Few Acute HIV-1 Symptoms and High Set-point Viral Load in Subtype C Infections

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Abstract

HIV-1 disease pathogenesis varies between individuals and is possibly determined during acute HIV infection (AHI). We set out to dissect HIV-1 viral diversity, evolutionary dynamics and innate immune responses during AHI and elucidate mechanisms involved in HIV-1 disease pathogenesis. Preliminary data suggests a role of the infecting subtype on expression of innate responses, with subsequent manifestation of acute retroviral syndrome (ARS) and regulation of viral replication.

Background

HIV-1 disease progression varies widely between individuals. This has been attributed to a combination of virological and immunological events during acute HIV infection (AHI). However, the exact mechanisms explaining virus-host interactions and their effect on disease pathogenesis remain unclear. We aimed to dissect HIV-1 viral diversity, evolutionary dynamics and innate immune responses during AHI and elucidate mechanisms involved in the regulation of disease.

Methods

A retrospective longitudinal analysis of data and samples from well characterized cohorts from Europe (Sweden [n=26]) and Africa (Kenya [n=32], Rwanda [n=14], Uganda [n=13], and Zambia [n=15]) were included (*fig 1*).

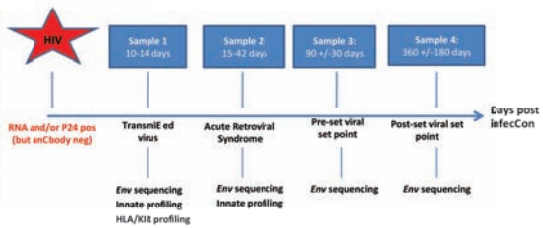

Figure 1: Outline of the study design illustrating detection of Acute HIV Infection (AHI), follow up time post infection, criteria used for longitudinal samples identification and specific lab processes included in every follow up time point.

Clinical data were assessed for acute retroviral syndrome (ARS), defined as any of 11 reported symptoms during AHI. HIV-1 *env* single genome sequencing (SGS) was done, with about 20 SGS clones generated from each time point. A selected panel of innate immune markers was profiled using the Meso Scale Discovery (MSD) electro-chemiluminescence-based platform.

Results

Overall, one hundred participants (samples from four time-points, n=374) were included. The median age at HIV infection was 30.3 (IQR; 24.3 – 36.1) years, with majority of participants being male (83%). Most of the participants were infected with HIV-1 subtypes A (41%), followed by B (19%) and C (17%) (*fig 2*).

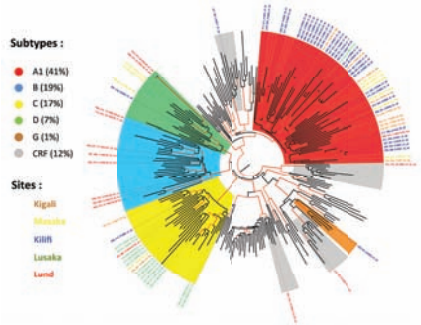

Figure 2: A phylogenetic tree illustrating the distribution of the infecting HIV-1 subtypes by participating sites (N=100).

HIV-1 subtype C-infected individuals were less likely to report ARS compared to those with non-C subtypes (n=8 [50.0%] vs. n=55 [78.6%], p=0.020), whilst subtype A-infected individuals were more likely to report ARS than those infected with non-A variants (n=34 [89.5%] vs. n=29 [60.4%], p=0.003) (*fig 3 [a]*).

The median set-point viral load was 41,000 (IQR 16,000 – 80,000) copies/ml. Subtype C-infected individuals were more likely to have higher set-point viral load than those infected with non-C variants (OR, 5.6 [95% CI 1.6 – 19.3], p=0.003) (*fig 3 [b]*).

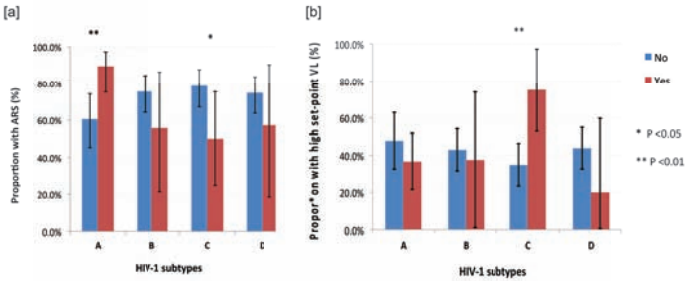

Figure 3: Bar graphs illustrating associations between [a] HIV-1 subtypes and proportion of individuals reporting acute retroviral syndrome (ARS), and [b] HIV-1 subtypes and proportion of individuals with high set-point viral load (>50,000 copies/ml) amongst acute HIV infected individuals (N=100).

Results

An exploratory analysis suggests associations between some specific innate markers and the infecting subtype, ARS and set-point viral load (fig 4 [a]). For example, individuals infected with HIV-1 non-C subtype mounted a stronger IL-4 response compared to those infected with subtype C. Individuals with stronger IL-4 responses reported more ARS and subsequent lower set-point viral load, compared to those with a weaker IL-4 response (fig 4 [b]). IL-4 is a proinflammatory marker that has been shown to be important for B-cell maturation and antibody production.

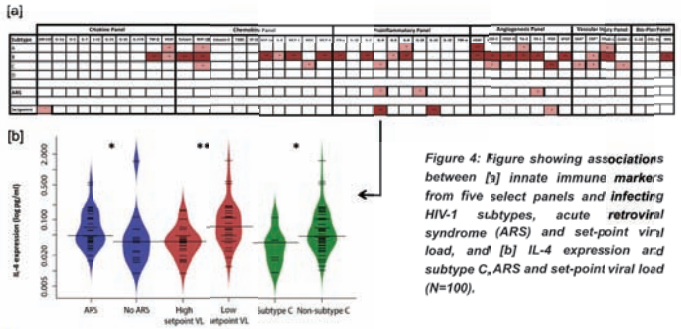

Figure 4: Figure showing associations between [a] innate immune markers from five select panels and infecting HIV-1 subtypes, acute retroviral syndrome (ARS) and set-point viral load, and [b] IL-4 expression and subtype C, ARS and set-point viral load (N=100).

Summary

Differences in expression of innate immune responses during AHI may be driven by the infecting subtype, and may contribute to ARS and subsequent control of viral replication. Further work is on-going to delineate the relationship between infecting subtype and innate immune responses, and their effect on ARS and disease progression.

Acknowledgement

Strengthening health research capacity in Africa

For more details and updates on this project, please e-mail ahassan@kemri-wellcome.org or visit our webpage (www.icahi.org)