Cytomegalovirus Shedding in Brazilian Pregnant Women Living With HIV and CMV Infection in Infants 0820

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BACKGROUND

- Cytomegalovirus shedding among *CMV-seropositive* women living with HIV (WLHIV) on combined antiretroviral therapy (HAART), and its impact on infant CMV infection in *non-breastfeeding settings*, remains unclear.
- We assessed maternal CMV shedding in urine from pregnancy through six weeks postpartum, determining the timing and incidence of infant CMV transmission from fetal life through 12 months of age. Potential impacts of CMV infection on infant growth and neurodevelopment were explored.

METHODS

We analyzed data from Brazilian participants of the International Prospective Cohort of HIV and ZIKA in Infants and Pregnancy Study (HIV-ZIP study)

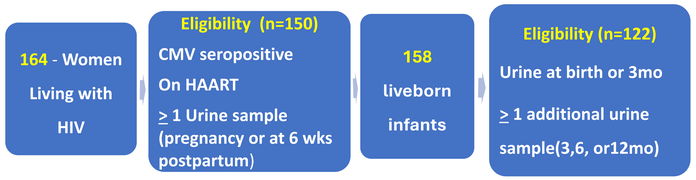


Fig 1- Selection Criteria of Mothers and Infants

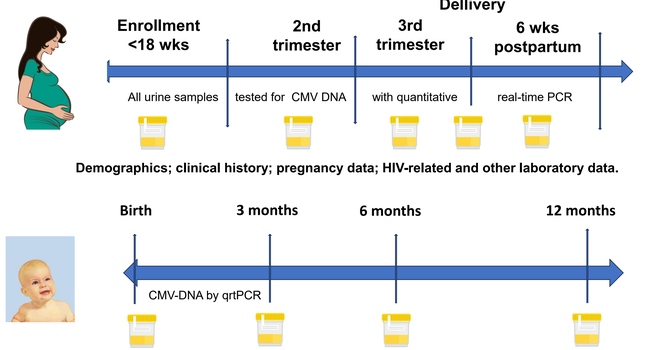


Fig 2-Clinical and Laboratory follow-up of mothers and infants

Definitions of CMV shedding and infection

- **Confirmed Congenital CMV (cCMV):** CMV-DNA detected in urine at birth **and** in a subsequent sample
- **Presumed cCMV:** Birth urine unavailable; CMV-DNA detected at 3 mo
- **No cCMV:** CMV-DNA negative at birth or, if unavailable, at 3 mo
- **Perinatal / Early postnatal CMV (Pe/ePn-CMV):** CMV-DNA negative at birth and positive at 3 mo.
- **Postnatal CMV (Pn-CMV):** CMV-DNA negative by 3 mo and positive at 6 and/or 12 mo
- **Maternal CMV shedding:** CMV-DNA detected in urine at any time

CMV shedding in urine occurred in 1/5 of pregnant WLHIV, particularly in women with low CD4+ counts and illicit substance use. Maternal CMV reactivation and household crowding (≥2 people per room) were linked to cCMV infection, whereas postnatal infection occurred infrequently in non-breastfed infants, mainly in mothers with lower CD4+ counts at 6 weeks postpartum, but was associated with stunting at one year of age.

RESULTS

All 150 women were CMV+. 725 urine samples tested for CMV-DNA (150 at enrollment, 147 in 2nd trim, 145 in 3rd trim, 142 at delivery, and 141 at six weeks postpartum).

Maternal CMV shedding



29 of 150 women (19.3%; 95%CI,13.3%–26.4%) shed CMV DNA in urine at least once

1st trimester (n=7), 2nd trim (n=7), 3rd trim (n=9), delivery (n=2), postpartum (n=14), multiple points (n=8).

qCMV-DNA 1.90 to 3.98 $\log_{10}$ cps/mL (median 2.44). CMV DNA levels did not vary by timing of collection

CMV shedders and non-shedders were demographically similar

Table 1: Adjusted Odds Ratios and 95% Confidence Intervals from Multivariable Logistic Regression Model Predicting factors associated with CMV Shedding at any Timepoint in Pregnancy to 6 weeks post-partum

Characteristics	Adjusted OR	95% Confidence Limits		Pr>ChiSq
Maternal age (years) <=18 vs. >18	0.913	0.131	6.353	0.9268
<High School vs. >high school	1.696	0.628	4.58	0.297
≥ 2 people vs. < 2 people per room.	0.51	0.105	2.471	0.4031
Illicit substance use during pregnancy vs. no	**6.309**	**1.325**	**30.043**	**0.0207**
<350 Lymphocytes at entry vs. >=350 cells/mm³	**8.156**	**2.625**	**25.345**	**0.0003**
Entry HIV-RNA (>=400 vs. <399 copies/ml)	1.29	0.46	3.619	0.6282
Any chronic conditions vs. none	1.349	0.51	3.568	0.5463
Any infections vs. none	0.578	0.116	2.88	0.5039
Any pregnancy complications vs. none	0.418	0.147	1.193	0.1031
Currently has a job vs. no job	0.863	0.306	2.434	0.7812

**Models include all variables in the table*

Infant CMV Infection

No infant tested positive by HIV RNA assays; 393 urine samples(101 at birth, 115 at 3, 98 at 6, and 79 at 12 months).

