Association between CD4, CD4/CD8 ratio and viral blips among virally suppressed HIV patients – a joint disease progression and time-to-event model

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#### Abstract

Aim Viral blips that occur among virally suppressed HIV-positive patients suggest immune activation and inflammation and associated with slower CD4 count and CD4/CD8 ratio normalisation. With the advances in HIV treatment, lifestyle and comorbidities begin to be a concern despite successful antiretroviral therapy. We reported a study incorporating the effect of CD4 and CD4/CD8 ratio normalisation on viral blips in joint disease progression (DP) and time-to-event (TTE) model. Methods A total of 152 HIV-positive patients receiving efavirenz therapy were recruited. Joint DP and TTE models on viral blip were developed for CD4 and CD4/CD8 ratio separately. Risk factors, such as smoking status, pack-year and comorbidity scores, were included in the analysis. Results Gompertz model best described the CD4 and CD4/CD8 ratio DP models, while viral blips data were fitted with the Cox proportional hazard model. History of opportunistic infections and changing of antiretroviral regimen significantly affect the baseline CD4 and CD4/CD8 ratio. Comorbidity score was significant in both CD4 (asymptote CD4) and CD4/CD8 ratio DP model (recovery rate). Increase in cumulative pack-year resulted in lower CD4/CD8 ratio recovery rate ( $\beta$  -0.02, 95%CI: -0.03 to -0.01; p<0.001). Active smokers with slow CD4 or CD4/CD8 ratio normalisation associated with more viral blips. Conclusion CD4 and CD4/CD8 ratio are significant risk factors of viral blips and potential markers of non-AIDS related morbidities in virally suppressed patients. Early identification of high-risk group with repeated viral load testing, lifestyle modification and comorbidities management should be emphasised in the HIV treatment long-term care plan.

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