

Missed opportunities for prevention of mother-to-child transmission in the United States

Andres F. Camacho-Gonzalez^{a,b}, Marie-Huguette Kingbo^c,
Ashley Boylan^b, Allison Ross Eckard^{a,b}, Ann Chahroudi^{a,b}
and Rana Chakraborty^{a,b}

Objective: To describe system failures potentially contributing to perinatal HIV transmission in the state of Georgia, United States, between 2005 and 2012.

Design: A retrospective chart review of antenatal and postnatal records of HIV-infected infants between 1 January 2005 and 31 December 2012.

Methods: Study participants included all HIV-infected infants referred for specialized management to the Ponce Family and Youth Clinic within Grady Health Systems in Atlanta. Main outcomes included identification of maternal, perinatal, and neonatal risk factors associated with vertical transmission.

Results: Twenty-seven cases were identified; 89% of mothers were African-American between 16 and 30 years of age. Seventy-four percent of women knew their HIV status prior to pregnancy, 44% had no prenatal care, and 52% did not receive combination antiretroviral therapy during pregnancy or intrapartum zidovudine. HIV-1 RNA near the time of delivery was available in only 10 of 27 mothers, and of those, only three had an undetectable HIV-1 RNA level. Caesarean section was performed in 70% of women. Of the 27 children, the mean gestational age was 37 (SD: 2.9) weeks, with 33% requiring neonatal ICU admission. Fifty-nine percent were men, and only 67% received postnatal zidovudine prophylaxis.

Conclusion: Mother-to-child transmission of HIV continues to occur in Georgia at unacceptable levels. Increased education with adherence to existing national guidelines, as well as coordinated efforts between healthcare and public health providers to improve linkage and retention in medical care are urgently needed to prevent further vertical transmission events in Georgia.

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Background

Strategies to prevent mother-to-child transmission (MTCT) of HIV-1 infection have evolved over three

decades [1–3]. With the implementation of current recommendations, the rate of perinatal HIV-1 transmission has dramatically decreased to less than 1% in the United States and Europe [4–8]. However, there remains

^aDivision of Pediatric Infectious Diseases, Department of Pediatrics, Emory University School of Medicine; Children's Healthcare of Atlanta, ^bPonce Family and Youth Clinic, Grady Infectious Diseases Program, Grady Health Systems, and ^cDepartment of Epidemiology and Biostatistics, Georgia State University, Atlanta, Georgia, USA.

Correspondence to Rana Chakraborty, MD, DPhil (Oxon), Emory University School of Medicine, 2015 Uppergate Dr Suite 500, Atlanta, GA 30322, USA.

Tel: +1 404 727 5642; e-mail: rchakr5@emory.edu

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an unacceptable annual rate of newly diagnosed HIV-1 infections among infants in parts of the United States associated with marked racial disparity, evident by a MTCT rate of 12.3/100 000 among African-Americans versus 0.5/100 000 in Caucasians [9]. In 2010, there were 162 cases of perinatally acquired HIV infections in the United States [10]. These numbers are higher than the Centers for Disease Control and Prevention (CDC) perinatal HIV elimination goal [11]. Recently, the CDC reported that missed opportunities were documented in 74.3% of infected children among 7757 mother-infant pairs in 15 US jurisdictions between 2005 and 2008 [12].

In well resourced settings, even one HIV-infected infant represents a system failure that necessitates urgent implementation of corrective measures [13]. This article documents persistent system failures in preventing perinatal HIV transmission over 8 years in infants referred from across the state of Georgia to a major pediatric HIV referral center in Atlanta.

Methods

We undertook a retrospective chart review of all perinatally acquired HIV infections in infants referred to and receiving care at the Ponce Family and Youth Clinic of the Grady Health Systems, born between 1 January 2005 and 31 December 2012. The clinic is the only pediatric HIV facility in Atlanta Metropolitan Statistical Area and the largest of its kind in North America.

The institutional review boards of Emory University and Grady Health Systems approved this study. Information was obtained from inpatient and outpatient clinical and laboratory records from infected infants and their mothers (when available). A questionnaire that included maternal and newborn information was applied to identify missed opportunities that may have resulted in HIV transmission events. In-utero HIV infection was defined as an infant

with a positive HIV DNA PCR within the first 48 h of life. Otherwise, infections were considered to be perinatally or postnatally acquired.

