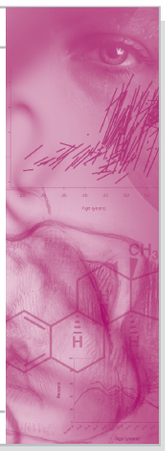
RESEARCH

Risk factors for perinatal HIV-1 transmission in pregnant women requiring lifelong antiretroviral therapy: A longitudinal study at a tertiary hospital in South Africa



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Objectives. To estimate the infant HIV-1 transmission rate and to evaluate risk factors for transmission in pregnant women at an Eastern Cape tertiary hospital requiring lifelong antiretroviral therapy (ART).

Methods. Pregnant women who initiated lifelong ART during pregnancy and others who conceived on lifelong ART were followed up antenatally, through delivery, until 6 weeks postpartum. A qualitative HIV-1 DNA polymerase chain reaction (PCR) was done on the infants at 6 weeks. Risk factors evaluated for perinatal HIV transmission included CD4 count, duration of ART, plasma HIV-1 RNA viral load (VL) at delivery, preterm birth, and mode of delivery.

Results. Data on 838 women with 858 live births are presented. The median CD4 count was 192 cells/µl, and the median duration of ART was 12 weeks. Of 618 women (73.7%) with VL results at delivery, 555 women (89.8%) had a VL <1 000 copies/ml.

HIV-1 DNA PCR was performed on 665 out of 831 infants (80%) from 6 weeks onwards. Transmission occurred in 16 infants (2.4%; 95% confidence interval (CI) 1.4 - 4.0). The transmission rate was 7.8% with maternal plasma VL ≥1 000 copies/ml (p=0.018), 4.2% with duration of ART <10 weeks (p=0.010), and 8.6% with preterm birth (p=0.046).

On multivariable regression analysis VL ≥1 000 copies/ml (adjusted odds ratio (AOR) 12.82; 95% CI 1.72 - 95.53) and duration of ART <10 weeks (AOR 4.91; 95% CI 1.40 - 17.18) remained significant predictors of transmission.

Conclusions. Maternal plasma VL at delivery and duration of ART are significant independent predictors of perinatal HIV-1 transmission, but transmission can occur with undetectable plasma VL at delivery.

Paediatric HIV-1 infection has virtually been eradicated in resource-rich countries, largely owing to the provision of multidrug combination antiretroviral therapy (ART) to all HIV-1-infected pregnant women, elective caesarean section (ELCS), and avoidance of breastfeeding. Currently fewer than 200 infants are born with HIV-1 infection annually in the USA, and fewer than 250 in Western Europe.[1,2] In contrast, sub-Saharan Africa bears much of the burden of worldwide infant HIV-1 infections – in 2008 almost 90% of the estimated 390 000 new paediatric infections occurred in this part of the world.[3]

Factors associated with perinatal HIV-1 transmission include the administration of ART, maternal CD4 count, maternal plasma HIV-1 RNA viral load (VL) at delivery, preterm birth, mode of delivery, and prolonged rupture of the membranes prior to delivery.[4-10]

Offering ELCS to all HIV-1-infected pregnant women in developing countries is seldom feasible or safe, given the high prevalence of infection among pregnant women, the higher risks of infectious morbidity that accompany caesarean section in these women,[11] and the shortages

of skilled staff and theatre facilities that characterise hospitals in many resource-poor settings.

An elevated maternal plasma VL remains an important risk factor for perinatal HIV-1 transmission, even for women on ART.[4] International recommendations on mode of delivery are currently guided by the result of VL assays around that time. In the UK planned vaginal delivery is an option exclusively for women who have been on ART and have an undetectable plasma VL near delivery.[12,13] In the USA women on ART are offered ELCS if their VL at delivery exceeds 1 000 copies/ml, with no consensus on mode of delivery if the VL is below this value.[14,15]

It has been suggested that vaginal delivery could be planned in women on ART who have an undetectable plasma VL at or near delivery. Previous studies have shown that perinatal HIV-1 transmission in these women is extremely uncommon.[4,16] In this study we sought to estimate the rate of infant HIV-1 transmission in pregnant women on lifelong ART for advanced immune suppression, and to explore risk factors for transmission.

