HIV Disease Progression in the First Year After Delivery Among African Women Followed in the HPTN 046 Clinical Trial

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Background: Starting lifelong antiretroviral therapy (ART) in HIV-infected pregnant women may decrease HIV progression and transmission, but adherence after delivery may be difficult, especially for asymptomatic women. We evaluated disease progression among HIV-infected women not on ART with CD4$^+$ lymphocyte counts above 200 cells per microliter at delivery.

Methods: We analyzed risk of death, progression to AIDS (stage IV or CD4 $<$ 200 cells per microliter), or to CD4$^+$ count $<$350 1 year after delivery among postpartum women enrolled to a prevention of breastfeeding transmission trial using the Kaplan–Meier method. In the primary analysis, women were censored if ART was initiated.

Results: Among 1285 women who were not WHO stage IV or less at 6 weeks postpartum, 49 (4.3%) progressed to stage IV/CD4 $<$200 cells per microliter or death by 1 year. Progression to CD4 $<$200 cells per microliter or death occurred among 16 (4.3%) of 441 women with CD4 count of 350–549 cells per microliter and 10 (1.6%) of 713 with CD4 counts $>$550 cells per microliter at delivery. CD4 $<$350 cells per microliter by 12 months postpartum occurred among 116 (37.0%) of 350 women with CD4 count 400–549 cells per microliter and 48 (7.4%) of 713 with CD4 count $>$550 cells per microliter at delivery.

Conclusions: Progression to AIDS or CD4 count $<$350 cells per microliter is uncommon through 1 year postpartum for women with CD4 counts over 550 cells per microliter at delivery, but occurred in over one third of those with CD4 counts under 550 cells per microliter. ART should be continued after delivery or breastfeeding among women with CD4 counts $<$550 cells per microliter if follow-up and antiretroviral adherence can be maintained.

Key Words: HIV, postpartum, disease progression

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BACKGROUND

A recent World Health Organization (WHO) programmatic update has suggested that all HIV-infected pregnant women should be considered for initiation of triple antiretroviral (ARV) regimens for prevention of mother-to-child transmission with consideration given to continuing all women on ARVs for life once initiated, regardless of starting CD4$^+$ lymphocyte count.[1] The recommendation for use of triple ARV regimens, rather than zidovudine alone during

pregnancy with additional peripartum ARV drugs for women with high CD4+ cell counts, is based on several considerations. Rapid initiation of combination ARV drugs without waiting for CD4 results in settings where CD4+ cell counts are often delayed assures treatment for women with low CD4+ lymphocyte counts who have the highest risk of transmission.[2] Using the same regimen for all pregnant women and other adults allows for streamlining of drug supply and provider training. In addition, treating HIV-infected persons at higher CD4+ cell counts resulted in lower risk of transmission to sexual partners in a recent trial.[3]

However, the risks versus benefits of continuing triple antiretroviral regimens started among generally healthy asymptomatic pregnant women with higher CD4+ lymphocyte counts after delivery or cessation of breastfeeding have not been evaluated adequately. The postpartum period is known in both resource-rich and resource-poor settings to be a high risk period for poor HIV treatment adherence, given the demands of newborn care and frequent lack of disclosure with recent diagnosis during pregnancy.[4] Especially in resource-limited settings, there is increased potential for disruption in care as traditionally many women travel away from home after delivery for extended stays with family, frequently far from ARV treatment centers. In addition, resource constraints at the country level may preclude provision of long-term therapy for women with higher CD4+ lymphocyte counts after cessation of breastfeeding without sacrificing treatment access for those who already meet WHO and the Ministry of Health treatment criteria.

Rates of disease progression among asymptomatic HIV-infected women during the first year after delivery have not been well documented in resource-limited settings. Thus, the purpose of this analysis was to assess HIV immunologic and clinical disease progression during the first 12 months postpartum among asymptomatic HIV-infected women with higher CD4 counts at delivery using data from a recently completed trial, HIV Prevention Trials Network (HPTN) 046.[5]

METHODS

HPTN 046 was a randomized, double-blinded placebo-controlled trial of an extended nevirapine regimen in infants for preventing the transmission of HIV through breastfeeding conducted in Zimbabwe, South Africa, Uganda, and Tanzania.[5] The protocol was approved by all relevant institutional review boards and regulatory bodies; all women provided written consent for themselves and their infants before enrollment.

