HIV-1 reservoir dynamics in early treated children with perinatally acquired HIV: does sex matter?

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Background

- Eliminating the HIV-1 reservoir is key to an effective HIV cure.
- In children, ART initiation before postnatal peak limits viral exposure, rapidly decreases the viral load, reduces the period of viremia, and might favourably impact the viral reservoir in the peripheral blood and other organs.
- A better understanding of the size and nature of the viral reservoir will help the design of cure strategies.
- We performed a longitudinal analysis of the total HIV reservoir in perinatally HIV-infected, early treated children.

Methods

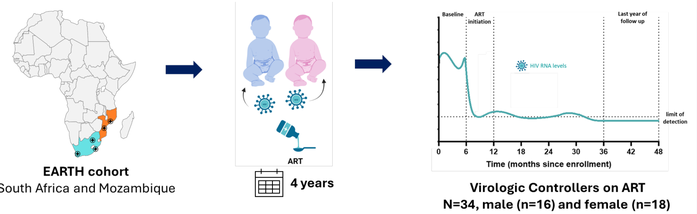

Figure 1: EARTH study cohort

Note: ART was initiated at a median of 34 days of life and the median time to viral suppression in virological controllers was 363 days on ART

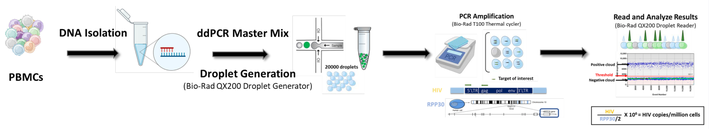

Figure 2: HIV reservoir quantification by droplet digital PCR (ddPCR)

The lower reservoir size in males after 4 years of ART is a novel finding, suggesting that sex differences should be considered to optimize HIV cure strategies in children.

Results

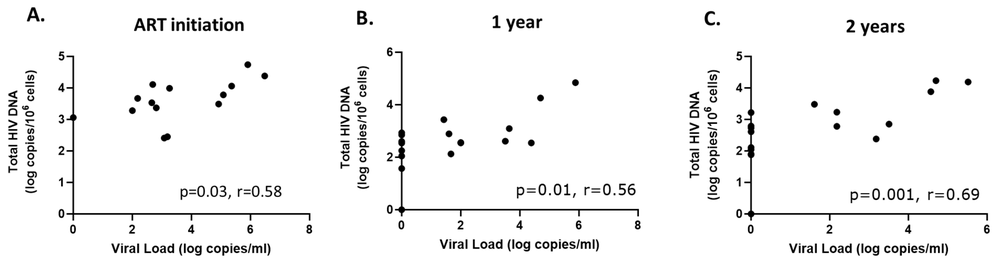

Figure 3: There was a positive correlation between baseline viral load and proviral load measured at A) ART initiation, B) 1 year, and C) 2 years of follow up.

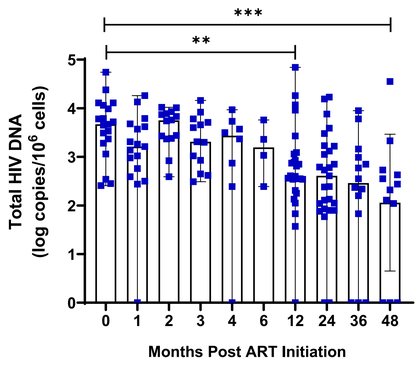

Figure 4: At ART initiation the median total HIV DNA level was 3.7 log copies/10^6 cells. The HIV DNA reservoir decreased gradually over the first 6 months (median=3.2 log copies/10^6 cells) of ART with significant decrease after 1 year (p=0.002). There was a further decline over the next 3 years (median=2.05 log copies/10^6 cells (p<0.0001).

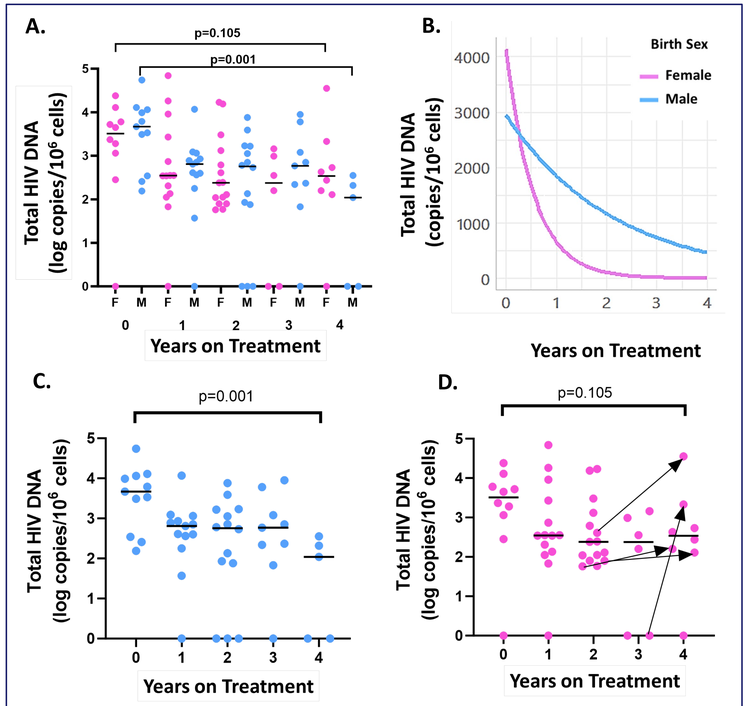

Figure 5: A) There was no difference in proviral load at ART initiation between sexes. B) Early reservoir decay is faster in females - for each year after treatment, males have 1.36 times higher reservoir size (p=0.217). C,D) But after 4 years, the HIV reservoir size decreased significantly from baseline in (C) males (p=0.001) but not (D) in females.

Conclusions

- After 3 years on ART, the viral reservoir continues to decline in males, while some females display an expansion of the viral reservoir. The underlying mechanisms need to be investigated further.

ADDITIONAL KEY INFORMATION

- This study was performed by the EPIICAL Consortium and funded by ViiV through Penta Child Health Research.
- The funder had no role in the conceptualization, analysis or results.