

1. Temporal effect of HLA-B*57 on viral control during primary HIV-1 infection

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Abstract

Background: HLA-B alleles are associated with viral control in chronic HIV-1 infection, however, their role in primary HIV-1 disease is unclear. This study sought to determine the role of HLA-B alleles in viral control during the acute phase of HIV-1 infection and establishment of the early viral load set point (VLSP).

Findings: Individuals identified during primary HIV-1 infection were HLA class I typed and followed longitudinally. Associations between HLA-B alleles and HIV-1 viral replication during acute infection and VLSP were analyzed in untreated subjects. The results showed that neither HLA-B*57 nor HLA-B*27 were significantly associated with viral control during acute HIV-1 infection (Fiebig stage I-IV, n=171). HLA-B*57 was however significantly associated with a subsequent lower VLSP ($p < 0.001$, n=135) with nearly 1 log₁₀ less median viral load.

Analysis of a known polymorphism at position 97 of HLA-B showed significant associations with both lower initial viral load ($p < 0.01$) and lower VLSP ($p < 0.05$). However, this association was dependent on different amino acids at this position for each endpoint.

Conclusions: The effect of HLA-B*57 on viral control is more pronounced during the later stages of primary HIV-1 infection, which suggests the underlying mechanism of control occurs at a critical period in the first several months after HIV-1 acquisition. The risk profile of polymorphisms at position 97 of HLA-B are more broadly associated with HIV-1 viral load during primary infection and may serve as a focal point in further studies of HLA-B function.

2. Advanced HIV Disease at Entry into HIV Care and Initiation of Antiretroviral Therapy During 2006-2011: Findings From Four Sub-Saharan African Countries.

Lahuerta M, Wu Y, Hoffman S, Elul B, Kulkarni SG, Remien RH, Nuwagaba-Biribonwoha H, El-Sadr W, Nash D; Clin Infect Dis. 2013 Dec 4.

Background. Timely antiretroviral therapy (ART) initiation requires early diagnosis of human immunodeficiency virus (HIV) infection with prompt enrollment and engagement in HIV care.

Methods. We examined programmatic data on 334 557 adults enrolling in HIV care, including 149 032 who initiated ART during 2006-2011 at 132 facilities in Kenya, Mozambique, Rwanda, and Tanzania. We examined trends in advanced HIV disease (CD4+ count <100 cells/ μ L or World Health Organization disease stage IV) and determinants of advanced HIV disease at ART initiation.

Results. Between 2006-2011, the median CD4+ count at ART initiation increased from 125 to 185 cells/ μ L an increase of 10 cells/year. Although the proportion of patients initiating ART with advanced HIV disease decreased from 42% to 29%, sex disparities widened. In 2011, the odds of advanced disease at ART initiation were higher among men (adjusted odds ratio [AOR], 1.4; 95% CI, 1.3-1.5), those on tuberculosis treatment (AOR, 1.6; 95% CI, 1.3-2.0), and those with a \geq 12 month gap in pre-ART care (AOR, 2.0; 95% CI, 1.6-2.6).

Conclusions. Intensified efforts are needed to identify and link HIV-infected individuals to care earlier and to retain them in continuous pre-ART care to facilitate more timely ART initiation.

3. Treatment as long-term prevention: sustained reduction in HIV sexual transmission risk with use of antiretroviral therapy in rural Uganda

Siedner, Mark J.a; Musinguzi, Nicholasb; Tsai, Alexander C.a,c; Muzoora, Conradb; Kembabazi, Annetb; Weiser, Sheri D.d; AIDS: 14 January 2014 - Volume 28 - Issue 2 - p 267-271

Abstract

Objectives: Suppressive antiretroviral therapy (ART) substantially decreases HIV transmission in clinical research settings. We sought to measure the frequency and correlates of periods of transmission risk among individuals taking ART during multiple years of observation in rural, southwestern Uganda.

Design: Observational cohort study.

Methods: We collected sexual behavior and viral load data in a Ugandan cohort of people living with HIV/AIDS from the time of ART initiation. We defined each 90-day visit as a potential transmission period if HIV-1 RNA was more than 400 copies/ml and the participant reported sexual transmission risk behavior, defined as unprotected sexual contact with at least 1 HIV-uninfected partners or partners of unknown serostatus in the prior 90 days.

Results: We evaluated data from 463 individuals on ART over a median 3.5 years of observation and 5293 total study visits. During that time, over half (259, 56%) had detectable viremia or reported sexual transmission risk behavior at least once. However, only 23 (5%) had both simultaneously, at 28 (<1%) of all visits. Transmission sexual behavior was reported at 6% of visits with detectable viremia. In multivariable regression modeling, correlates of transmission risk periods included younger age, lower CD4+ cell count, low household asset ownership and increased internalized stigma.

Conclusion: Although detectable viremia and/or sexual transmission risk behavior occurred in over half of individuals, ART reduced periods of HIV transmission risk by over 90% during up to 6 years of observation time. These findings provide further support for provision of ART, along with interventions to promote long-term adherence, to reduce HIV transmission in HIV-endemic settings.

4. 'If I am given antiretrovirals I will think I am nearing the grave': Kenyan HIV serodiscordant couples' attitudes regarding early initiation of antiretroviral therapy

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Abstract

Objectives: Early initiation of antiretroviral therapy (ART) – that is, at higher CD4+ cell counts (>350 cells/ μ l) – is a potent HIV prevention strategy. The WHO recommends ART initiation by all HIV-infected individuals in HIV serodiscordant relationships to prevent HIV transmission, yet the acceptability of early ART among couples has not been well studied.

Design: Qualitative study exploring HIV serodiscordant couples' attitudes toward early initiation of ART.

Methods: We conducted eight focus group discussions and 20 in-depth interviews with members of heterosexual HIV serodiscordant couples in Kenya. Investigators iteratively applied inductive and deductive codes, developed matrices to identify patterns in codes, and reached consensus on key attitudes (motivations and barriers) related to early ART and one central, emerging theme.

Results: Most participants expressed interest in early initiation of ART, with maintaining health and preventing HIV transmission as key benefits. However, many identified personal concerns and potential barriers to wider community acceptance, including side-effects, adherence to life-long treatment, and stigma. The meaning of ART emerged as a fundamental consideration, with initiating therapy perceived as emblematic of the final stage of AIDS, when one was 'nearing the grave.' One particular challenge was what early ART might signify for someone who looks and feels healthy.

Conclusion: HIV serodiscordant couples recognized the potential benefits of early ART, but ART was frequently viewed as signifying AIDS and approaching mortality. Potential implementation of early ART presents challenges and an opportunity to re-orientate individuals toward a new image of ART as health-preserving for patients and partners.