Results

Between the years 2005 and 2012, 27 infants were identified as HIV-infected. Risk factors for MTCT of HIV identified through the screening questionnaire are presented in Table 1. The majority of women were African-Americans (89%) between 16 and 30 years (63%). Only 44% received prenatal care. Seventy-four percent of women (20/27) knew their HIV status prior to pregnancy, yet only 10 (50%) of them received prenatal care. Illicit substance use was identified in nine (33%), with cocaine and marijuana being the drugs of choice either alone or in combination. Among the 20 women who knew they were HIV-infected during their pregnancy, nine (45%) did not receive combination antiretroviral therapy (cART), and five (25%) did not receive intrapartum zidovudine (ZDV). CD4⁺ T-cell count was available in only nine of 27, with three women documented to have at least 500 cells/ μ l. HIV RNA at the time of delivery was available in only 10 of 27 women, and, of these, only three had an undetectable plasma level. Of the three mothers, obstetric risk factors or complications probably contributed to perinatal HIV transmission and were therefore not considered as missed opportunities. The first mother gave birth to an infant at 39 weeks gestation, and received prenatal care from 8 weeks gestation and cART throughout her pregnancy with a CD4⁺ T-cell count at the time of delivery of 583 cells/ μ l. Pregnancy was complicated by placenta previa and premature rupture of membranes of unknown duration. The infant was born by C-section and both the mother and the newborn received prophylaxis with ZDV during labor and for 6 weeks postnatally. The infant was formula-fed, but the HIV DNA PCR was reported as positive at 4 weeks of life. A second mother received appropriate HIV management throughout pregnancy and

Table 1. Risk factors for mother-to-child transmission of HIV.

Risk factor	Yes N (%)	No N (%)	Unknown N (%)
Maternal/Prepartum			
Prenatal care	12 (44)	12 (44)	3 (11)
Illicit substance use	9 (33)	10 (37)	8 (30)
Antiretrovirals throughout pregnancy	12 (44)	14 (52)	1 (4)
Delivery/Intrapartum			
Rupture of membranes prior to delivery	6 (22)	3 (11)	18 (67)
ZDV at delivery	14 (52)	9 (33)	4 (19)
Maternal undetectable HIV-1 RNA at time of delivery	3 (11)	7 (26)	17 (63)
Maternal CD4 ⁺ count <200 cells/ μ l	2 (7)	7 (26)	18 (66)
Vaginal delivery	8 (30)	19 (70)	–
Infant/Postpartum			
Neonatal antiretroviral prophylaxis	18 (67)	7 (26)	2 (7)
Breastfeeding	1 (4)	19 (70)	7 (26)

ZDV, zidovudine.

delivery, but had placental abruption. HIV infection was diagnosed in her infant at 6 weeks of life. The third mother gave birth at 36 weeks gestation to dizygotic twins, in which twin A was infected and twin B was not. She received prenatal care from the third trimester when her HIV RNA level was 123 000 copies/ml and CD4⁺ T-cell count was 277 cells/ μ l. The mother commenced cART achieving undetectable plasma HIV RNA level at the time of delivery. The newborn was immediately initiated on oral ZDV and formula-fed. HIV DNA PCR at birth was reported as positive and the infant considered to have been infected *in utero*. HIV genotype assays obtained at the initial postnatal visit reported wild-type virus for all three infected infants.

Twenty-two percent of mothers had premature rupture of membranes, and the most common mode of delivery was C-section (70%). Of the mothers who gave birth vaginally, two had known and detectable HIV RNA plasma level at the time of delivery. The first mother was diagnosed during pregnancy and prescribed cART; however, compliance was poor and the HIV RNA level at time of birth was 231 000 copies/ml. She received intrapartum ZDV, but the infant did not receive postpartum ZDV. An HIV diagnosis was made in the infant at 1 month of age. The second mother tested HIV-positive 1 year prior to her pregnancy, but used illicit substances, reported being homeless and did not receive any prenatal care. HIV RNA level at the time of delivery was 124 890 copies/ml and her CD4⁺ T-cell count was 67 cells/ μ l. Although she did not receive intrapartum ZDV, oral ZDV was administered as postnatal prophylaxis soon after birth. Her infant was diagnosed with HIV infection at 3 weeks of age.

