

6633 Transmission of Congenital and Postnatal Cytomegalovirus (CMV) Among HIV-Exposed Infants: The Effect of Prenatal Maternal Highly Active Antiretroviral Treatment (HAART)

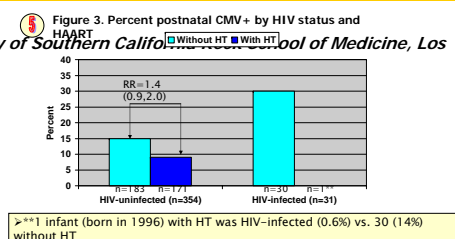
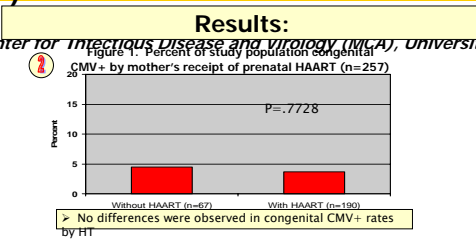
ABSTRACT
 Background: Before the use of HAART (HT) to prevent perinatal HIV transmission, rates of congenital CMV were high in HIV-infected infants. This study examines perinatal CMV rates among HIV-infected and HIV-exposed but uninfected infants after HT became standard of care in our clinic.
Methods: Infants born from 1988-2002 to HIV-infected women were evaluated for congenital CMV infection (a positive oral or urine CMV culture obtained in the first 3 weeks of life, n=257 infants tested) and postnatal CMV (excluding the first 3 weeks, a positive test in the first 6 months of life, n=385 infants tested). Prenatal maternal HT was defined here as triple anti-retroviral therapy. All infants with maternal HT received at least 6 weeks of ZDV.
Results: 61% of our study population was Hispanic and 31% Black. Mother's median age at child's birth was 28.2 years. Rates of congenital CMV did not change with HT use (4.5% with HT vs. 3.7% without HT) or by infant HIV infection status. However, rates of postnatal CMV transmission were significantly (P<.05) lower for those with HT (9.2%) compared to those without HT (17.4%). Not receiving HT remained significantly associated with increased postnatal CMV+ (OR=2.1, 95%CI = 1.1, 4.0) controlling for infant's gender, birth weight and gestational age. Among the HIV-infected infants (n=31), all except 1 infant did not receive HT and 30% of them were postnatal CMV+. Among the HIV-uninfected infants (n=354), the incidence of postnatal CMV+ was lower among those with HT (9.3%) compared to those without HT (15.2%) although statistical significance was not reached (P=.09). For HIV-uninfected infants without HT, 11.5% of those who were postnatal CMV+ had either symptoms lasting more than 2 months during the first year of life of failure to thrive, lymphadenopathy, splenomegaly, hepatomegaly, or neurologic impairment compared to 2.1% of those who were postnatal CMV- (P<.05). No HIV-uninfected infants with HT had any of these symptoms.
Conclusions: In our population, while rates of

Methods:
Study Group:
 • Infants born 1988-2002 to HIV-infected women and followed at the Maternal Child Adolescent Center for Infectious Diseases and Virology (MCA) at the Los Angeles County+University of Southern California Medical Center (LAC+USC)
 • MCA is the largest perinatal HIV specialty and referral center in LAC
 • Approx. 45 HIV+ women deliver annually at the Medical Center
 • HAART became standard of care at MCA in 1996
 • MCA has had no mother-child HIV transmissions since 1996 among women in our program
Definitions:
Congenital CMV infection: A positive oral or urine CMV culture in first 3 weeks of life
Postnatal CMV infection: A positive oral or urine CMV culture between the first 3 weeks to 6 months of life, excluding those with a positive congenital CMV+ culture
Prenatal maternal HAART: Antiretroviral therapy with ≥3 drugs prescribed to mother any time during pregnancy
Symptoms potentially CMV related: failure to thrive, lymphadenopathy, splenomegaly, hepatomegaly, neurologic impairment.
Data:
 • Demographic, laboratory results and treatment data were collected as part of the MCA Natural History Study
 • Multiple CMV oral and urine cultures for infants were collected
 • Birth characteristics, symptoms lasting more than 2 months during the first year of life, and prenatal HT were collected during 6 month chart reviews as part of the CDC Pediatric Spectrum of Disease (PSD) study

Table 1: Description of study population and percent CMV positive (N=612)