Setting

Frere Maternity Hospital is a poorly staffed tertiary facility in East London, a city situated on the Eastern Cape coastline. This hospital serves as a referral centre for a large geographical area within the Eastern Cape province of South Africa. The HIV seroprevalence among pregnant women in this province is 29%.[17] An estimated 11 - 13% of HIV-1-infected pregnant women have CD4 counts <200 cells/µl,[2,6] reflecting in part the proportion with advanced disease in need of lifelong treatment.

Just over 7 000 babies are born annually at Frere Hospital. Caesarean sections are reserved for obstetric reasons in all pregnant women. Approximately 11% of all deliveries of live infants at this institution are ELCSs (unpublished data).

Methods

Requirements for lifelong ART at our antenatal care centre included pregnant women with World Health Organization (WHO) stage 4 disease, or with a CD4 count <250 cells/µl. Women initiated on ART during pregnancy were expected to continue treatment for life.

This study was undertaken between 1 January 2006 and 31 December 2008. Women initiated on lifelong ART during pregnancy and others who conceived on ART were followed up until 6 weeks after delivery. Details on age, parity, CD4 count, VL, gestation at ART commencement, duration of ART, VL at delivery, gestation at delivery, mode of delivery and infant details were obtained. Gestational age was determined by ultrasound examination. For women who conceived on lifelong ART, CD4 counts and VL assays were additionally obtained at confirmation of pregnancy.

CD4 counts were measured locally by flow cytometry, and VL assays were done at a regional laboratory using the nucleic acid sequence-based amplification (NASBA) procedure (NucliSens HIV-1 QT, bioMerieux, Boxtel, The Netherlands).

VL assays were repeated a day before ELCS, at the onset of labour, at the onset of induction of labour, or within a week after delivery. An undetectable plasma VL (<50 copies/ml) at delivery was arbitrarily assigned a value of 20 copies/ml.

ELCSs were done for obstetric indications. ELCS was defined as caesarean section prior to the onset of labour and prior to rupture of the membranes. Preterm birth in this cohort was defined as birth before 34 weeks' gestation. Low-birth-weight (LBW) infants were identified by birth weight <2 500 g.

At birth the neonate was given a single dose of nevirapine (sd-NVP), 2 mg/kg, followed by zidovudine (AZT), 4 mg/kg/dose, 12-hourly, for a week. Before January 2007 newborns received only sd-NVP, since AZT syrup was not available at our institution.

Method of infant feeding, classified as exclusive breastfeeding, exclusive formula feeding or mixed feeding, was recorded at 6 weeks.

From 6 weeks onwards a heel-prick dried blood spot (DBS) was collected from the infant and sent to a regional laboratory, where a qualitative HIV DNA polymerase chain reaction (PCR) was performed using the Amplicor Roche version 1.5 Prototype DNA Kit (Roche Diagnostics, Inc., Alameda, Calif.). An infant was classified as HIV-1 infected if the PCR specimen tested positive, or if the infant died from an HIV-related condition before PCR testing. Twins were counted as separate mother-infant pairs and tested individually.

Data were analysed using Epi-info software version 3.2.2 (Centers for Disease Control and Prevention (CDC), Atlanta, Ga, 2005). Continuous data are presented as medians with interquartile ranges (IQRs). Categorical data are presented as proportions with 95% confidence intervals (CIs). Dichotomous data comparisons were done by means of a chi-square test or Fisher's exact test. Variables studied as risk factors for transmission included: CD4 <250 cells/µl, timing of ART, duration of ART, type of ART, mode of delivery, preterm birth, VL at delivery, and neonatal characteristics. A univariable logistic regression analysis was performed for potential risk factors, from which a multivariable logistic regression model was constructed with adjusted odds ratios (AORs) and 95% CIs.

Study approval was obtained from the hospital's research and ethics committee.

Results

Between 1 January 2006 and 31 December 2008, 1 030 eligible pregnant women accepted entry into our antenatal care centre. Two women declined further participation, and

another 2 did not return after initial ART preparation. Of the remaining 1 026 women, 113 had ongoing pregnancies, 44 (4.3%) were lost to follow-up, and 31 (3.0%) experienced pregnancy losses. Data on 838 women with 858 live births (including 20 twin pairs) are presented.

Table I summarises the characteristics of the 838 pregnant women on ART with live births. Their median age was 29 years. Two hundred and eighty-three women (33.8%) were primigravidas. Women initiated on ART during pregnancy constituted 74% of this cohort. The median CD4 count was 192 cells/µl, and 646 women (77.0%) had CD4 counts <250 cells/µl. Although the median duration of ART during pregnancy was 12 weeks, 340 women (40.6%) received ART for less than 10 weeks. Maternal plasma VL results at delivery were available for 618 women (73.7%). Of this group 555 women (89.8%) had a VL <1 000 copies/ml and 448 (72.5%) had an undetectable VL.

