

Advances in viral pathogenesis

OC 50 Baseline viral load impacts the aging process in infants with perinatally acquired HIV enrolled in the EARTH cohort

Authors

M.R. Petrara¹, E. Ruffoni¹, G.R. Pascucci², E. Morrocchi², F. Carmona¹, C. Giaquinto³, N. Cotugno¹, P. Rossi¹, S. Giunco⁴, P. Palma², A. De Rossi^{1,4}, within the EPIICAL Consortium

Affiliation

¹Immunology and Diagnostic Molecular Oncology Unit, Veneto Institute of Oncology IOV-IRCCS, Padova, Italy, ²Research Unit of Clinical Immunology and Vaccinology, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy, ³Department of Women's and Children's Health, University of Padova, Division of Pediatric Infectious Diseases, Padova, Italy, ⁴Oncology and Immunology Section, Department of Surgery, Oncology and Gastroenterology, University of Padova, Italy

ABSTRACT

Backgrounds: The aim of this study is to define the impact of baseline viral load on the premature aging process in infants with perinatally acquired HIV (PHIV), from the Early Anti-Retroviral Treatment in HIV children (EARTH) cohort.

Methods: Thirty-six PHIV infants, ART-naïve at enrolment, with a median age of 1.6 (1.3-2.5) years, were studied for their immune aging profile (activated, senescent and exhausted T cells) by flow cytometry. Relative telomere length, T-cell receptor excision circle (TREC), and HIV-DNA in peripheral blood mononuclear cells (PBMC) were measured by multiplex real-time PCR, real-time PCR and ddPCR, respectively. Statistical analyses were performed using SigmaPlot software.

Results: Plasmaviremia significantly correlated with HIV-DNA in PBMC ($r=0.525$, $p=0.003$). According to plasmaviremia at enrolment, PHIV infants were divided in group 1 (VL <25 percentile of Log₂ HIV-RNA) and group 2 (>75 percentile of Log₂ HIV-RNA). Baseline levels of HIV-DNA in PBMC were significantly higher in group 2 than in group 1 (1159 [617-4426] vs 89 [9-1607] copies/106 PBMC, $p=0.011$). Similarly, group 2 had higher percentages of activated, senescent and exhausted CD4 and CD8 T cells than group 1 (table). Relative telomere lengths were significantly shorter in group 2 than in group 1 (1.82 [1.68-1.90] vs 1.93 [1.78-2.26], $p=0.020$). TREC levels were lower in Group 2 than in Group 1 (518 [426-666] vs 647 [538-865], $p=0.061$).

Conclusions: Higher levels of viral load strongly correlates with HIV-DNA in PBMC and lead to higher immune activation, senescence and exhaustion, thus suggesting that baseline levels of plasmaviremia may accelerate the aging process.

Parameters Median [IQR]	group 1 (n=16)	group 2 (n=20)	p-value
%CD4 activation (CD3+CD4+CD38+HLA-DR+)	1.56 [1-2.21]	3.36 [2.60-9.55]	<0.001
%CD8 activation (CD3+CD8+CD38+HLA-DR+)	1.75 [1.06-2.15]	3.51 [2.59-9.13]	<0.001
%CD4 senescence (CD3+CD4+CD28-CD57+)	0.53 [0-6.67]	23.13 [18.79-35.33]	<0.001
%CD8 senescence (CD3+CD8+CD28-CD57+)	26.22 [11.29-39.45]	44.97 [31.96-61.32]	<0.001
%CD4 exhaustion (CD3+CD4+PD-1+)	7.04 [5.17-10.77]	15.25 [9.23-20.11]	0.013
%CD8 exhaustion (CD3+CD8+PD-1+)	14.66 [7.04-19.80]	7.54 [4.52-9.75]	0.028