This analysis includes women who provided informed consent and were screened during the third trimester of pregnancy up to 7 days postpartum whose infants were eligible and randomized. To be eligible, women had to have confirmed HIV-1 infection, be at least 18 years old, intend to breastfeed, and not have any serious medical condition that would interfere with breastfeeding or study participation. Their infants had to be HIV uninfected at 3 days of life under version 2.0 and at 6 weeks of age in version 3.0. Maternal care and follow-up were the same in both versions. Maternal ARV regimens were not provided through the study but were available in accordance with the local standard of care, which primarily consisted of combination ARV therapy for women with CD4+ lymphocyte counts below 200 cells per microliter and maternal and infant single-dose nevirapine for those with higher CD4+ cell counts. Enrollment occurred between February 2007 and March 2010. Infants were enrolled at 3 days postpartum under version 2.0 and at 6 weeks postpartum in version 3.0, but all women were enrolled by 7 days postpartum and had study visits at delivery or within 7 days postpartum, at 2 and 6 weeks, and at 3, 6, and 12 months postpartum. At each visit, an interim medical history and symptom-directed physical examination were completed. Maternal HIV disease staging was completed using the WHO staging system,[6] and a complete blood count and CD4+ lymphocyte count were obtained in laboratories certified by the National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS Quality Assurance Program (Figs. 1 and 2)

Statistical Analyses

To assess maternal disease progression over time, we used the Kaplan–Meier method to estimate the cumulative proportion of mothers who progressed to 1 of 4 surrogate disease end points at 6 and 12 months postpartum. Two of the end points described CD4+ lymphocyte decline from baseline at delivery: time to (1) CD4+ lymphocyte counts below 200 cells per microliter and (2) CD4+ lymphocyte counts below 350 cells per microliter. Women were censored at the time of ART initiation. The other 2 end points described progression to clinical AIDS or death from 6 weeks postpartum: (3) WHO clinical stage III or IV or death and a combined end point of (4) WHO clinical stage IV, CD4+ lymphocyte count below 200 cells per microliter, or death. Mothers were excluded from the analysis of the first 2 end points if they had delivery CD4+ lymphocyte counts below 200 and 350 cells per microliter, respectively, whereas the third analysis excluded those mothers who were stage III or IV at 6 weeks postpartum or who had started ART before 6 weeks; and finally, the fourth analysis excluded those mothers who were stage IV at 6 weeks, had taken ART before six weeks, or had CD4+ lymphocyte counts below 200 cells per microliter before 6 weeks. For the combined end points, 3 and 4, time to event was calculated as the minimum event time if a mother had more than one of the qualifying outcomes. For the third end point, women were censored at time of ARV initiation after 6 weeks or at the last visit through 12 months postpartum if they did not die or progress to WHO stage III or IV. For the fourth end point, women were censored at the time of ARV initiation after 6 weeks postpartum or at last CD4+ measure above the threshold of 200 cells per microliter through 12 months postpartum if they did not die or progress to WHO stage IV. Because ARV initiation is likely to be informative, a combined end point analysis was also performed where the time to event was the minimum visit in which the above thresholds (points 1–4) were crossed or ARV treatment was initiated. All participants in whom the end point was not observed were censored at their last visit time. Maternal death incidence was calculated by dividing the number of deaths by the total person-years through 12 months of follow-up and stratified by CD4+ lymphocyte counts at delivery.