The ART regimens used during pregnancy were a combination of two nucleoside reverse transcriptase inhibitors, with either efavirenz (EFV) (*N*=733; 87.5%), nevirapine (NVP) (*N*= 97; 11.6%), or lopinavir/ritonavir (LPV/r) (*N*=8; 1.0%). Drug substitutions were relatively common, performed on 59 women (7.0%). The principal reason for ART substitutions was discontinuation of EFV during the first trimester in women who conceived on ART. EFV was switched to NVP in 48 cases and to LPV/r in 7. More detailed analyses of maternal outcomes and birth defects following EFV use in this cohort are published elsewhere.[18,19]

Table I. Baseline demographic characteristics of pregnant women requiring lifelong ART who gave birth to live infants (*N*=838)

Median age (yrs) (IQR)	29 (25 - 33)
Primigravidas (%)	283 (33.8)
Women initiated on ART antenatally (%)	624 (74.5)
Median CD4 count (cells/µl) (IQR)	192 (126 - 245)
CD4 <250 cells/µl (%)	646 (77.1)
Median duration of ART (wks) (IQR)	12 (6 - 30)
Duration of ART <10 wks (%)	340 (40.6)
Mean VL at delivery (copies/ml)*	8 220 (SD 69 790)
<1 000 copies/ml (%)	555/618† (89.8)
<50 copies/ml (%)	448/618 (72.5)
Planned vaginal birth (%)	745 (88.9)
Planned ELCS (%)	92 (11.0)
Median gestation at delivery (wks) (IQR)	39 (38 - 40)
Delivery <34 weeks (%)	49 (5.8)
Mode of delivery	
ELCS (%)	87 (10.4)
EMCS (%)	160 (19.1)
NVD (%)	570 (68.0)
AVD (%)	20 (2.4)
Laparotomy for extra-uterine pregnancy (%)	1 (0.1)
Delivery outside hospital (%)	98 (11.7)

*VL <50 copies/ml was assigned a value of 20 copies/ml.
†Results for VL assays at delivery were available for 618 women (73.7%).
IQR = interquartile range; VL = viral load; SD = standard deviation; ELCS = elective caesarean section; EMCS = emergency caesarean section; NVD = spontaneous vaginal delivery; AVD = assisted vaginal delivery.

The median gestation at delivery was 39 weeks. Vaginal birth was planned for 745 women (88.9%), and ELCS for 92 (11.0%). One woman was scheduled for a laparotomy for advanced extra-uterine pregnancy. Forty-nine women (5.8%) delivered preterm. Eighty-seven women (10.4%) had ELCSs done, mainly for previous caesarean section or breech presentation at term. Nearly 20% of women had emergency caesarean sections (EMCSs), predominantly for fetal distress or poor progress during labour. The majority of women (68.0%) had spontaneous vaginal deliveries (NVDs). Only 20 women (2.4%) had assisted vaginal deliveries (AVDs) – ventouse, forceps or vaginal breech deliveries. Ninety-eight women (11.7%) gave birth at another hospital, at a midwifery obstetric unit, at home, or en route to hospital.

Of the 858 liveborn infants, 439 (51.2%) were male. The median birth weight was 3 000 g. Fifty-five infants (6.4%) were born preterm, whereas 181 (21.1%) were of low birth weight (LBW). Neonatal deaths (*N*=18) were almost exclusively due to preterm birth and intrapartum asphyxia. Neonatal prophylaxis uptake of sd-NVP and AZT was relatively high (*N*=698, 81.4%).

Of the 9 deaths that took place before HIV-1 DNA PCR testing, 2 were clearly caused by HIV-related illnesses. Both infants were malnourished and had tuberculosis (TB). Six hundred and sixty-five out of 831 infants (80.0%) were tested for HIV from 6 weeks onwards, 586 (88.1%) within 2 months of birth. A positive PCR result was obtained in 14 infants. Including the infant deaths from HIV, the number of infected infants totalled 16 out of 667 – an overall transmission rate of 2.4% (95% CI 1.4 - 4.0).

