Association between HIV-specific Antibodies and HIV Reservoir Markers in Early Treated Thai Children

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BACKGROUND

- Children who initiated early antiretroviral therapy (ART) are potential candidates for sustained virologic remission, due to limited time of virus establishment and prompt ART initiation, thus restricted HIV reservoir.[1,2]
- Low antibody responses to HIV proteins in children were reported to be associated with low total HIV reservoir size.[3]

OBJECTIVE

- This study aimed to characterize HIV protein-specific antibodies and HIV reservoir markers in children who initiated early ART and had sustained virological suppression.

METHODS

Children with perinatally-acquired HIV born during 2014-2018 from Thai national cohort with

- **ART initiation < 6 months of age**
- **Sustained virological suppression** (HIV RNA <200 c/mL)

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HIV-specific antibodies determined by

- Chemiluminescent microparticle immunoassay (CMIA)
- Western blot to 10 proteins: Env (gp160, gp120, gp41), Pol (p65, p51, p31), and Gag (p55, p40, p24, p18)

HIV reservoir markers by tat/rev induced limiting dilution assay (TILDA) and integrated HIV DNA at CRCHUM.

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Statistical Analysis

- Proportion of children with seropositive to each HIV-specific protein by Western blot was compared using Fisher exact test, grouping by seropositivity by CMIA and detected HIV reservoir markers by TILDA.

RESULTS: HIV-specific antibodies

- From March to April 2024, 23 children with median age of 8.4 (IQR 7.0-9.5) years were enrolled.
- One-third of children with HIV seropositive by CMIA (n=9) had response to Env-gp160 protein, compared with none among children with HIV seronegative (33% vs 0%, p=0.04). Likewise, low response to Env-gp41 protein (11% vs 0%, p=0.39).
- Children with HIV seropositive by CMIA (n=9) had significantly higher response to Gag-p24 (89% vs 43%, p=0.04) (Figure 1).

Children with early ART had *low HIV-specific antibodies to Env.*

No association in HIV reservoir markers by TILDA and proportion of HIV-specific Abs responses.

Association of HIV reservoir markers and HIV-specific antibodies by Western blot assay

- Seven children had detectable HIV reservoir markers by TILDA assay.
- Proportion of children with positive HIV-specific antibodies by Western blot assay were not statistically different between children with undetectable TILDA assay (n=11) and detectable TILDA (n=7) (Figure 2).
- HIV-specific antibodies by Western blot among children with integrated HIV DNA > or ≤ 50 copies/10^6 $CD4^+$ T cells (p>0.05) were not different.

Table 1. Characteristics of children.

Characteristics	Median (IQR)
Age (years)	8.4 (7.0-9.5)
Age at ART initiation (days)	73 (45-99)
Current $CD4^+$ T cells (cells/mm^3)	814 (670-1191)
HIV seropositive by CMIA, n (%)	9 (39.1%)
HIV seropositive by Western blot, n (%)	14 (60.9%)
● Env	3 (13.0%)
● Pol	10 (43.5%)
● Gag	14 (60.9%)
Integrated HIV DNA (copies/10^6 $CD4^+$ T cells)	47 (15-87)
HIV reservoir detectable by TILDA, n (%)	7/18 (38.9%)

CMIA: Chemiluminescent microparticle immunoassay; IQR: Interquartile range; TILDA: tat/rev induced limiting dilution assay

Figure 1. Seropositivity rates to HIV peptide by Western blot, grouped by seropositivity by CMIA.

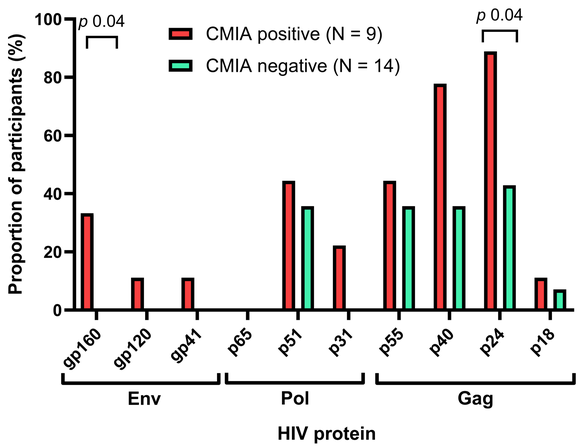
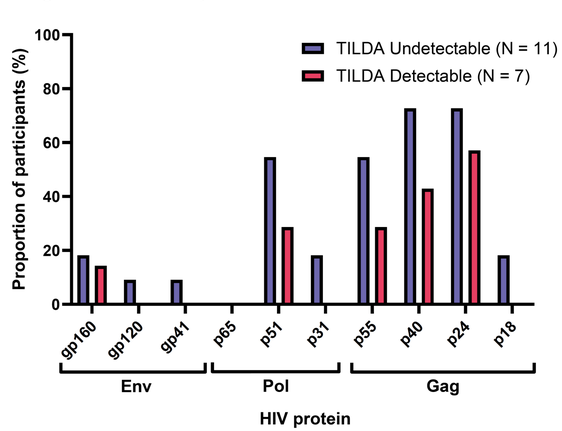


Figure 2. Seropositivity rates to HIV peptide by Western blot, grouped by HIV reservoir markers using TILDA assay.



DISCUSSION

- HIV reservoirs, in latently infected CD4+ T cells as integrated provirus were obstacles to ART-free HIV remission.[4] One-third of our early-treated children cohort had detected HIV reservoir markers by TILDA, similar to results in adults treated during acute HIV infection.[5,6]
- The lower frequency of detected HIV protein-specific antibodies in children on suppressive ART was previously demonstrated to correlate with low total DNA reservoir size.[7] However, in this study using more sensitive assays by integrated DNA and replication-competent reservoirs, no difference in HIV peptide-specific antibody profiles was demonstrated.

CONCLUSIONS

- Children with early ART had low Env-specific antibodies.
- No strong association between HIV-specific antibody responses by Western blot and HIV reservoir markers by TILDA or integrated HIV DNA levels was found.
- Identification of potential candidates for ART-free HIV remission should consider both HIV-specific antibody and reservoir markers criteria.

REFERENCES

[1]Chun TW, Moir S, Fauci AS. Nat Immunol. 2015;16:584-9. [2]Massanella M, Puthanakit T, Leyre L, et al. Clin Infect Dis. 2021;73:427-38. [3]Rocca S, Zangari P, Cotugno N, et al. J Pediatric Infect Dis Soc. 2019;8:433-8. [4]Kulpa DA, Paiardini M, Silvestri G. Nat Rev Immunol. 2025. [5]Massanella M, Bender Ignacio RA, Lama JR, et al. Lancet Microbe. 2021;2:e198-e209. [6]Leyre L, Kroon E, Vandergeeten C, et al. Sci Transl Med. 2020;12. [7]Rocca S, Zangari P, Cotugno N, et al. J Pediatric Infect Dis Soc. 2019;8:433-8.

ADDITIONAL KEY INFORMATION

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