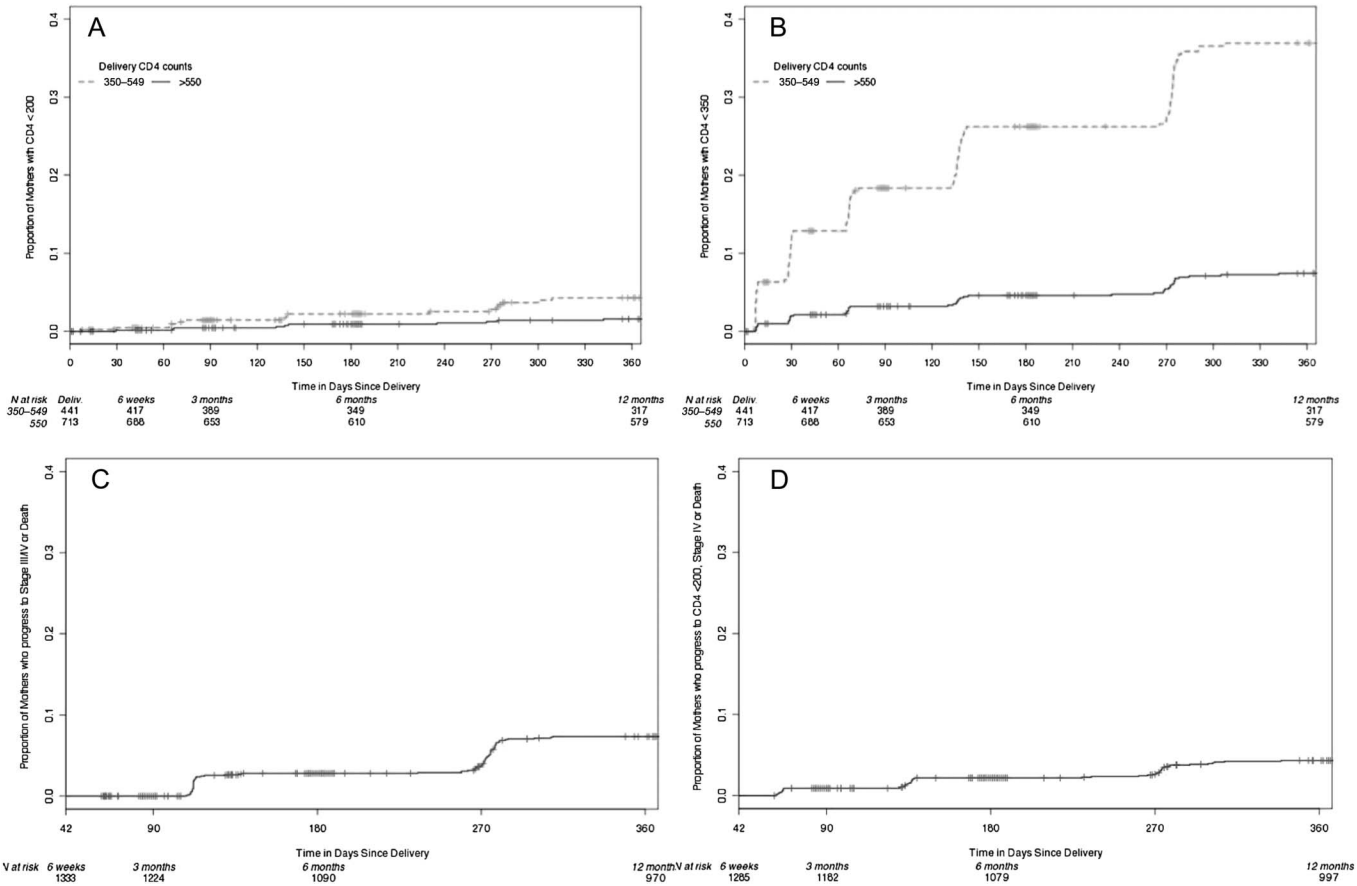

FIGURE 1. Time to (A) CD4$^+$ lymphocyte counts below 200 cells per microliter, (B) CD4$^+$ lymphocyte counts below 350 cells per microliter, (C) WHO clinical stage III/IV or death, and (D) WHO clinical stage IV, CD4$^+$ count $<$200 cells per microliter, or death.

RESULTS

From February 2007 to March 2010, 2025 women enrolled into HPTN 046, including 1430 (70.7%) with CD4$^+$ lymphocyte counts above 350 cells per microliter (Table 1). WHO clinical staging was available at 6 weeks postpartum in 1945 women; 1855 (96%) were stage I or II. Women without WHO clinical staging at 6 weeks had similar demographic characteristics and baseline CD4$^+$ lymphocyte counts compared with those with staging (data not shown). Twenty-eight percent of the women received triple ART regimens during pregnancy. Other baseline characteristics are summarized in Table 1.