On univariable analysis (Table II), duration of ART ≥8 weeks was associated with a modest reduction in transmission rate: 1.9% versus 3.5% with ART <8 weeks (p=0.176). A significant difference in transmission rate was observed at a cut-off of 10 weeks: the transmission rate was 1.2% versus 4.2% with ART <10 weeks (p=0.010). The transmission rate also varied significantly with plasma VL at delivery: 7.8% with VL ≥1 000 copies/ml versus 1.5% with VL <1 000 copies/ml (p=0.018). Preterm birth increased the transmission rate more than 4-fold: 8.6% with preterm birth versus 2.1% with delivery beyond 34 weeks (p=0.046).

Infant birth weight was marginally associated with transmission: 4.4% in LBW infants versus 1.9% in infants with a birth weight ≥2 500 g (p=0.086). Although the planned mode of delivery did not influence transmission rates, there was a tendency toward a higher transmission rate with NVD versus other modes of delivery (3.0% v. 1.3%; p=0.088). No HIV-1-infected infants were born to the women who had ELCSs.

Table II. HIV-1 transmission in women requiring lifelong ART – univariable analysis

Variable	*N*	*n*	%	*p*
Total	667*	16	2.4	
Timing of ART				
Antenatal ART	495	14	2.8	0.175
Conception on ART	172	2	1.2	
CD4 count (cells/µl)				
CD4 <250	516	12	2.3	0.508
CD4 ≥250	151	4	2.6	
Type of ART				
NVP-based ART	79	1	1.3	0.416
EFV-based ART	588	15	2.6	
Duration of ART				
<8 wks	201	7	3.5	0.176
≥8 wks	466	9	1.9	
Duration of ART				
<10 wks	263	11	4.2	0.010
≥10 wks	404	5	1.2	
VL at delivery				
≥1 000 copies/ml	51	4	7.8	0.018
<1 000 copies/ml	456	7	1.5	
Preterm birth				
<34 wks	35	3	8.6	0.046
≥34 wks	632	13	2.1	
Planned mode of delivery				
Vaginal birth	583	15	2.6	0.381
ELCS	83	1	1.2	
Actual mode of delivery				
NVD	434	13	3.0	0.088
AVD	20	0	0	
EMCS	131	3	2.3	
ELCS	81	0	0	
Place of delivery				
Outside hospital	81	3	3.7	0.306
Inside hospital	586	13	2.2	
Gender of neonate				
Male	338	10	3.0	0.177
Female	329	6	1.8	
Birth weight				
<2 500 g	136	6	4.4	0.086
≥2 500 g	531	10	1.9	
Neonatal prophylaxis				
sd-NVP only	105	3	2.9	0.474
sd-NVP + AZT	562	13	2.3	
Infant feeding				
Breastfeeding	33	0	0	0.440
Formula feeding	634	16	2.5	

*Includes the infants tested for HIV plus the 2 infants who died from HIV.
ELCS = elective caesarean section; EMCS = emergency caesarean section; NVD = spontaneous vaginal delivery; AVD = assisted vaginal delivery; *N* = number of mother-infant pairs (twins were counted separately); *n* = number of infected infants.
p was obtained by chi-square test for duration of ART, mode of delivery and gender. For all other variables the value of *p* was obtained using Fisher's exact test.

Variables such as the timing of ART, type of ART, CD4 count, place of delivery, gender and neonatal prophylaxis did not meaningfully affect transmission rates. Forty-four infants (5.3%) were reportedly exclusively breastfed, 33 (75.0%) of whom were tested, with none infected.

In a subgroup of 294 women with duration of ART ≥10 weeks and plasma VL <1 000 copies/ml at delivery, the transmission rate was 0.3% (95% CI 0.0 - 1.9). Only 1 infant was infected, born to a woman in whom ELCS was planned at 38 weeks' gestation. She presented with pre-labour rupture of membranes of longer than 4 hours' duration, and underwent an EMCS 2 hours later.

In another subgroup of 96 women who initiated ART at a pre-therapy VL ≥100 000 copies/ml, plasma VL reduction

to undetectable levels occurred in 40 cases (42%), after a mean of 12 weeks of treatment. The women who achieved this precipitous reduction in VL included 3 who gave birth within 6 weeks of commencing ART. The infant HIV transmission rate (77 out of 96 infants tested) was 6.3% (95% CI 0.8 - 20.8) when the VL was undetectable at delivery versus 6.7% (95% CI 1.4 - 18.3) with a detectable VL (p=0.659).

