Genital tract cellular activation and inflammation associated with highly prevalent sexually transmitted infections and bacterial vaginosis in adolescent women at risk for HIV infection

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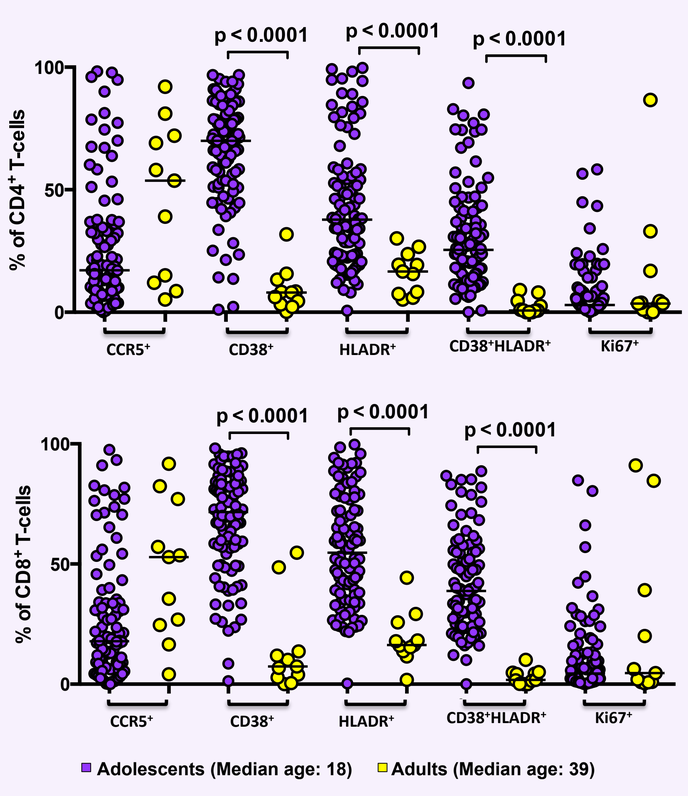
INTRODUCTION

The biological mechanisms underlying HIV risk in younger women is unclear. HIV is primarily transmitted across the genital mucosa and preferentially infects CD4⁺ T-cells. We investigated the influence of asymptomatic sexually transmitted infections (STIs) and bacterial vaginosis (BV) on CD4⁺ T-cell activation and inflammation in the genital tracts of adolescents from South Africa.

METHODS

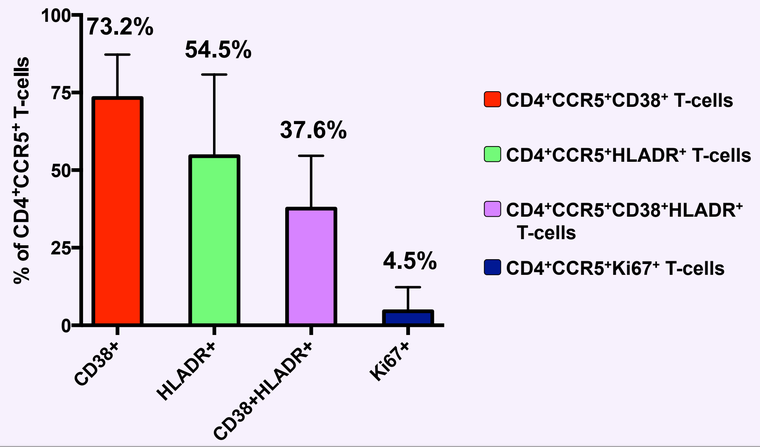
As part of a longitudinal cohort study involving 16-22 years old young women, cervical mononuclear cells were obtained from 149 adolescents by cytobrush and the T-cell expression of activation and proliferation markers (CD38, HLADR, Ki67) was measured by FACS. Women were tested for bacterial vaginosis (BV) and STIs (*C. trachomatis, N. gonorrhoea, T. vaginalis, M. genitalium*, HSV-1 & 2, *H. ducreyi*, *T. pallidum* and *L. venereum*). For comparison, 11 HIV-negative adult women were also included (Jaspan et al, 2009). An array of 48 inflammatory, anti-inflammatory, regulatory and hematopoietic cytokines was measured using Luminex

Adolescents generally have higher T-cell activation levels compared to adults



Adolescents (median:18yr; IQR: 18-19yr) had significantly higher frequencies of activated CD4⁺ and CD8⁺ T-cells (each p<0.0001) compared to adult women. The frequency of proliferating cells also tended to be higher in the younger women. In contrast, adolescents had lower CCR5 expression compared to adults.

High frequencies of activated genital CCR5⁺ T-cells may increase susceptibility to HIV



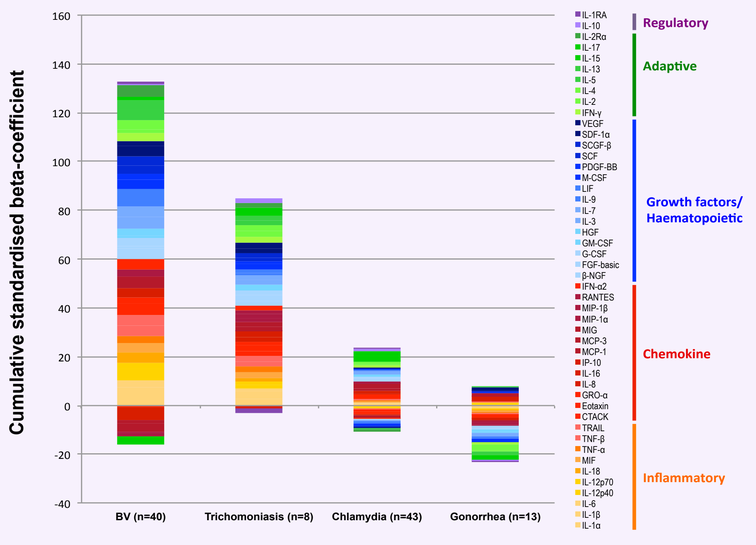
Activated CCR5⁺ T-cells represent the preferred target cells for HIV infection and the level of expression of these markers are essential in determining an individual's susceptibility to HIV infection. Most of CCR5⁺ CD4 T-cells obtained from the genital tract co-expressed high levels of CD38 and HLADR, suggesting that there are relatively high numbers potential HIV target cells in the genital tract of adolescents.