Maternal disease progression rates both with censoring at ARV initiation and with ARV initiation included in the end point are summarized in Table 2. Among women who had CD4$^+$ cell count results available at delivery and postpartum sampling (Table 2), 16 (4.3%) of those with counts between 350 and 549 cells per microliter dropped to below 200 cells per microliter by 1 year compared with 10 (1.6%) of those starting above 549 cells per microliter (Fig. 1A). Among women who had a CD4$^+$ lymphocyte count between 400 and 549 cells per microliter at delivery, 116 (37%) dropped under 350 cells per microliter by 1 year after delivery, whereas 48 (7.4%) of those with a CD4$^+$ cell count of $\geq$550 cells per microliter at delivery dropped below this threshold (Fig. 1B). When adding ARV initiation to the end point rather than censoring, rates of the end point of CD4$^+$ count $<$200 cells per microliter or ARV initiation more than doubled for women with CD4$^+$ counts between 350 and 549 cells per microliter but did not change appreciably for the end point including dropping to CD4$^+$ count below 350 cells per microliter or for those starting above a CD4$^+$ count of 550 cells per microliter (Figure 2). For women who started in stages I to III, 49 (4.3%) died or progressed to AIDS based on stage IV conditions or CD4$^+$ lymphocyte count below 200 cells per microliter by 12 months after delivery, censoring for ARV initiation (Fig. 1C and D; Table 2). When including ARV initiation in the end point, 88 (7.7%) met the progression criteria. By 12 months, 83 (7.4%) women starting in clinical stage I or II progressed to stage III or IV, whereas 159 (13.4%) progressed to stage III or IV or initiated ARV. Of the 74 women initiating ARV by 12 months after delivery, 57 (77%) had nadir CD4$^+$ lymphocyte counts below 200 cells per microliter before initiation, 10 (14%) were between 200 and 300 cells per microliter, and 7 (9%) remained above 300 cells per microliter. The reasons for initiation of ARV at higher CD4$^+$ counts were not documented.

Twelve (1%) women who were not stage IV at their 6-week postpartum assessment developed 13 clinical stage IV end points by 12 months after delivery. These end points included 5 cases of extrapulmonary tuberculosis, 2 cases each of HIV wasting ($>$10% weight loss plus either unexplained

