BACKGROUND

HIV infection has become a chronic disease condition due to advances in antiretroviral treatment (ART). However, people living with HIV appear to have higher rates of age-associated illnesses (frailty, metabolic, cardiovascular, bone and neurodegenerative disorders, and cancer), compared to general population.

ART is not able to eradicate the virus which, likely through the damage of gut mucosa and the release of PAMPS and DAMPs into circulation, induces an inflammatory/immune activated status, that causes biological and immunological senescence, and increases vulnerability for age-linked comorbidities.

Studies on children (0-5 years) with perinatal acquired HIV infection showed that these patients exhibit premature aging and accelerated immune senescence compared to healthy children [1]. Moreover, the timing of ART initiation appears important for consequences on the immune and biological aging profile of children with perinatal HIV [2,3].

Few data are available on adolescent adult with perinatal acquired HIV; thus, the assessment of aging biomarkers and their relation with the HIV reservoir becomes a priority to characterize and monitor adolescent/young adult with perinatal acquired HIV (PHIV).

RESULTS

1. Comparison of immune profile between PHIV adolescent/young adult and healthy controls.

    | Characteristic | PHIV (n=18) | Healthy controls (n=23) | p-value |
    |---------------|------------|------------------------|---------|
    | Age (years)   | 27.0[19.8-34.2] | 22.7[16.3-30.2] | 0.001   |
    | Age at ART initiation (years) | 3.5[1.8-6.3] | 6.7[4.4-11.2] | 0.001   |
    | Time on ART (years) | 22.6[11.6-34.7] | 22.5[11.6-34.7] | 0.999   |

Compared to healthy controls, PHIV have higher levels of immune aging profile (CD4/CD8 ratio, activation, senescence, exhaustion and regulatory T and B cells), cellular aging markers (TREC and RTL), and functional muscle wasting and degeneration biomarkers (NCAM1 and CAF).

2. Spearman correlation plot of HIV reservoir with immune, biological and functional markers of aging.

    - HIV reservoir positively correlates with immune senescent, activated and exhausted T and B cells, inversely correlates with regulatory T and B cells, TREC and RTL, and positively correlates with NCAM1 and CAF.

CONCLUSIONS

Our findings provide evidence that PHIV adolescent/young adult experiences premature aging, and reinforce the relationship between the HIV reservoir and immune senescence.

In addition, our findings demonstrate for the first time that the HIV reservoir positively correlates with circulating degeneration biomarkers, thus adding new tools for minimally invasive monitoring of biological aging in this population over time.

REFERENCES


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PATIENTS AND METHODS

Forty-one PHV adolescents/young adults (PHIV/AA) (age 16 - 30 years) under antiretroviral therapy and with undetectable viremia for at least 10 years, and 23 aged-matched healthy controls were enrolled in this study. The immune aging profile (activated, senescent, exhausted and regulatory T and B cells) was studied by flow cytometry [4]. HIV RNA and cell-associated HIV RNA in PBMC were measured by ddPCR and real-time PCR, respectively [3]. Levels of T-cell receptor excision circle (TREC) and relative telomere length (RTL) were quantified by multiplex real-time PCR [3]. Circulating muscle wasting and degeneration biomarkers NCAM1 (neural cell adhesion molecule) and CAF (C-terminal Agrin Fragment), associated with aging and sarcopenia, were assessed by ELISA. Statistical analyses were performed using RStudio software and data were adjusted by age.

Characteristics of studied cohorts

- Age (years): 27.0[19.8-34.2] vs 22.7[16.3-30.2] (p=0.001)
- Age at ART initiation (years): 3.5[1.8-6.3] vs 6.7[4.4-11.2] (p=0.001)
- Time on ART (years): 22.6[11.6-34.7] vs 22.5[11.6-34.7] (p=0.999)