Quantitative HIV-1 Specific Antibodies as Predictors of Blood HIV-1 DNA Levels

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BACKGROUND

- Antiretroviral therapy (ART) reduces HIV-1-related morbidity and mortality in children but does not prevent the establishment of a persistent replication-competent HIV-1 reservoir.
- We examined the utility of using plasma HIV antibody levels as a screening test for low circulating cell-associated HIV-1 DNA levels in children and adolescents with perinatal HIV-1 infection.

METHODS

Participants

- 514 longitudinally-collected plasma specimens from 61 perinatally-infected participants and enrolled in the Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol (PHACS AMP).
  - Achieved sustained virologic suppression (VS, HIV-1 plasma levels <400 copies/mL at or before 5 years of age on ART)
  - Maintained VS, allowing for isolated viral loads ≥400 copies/mL
- 20 perinatally HIV-1-exposed, uninfected children studied through 2 years as controls (PHEU).

Measures

Antibody levels to HIV-1 envelope (gp160, gp41), gag (capsid, p24; matrix, p17); RT (p66/51), and integrase (p31) were quantified by ELISA; PBMC HIV-1 DNA levels were measured by droplet digital PCR.

Analyses

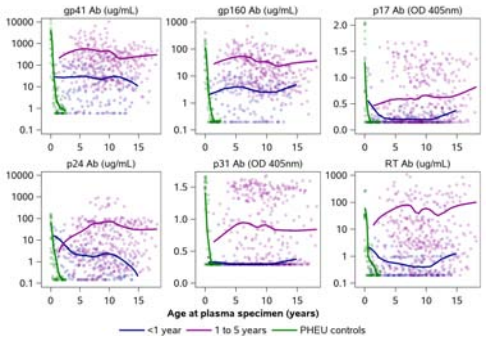
Receiver operator curve (ROC) analyses, stepwise regression, and the random forest method were used to identify the most predictive antibodies for low HIV-1 DNA levels (<100 and <10 copies per million PBMCs).

Characteristics of cohorts with HIV-1 infection

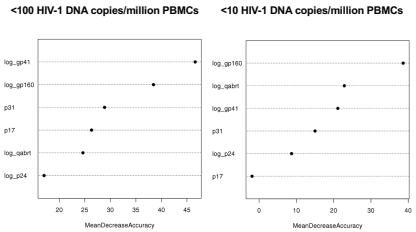
	Total (N=61)	Age at virologic suppression <1 year old (N=13)	Age at virologic suppression 1 to 5 years old (N=48)
Age at ART initiation (months)			
Median	14.4	2.1	20.9
Q1, Q3	3.1, 31.6	1.7, 3.1	9.0, 41.0
Age at confirmed virologic suppression (months)			
Median	34.3	8.0	43.5
Q1, Q3	15.8, 56.4	7.6, 9.8	31.2, 58.9
Age at first HIV-1 Antibody specimen (months)			
Median	54.4	6.8	58.9
Q1, Q3	23.2, 82.1	4.6, 15.0	41.6, 88.4
Age at first analyzed PBMC specimen (months)			
Median	50.8	6.8	58.0
Q1, Q3	19.7, 82.1	2.5, 21.4	31.9, 88.4

Plasma antibody levels to HIV-1 gp41 and gp160 may be used to identify virologically-suppressed children on ART with low circulating cell-associated HIV-1 DNA levels.

LOESS trajectories of antibody levels

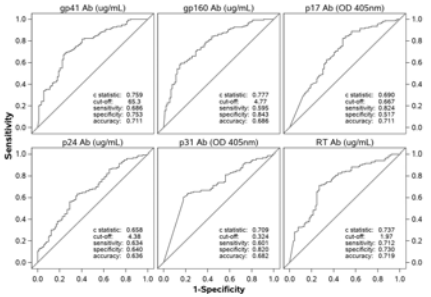


Random forest variable importance plots

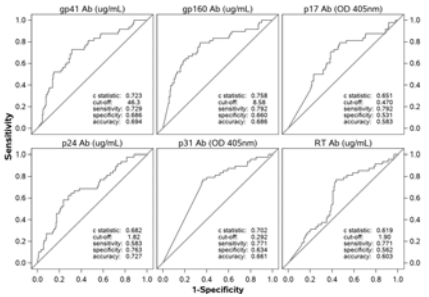


HIV-1 antibody level ROC curves

<100 HIV-1 DNA copies/million PBMCs



<10 HIV-1 DNA copies/million PBMCs



RESULTS

- Antibody levels to all six HIV-1 proteins were high and remained high or increased longitudinally in children with VS between 1-5 years of age.
- In children with VS <1 year of age, antibodies to p17, p24, and RT decreased throughout follow-up; gp160 and gp41 antibodies were low and remained low; p31 antibodies were either exceedingly low or undetectable.
- The stepwise regression model suggested that gp41 and gp160 were useful predictors of low HIV-1 DNA levels; c-statistics including all antibodies ranged from 0.75 to 0.77.
- The random forest method also identified gp41 and gp160 as important predictors of low HIV-1 DNA; area under the curve estimates using all HIV-1-specfic antibodies ranged from 0.74 to 0.81.

CONCLUSIONS

HIV-1 antibody levels to gp41 and gp160 may be useful markers of low circulating cell-associated HIV-1 DNA levels in virologically-suppressed children on ART. Validation in larger cohorts will facilitate development of screening algorithms for use in pediatric cure or remission studies in resource-limited settings.

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