CMV Viraemia Is Associated With Mortality Among Children With HIV Starting ART in Sub-Saharan Africa

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Background

Cytomegalovirus (CMV) co-infection is associated with mortality in adults with HIV, but the association between CMV viraemia and mortality in children with HIV is uncertain.

Methods

497 children (mean age 6.5 years, standard deviation ±4.2; 48% male) enrolled in the ARROW trial in Uganda and Zimbabwe had CMV viraemia quantified: at ART initiation; after 12 weeks; and after 84 weeks post-initiation in a case-cohort design. Cases were those who died, had new or recurrent WHO Stage 4 events, or had poor response to ART (CD4<15%). **Assay differed by country.** In Zimbabwe, the Abbot RealTime CMV assay was used (upper and lower limits of detection (ULLD) 156 million IU/mL - 50 IU/mL. In Uganda, Great Ormond Street's CMV assay was used (ULLD 12 million IU/mL – 120 IU/mL). **Associations between baseline CMV viraemia and subsequent mortality were evaluated using multivariable Cox regression models, adjusting for HIV viral load, CD4 percentage and IL6 at ART initiation.**

In two studies in Uganda and Zimbabwe, CMV viraemia at the point of ART initiation was independently associated with mortality in children.

Results

JCRC = Joint Clinical Research Centre; PIDC = Paediatric Infectious Disease Clinic, Mulago Hospital

Factor at ART initiation	Overall (N=497)	Cases (N=104)	Controls (N=393)
Site			
Uganda Entebbe (non-urban)	57 (11.5%)	15 (14.4%)	42 (10.7%)
Uganda JCRC (urban)	142 (28.6%)	28 (26.9%)	114 (29.0%)
Uganda PIDC (urban)	135 (27.2%)	26 (25.0%)	109 (79.6%)
Zimbabwe Harare (urban)	161 (32.4%)	33 (31.7%)	128 (79.5%)
In immunology sub-study	256 (51.5%)	15 (14.4%)	241 (61.3%)
Male sex	238 (47.8%)	52 (50.0%)	186 (47.3%)
Age, years; mean (SD)	6.5 (4.2)	6.1 (4.1)	7.7 (4.4)
Viral load, copies/mL; median (IQR)	238 850 (81 330, 641 190)	290 236 (144 434, 757 040)	226 326 (68 571, 614 519)
CD4%; median (IQR)	11.4 (6.0, 17.0)	5.1 (2, 10)	13.0 (8.0, 19.0)
WHO clinical stage			
1	9 (1.8%)	3 (2.9%)	6 (1.5%)
2	147 (29.6%)	23 (22.1%)	124 (31.6%)
3	263 (52.9%)	57 (54.8%)	206 (52.4%)
4	78 (15.7%)	21 (20.2%)	57 (14.5%)
CRP concentration, mg/L; median (IQR)	4.5 (1.4, 14.6)	7.5 (1.6, 20.0)	4.1 (1.4, 13.2)
IL6 concentration, pg/mL; median (IQR)	6.2 (4.7, 9.5)	8.3 (5.5, 12.5)	5.8 (4.6, 8.9)

	Unadjusted HR (95%CI)	P	Adjusted* HR (95%CI)	P
CMV detectable vs. not detectable				
Uganda	3.03 (1.10, 8.33)	0.03	2.86 (1.02, 8.33)	0.045
Zimbabwe	2.00 (0.23, 16.7)	0.52	2.08 (0.22, 20.0)	0.52
1 Log_{10} increase in CMV				
Uganda	1.03 (0.48, 2.20)	0.95	0.83 (0.37, 1.88)	0.66
Zimbabwe	2.37 (1.52, 3.68)	<0.001	2.35 (1.34, 4.12)	0.003

*Adjusted for Participation in the Immunology sub-study, CD4 and IL6

CMV viraemia was associated with mortality — but the relationship differed by country / assay type.

Conclusions

CMV viraemia at the time of ART initiation is associated with mortality in children with HIV in sub-Saharan Africa, **independent of HIV viral load, immunosuppression and IL6.**