olymorphisms in a Kenyan perinatal human immunodeficiency virus type 1 cohort: association with increased 2-year maternal mortality.

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Abstract

The CCR5 chemokine receptor acts as a coreceptor with CD4 to permit infection by primary macrophage-tropic human immunodeficiency virus type 1 (HIV-1) strains. The CCR5Delta32 mutation, which is associated with resistance to infection in homozygous individuals and delayed disease progression in heterozygous individuals, is rare in Africa, where the HIV-1 epidemic is growing rapidly. Several polymorphisms in the promoter region of CCR5 have been identified, the clinical and functional relevance of which remain poorly defined. We evaluated the effect of 4 CCR5 promoter mutations on systemic and mucosal HIV-1 replication, disease progression, and perinatal transmission in a cohort of 276 HIV-1-seropositive women in Nairobi, Kenya. Mutations at positions 59353, 59402, and 59029 were not associated with effects on mortality, virus load, genital shedding, or transmission in this cohort. However, women with the 59356 C/T genotype had a 3.1-fold increased risk of death during the 2-year follow-up period (95% confidence interval [CI], 1.0-9.5) and a significant increase in vaginal shedding of HIV-1-infected cells (odds ratio, 2.1; 95% CI, 1.0-4.3), compared with women with the 59356 C/C genotype.