The CARMA Study: Children on early suppressive ART Total HIV-1 DNA quantitation 12 years post ART initiation.
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Background: Future strategies aimed at achieving antiretroviral therapy (ART)-free HIV remission are likely to target individuals with a limited size of viral reservoir. We investigated factors associated with low reservoir measured as total HIV-1 DNA in PBMCs in children with perinatally acquired HIV-1 infection (PaHIV) from 5 European pediatric centers (UK, Spain and Italy) in the EPIICAL consortium.

Methods: 40 children with PaHIV commenced ART <2 years of age, suppressed within 12 months of start and remained suppressed (viral load, (VL) <50 copies/ml) for at least 5 years. Total HIV-1 DNA was measured in isolated PBMCs by quantitative real time PCR (copies/million PBMCs). Factors associated with total HIV-1 DNA were analyzed using generalized additive mixed models. Age at ART, VL at ART initiation, and baseline % CD4 effects were tested including smoothing splines to test non-linear association. ART drug combination of each patient was included as random effects.

Results: Of 40 perinatally infected children, 27 (67.5%) female, 21 (52.5%) Black/Black African, 13 (32.5%) Caucasian, 10 were seronegative on 4th generation HIV antibody/antigen at a median [IQR] of 12.2 [8.03; 15.6] years of age. Total HIV-1 DNA measured at a median of 12 [7.3; 15.4] years after ART initiation was below level of detection in 5 children, with a median of 50.9 [25.3, 117.3] copies/10^6 PBMC in the remaining 35 children. DNA levels were positively associated with age and viral load at ART initiation and baseline % CD4 (Figure1). While ART initiation presented a quasi-linear association (coef=0.15 (0.6), p=<0.001), the effect of VL (coef=0.35 (0.16), p=0.032) is only noticeable when >6logs. The effect of baseline % CD4 (coef=0.03 (0.01), p=0.049) was not maintained above 40%.

Conclusion: In this early treated PaHIV cohort on sustained suppressive ART for more than a decade, total HIV-1 DNA was undetected in one eighth. Lower DNA levels were associated with younger age at ART initiation, VL <6logs at ART initiation, and lower CD4 %, supporting current global guidelines of early diagnosis and ART initiation for all infants.