

CONGENITAL CYTOMEGALOVIRUS INFECTION IN INFANTS BORN TO HIV-INFECTED MOTHERS: PREVALENCE AND RISK FACTORS.

FRENCH PERINATAL COHORT EPF (ANRS C01/10/11)

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ABSTRACT

Background: In developed countries, 0.3% to 0.5% of all newborns are congenitally infected by cytomegalovirus (CMV) with the risk of sensorineural hearing loss or mental retardation. Few results about congenital CMV infection in infants born to HIV-infected women have been reported. We aimed to estimate the prevalence of congenital CMV infection and perinatal risk factors among children enrolled in the ANRS French Perinatal Cohort (EPF), a national multicenter prospective cohort of mother-to-child HIV transmission.

Methods: All infants born between 1993 and 2004 in EPF sites and screened for CMV were included in the analysis. As part of the standardized follow-up of infants born alive during that period in participant maternities, a urine sample was obtained within the ten first days of life. These urine samples were tested for CMV, using rapid viral culture from 1993 to 2001 and CMV real-time PCR since 2001.

Results: Between 1993 and 2004, 5052 of the 7567 newborns included in EPF were screened for CMV. The prevalence of CMV infection was 2.4% (115 positive tests; 95% confidence interval CI: 2.0- 2.8%), and 51.6% were born to mothers with a documented and positive serological CMV test at delivery: time from seroconversion was unknown for most of them; it occurred during pregnancy in at least 0.7% (N=19) of them. As expected, congenital CMV infection tended to be more frequent in case of maternal seroconversion (2/19; 10.5% versus 10/540; 1.9%; p=0.06).

The prevalence of congenital CMV infection was significantly higher in HIV-infected newborns (10.2% ; 13/127; 95% CI: 5.6-16.9%) than in uninfected ones (2.2% ; 102/4704; 95% CI: 1.8-2.6%; p<0.01). Among children term born and HIV uninfected, year of delivery, maternal young age, and maternal low CD4 T cell count near delivery (<200 CD4 cells/mm³) were factors independently associated with congenital CMV infection in a logistic regression.

Conclusion: The prevalence of congenital CMV infection was high in children born to HIV- infected mothers, with a high risk of co-infections among HIV-infected infants.

OBJECTIVE

To estimate the prevalence of neonatal CMV infection and to identify perinatal risk factors among children born to HIV1-infected mothers between 1993 and 2004

STUDY POPULATION

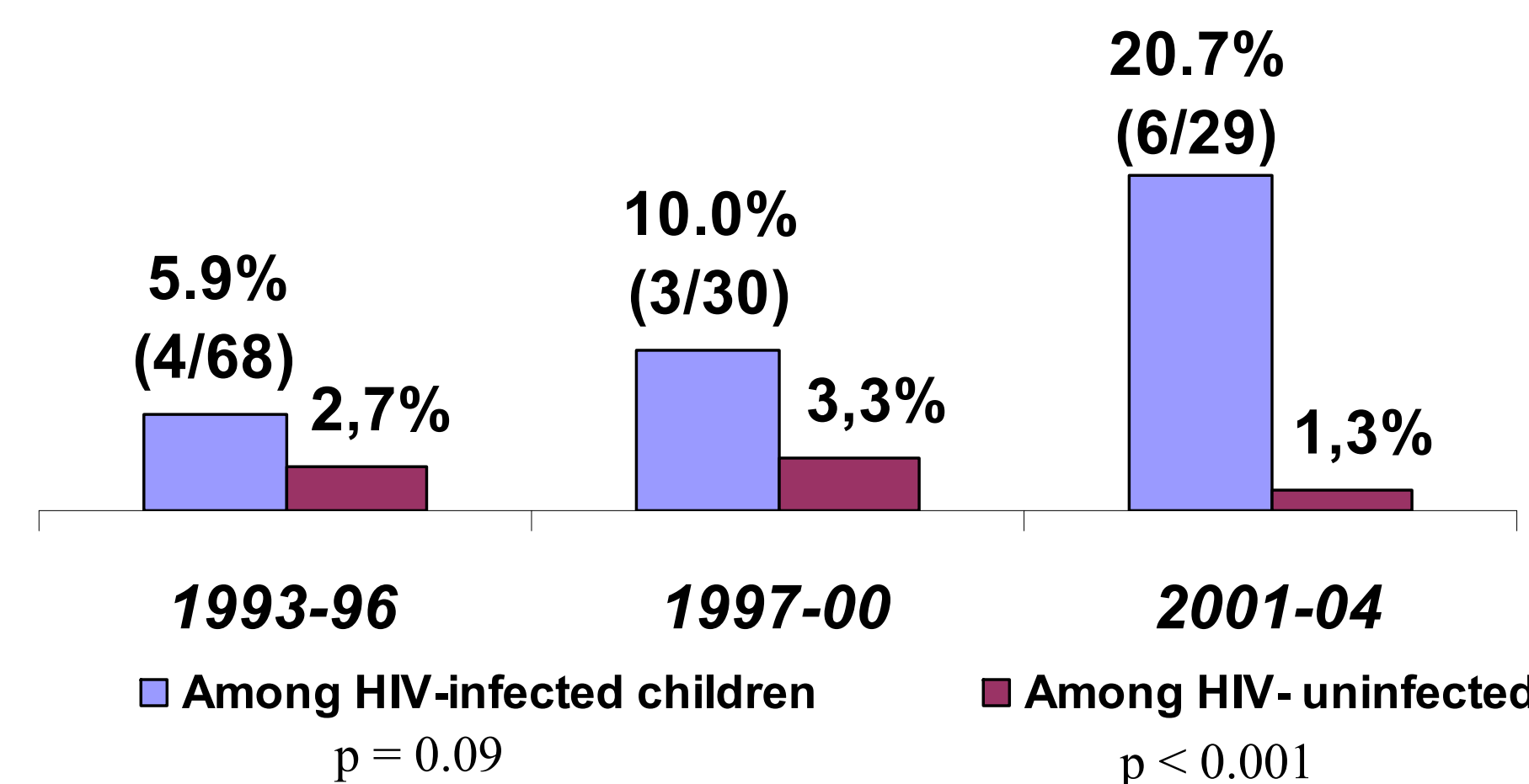
The ANRS French Perinatal Cohort (EPF)