Characteristic:	Total (n=612)	Congenital (n=257)	Postnatal (n=385)
Race:			
white	28 (7)	1 (8)	7 (26) *
black	12 (31)	5 (6)	12 (10)
hispanic	29 (61)	4 (2)	33 (14)
other	3 (1)	0 (0)	0 (0)
Sex:			
male	22 (55)	6 (4)	32 (15)
female	18 (45)	4 (3)	20 (12)
HIV status:			
positive	36 (9)	1 (4)	9 (29) **
negative	37 (91)	9 (4)	43 (12)
Mother IDU:			
yes	71 (17)	2 (5)	9 (15)
no	33 (82)	8 (4)	40 (13)
unk	4 (1)		
Type of delivery			
vaginal	27 (67)	39 (15)	7 (4)
c-section	12 (30)	11 (9)	3 (4)
unk	1 (3)		
Gestational age:			
premature (<37 wks)	85 (21)	2 (5)	13 (17)
full-term (>37 wks)	30 (75)	7 (3)	13 (13)
unk	18 (4)		37
		Congenital	Postnatal
		CMV+ CMV-	CMV+ CMV-
Mean birth weight (gms)	3006	2982 317 *	3113 310
Mother's characteristics:			
Mean age (yrs.) at delivery	28	27 28	28 28
Mean prenatal nadir CD4 cells/mm ³	348	318 352	316 354
Mean highest viral HIV RNA (log copies/ml)	3.2	2.8 3.3	3.5 3.2

* P<.05, ** P<.01, +comparing whites to non-whites



Background and Objectives:

- After 1994 when AZT was shown to reduce perinatal HIV transmission by two-thirds, antiretroviral treatment (ART) during pregnancy, labor and delivery and postnatally to the newborn became standard of care for prevention of perinatal HIV transmission.
- Since the introduction of highly active ART (HAART) in 1996, these therapies have reduced perinatal HIV transmission to <1%.
- The impact of HAART (HT) on reducing congenital and postnatal CMV+ rates in HIV-exposed infants has not been studied.
- Demonstrating a benefit of HT on CMV transmission among HIV-exposed infants would be useful in counseling our HIV+ pregnant patients.

• 199 (48%) infants were born 1988-1996 and 213 (53%) 1997-2002
 • 199 (48%) of infants born 1988-2002 had mothers who were HIV-infected and 213 (53%) had mothers who were HIV-uninfected
 • Risk ratios were calculated as the rate among those without HT compared to those with HT
 • To use the maximum amount of data, postnatal CMV+ rates are shown for the 385 infants with at least 1 culture between the first 3 weeks to 6 months of life with the caveat that there could be some misclassification
 • Repeated analyses of postnatal CMV+ rates among infants who had both a congenital and postnatal test (n=230) showed the

> Most infants were hispanic or black, delivered vaginally, full-term and of normal birth weight
 > For congenital CMV, only mean birth weight was significantly lower for CMV+ vs. CMV-
 > For postnatal CMV, whites vs. nonwhites and HIV+ vs. HIV- were significantly

Table 2. Percent postnatal CMV+ by HAART and selected characteristics (n=385)

Characteristic:	Without HAART		P value	With HAART		P value
	No.	(%)		No.	(%)	
Delivery:						
C-sect	3	(8)	P=.09	8	(9)	P=.7287
Vaginal	30	(19)		9	(10)	
Mother's nadir CD4:						
≤ 200	9	(31)		2	(7)	P=.5943
>200	12	(14)	P<.05	9	(9)	
Mother's highest HIV RNA:						
> 400	15	(25)	P=.167	6	(7)	P=.3831
≤ 400	5	(16)		5	(12)	
Race:						
White	5	(31)	P=.128	2	(18)	P=.2908
Non-white	30	(16)		15	(9)	

> Lower maternal CD4 was associated with postnatal CMV+ for those without HT

Conclusions:

- While most of the reduction in postnatal CMV+ transmission at MCA was due to prevention of HIV transmission, importantly we saw postnatal CMV+ rates reduced in HIV-uninfected infants and fewer symptoms potentially related to CMV
- Without HAART, more severe immunodeficiency in the mother (i.e. lower CD4 counts) may allow for ongoing shedding and opportunities for postnatal CMV transmission
- For HIV-exposed children, there may be many health benefits to early identification and treatment of their HIV+ pregnant mothers
- Further study is needed to examine mechanisms of