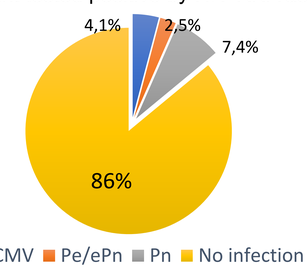


Fig 3- Infant CMV according to classification of infection

17 of 122 infants (13.9%; 95%CI,8.0%–20.0%) had CMV-DNA in urine: 2.61 to 6.08 $\log_{10}$ copies/mL (median 2.61), similarly in congenital and perinatal/postnatal infections.

Infant Number	Birth	3 months	6 months	12 months
Confirmed Congenital infection (cCMV)				
2	5.96 $\log_{10}$ cps/mL	5.36	3.56	5.09
5	3.80	5.25	5.62	4.24
Presumed Congenital Infection / early perinatal				
1	No Sample (NS)	2.70	2.80	NS
3	NS	5.33	4.24	NS
4	NS	5.23	5.24	3.91
Perinatal/early postnatal infection (Pe/ePn)				
6	Undetectable (U)	2.92	2.91	3.67
7	U	2.90	NS	NS
8	U	3.79	U	5.39
Post-natal Infection (Pn)				
9	U	U	NS	2.61
10	U	U	NS	3.41
11	U	U	U	5.22
12	U	NS	U	5.41
13	U	U	U	6.08
14	U	U	U	5.07
15	U	U	U	4.65
16	U	U	NS	4.78
17	U	NS	NS	5.06

Table 3. Adjusted Odds Ratios and 95% Confidence Intervals from Multivariable Logistic Regression Models Predicting factors associated with cCMV and Pe/Pn CMV in infants compared to infants without CMV shedding in the first year of life.

Characteristics	Congenital CMV infection		Perinatal/Post natal CMV	
	Odds ratio (CI95%)	P-value	Odds ratio (CI95%)	P-value
Maternal Age	0.9 (0.7-1.1)	0.23	1.1 (0.9-1.2)	0.38
Completed High School	3.9 (0.3-46.6)	0.29	1.6 (0.5-5.9)	0.45
People per room in the household >=2	**29.7 (1.7-512.7)**	**0.02**	0.5 (0.1-4.9)	0.57
Maternal CMV shedding during gestation	**22.3 (1.2-421.1)**	**0.04**	0.2 (0.1-2.4)	0.22
Maternal lymphocytes at 6 weeks postpartum (<350 cells/mm³)	0.4 (0.1-11.1)	0.60	**5.1 (1.2-23.3)**	**0.03**
Mother has Job	1.5 (0.2-13.4)	0.71	1.2 (0.3-4.6)	0.74

Infant Growth, Ophtalmological and Neurological outcomes

- Anthropometry at birth did not differ by CMV status.
- Hearing screening with OEA showed higher failure rates in cCMV at all time points, reaching statistical significance at 12 months of age.
- No infants with CMV failed ophthalmologic examinations.
- Postnatal CMV shedding independently predicted stunting in a logistic regression model.
- Bayley (BSID-III-ST) indicated that most infants developed within normal limits.
- No differences in overall neurodevelopmental risk were observed by CMV status.

CONCLUSIONS

- 20% of pregnant WLHIV on HAART exhibited intermittent CMV-DNA shedding in urine during pregnancy or up to six weeks postpartum.
- Illicit substance use and low CD4+ T-cell counts were the strongest predictors of maternal viruria.
- 14% of infants acquired CMV infection—4% congenitally and 10% postnatally.
- Congenital CMV infection was associated with maternal CMV shedding during pregnancy and household crowding (>2 persons/room).
- Postnatal CMV infection was more common in infants from mothers with lower CD4+ counts at 6 weeks postpartum.
- CMV infection was not associated with infant acute morbidity or impaired neurodevelopment, although postnatal CMV infection was associated with stunting at one year.

PLAIN LANGUAGE SUMMARY

There is an ongoing risk of CMV replication and transmission in women living with HIV, even under effective antiretroviral therapy. Strengthening immune monitoring, addressing behavioral risk factors, and improving early infant CMV screening may help mitigate infection-related outcomes in this high-prevalence setting.