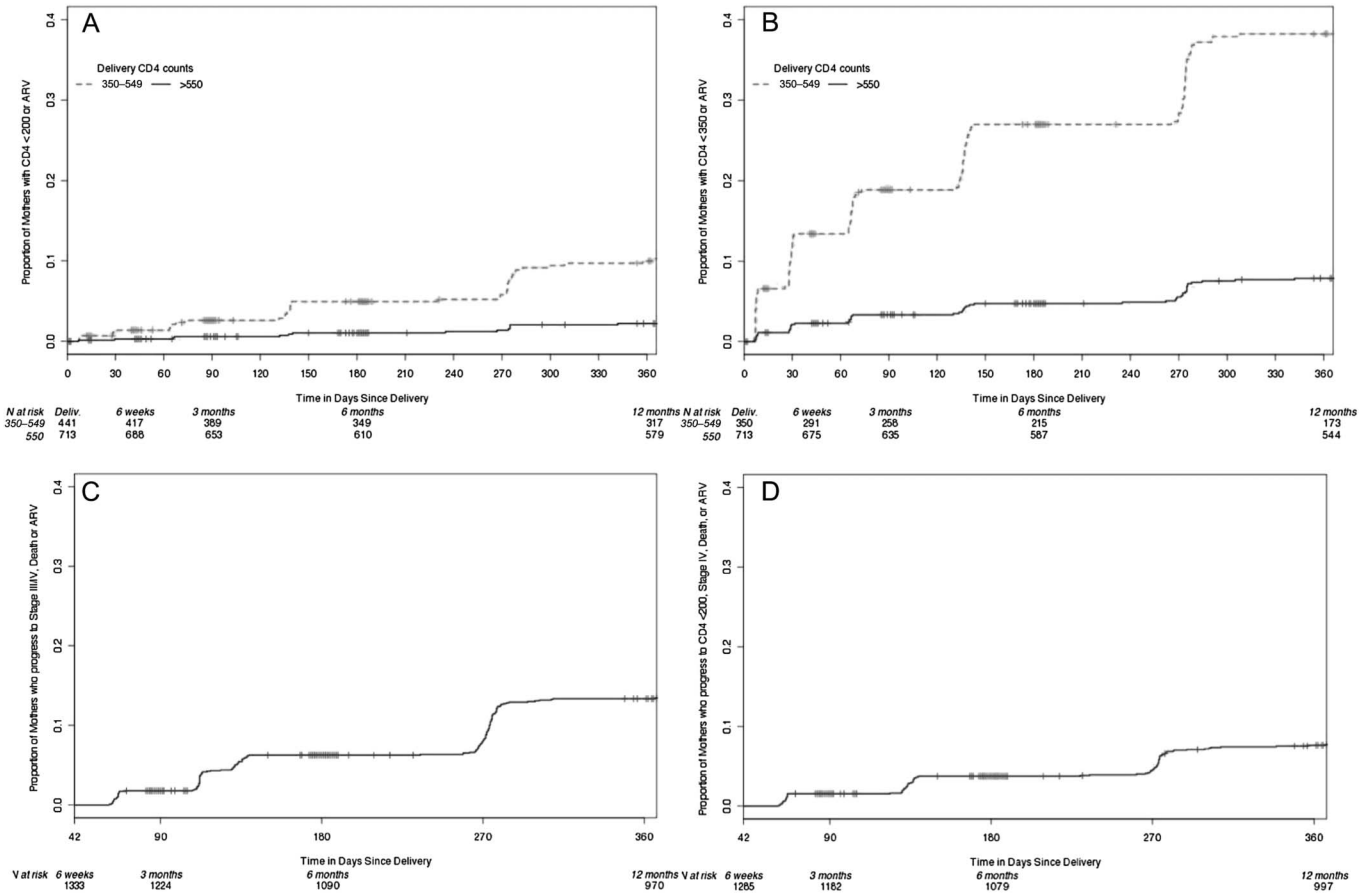

FIGURE 2. Time to ART initiation or (A) CD4+ lymphocyte counts below 200 cells per microliter, (B) CD4+ lymphocyte counts below 350 cells per microliter, (C) WHO clinical stage III/IV or death, and (D) WHO clinical stage IV, CD4+ count <200 cells per microliter, or death.

diarrhea for over 30 days or chronic weakness and unexplained fever for over 30 days), *Pneumocystis jiroveci* pneumonia, and extrapulmonary cryptococcosis, and 1 case each of central nervous system toxoplasmosis and symptomatic HIV-associated nephropathy/cardiomyopathy. Sixteen (0.8%) of enrolled women died during the first year after delivery (see **Table S1, Supplemental Digital Content**, http://links.lww.com/QAI/A443). Cause of death was unknown in 7 cases and had varied causes in the other 9. Only 1 of the 9 deaths (11%) with known causes was potentially secondary to an AIDS-defining condition and only 2 women who died had a CD4+ cell count below 200 cells per microliter at the visit before death. Maternal death rates per 100 person-years stratified by CD4+ lymphocyte count at delivery are shown in Table 3. The rates of death did not differ significantly by CD4 stratum, but number of events were low. Eleven (68.8%) of the deaths occurred among women with CD4+ lymphocyte counts over 350 cells per microliter at the visit before their death.

DISCUSSION

The pregnant and postpartum HIV-infected women enrolled to this trial were representative of the women seen at clinical research sites in sub-Saharan Africa[7,8] and had a range of CD4+ lymphocyte counts at delivery, with 70% above 350 cells per microliter, the current threshold for initiation of ARV therapy in many countries.[9] Less than 5% had stage III or IV disease at baseline, whereas 9% had CD4+ lymphocyte counts below 200 cells per microliter, suggesting that symptoms do not reliably indicate those most in need of ARV therapy. In addition, with the current CD4+ count threshold of 350 cells per microliter, symptoms will not identify many of those who need therapy.

Given the standard of care existing at the sites during the HPTN 046 trial, asymptomatic women with CD4+ lymphocyte counts above 350 cells per microliter did not meet WHO or country-specific criteria for ARV therapy. Within this context, we carefully monitored the women study participants for disease progression to initiate treatment if needed. This close follow-up also provided the opportunity to help inform future treatment recommendations. Women who were asymptomatic (WHO clinical stage I or II at baseline) had a relatively low risk (7.4%) of progressing to symptomatic HIV disease within 1 year postpartum, emphasizing the need for CD4+ lymphocyte testing to target therapy for those individuals at highest risk for disease progression in settings where universal treatment is unaffordable. Among women

TABLE 1. Maternal Baseline Characteristics (n = 1995)