- Prospective multicenter national cohort of HIV-infected mother/child pairs
- Follow up every 6 months :
 - 2 years old for uninfected children
 - 18 years old for infected children

Study population and CMV diagnostic

- Neonates born alive to HIV1 – infected mothers between 1993 and 2004 (N=7 567)
- 67% of neonates were screened for CMV within the first 10 days of life as part of routine evaluation
- Diagnostic on urine sample: rapid culture from 1993 to 2001 ; CMV real-time PCR since 2001

Fig 1 – Prevalence of congenital CMV infection (ANRS EPF 1993-2004)



	Urine tested		Congenital CMV infection	
	N	n	%	95% CI
Among all tested children	4831	115	2.4	(2.0 - 2.8)
<i>born to mothers known as CMV+</i>	2484	75	3.0	(2.3 - 3.7)
According to HIV child infection				
HIV1 - uninfected	4704	102	2.2	(1.8 - 2.6) p < 0,01
HIV1 - infected	127	13	10.2	(5.6 -16.9)

RESULTS

- **67% (5052 / 7567) neonates screened between 1993 and 2004**
- **Prevalence of congenital CMV infection (Fig 1) : 2.4%** (115/4831; 95%CI: 2.0-2.8%)
 - significantly higher in HIV1-infected children: **10.2 % versus 2.2% in uninfected** (p<0.01)
- **Factors associated with congenital CMV in term born HIV-uninfected during HAART era (Table 1):**

- decreasing risk with year of delivery, older maternal age, and higher CD4 cell count
- lower risk in case of starting ART at first trimester than second trimester among mothers who need ART for themselves

Table 1 – Factors associated with congenital CMV infection in term born HIV-uninfected children during HAART era (ANRS EPF 1997-2004)

	N (tested)	Univariate analysis (N=3375)		Logistic regression (N=3158)				
		n (CMV+)	%	crude OR	p	adj OR	CI95%	p
Year of delivery								
2003-2004	994	8	0.8	1	<0.01	1		<0.01
2001-2002	1038	14	1.4	1.7		1.6	0.6-3.8	
1999-2000	770	20	2.6	3.3		3.3	1.4-7.7	
1997-1998	573	22	3.8	4.9		4.1	1.8-10.1	
Geographical origin								
Other	1370	20	1.5	1	0.15	1		0.16
Sub-Saharan African	1996	43	2.2	1.5		1.5	0.8-2.5	
Maternal age								
≥ 25 years old	2934	49	1.7	1	0.01	1		0.02
< 25	441	15	3.4	2.1		2.1	1.1-3.8	
Type of prepartum ARV								
HAART	1622	33	2.0	1	0.84			
Bitotherapy	994	17	1.7	0.8				
Monotherapy	667	13	2.0	1.0				
Untreated	83	0	0.0	-				
Time at starting ARV								
Started before pregnancy	976	13	1.3	1	0.01	1		0.03
4 – 13 gestational weeks	177	2	1.1	0.8		0.9	0.2-3.9	
14 - 20 wks	404	14	3.5	2.7		2.2	1.0-4.9	
21 - 26 wks	476	16	3.4	2.6		2.6	1.2-5.7	
≥ 27 wks	1239	18	1.5	1.1		1.0	0.5-2.2	
Untreated	83	0	0.0	-		-	-	
CD4 cell count at delivery								
≥200 cells/mm ³	2966	52	1.8	1	0.02	1		0.02
<200 cells/mm ³	299	11	3.7	2.1		2.2	1.1-4.3	
HIV1 RNA at delivery								
< 400 c/mL	2101	34	1.6	1	0.25			
[400 – 1 000[c/mL	286	7	2.5	1.5				
≥ 1 000 c/mL	849	21	2.5	1.5				
Child gender								
Girls	1613	24	1.5	1	0.09	1		0.09
Boys	1744	40	2.3	1.6		1.6	0.9-2.7	

CONCLUSION

- Prevalence of congenital CMV infection:**
- high among HIV-infected children
 - decreasing in HIV-uninfected children in HAART era
- The restoration of CD8 functions and rapid control of CMV viremia may explain the decrease of CMV transmission for mothers who had early initiation of ART during pregnancy