Joint evolution of CD4 and Viral load trajectories over 2 years in an early-treated pediatric African cohort

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Background

In response to antiretroviral therapy (ART), some patients experience a discordant response, characterized either by a high CD4+ cell count despite persistent viremia or by viral suppression with low CD4+ cell count. Little is known about the meaning of discordant responses in children reported to be 10-20%. In this study we analyse virologic and immunologic phenotypes, including a discordant response based on trajectories instead of arbitrary thresholds.

Methods

59 infants born with HIV and treated before 90 days of life
EARTH Cohort: Prospective cohort enrolling perinatally HIV infected infants from South Africa and Mozambique

The endpoints were the **2-years follow up** of **Viral load (VL)** and **percentage of CD4**

KmL3D R package that implements k-means dedicated to **clustering joint-trajectories** was used to calculate CD4 and VL trajectories . Optimum number of clusters was based on the Calinski-Harabatz criterium. Comparisons between clusters were assessed by the Kruskal-Wallis and Fisher test.

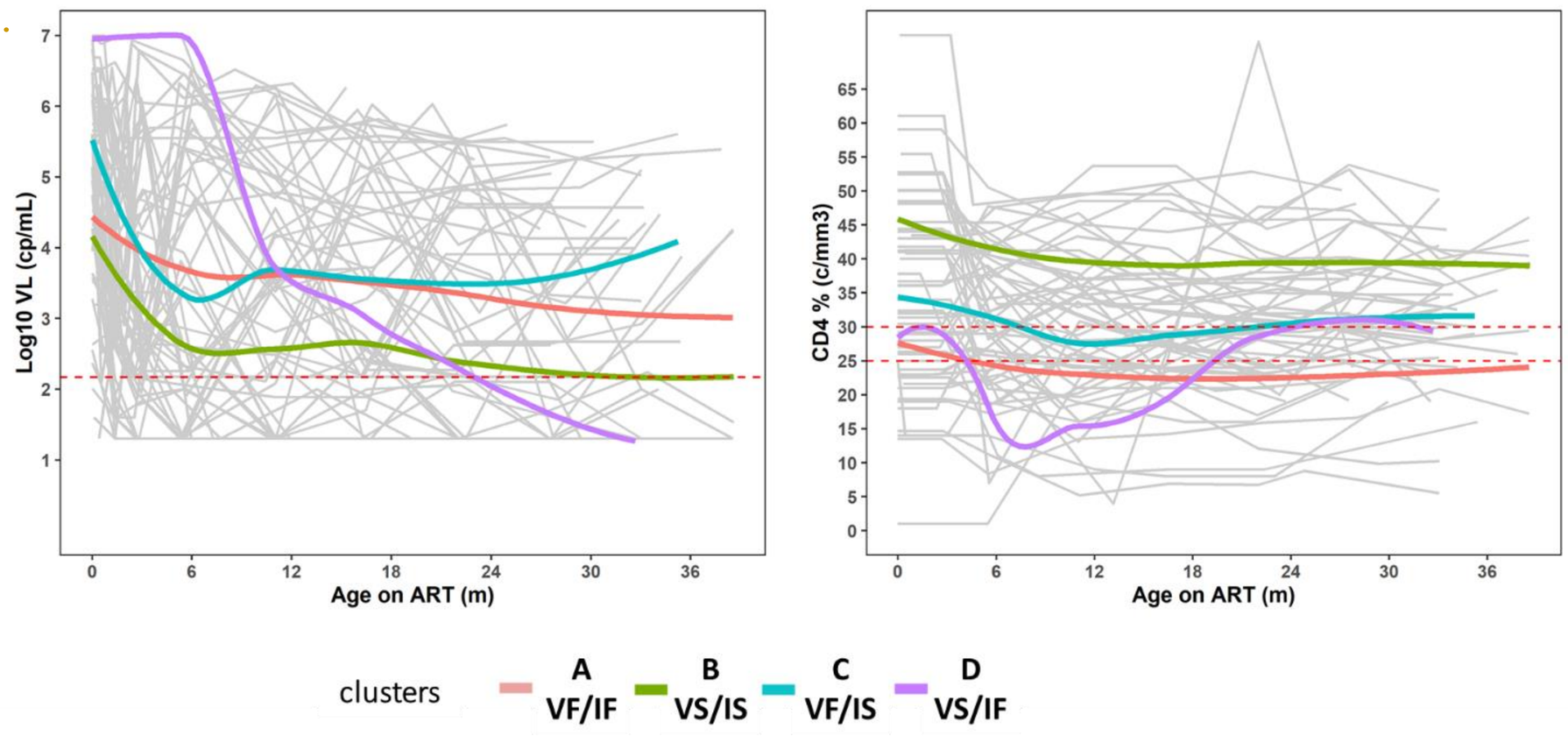
Results

A total of 59 patients with at least 5 measurements of CD4 and VL were included in this study. Four robust clusters were selected. The participants in Cluster A (23/59 (39.0%)) presented virological failure and poor %CD4 reconstitution after treatment. They were treated later, and they had high VL and low %CD4 at ART initiation. Cluster B (19/59 (32.2%)) had participants who achieved viral suppression and had consistently high %CD4.

A total of **17/59 (28.8%) patients presented discordant responses**. Patients included in Cluster C (16/59 (27.1%)) presented **a viral failure and high good CD4 reconstitution**, and patients included in Cluster D (1/59 (1.7%)) also presented discordant response, in this case viral suppression and poor CD4 reconstitution.

Despite acceptable CD4 levels, patients with discordant responses presented higher rates of clinical progression (37.5%) (WHO stage III-IV) than those with viral suppression and good CD4 response (1/19 (5.3%)), p=0.015. Patients with discordant responses were more frequently treated with ART regimens including protease inhibitors (p=0.047).

Figure 1.



Conclusions

A higher rate of discordant responses was present in this study (28.8%) compared to previous reports. The characterization of immunologic and virologic status of the patients could help on the design of personalized therapeutic interventions and on identifying patients for trials.