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THE EFFECT OF HIV SUBTYPE ON RAPID DISEASE PROGRESSION IN RAKAI, UGANDA

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METHODS: A retrospective study in Rakai, Uganda identified 140 HIV seroconverters with subtype data determined by MHAacd and viral load by Roche Amplicore v1.5. All viral loads were converted to log₁₀ scale. An additional 127 HIV seroconverters had subtype and viral load data but no CD4 counts available. AIDS was defined as a CD4 <250 at which point individuals were eligible for PEPFAR-based ART. HIV co-receptor tropism was generated by Monogram BioSciences.

RESULTS: The mean follow-up time for the 140 subjects was 5.1 years (IQR 4.0 to 6.7). In that time frame, 23 subjects had died and 58 had developed AIDS. Of the 17 subtype-A-infected subjects 5 (29%) had AIDS, but none had died. This differed significantly ($p < 0.01$) from the 80 subtype-D-infected individuals among whom 47 (59%) had progressed to AIDS or died, and the 21 (57%) of 37 individuals with recombinant strains who had progressed to AIDS or died. There were 5 individuals with multiple strains who all had progressed to AIDS (median 6.1 years). Viral load was higher in those with disease progression for all subtypes ($p < 0.05$). When controlling for the effect of HIV viral load D and recombinant subtypes were still significantly more pathogenic than subtype A ($p < 0.05$ based on a Cox proportional hazards regression model). In a cohort of 227 HIV seroconverters followed over 2 years, 5.9% (8 of 136) of subtype D and 4.1% (2 of 49) of recombinant infected HIV⁺ individuals died within 24 months, whereas none of the 34 subtype-A infected or 8 multiply infected individuals had died. HIV viral load did not predict death within 24 months of infection; the median log₁₀ viral loads for death within 24 months vs others was 4.74 (IQR 4.08 to 5.25) vs 4.66 (IQR 4.20 to 5.46). In a separate subsample, X4 phenotype was present in 24% (19 of 79) of subtype D samples, 14% (3 of 21) of recombinants and 0% (0 of 21) of subtype-A-infected subjects.

Furthermore, 15% (2 of 13) HIV seroconverters infected with subtype D developed X4 phenotype tropism within in one year of infection.

CONCLUSIONS: Viral load had a significant effect on disease progression over longer follow-up time, but did not predict death within 24 months of infection. Subtype D and recombinant strains incorporating subtype D are pathogenic than subtype A, probably due to the increased frequency X4 co-receptor tropism in subtype D. These findings suggest that knowledge of HIV subtype might be useful in clinical management of HIV infection in Uganda.

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