Undetectable Viral Load? Not Necessarily in Semen

April 3, 2012 By Tim Horn

Undetectable viral loads in blood is not a guarantee that HIV is also undetectable in semen, according to a new study involving 101 HIV-positive men who have sex with men (MSM) conducted in Boston and published online ahead of print by the journal AIDS. Of the 83 men with undetectable virus in blood samples, roughly a quarter of them—21 MSM in total—had semen with detectable HIV.

Though the study conducted by Joseph Politch, PhD, of Boston University School of Medicine and his colleagues didn't look at whether those with low-but-detectable levels of HIV in their semen were necessarily more likely to transmit the virus than those with undetectable seminal viral loads, the authors nevertheless caution that a risk of ongoing HIV transmission potentially remains in the absence of barrier protection during sexual activity. "Until more information on transmission risk in MSM is available," they write, "it would be prudent to advise sexually active HIV-infected MSM to use condoms and other risk-reduction strategies throughout all stages of HIV disease regardless of HIV treatment status."

Politch and his colleagues note that antiretroviral therapy is undoubtedly associated with a reduced risk of HIV transmission during sexual activity. In prefacing their own data, the authors reiterate the results of HPTN 052, which demonstrated that ARV therapy led to a 96 percent reduction in HIV transmission risk among HIV-discordant heterosexual couples, along with a study among MSM conducted over a decade ago concluding that HIV treatment decreases the transmission risk by roughly 60 percent.

Yet, according to the authors, "MSM have experienced a resurgent HIV epidemic in the [ARV treatment] era. Many HIV-infected MSM continue to engage in unsafe sex, and sexually transmitted infections (STIs) or other factors may promote genital HIV shedding and transmission in this population despite [ARV therapy]."

Though the "resurgent HIV epidemic" is undoubtedly multifactorial—roughly 20 percent of those living with HIV, including many MSM, are not aware they are infected and have thus not received personalized care and counseling—Politch's group set out to explore an important factor associated with HIV transmission: the prevalence of seminal HIV shedding among HIV-positive MSM receiving ARV therapy, and how it relates to a number of clinical, behavioral and biological variables.

The study recruited HIV-positive participants from Fenway Health, a clinic catering to the health care needs of the lesbian, gay, bisexual and transgender community in Boston. Paired blood and semen samples were collected from the 101 study volunteers. Clinical and behavioral data were obtained from medical records and questionnaires. Evidence of genital herpes and genital inflammation were also assessed using laboratory tests.

The men were predominately white (74 percent), and virtually all (97 percent) identified themselves as MSM. The average age of the study volunteers was 43. Eighty percent had been on ARV therapy for more than a year; all had been on HIV treatment for at least three months.

Twenty-seven percent reported only engaging in protected sexual intercourse within the three months before study enrollment and were thus classified as low risk for acquiring a sexually transmitted infection (STI). Seventy-three percent were classified as high risk for having an STI, based on self reports of unprotected sexual intercourse in the past three months.

Nine men, all belonging to the high-risk group, tested positive for an STI within seven days before their official start in the study. Sixty-three percent of the men were positive for genital herpes, or herpes simplex virus-2, HSV-2, antibodies.

Eighteen of the 101 MSMs enrolled in the study had detectable HIV in their blood samples. The average viral load among these men was 560, but it ranged from 80 to more than 600,000. Nine (50 percent) of the men with detectable blood-based viral loads also had detectable HIV levels in their semen.

Eighty-three of the 101 MSM had undetectable levels of HIV in their blood samples. Though most also had undetectable HIV in their semen samples, 21 (25 percent) had detectable seminal viral loads.

Politch and his team note, however, that HIV levels—free-floating HIV-RNA and both HIV-RNA and HIV-DNA in cells—were significantly higher among those with detectable blood-based viral loads, compared with those with undetectable blood-based viral loads. For example, whereas the average free-floating viral load was 4,438 copies among those with detectable blood-based HIV levels, it was 51 copies among those with undetectable blood-based HIV levels.

Whether or not the free-floating virus detected in the semen samples of those with undetectable blood-based viral loads is of high enough quantity and/or quality to establish infection in a sexual partner wasn’t explored by the researchers.

The authors did note, however, that the prevalence of HIV shedding among those with undetectable blood-based viral loads documented in this study proved higher than has been reported in other studies. “This is likely due to the high prevalence of STIs and genital inflammation in our sexually active MSM cohort.”

Indeed, among the three factors associated with having detectable seminal viral loads among

those with undetectable blood-based levels, having an STI was associated with a 29-fold increase in the risk, compared with those who didn't have an STI. Being positive for HSV-2 was not associated with have a detectable seminal viral load.

As for the other two factors, genital inflammation—notably an increase in tumor necrosis factor-alpha, an inflammatory marker—was associated with a 14-fold increase in the risk, whereas unprotected insertive anal sex with an HIV-positive person—"topping" a positive partner without a condom—was associated with a sevenfold increase in the risk of having detectable HIV in semen even when HIV is undetectable in blood samples.

"In light of recent evidence that even low amounts of HIV in semen could pose a transmission risk in MSM, who are more vulnerable to HIV infection than heterosexual men, this information has potential clinical significance for the HIV epidemic in MSM," the authors conclude. "HIV-infected men who engage in unprotected intercourse may use [ARV therapy] and viral load status in their sexual decision-making, and being on [ARV therapy] or having an undetectable blood viral load may relax concerns about transmitting HIV. Therefore, MSM at risk for transmitting HIV may believe that they have a low risk based on incorrect assumptions that [ARV therapy] eliminates HIV from semen."

Of particular concern to the study investigators is that ongoing replication of the virus in the genital tract, in the presence of ARV therapy, can lead to the accumulation of drug-resistance mutations and the possible spread of treatment-resistant virus. This, they point out, "may contribute to the high prevalence of antiretroviral drug-resistant HIV in HIV-infected individuals in the United States [who have not yet started ARV therapy]."

In addition to the suggestion that condom use continue to be promoted as a harm-reduction strategy among HIV-positive MSM who are otherwise responding well to ARV treatment, the authors also note the need to "promote the aggressive diagnosis and treatment of STIs."

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