Characteristic	N (%)
Enrollment site	
Chitungwiza, Zimbabwe	664
Kampala, Uganda	705
Dar es Salaam, Tanzania	218
Durban, South Africa	408
Median Age, yr (range)	27 (18–46)
Marital status	
Never married/not living with partner	596 (29%)
Married	757 (37%)
Living with partner	604 (30%)
Separated/divorced/widowed	68 (3%)
Antiretrovirals received during pregnancy before delivery	—
None or only intrapartum prophylaxis	583 (25%)
1 or 2 drugs	868 (43%)
3 drugs	574 (28%)
$CD4^+$ lymphocyte count (cells/μL; n = 2022)	—
<200	171 (9%)
200–349	421 (21%)
350–549	594 (29%)
≥550	836 (41%)
WHO stage assessed at 6 wk postpartum (n = 1945)	—
I	1568 (81%)
II	287 (15%)
III	84 (4%)
IV	6 (<1%)

with $CD4^+$ cell counts between 400 and 549 cells per microliter at baseline, 37% dropped to below 350 cells per microliter at 1 year, indicating a need for ARV therapy and suggesting that women in this range should be offered continuation of therapy after cessation of perinatal transmission risk. These findings are similar to data from the multicountry MTCT-Plus Initiative, which found that women stopping a variety of ARV regimens for prevention of perinatal transmission had a 46% risk of dropping below 350 cells per microliter by 24 months postpartum when the initial $CD4^+$ cell count during pregnancy was 400–499 cells per microliter.[10] A study from Haiti found that women stopping antiretroviral prophylaxis at delivery with a $CD4^+$ lymphocyte count between 350 and 499 cells per microliter dropped to the threshold of 350 cells per microliter requiring therapy at a median of 19 months after delivery compared with a median of 71 months to reach this threshold among women with $CD4^+$ cell counts at or above 500 cells per microliter at delivery.[11] These data are also consistent with a study from Brazil, which showed that among women discontinuing ARV agents after delivery, the group with levels between 250 and 500 cells per microliter had a risk of progression to stage II or III events that was 2.5 times higher than women with $CD4^+$ counts above 500 cells per microliter.[12] The importance of $CD4^+$ lymphocyte results for predicting progression were also shown in a study from Kenya demonstrating that CD4 counts and percentage during pregnancy were most predictive of mortality over the first 2 years postpartum compared with total lymphocyte count, hemoglobin, HIV RNA level, or body mass index.[8]

Among women in the 350–550 cells per microliter $CD4^+$ lymphocyte group, continuation would also have benefits in reduction of heterosexual transmission to discordant partners. This conclusion is based on the results from a large randomized trial of discordant couples, which found that treating HIV-infected subjects with $CD4^+$ lymphocyte counts between 350 and 550 cells per microliter reduced linked transmissions to partners by 96% as compared with delaying therapy until the $CD4^+$ lymphocyte count drops below 250 cells per microliter or symptomatic illness occurred.[3] Although earlier treatment at higher $CD4^+$ levels above 550 cells per microliter may also reduce the risk of sexual transmission, the benefit in the group with higher counts has not been proven. Women beginning ARVs in pregnancy with $CD4^+$ cell counts between 350 and 550 cells per microliter should be counseled about the potential benefit of reduced sexual transmission when they are considering whether or not to continue ARVs after delivery.

Intensive counseling for adherence to the regimen must be provided for women who choose to continue ARVs after cessation of mother-to-child HIV transmission risk, as adherence has been shown to decrease markedly once the incentive of transmission prevention has ended. A recent meta-analysis reported a pooled estimate of adequate adherence (>80% of doses) of 75.7% [95% confidence interval (CI): 71.5% to 79.7%] during pregnancy compared with 53.0% (95% CI: 32.8% to 72.7%, $P = 0.005$) during the postpartum period.[4] This study included women from a range of low-, middle-, and high-income countries. Likewise, in several reports from African sites, HIV-infected women were at particularly high risk for loss to follow-up with ≥50% defaulting on their maternal child health appointments after delivery in some studies.[13–16] Travel away from home to stay with family for several months after the birth of a child is common. In addition, many women have not disclosed their HIV status to partners or family members making adherence challenging, especially if residing with relatives.[17] Poor adherence increases the risk of development of viral resistance and treatment failure.[18] Concerns regarding development of resistance may be especially important, given the current WHO recommendations for efavirenz-based first-line therapies that require a single mutation for resistance.[9] Clearly, support for adherence and follow-up after delivery will need to be intensified for women planning to continue ARV agents postpartum.

