Early Cytomegalovirus (CMV) Viraemia and Clinical Outcomes in HIV- infected Children in the Early ART Era

Nei-yuan Hsiao[1], Kennedy Otwombe[2], Landon Myer[3], Avy Violari[2], Diana Gibb[4], Ravindre Panchiar[2], Abdel Babiker[4], Patrick Jean-Phillipe[5], Mark Fredric Cotton[6]

[1]Clinical Laboratory Sciences, National Health Laboratory Service/University of Cape Town, Cape Town, South Africa,[2]Perinatal HIV Research Unit, Johannesburg, South Africa,[3]Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa,[4]Medical Research Council UK, London, United Kingdom,[5]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States,[6]Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa

Background: Cytomegalovirus (CMV) is an important cofactor for HIV disease progression and is associated with poor outcomes in HIV-infected infants not on antiretroviral therapy (ART)[1]. In sub-Saharan Africa, 90% of infants acquire CMV post-natally in their first year of life but its effect on HIV infection among infants on ART is unknown.

Methods: Effect of early CMV viraemia in HIV infected infants was examined in the Children with HIV Early Antiretroviral Therapy Study (CHER) cohort. Early CMV viraemia was determined by Roche CAP/CTM CMV PCR (Roche Molecular Diagnostics, Branchburg, New Jersey) on CHER baseline plasma samples.

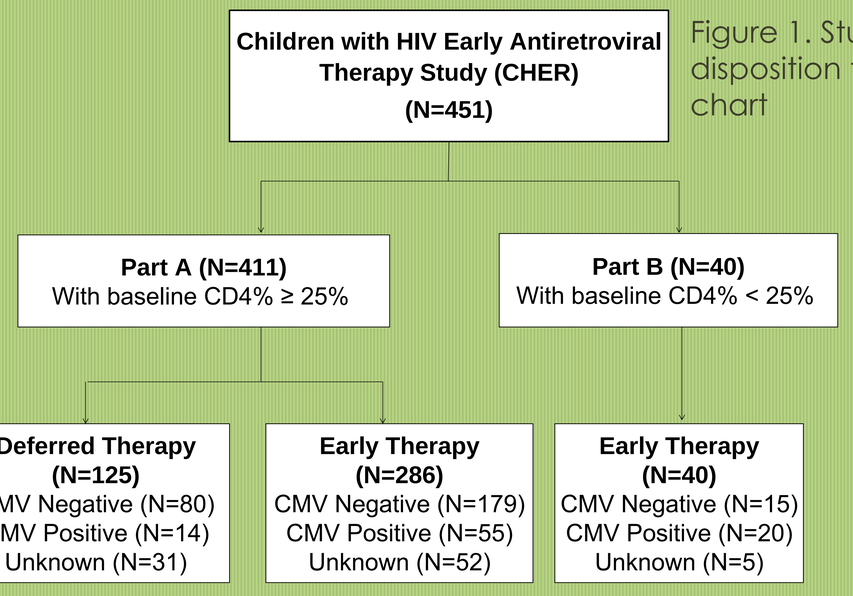


Figure 1. Study disposition flow chart

Results:

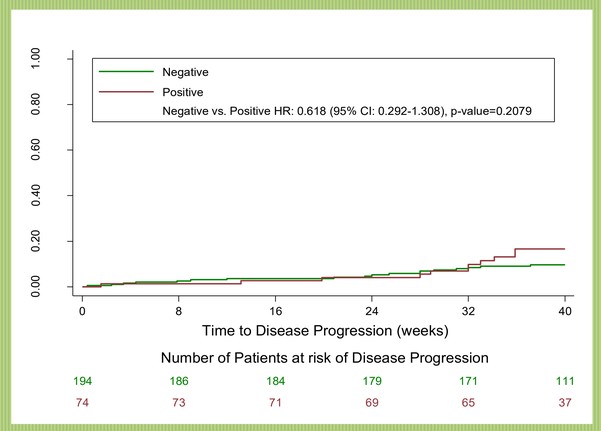
Table 1 Comparison of baseline characteristics by CMV status

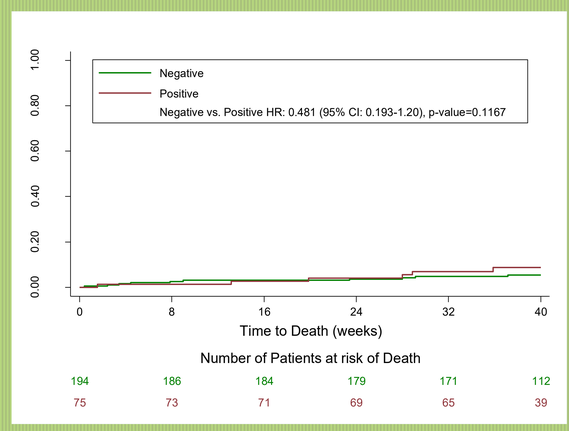
Variable	CMV Positive (N=89)	CMV Negative (N=274)	P-Value
Median Age in weeks (IQR)	7.9 (7.0- 9.6)	7.6 (6.7- 9.0)	0.0953
Median CD4% (IQR)	30.4 (23.4- 34.2)	37.5 (30.8- 43.7)	<.0001
HIV Viral Load			
10,000-100,000 (%)	2/89 (2)	17/274 (7)	0.1453
100,000-500,000 (%)	14/89 (16)	75/274 (27)	0.0265
>500,000 (%)	73/89 (82)	182/274 (66)	0.0052
Any History of breast feeding	14/89 (16)	21/274 (8)	0.025
Median Weight-for-age z-score (IQR)	-1.5 (-2.3,-0.8)	-1.0 (-1.9,-0.2)	0.0004
Median Height-for-age z-score (IQR)	-1.9 (-2.4,-1.0)	-1.4 (-2.3,-0.4)	0.0097

Table 2 Comparison of one year outcomes by CMV status

Variable	CMV Positive (N=89)	CMV Negative (N=274)	P-Value
Weeks of follow-up (IQR)	39.9 (32.3-40)	39.9 (36-40)	0.4325
Deaths (%)	11/89 (12)	26/274 (9)	0.4368
Lost to follow-up (%)	3/89 (3)	9/274 (3)	0.9685
Median Weight-for-age z-score (IQR)	-0.56 (-1.5,0.2)	-0.21(-1.1,0.5)	0.0336
Hospitalisations			
Number of children (%)	28/89 (31)	73/274 (27)	0.3782
Number hospitalisations	46	109	0.1365
Severe CDC stage B events			
Number of children (%)	9/89 (10)	24/274 (9)	0.6996
Number of events	9	24	0.7132
CDC stage C events			
Number of children (%)	9/89 (10)	19/274 (7)	0.3289
Number of events	9	21	0.4866
AIDS Encephalopathy (%)	7/89 (8)	9/274 (3)	0.0674

Figure 2a(left) and 2b(right). Time to disease progression(2a) and death(2b) by CMV status among participants receiving early ART





Conclusion: Our study confirms that early CMV viraemia is associated with breastfeeding exposure and poorer immunological status prior to ART initiation. Early ART appears to ameliorate most effects of concurrent CMV infection.

Reference:

1: Kovacs A, Schluchter M, Easley K, Demmler G, Shearer W, La Russa P, Pitt J, Cooper E, Goldfarb J, Hodes D, Kattan M, McIntosh K. Cytomegalovirus infection and HIV-1 disease progression in infants born to HIV-1-infected women. Pediatric Pulmonary and Cardiovascular Complications of Vertically Transmitted HIV Infection Study Group. N Engl J Med. 1999 Jul 8;341(2):77-84.