

Chemokines in breastmilk are associated with mother-to-child HIV-1 transmission.

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Abstract

INTRODUCTION:

CC and CXC chemokines may play a role in mother-to-child HIV-1 transmission by blocking HIV-1 binding to chemokine receptors and impeding viral entry into cells.

METHODS:

To define correlates of breastmilk chemokines and associations with infant HIV-1 acquisition, chemokines in breastmilk and infant HIV-1 infection risk were assessed in an observational, longitudinal cohort study. We measured MIP-1alpha, MIP-1beta, RANTES, and SDF-1 in month 1 breastmilk specimens from HIV-1-infected women in Nairobi and HIV-1 viral load was calculated in maternal plasma and breastmilk at delivery and 1 month postpartum. Infant infection status was determined at birth and months 1, 3, 6, 9, and 12.

RESULTS:

Among 281 breastfeeding women, 60 (21%) of their infants acquired HIV-1 during follow-up, 39 (65%) of whom became infected intrapartum or after birth. MIP-1alpha, MIP-1beta, RANTES, and SDF-1 were all positively correlated with breastmilk HIV-1 RNA ($P < 0.0005$). Women with clinical mastitis had 50% higher MIP-1alpha and MIP-1beta levels ($P < 0.001$ and $P = 0.006$, respectively) and women with subclinical mastitis (breastmilk Na(+)/K(+) > 1) had approximately 70% higher MIP-1alpha, MIP-1beta and RANTES ($P < 0.002$ for all) compared to women without mastitis. Independent of breastmilk HIV-1, increased MIP-1beta and SDF-1 were associated with reduced risk of infant HIV-1 (RR=0.4; 95% CI 0.2-0.9; $P = 0.03$ and RR=0.5; 95% CI=0.3-0.9; $P = 0.02$, respectively) and increased RANTES was associated with higher transmission risk (RR=2.3; 95% CI 1.1- 5.3; $P = 0.04$).

CONCLUSIONS:

These observations suggest a complex interplay between virus levels, breastmilk chemokines, and mother-to-child HIV-1 transmission and may provide insight into developing novel strategies to reduce infection across mucosal surfaces.