Overall, 4 out of 360 infants (1.1%) born to women with an undetectable plasma VL at delivery were infected. The mean duration of ART was only 9 weeks (range 6 - 13 weeks) in the 4 women with infected infants, compared with 19 weeks (range 1 - 42 weeks) in the 356 women with uninfected infants.

Following a univariable regression analysis, the final multivariable regression model included 507 mother-infant pairs with 11 infected infants for analysis, as shown in Table III. Duration of ART <10 weeks and VL ≥1 000 copies/ml remained significant predictors of infant HIV transmission. Duration of ART <10 weeks was associated with a more than 4-fold increase in transmission, and VL ≥1 000 copies/ml increased transmission by almost 13-fold. Preterm birth, LBW and spontaneous vaginal delivery lost statistical significance on multivariable regression analysis.

HIV infection status was not obtained for 166 infants (20%). A comparative analysis of mother-infant pairs was done (data not shown) between HIV- tested and untested infants, which included all demographic characteristics

Table III. Univariable and multivariable regression analyses of risk factors for perinatal HIV-1 transmission in women requiring lifelong ART

Variable	OR (95%CI)	*p*-value	AOR (95% CI)*	*p*-value
Timing of ART				
Antenatal ART	2.47 (0.56 - 11.00)	0.234		
Conception on ART	1.00			
CD4 count				
<250	0.88 (0.28 - 2.75)	0.819		
≥250	1.00			
Type of ART				
NVP-based ART	0.49 (0.06 - 3.76)	0.492		
EFV-based ART	1.00			
Duration of ART				
<10 wks	3.48 (1.20 - 10.14)	0.022	4.91 (1.40 - 17.18)	0.013
≥10 wks	1.00			
VL at delivery				
≥1 000	5.46 (1.54 - 19.34)	0.003	12.82 (1.72 - 95.53)	0.013
<1 000	1.00			
Preterm birth				
<34 wks	4.46 (1.21 - 16.46)	0.014	13.48 (0.64 - 285.80)	0.095
≥34 wks	1.00			
Planned mode of delivery				
Vaginal	2.19 (0.29 - 16.81)	0.450		
ELCS	1.00			
Actual mode of delivery				
NVD	2.37 (0.67 - 8.39)	0.182	1.86 (0.54 - 6.47)	0.328
Caesarean section	1.00			
Place of delivery				
Outside hospital	1.70 (0.47 - 6.08)	0.418		
In hospital	1.00			
Gender of neonate				
Male	1.64 (0.59 - 4.57)	0.343		
Female	1.00			
Birth weight				
<2 500 g	2.41 (0.86 - 6.74)	0.095	0.71 (0.13 - 3.91)	0.691
≥2 500 g	1.00			
Neonatal prophylaxis				
sd-NVP only	1.24 (0.35 - 4.44)	0.739		
sd-NVP + AZT	1.00			

*507 mother-infant pairs included in adjusted analysis; adjusted for duration of ART, VL, mode of delivery, preterm birth, and birth weight.
OR = unadjusted odds ratio; AOR = adjusted odds ratio; CI = confidence interval; ELCS = elective caesarean section; NVD = spontaneous vaginal delivery.

and risk variables used in the study. The tested and untested groups were matched for all parameters, but differed significantly for mode of delivery and neonatal prophylaxis. Mothers of untested infants had fewer ELCSs (6.0% v. 12.2%; p=0.009) and more NVDs (76% v. 65%; p=0.003), and more untested infants received sd-NVP only (24.7% v. 15.8%; p=0.005).

Discussion

In this largely observational study we examined perinatal HIV-1 transmission and its associated risk factors in women who exclusively required lifelong ART for their own health. The overall transmission rate of 2.4% is consistent with transmission rates of between 1.0 and 4.3% observed elsewhere in South Africa and internationally, following combination ART use in pregnancy.[4,20-25]

Our data provide further reassurance on the effectiveness of ART in reducing infant HIV transmission in women with advanced immune suppression. In the absence of treatment these women generally account for the highest risk of infant transmission, between 39% and 43%.[5,7,26]

The main determinants of HIV transmission were maternal plasma VL at delivery and duration of ART. Duration of ART <10 weeks increased the rate of transmission nearly 5-fold, while a VL ≥1 000 copies/ml was associated with a more than 12-fold higher rate of transmission. The transmission rate was 0.3% in the infants of women with a VL <1 000 copies/ml at delivery and who received >10 weeks of ART during pregnancy. Preterm birth was associated with a higher transmission rate, but the relatively small number of infants that were followed up precludes definitive conclusions on the association between this variable and HIV transmission.