In our study, women with $CD4^+$ lymphocyte counts of 550 cells per microliter or higher had a lower risk of disease progression with only 7.4% dropping below 350 cells per microliter and 1.6% below 200 cells per microliter by 1 year postpartum without ARVs. These results are consistent with data from the MTCT-Plus Initiative, which demonstrated that 18.5% of women with initial $CD4^+$ cell counts above 500 cells per microliter during pregnancy progressed to counts below 350 cells per microliter by 24 months after delivery.[10] The group of women with $CD4^+$ cell counts above 550 cells per microliter would be expected to have a low risk of disease progression even with discontinuation of ARVs after pregnancy and breastfeeding, so could discontinue therapy if

TABLE 2. Cumulative Rates of (A) CD4 + Cell Decline or Death Stratified by CD4+ Cell Count at Delivery and (B) Progression to Clinical AIDS or Death at 6 and 12 months Among Women Not on Combination Antiretroviral Therapy Before Delivery

A. End Points: CD4 Decline or Death

	1. Number (%) of those who drop below 200 cells/μL stratified by baseline CD4 count				2. Number (%) of those who drop below 350 cells/μL stratified by baseline CD4 count			
Baseline CD4 count, cells/μL	Delivery 350–549		Delivery ≥550		Delivery 400–549		Delivery ≥550	
N	441		713		350		713	
	End point reached	Cumulative rate (95% CI)	End point reached	Cumulative rate (95% CI)	End point reached	Cumulative rate (95% CI)	End point reached	Cumulative rate (95% CI)
6 mo postpartum	End point censored at ARV initiation							
	9	2.2% (0.8% to 3.7%)	6	0.9% (0.2% to 1.6%)	86	26.2% (21.3% to 30.9%)	31	4.6% (3.0% to 6.2%)
	End point includes ARV initiation							
	20	4.9% (2.8% to 7.0%)	7	1.1% (0.3% to 1.8%)	89	27.0% (22.0% to 31.6%)	32	4.7% (3.1% to 6.3%)
12 mo postpartum	End point censored at ARV initiation							
	16	4.3% (2.2% to 6.3%)	10	1.6% (0.6% to 2.5%)	116	37.0% (31.3% to 42.1%)	48	7.4% (5.4% to 9.4%)
	End point includes ARV initiation							
	39	10.3% (7.1% to 13.3%)	14	2.2% (1.1% to 3.4%)	121	38.2% (32.5% to 43.4%)	51	7.9% (5.8% to 10.0%)

B. End points: progression to clinical AIDS or death

	3. Number (%) stage I to II at baseline, progress to stage III or IV or death		4. Number (%) stage I to III at baseline, progress to stage IV, CD4 <200 cells/μL or death	
Baseline	6 wk postpartum		6 wk postpartum	
CD4 count, cells/μL	Any		>200	
N	1333		1285	
	End point reached	Cumulative rate (95% CI)	End point reached	Cumulative rate (95% CI)
6 mo postpartum	End point censored at ARV initiation			
	34	2.8% (1.9% to 3.7%)	26	2.2% (1.3% to 3.0%)
	End point includes ARV initiation			
	78	6.3% (4.9% to 7.6%)	45	3.7% (2.7% to 4.8%)
12 mo postpartum	End point censored at ARV initiation			
	83	7.4% (5.8% to 8.9%)	49	4.3% (3.2% to 5.5%)
	End point includes ARV initiation			
	159	13.4% (11.4% to 15.3%)	88	7.7% (6.1% to 9.2%)

desired. These findings underscore the utility of CD4+ lymphocyte testing and suggest that in this group of women, more data are needed regarding the risks and benefits of continuing ARVs after risk of mother-to-child transmission of HIV has passed.

