19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE CENTRO CONGRESSI EUROPA
RESEARCH and CARE: FROM BENCH, TO BEDSIDE, TO COMMUNITY
Promosso da SIMIT
16° CONGRESSO NAZIONALE ICAR Italian Conference on AIDS and Antiviral Research
P 102
POSTER 4 YOU ICAR 2024

HIV acquisition at birth does not drive T-cell dysfunction in Heavily Treatment Experienced (HTE): data from the Prestigio Registry

Valeria Bono[1], Camilla Tincati[1], Vincenzo Spagnuolo[2], Laura Galli[2], Antonio di Biagio[3], Matteo Augello[1], Roberta Rovito[1], Garlassi Elisa[4], Maria Cristina Moioli[5], Emanuele Focà[6], Antonella Castagna[2], Giulia Marchetti[1]

1. Clinica di Malattie Infettive, San Paolo Hospital, University of Milan, Milan, Italy, 2. Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, 3. Department of Infectious Disease, IRCCS AOU San Martino IST, (DISSAL), University of Genoa, Italy., 4. Malattie Infettive Arcispedale S. Maria Nuova-IRCSS, Reggio Emilia, Italy, 5. Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, 6. Division of Infectious and Tropical Diseases, ASST Spedali Civili Hospital, University of Brescia, Brescia, Italy.

Introduction

Individuals with HIV vertical transmission (VT) are exposed to both HIV and combination antiretroviral therapy (cART) from young age. In this setting, suboptimal adherence to cART may lead to viral failure and therapeutic burden (HTE, Heavily Treatment Experienced individuals), which drive immune impairment. Indeed, unfavourable clinical and viro-immunologic outcomes have also been described in HTE without VT. Whether HTE with VT feature disrupted T-cell homeostasis is unknown. We therefore investigated T-cell dysfunction in HTE with and without VT, also according to viral load (VL).

Methods

HTE VT and matched HTE no-VT from the Prestigio Registry were enrolled and classified according to undetectable (VL<50 cp/mL) or detectable viremia (VL>200 cp/mL). We measured senescence (CD57), activation (HLA-DR/CD38) and exhaustion (PD-1/TIGIT) in CD4/CD8 T-cells by flow cytometry. Age/sex-matched HIV-individuals were enrolled as controls. Kruskal-Wallis and Mann-Whitney test were used for statistics.

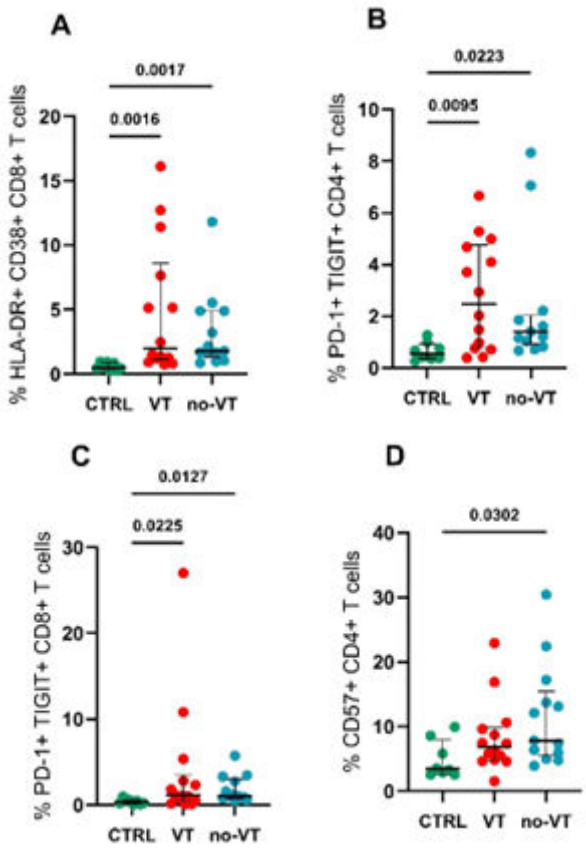
Results

We evaluated 16 VT and 16 no-VT HIV individuals. In each group, 50% were viremic and 50% were aviremic. VT were younger than no-VT (31yrs, IQR 27-33 vs 56, IQR 54-59; p<0.0001), yet duration of HIV infection was comparable in the two groups (31yrs, IQR 27-33 vs 30yrs, IQR 25-32; p=0.7).

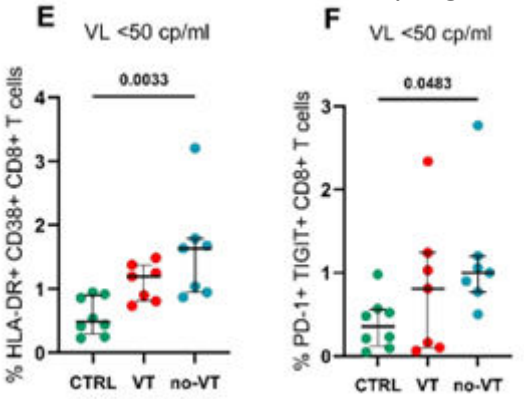
Table 1

Demographical and Viro-immunological parameters	VT (N=16)	no-VT (N=16)	p-value
Age at sampling, (years), ***median (IQR)***	31 (27-33)	56 (54-59)	**<0.0001**
Sex female, ***[n (%)]***	10 (62.5)	10 (62.5)	1.000
Time since HIV diagnosis, (years), ***median (IQR)***	31 (27-33)	30 (25-32)	0.724
CD4+ nadir, (cells/mm^3), ***median (IQR)***	90 (16-186)	127 (21-200)	0.745
CD4+ at sampling, (cells/mm^3), ***median (IQR)***	394 (179-1011)	547 (149-770)	0.545
CD8+ at sampling, (cells/mm^3), ***median (IQR)***	806 (571-1117)	672 (510-949)	0.406
HIV-RNA at sampling, *[n (%)]*			
<50 copies/mL	8 (50%)	8 (50%)	1.000
>200 copies/mL	8 (50%)	8 (50%)	

VT and no-VT HTE showed similar senescent, activated and exhausted T-cells. Interestingly, compared to HIV- controls, both VT and no-VT displayed higher: i) activated CD8+HLA-DR+CD38+ (Fig.1A); ii) exhausted PD-1+TIGIT+ CD4 (Fig.1B) and CD8+ (Fig.1C). In contrast, senescent CD57+CD4+ were increased only in no-VT compared to controls (Fig.1D).



When stratifying by viremia, these differences were retained in the viremic VT and no-VT groups, whereas no differences were registered in their aviremic counterparts, except for activated (Fig.1E) and exhausted (Fig.1F) CD8 T-cells which were consistently higher in no-VTs than in HIV-.



Conclusion

Irrespective of HIV transmission mode, compared to HIV-, HTE show greater T-cell senescence, activation and exhaustion which appear to be driven by uncontrolled viremia. Despite no differences according to transmission modality, our findings of higher CD8+HLA-DR+CD38+ and CD8+PD-1+TIGIT+ in no-VT with suppressed viral load compared to HIV-, point to greater immunological dysfunction in HTE without vertical transmission, that might possibly reflect their older age. The link(s) between age-related immunesenescence, HIV mode of infection and persistent viral replication in the pathogenesis of HTE merits further studies.