Of the 27 infants, the mean gestational age was 37 (SD: 2.9) weeks. Eleven percent ($n=3$) had a positive HIV DNA PCR at birth and probably acquired HIV infection *in utero*. Fifty-nine percent were boys, and 67% were prescribed AZT prophylaxis (data on ZDV prophylaxis were unavailable for two participants). Thirty-three percent required neonatal ICU admission. Seventy percent were exclusively formula-fed (no feeding history was available in seven participants), with one mother acknowledging that she had breastfed her baby for 3 months because of undiagnosed maternal HIV infection. Among the whole cohort, the median age for the first positive HIV DNA PCR was 1 month (range: 0–30 months). Stratifying by timing of maternal HIV diagnosis (prepregnancy, during pregnancy through delivery, or postpartum), a prepregnancy or during pregnancy through delivery diagnosis was associated with the infant's first positive HIV DNA PCR at a median age of 1 month compared with 20 months in those mothers who were diagnosed postpartum. Most infected infants were enrolled in HIV care at a median age of 2 months (range: 0–34 months).

Discussion

Perinatal transmission of HIV has decreased significantly so that current estimates indicate that less than 200 HIV-infected infants are now born annually in the United States [14,15]. However, the ultimate goal should be to achieve and sustain the elimination of MTCT of HIV. In 24 of the 27 cases of perinatal HIV transmission described in this study, limitations in healthcare delivery and uptake were identified as a significant risk factor among vulnerable HIV-infected pregnant women, resulting in preventable adverse neonatal outcomes. Implementation of targeted interventions specifically addressing linkage and retention in medical care can prevent such consequences in at-risk individuals. In our study, half of the HIV-infected women did not receive any prenatal care and half did not receive cART as prophylaxis and treatment during pregnancy or delivery, missing critical opportunities for early diagnosis and treatment. Most striking 74% of women who transmitted HIV infection to their infants knew their status prior to their pregnancy. A lack of willingness to be treated, sociobehavioral barriers for treatment (HIV disclosure and stigma), socioeconomic factors, and/or failure of service agencies to fully engage clients could all be reasons for this lack of linkage to and retention in medical care.

There is an urgent need to identify and implement effective interventions to improve linkage and retention if we are to eliminate MTCT of HIV among these most vulnerable HIV-infected women. The CDC has developed a framework specifically directed toward perinatal HIV transmission elimination in the United States, which includes comprehensive reproductive health and family planning, preconception methods for HIV-infected women, and HIV testing for all women of child-bearing age. In addition, current guidelines recommend repeat third trimester testing in areas of high HIV prevalence [16]. To further decrease MTCT of HIV, targeted efforts toward real-time case finding of all HIV-infected pregnant women and their exposed infants is required [17]. Designing, optimizing, and implementing this framework becomes even more important as the prevalence of HIV among women of child-bearing age increases [18].

In our study, only 67% of exposed infants received ZDV prophylaxis, and an HIV DNA PCR was obtained as late as 30 months in some participants. This suggests that some obstetric and pediatric centers do not follow standard-of-care guidelines, which includes assessment of maternal HIV status during labor by rapid testing and prompt intervention in exposed infants. Georgia law formally adopted opt out HIV testing only in 2007 and still does not mandate third trimester testing, although legislature is currently being reviewed to make such testing mandatory. Better education and more formal communication among clinicians caring for pregnant women and high-

risk neonates are urgently needed. Del Bianco *et al.* [19] identified similar risk factors in Texas documenting high perinatal transmission of HIV related to inadequate prenatal care, failure to receive antiretroviral therapy during pregnancy, detectable viral load, and intravenous drug abuse.

We describe 27 cases of perinatal HIV infections managed at a large pediatric HIV clinic over an 8-year period. Although they are likely representative of all the cases from Georgia over this time period, the exact number of perinatal HIV transmissions is unknown. Data from the Enhanced Perinatal HIV Surveillance (EPS) programme in Georgia stated that the rate of perinatal HIV transmission in the state between 2005 and 2010 was 2.5% compared with 2% nationally. However, this may likely underestimate the true number, as a large proportion of HIV-exposed infants followed in the EPS programme in Georgia had an “indeterminate” HIV status (53% compared with 27% nationally), precluding an accurate calculation of MTCT rates. Improvement in Georgia’s surveillance system is required [18].

The major limitations of this article include not having a comparison group of HIV-infected nontransmitting women. This reflects on the clinic, which serves as a major referral center for pediatric HIV care for the state of Georgia. Inherent to retrospective studies from a single site, there was missing information on a number of key determinants affecting MTCT of HIV including adherence to cART during pregnancy.

Although the United States has significantly decreased the rate of MTCT of HIV, even one newly infected infant can reflect poorly on healthcare and public health providers. Implementing effective interventions that address linkage and retention in medical care for vulnerable populations, while improving and maintaining provider education on MTCT of HIV, is critical if the goal of elimination is to be eventually realized in the United States.

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Conflicts of interest

There are no conflicts of interest.

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