There is also a need for operational research that investigates better ways to achieve high levels of adherence to ARV drugs among both pregnant and postpartum women and to decrease loss to follow-up among HIV-infected pregnant women. In areas where implementation of universal treatment is currently not feasible for cost, supply, and logistic reasons, targeting therapy to groups at highest risk for disease progression and transmission to their infants based on their CD4+ cell counts remains necessary. Even with implementation of the strategy of starting lifelong therapy for all pregnant women, CD4+ lymphocyte testing may be helpful to target women with low CD4+ cell counts for increased support and provision of opportunistic infection prophylaxis. Events occurring among the postpartum women were rare but similar to those reported in the HPTN052 study discussed above, with deaths (0.8%) and extrapulmonary tuberculosis (0.2%) being the most frequent serious events in the current study.[3] Causes of death were heterogeneous with only 2 cases occurring with proximate CD4+ lymphocyte counts under 200 cells per microliter and only 1 case (probable meningitis) likely AIDS defining. Other infections (malaria and hepatitis) and comorbidities (anemia,

TABLE 3. Maternal Death Rates per 100 Person-years Stratified by CD4+ Lymphocyte Count

CD4 at Delivery	Deaths	Person-years	Death Rate (Deaths per 100 person-years)	95% CI
<200	2	132.47	1.51	0.18 to 5.45
200–349	2	353.08	0.57	0.07 to 2.05
350–550	5	510.06	0.98	0.32 to 2.29
>550	7	726.90	0.96	0.39 to 1.98

diabetes, pancreatitis, and cardiac failure) contributed to deaths, and some of these conditions may have been ameliorated by earlier ARV. Incomplete data on causes of death limit the conclusions that can be drawn.

Availability of ARV therapy for women with $CD4^+$ lymphocyte counts below 200 cells per microliter in the current HPTN 046 study seems to have lowered the risk of death compared with earlier studies in similar populations. The HPTN 024 study, conducted among pregnant women in Malawi, Zambia, and Tanzania between 2001 and 2003, at a time when antiretroviral therapy was not widely available in those settings, reported death rates over the first year postpartum of 6.1 per 100 person-years among women with $CD4^+$ lymphocyte counts below 200 cells per microliter at delivery, 1.1 per 100 person-years with $CD4^+$ cell count of 200–500 cells per microliter, and 0.4 per 100 person-years for those with $CD4^+$ cell counts over 500 cells per microliter. No deaths occurred among 331 HIV-uninfected women in the study.[19] No ARV therapy was available to women after delivery in that study. In a retrospective review of a cohort of women delivering in Malawi in 2008 who received postpartum ARV therapy if they had WHO stage III or IV disease or $CD4^+$ lymphocyte count below 250 cells per microliter, the mortality rate over 18–20 months postpartum was 4.24 deaths per 100 person-years among 173 consecutive HIV-infected women and 0 among HIV-uninfected delivering at the same sites.[20]

There are certain limitations to these findings including incomplete data on causes of death and lack of longer term follow-up. Data on the use of hormonal contraception are not available, but unlikely to have influenced the findings, based on data from Kenya among postpartum women that found no differences in $CD4^+$ cell count or HIV RNA changes with use of hormonal contraceptives compared with no use.[21] Despite these limitations, there are also a number of strengths of the HPTN 046 study including the large number of participants followed in 4 African countries and excellent retention that allowed careful monitoring of serial $CD4^+$ lymphocyte counts and end point ascertainment over the first year after delivery. Because WHO and in-country guidelines in place during the study did not recommend ARV treatment for asymptomatic individuals with $CD4^+$ cell counts above 200 cells per microliter, these data from HIV-infected women in the first year after delivery can help inform evolving guidelines about continuation of ARV after delivery.

Data from follow-up of the HIV-infected women enrolled to the HPTN 046 study are informative on the risk of disease progression among postpartum women in resource-limited settings. Women with $CD4^+$ lymphocyte counts between 4000 and 550 cells per microliter in pregnancy had a 1 in 3 risk of progressing to indications for ARV therapy within 1 year of delivery based on the current WHO recommendations. Given these findings, this group of women should be counseled regarding the benefits of continuing ARVs after the need for ARVs for prevention of transmission is completed. Those who are interested in continuing ARVs should be provided with support for disclosure to family members, treatment adherence, and regular follow-up visits. Pending more data on long-term outcomes from ongoing trials, women with $CD4^+$ lymphocyte counts above 550 cells per microliter could be presented with information regarding the potential benefits and risks of continuing ARVs and supported in their decision to stop or continue ARVs after the indication for prevention of mother-to-child transmission of HIV has ceased.

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