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Associations between biomarkers of systemic immune activation and clinical, demographic and treatment characteristics of HIV-infected African adults

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Statement of the Problem: The importance of chronic systemic immune activation in the pathogenesis and clinical pathology of HIV has received limited attention in Africa, despite the fact that these populations likely have higher background levels of inflammation than their developed world counterparts. This study explored associations between systemic immune activation and patient characteristics, geographic location, coinfections and type of therapy. Methodology & Theoretical Orientation: Twelve biomarkers of immune activation (Figure 1) were measured before and during the first two years of virally-suppressive antiretroviral therapy (ART) using a multivariable model based on a doubly-repeated measures analysis of variance design, including 341 observations from HIV-1-infected participants from Nigeria, South Africa and Zambia in the analysis. Findings: Significant reductions in levels of all biomarkers were recorded after ART initiation, with changes in viral load (VL) and CD4 count being the most important contributors. Interesting associations were found between increasing age and β2M, and between body mass index and IL-6, β2M and LBP. Women had higher levels of IP-10 than men, despite equivalent VLs. TGF-β1 was highest in Zambian participants and associated with sub-optimal immune reconstitution on ART. After 2 years, Zambian participants had higher levels of TNF-α, MCP-1 and IL-8 when compared to South African participants. Tuberculosis co-infection at ART initiation was associated with elevated levels of sCD14, IL-6 and β2M at various timepoints. Hepatitis-B coinfected participants had higher levels of MCP-1 at month 12. Participants receiving cotrimoxazole prophylaxis had reduced levels of the microbial translocation biomarker LBP, while those receiving d4T/AZT versus TDF had higher levels of TGF-b1, IL-6 and CRP, and lower levels of sCD14. Conclusion & Significance: The results demonstrate the dynamic and multifactorial nature of systemic immune activation in the presence of virally-suppressive ART. The specific impact of geographic region, co-infections and type of therapy deserve further study.

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