Acute Maternal HIV Infection during Pregnancy and Breast-Feeding: Substantial Risk to Infants

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We know, in theory and increasingly in practice, how to dramatically reduce rates of mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) type 1 (HIV-1). Specifically, perinatal transmission of HIV-1 can be lowered from 40% [1, 2] to <2% [3] with the use of a combination of antiretroviral drugs during pregnancy and labor (with or without cesarean section); brief infant prophylaxis with antiretroviral agents; and avoidance of breast-feeding. However, this reduction can be achieved only when we are aware of the presence of maternal HIV-1 infection and are able to intervene.

The Joint United Nations Programme on HIV/AIDS estimated that, in 2007, only 1 in 3 HIV-infected pregnant women worldwide received any intervention to prevent MTCT [4]. Implementation of MTCT prevention interventions has been hindered by a multitude of factors globally, including limited or late access to antenatal care and to maternal HIV and CD4 testing; scarcity of trained health care workers to administer testing and treatment; cost of and adherence to antiretroviral drugs; and concerns regarding the safety, cost, and acceptability of replacement feeding. In this editorial commentary, we focus on one particularly formidable challenge to MTCT prevention efforts—one that has largely been overlooked: maternal HIV-1 acquisition during pregnancy or breast-feeding.

This issue of the Journal includes an interesting and important report by Liang et al [5] that describes a very high rate of breast-feeding–related MTCT of HIV-1 in association with postpartum acute maternal HIV-1 infection. The authors identified 104 women in China who were infected with HIV-1 between 1994 and 2000—almost certainly through early postpartum receipt of infected blood products—and who exclusively breast-fed their children for some period without any intervention for the prevention of MTCT. Of the 106 children born to these mothers, 36 (35.8%) were infected with HIV-1. Among women who are chronically infected with HIV and who breast-feed for 18–24 months, one would expect that approximately 9%–16% of their children would become infected through breast-feeding [2, 6]. The rate of breast-feeding–related MTCT observed in the study by Liang et al is notably higher than such estimates noted among chronically infected women, but it is consistent with previously reported rates of breast-feeding–related MTCT among women who experienced seroconversion postpartum (see below).

Primary HIV-1 infection is associated with very high levels of HIV-1 RNA [7, 8]. In turn, the maternal plasma HIV-1 RNA level is one of the most important predictors of perinatal HIV-1 transmission (although transmission or nontransmission can occur at any plasma HIV-1 RNA level) [9, 10]. It is, therefore, not surprising that very high rates of MTCT have been observed among women who experienced seroconversion during pregnancy or breast-feeding [11–14], although this has not been universally documented [15]. One of the earliest studies to describe high rates of MTCT among breast-feeding women with new HIV-1 infections was conducted in Rwanda; among 15 mothers who were HIV-1 seronegative at delivery and who became HIV-1 seropositive postpartum, 8 of their infants (53%) were infected postnatally [12]. An earlier review (based on limited data at the time) estimated that the rate of MTCT among breast-feeding mothers infected with HIV-1 postnatally was 29% [13]. A larger study that was recently conducted in Zimbabwe found a postnatal MTCT rate of 36% among 336 breast-feeding moth-
ers who tested negative for HIV-1 at ≥3 months postpartum and who then tested HIV-1 positive at a subsequent postpartum visit (or who had undetectable HIV-1 RNA at baseline and a subsequent positive result of HIV-1 enzyme-linked immunosorbent assay) [14]. These estimates are very similar to the MTCT rate (35.8%) reported by Liang et al in this issue of the Journal.

Interestingly, duration of breast-feeding was not associated with MTCT in the study by Liang et al (although a nonsignificant trend toward more transmission in association with a longer duration of breast-feeding appeared to be present). The authors plausibly hypothesize that the very high maternal HIV-1 RNA level occurring in individuals with primary HIV-1 infection may have led to very high rates of MTCT shortly after infection, thus overwhelming any potential effect of longer exposure to breast-feeding on MTCT.

Postpartum transfusion-associated HIV-1 infection (as described in the report by Liang et al) should be increasingly rare as blood-supply safety improves, including in countries with a high prevalence of HIV-1 [16]. However, HIV-1 transmission after a negative antenatal screening test result is not rare, and this report from Liang et al highlights the broader problem of acute HIV-1 infection during pregnancy and breast-feeding. In settings where there is a high general incidence of HIV-1, new maternal infections may be responsible for a substantial proportion of MTCT. HIV-1 seroconversion rates of 4.8 cases/100 person-years among peripartum women in Zimbabwe [17] and 3.5 cases/100 person-years among postpartum women in Rwanda [18] have been documented. A recent study conducted in Botswana also demonstrated a high rate of HIV-1 sero-incidence among pregnant and postpartum women [19]. Of 400 women who had tested negative for HIV-1 during pregnancy (a median of 17 weeks earlier), 5 (1.3%) tested positive for HIV-1 at delivery; of 244 women who tested negative during pregnancy, 7 (2.9%) tested positive when retested at child immunization visits occurring at a median of 62 weeks after the first test (leading to an estimated annual peripartum HIV-1 incidence rate of 1.8%) [19]. Of note, in these studies, it is not possible to determine the exact timing of infection, given the range in timing of testing and the window of time during which the HIV screening tests were used (in contrast, infection of the women included in the study by Liang et al very likely occurred at the time of postpartum transfusion).

In most settings, MTCT associated with acute maternal infection is a minor contributor to overall MTCT. However, its relative importance will increase as programs control MTCT among women with established chronic infections. For example, in Botswana, MTCT has been greatly reduced by a comprehensive national MTCT prevention program, and recent data suggest that MTCT related to new maternal HIV-1 infection after antenatal HIV screening could account for >40% of all ongoing MTCT [19].

Programs seeking to eliminate MTCT must take into consideration ongoing risks of HIV acquisition by mothers after antenatal testing, whether those risks are medical or sexual, and they must identify new cases of HIV infection through the retesting of women at key encounters with the health care system. Testing during late pregnancy, at labor and delivery, at child health care visits, or at a combination of these times would allow detection of incident maternal cases and provision of late antiretroviral interventions to infected women and prophylaxis to their infants, as well as either avoidance of breast-feeding or use of antiretroviral of interrupt transmission via breast-feeding. The optimal prevention and retesting policies have not yet been defined in those resource-limited settings with a high HIV-incidence, where health care systems are struggling to meet current needs. The study by Liang et al highlights the importance of identifying new peripartum maternal HIV infections in unfortunate instances where a negative antenatal test result is not the final word.

References


