Abstract

We aimed to determine whether endothelial activation biomarkers increase after HIV-1 acquisition, and whether biomarker levels measured in chronic infection would predict disease progression and death in HIV-1 seroconverters. HIV-1-seronegative Kenyan women were monitored monthly for seroconversion, and followed prospectively after HIV-1 acquisition. Plasma levels of angiopoietin-1 and angiopoietin-2 (ANG-1, ANG-2) and soluble vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), and E-selectin were tested in stored samples from pre-infection, acute infection, and two chronic infection time points. We used nonparametric tests to compare biomarkers before and after HIV-1 acquisition, and Cox proportional-hazards regression to analyze associations with disease progression (CD4 <200 cells/μl, stage IV disease, or antiretroviral therapy initiation) or death. Soluble ICAM-1 and VCAM-1 were elevated relative to baseline in all postinfection periods assessed ($P < 0.0001$). Soluble E-selectin and the ANG-2:ANG-1 ratio increased in acute infection ($P = 0.0001$), and ANG-1 decreased in chronic infection ($P = 0.0004$). Among 228 participants followed over 1028 person-years, 115 experienced disease progression or death. Plasma VCAM-1 levels measured during chronic infection were independently associated with time to HIV progression or death (adjusted hazard ratio 5.36, 95% confidence interval 1.99–14.44 per log10 increase), after adjustment for set point plasma viral load, age at infection, and soluble ICAM-1 levels. HIV-1 acquisition was associated with endothelial activation, with sustained elevations of soluble ICAM-1 and VCAM-1 postinfection. Soluble VCAM-1 may be an informative biomarker for predicting the risk of HIV-1 disease progression, morbidity, and mortality.