VL suppression during pregnancy is clearly an important objective in reducing HIV transmission, but by no means the only one. Plasma VL reduction to undetectable levels usually occurs following 24 weeks of treatment in ART-naïve individuals.[15] We have, however, observed complete plasma VL suppression within 12 weeks of initiating ART at a pre-therapy VL >100 000 copies/ml, with similar infant HIV transmission rates between those with undetectable and detectable VLs at delivery. Although this group of women was very small, and we did not demonstrate timing of transmission (*in utero* v. intrapartum), this finding nonetheless raises questions regarding the exclusive use of VL internationally when deciding on the mode of delivery.[12-15]

Furthermore, the 4 women (1.1%) with an undetectable plasma VL at delivery who gave birth to infected infants had received ART for a mean period of only 9 weeks. This treatment period may not have been sufficient to prevent *in utero* fetal infection or suppress the VL in the genital tract to undetectable levels, and may account for the observed HIV transmission despite undetectable plasma VLs at delivery.

Compartmentalisation of the genital tract is known to occur, with continued shedding of genital tract virus in up to 15% of women on ART with low or undetectable plasma VLs.[27] Cell-associated genital tract virus shedding has been shown to be a risk factor for infant HIV transmission.[28]

The optimal duration of ART required to prevent *in utero* fetal infection or to ensure a safe vaginal birth is uncertain. The current South African prevention of mother-to-child transmission guidelines do not provide any recommendations on the optimal time to initiate ART during pregnancy. In this document optimal ART is defined as duration of treatment ≥4 weeks.[29] The British HIV Association guidelines recommend starting short-term ART by 28 weeks' gestation, but earlier where necessary.[12] In the absence of any treatment, *in utero* transmission – which accounts for a third of all transmissions – occurs almost exclusively in the last 2 months preceding delivery.[30] Covering this period of pregnancy with ART as pre-exposure prophylaxis would seem reasonable, at least to avert *in utero* transmission. Support for this treatment duration has previously been shown in randomised studies with AZT monotherapy.[31]

Current trends of performing ELCS based on the presence of maternal HIV infection or the result of pre-delivery VL were not followed for this cohort. Vaginal birth was planned for 89% of women and ELCSs were done for obstetric indications. The ELCS rate was low (10%), consistent with the rate in the overall obstetric population at our institution. No association between mode of delivery and transmission rate was found. However, the lack of association may be due to the limited number of women who had ELCSs. ELCS rates from international studies on ART and even some South African studies were higher, with rates varying between 34% and 70%.[21-25] However, in none of these studies was a clear relationship demonstrated between ELCS and HIV transmission. Whether ELCS provides further protection against HIV transmission seems plausible but is currently unclear.

Gender differences in transmission rates have been reported in some studies but not in others.[6,23,25] The European Collaborative Study found a 1.5-fold increase in the transmission rate for girls. This gender effect was limited to infants born by ELCS, and the effect was lost in women on ART.[32] The Italian Register for HIV in Children found a 43% reduction in transmission rate for boys, limited to infants born after 1995. Similarly, no gender effect was observed for the subgroup of women on ART.[33] The reasons why girls are more likely to acquire HIV infection compared with boys are unclear. Furthermore the sex ratios at birth in these cohorts were 1.09 in favour of boys – considerably higher than the population sex ratios of 1.05 to 1.06 of the countries that participated[34] – suggesting the possibility of under-representation of girls. In our study infant gender was not a risk factor for transmission. Further work is needed in understanding infant gender and HIV transmission.

This study had some limitations. Maternal plasma VL results at delivery were not available for 26% of women, and 20% of infants were not tested. We were unable to determine the extent, if any, to which the differences

between HIV-tested and untested infants may have adversely influenced the overall transmission rate.

Conclusions

The rate of infant HIV-1 transmission in this cohort was low, notwithstanding a policy of planned ELCS for obstetric reasons. Pregnant women with indications for lifelong treatment should be fast-tracked for access to ART before 30 weeks' gestation. Plasma VL at delivery strongly predicts infant transmission, but an undetectable VL does not eliminate the risk. The optimal route of delivery of the HIV-exposed fetus remains unclear.

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