STI & Bacterial vaginosis prevalence

	Visit 1
Chlamydia trachomatis	**41.6%** (62/149)
Neisseria gonorrhoea	**11.4%** (17/149)
Trichomonas vaginalis	**7.4%** (11/149)
HSV-2	**4.7%** (7/149)
Mycoplasma genitalium	**4.0%** (6/149)
Candida species	**6.8%** (10/148)
Bacterial Vaginosis	**48.0%** (71/148)
Total	149

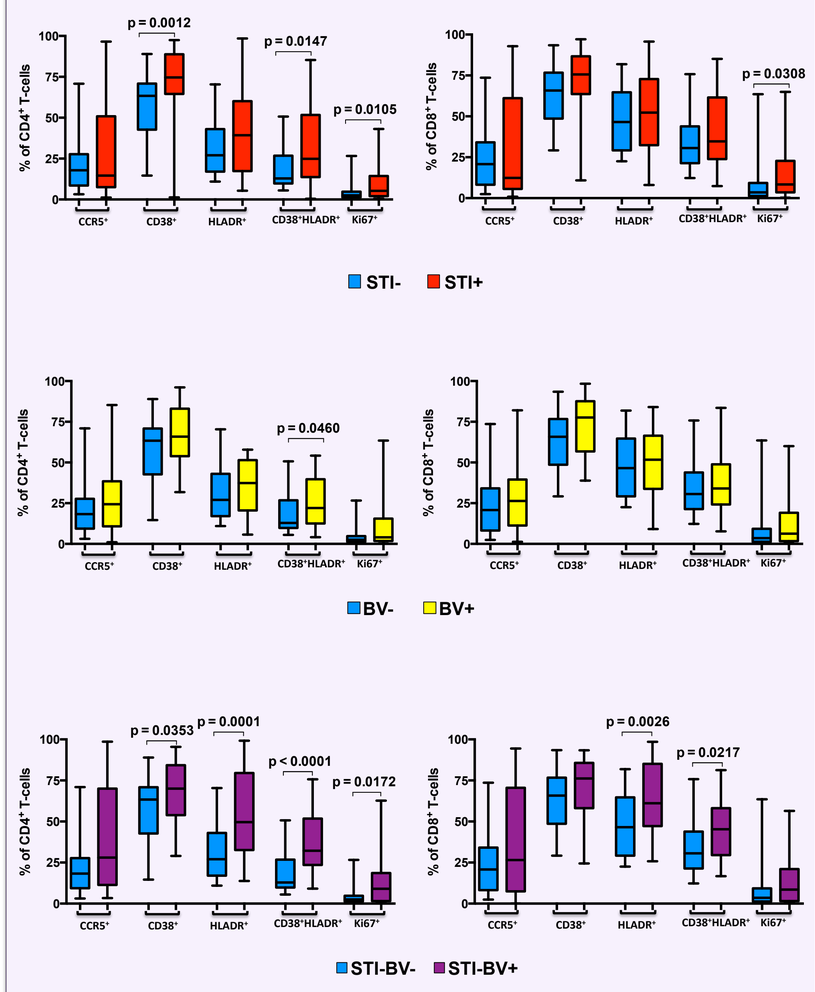
71% of all participants enrolled in this study had at least one STI/BV with 16% having multiple STIs. The prevalence of chlamydia of 41.6% was especially high compared to the national statistic of about 11%.

Bacterial vaginosis & STIs were associated with higher levels of inflammation



The impact of each STI/BV on the genital inflammatory milieu was compared for each cytokine. Overall, BV was the most inflammatory, although some of the inflammatory and adaptive cytokines were downregulated. *Trichomonas vaginalis* was the most inflammatory STI in this cohort while *Chlamydia trachomatis* and *Neisseria gonorrhoea* were associated with much lower inflammation levels.

STIs and Bacterial vaginosis result in a cummulative increase in genital T-cell activation



Having at least one STI, despite being asymptomatic, was accompanied by a general increase in T-cell activation, especially for the CD4⁺ T-cell population. The same trend was seen for participants with BV, where CD38⁺HLADR⁺ expression was upregulated in CD4⁺ T-cells. Having both STIs and BV appears to have a cummulative effect where the upregulation of CCR5 and the activation markers was more pronounced.

CONCLUSION

Adolescents are known to bear the burden of the HIV epidemic in South Africa, especially young women, with about 76% of HIV-positive young people in sub-Saharan Africa being female. We found significantly heightened levels of genital immune activation in the South African young females from this cohort, compared to adult women. This could be partly due to the particularly high prevalence of STIs (though asymptomatic) and BV among this population. Having higher genital inflammation and higher frequencies of activated potential target cells could put them at higher risk of infection and may explain the greater vulnerability of adolescents to HIV.

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