measurements of height, weight, BMI, MUAC and skinfold thicknesses at four sites (triceps, biceps, subscapular and suprailiac) are generally useful to monitor adiposity during pregnancy and lactation. Change in weight is also appropriate for identifying women at nutritional risk and in need of intervention.

Anthropometry is inexpensive, reliable if the measurer is well trained and feasible for both health facilities and fieldwork. Assessment of FFM is more complex and will require other types of measurements.

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Table 1. Recommended weight gain during pregnancy

| BMI before pregnancy | Total weight gain (kg) | Weekly weight gain (kg) during 2nd and 3rd trimesters |
|----------------------|------------------------|--|
| <19.8 | 12.5–18.0 | 0.5+ |
| 19.8–25.9 | 11.5–16.0 | 0.5 |
| 26.0–29.0 | 7.0–11.5 | 0.3 |
| >29.0 | <7.0 | 0.25 |