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Total HIV-1 Nucleic Acid Increases Precede Plasma RNA Rebound During Pediatric ATI

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BACKGROUND

In the absence of a reliable biomarker for HIV cure/remission, analytical treatment interruptions provide the only means for evaluating cure/remission interventions. Children who acquire HIV in utero are hypothesised to have higher cure potential due to immune ontogeny that restricts the ability of HIV to establish a large latent reservoir in the setting of very early antiretroviral therapy (ART). However, this limited immune exposure to HIV may increase the risk of acute retroviral syndrome (ARS) in children who later undergo ATI in studies designed to assess HIV cure/remission. To monitor for viral rebound, frequent plasma viral load testing is undertaken, but due to low blood sample volumes in children these samples are often diluted, and this reduces assay sensitivity. We hypothesised that Point-of-care (PoC) testing of total nucleic acid (TNA) in whole blood would detect increases in TNA prior to or at viral rebound as measured by standard HIV-1 RNA plasma assays.

METHODS

To test this hypothesis, we monitored HIV-1 TNA via PoC testing using the Cepheid GeneXpert Qual XC assay, which requires 100ul of whole blood per test. At the same time, we measured plasma HIV-1 RNA via standard testing using the Aptima HIV-1 Quantitative assay which requires 1ml whole blood for 500ul of plasma needed. This monitoring was done in 15 study participants from a very early ART-treated cohort of children living with HIV who underwent ATI in KwaZulu-Natal, South Africa.

Figure 1. HIV-1 TNA Changes Precede Plasma Viral Rebound During ATI

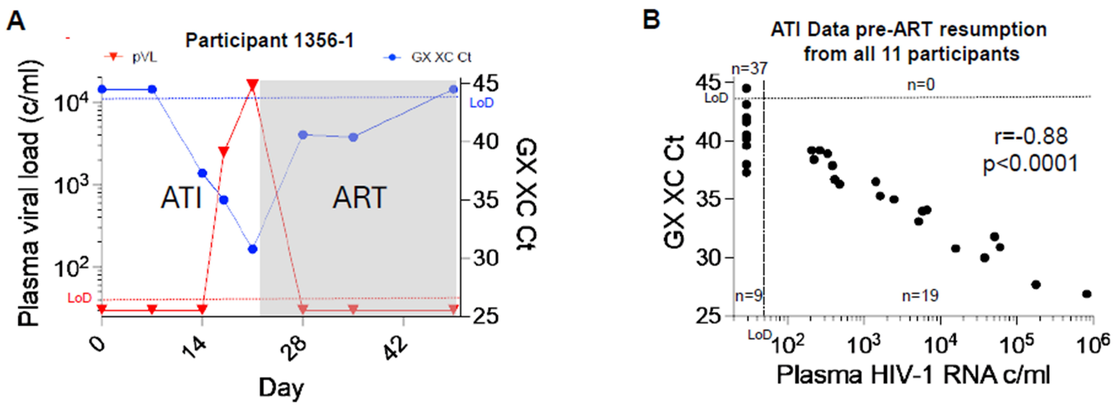


Fig 1(A) Data from a representative participant,1356-1, during ATI and following ART resumption (**B**) ATI data from all 11 participants from ATI initiation prior to ART resumption. Correlation between the Cepheid Xpert ® HIV-1 Qual XC TNA Ct and plasma HIV-1 RNA viral load (c/ml), Spearman r=-0.88, p<0.0001. Excluding datapoints where both Xpert ® HIV-1 Qual XC TNA and plasma HIV-1 RNA viral load were undetectable, r=-0.94, p<0.0001.

Increases in Point-of-Care Total HIV-1 Nucleic Acid Precede Plasma RNA Rebound During Pediatric ATI

RESULTS

Plasma viral rebound occurred in 11 of the 15 participants who underwent ATI. In several instances, HIV-1 TNA became detectable prior to the plasma RNA (Fig 1A&B). There were no cases of HIV-1 RNA being detectable without detection of TNA (Fig 1B). In this group of very early ART-treated children, who were aviremic and had low total HIV-1 DNA loads prior to ATI, plasma viral load and GeneXpert TNA Ct were strongly inversely correlated during the ATI period (r=-0.88, p<0.0001).

CONCLUSION

These data indicate that PoC testing of TNA on whole blood would contribute to safety monitoring in pediatric ATI studies, as a biomarker of imminent plasma HIV-1 RNA rebound. This would enable clinicians to be alerted early to the possibility of ARS and, potentially, the need to reinitiate ART, depending on the study design. At the same time, the low volume of blood sample required for the TNA assay allows for the frequent screening needed during paediatric ATI studies without compromising sensitivity.

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