Abstract

BACKGROUND: Several mucosal innate immune proteins exhibit HIV inhibitory activity and their analogues are potential microbicide candidates. However, their clinical associations and in-vivo role in cervicovaginal host defense against HIV acquisition are poorly defined. METHODS: Cervicovaginal secretions (CVSs) were collected from HIV uninfected Kenyan sex workers at enrolment into an HIV prevention trial. After trial completion, CVS from participants acquiring HIV (cases) and matched controls were assessed for levels of innate immune factors and HIV neutralizing capacity, by blinded investigators. Cross-sectional and prospective associations of innate immune factors were examined. RESULTS: CVS contained high levels of defensins (human neutrophil peptide-1-3 and human beta defensin-2-3), LL-37 and secretory leukocyte protease inhibitor. Regulated upon activation normal T-cell expressed and secreted levels were lower, and IFNalpha was undetectable. CVS from 20% of participants neutralized a clade A primary HIV isolate, and 12% neutralized both clade A and C isolates. HIV neutralization was correlated with human neutrophil peptide-1-3 (alpha-defensins) and LL-37 levels. However, alpha-defensin and LL-37 levels were increased in participants with bacterial sexually transmitted infections and were independently associated with increased HIV acquisition in multivariate analysis. CONCLUSIONS: Despite significant HIV inhibitory activity, cervicovaginal levels of alpha-defensins and LL-37 were associated with increased HIV acquisition, perhaps due to their association with bacterial sexually transmitted infections.