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Undetectable blood viral load and HIV transmission risk: results of a systematic review

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The sexual transmission of HIV occurs after an exposure to fluids that contain HIV, such as semen and fluids from the vagina and rectum. Research shows that a higher amount of HIV (viral load) in these fluids increases the risk of HIV transmission and that a lower viral load decreases the risk.[1]

Treatment, viral load and HIV transmission

The viral load in the blood of a person living with HIV is measured to monitor the success of antiretroviral therapy (also called ART, HAART or cART). Successful HIV treatment can reduce the viral load in the blood (and other bodily fluids) to undetectable levels and thereby reduce the risk of sexual HIV transmission. In fact, a research study known as HPTN 052 found that the risk of HIV transmission among heterosexual serodiscordant couples was 96% lower when the HIV-positive partner was on treatment.[2] (In serodiscordant couples, one partner is HIV-positive and the other is HIV-negative.)

Undetectable viral load does not mean that there is no virus, but rather that the amount of HIV in a bodily fluid is below a level that tests can detect. (Tests used in some places, such as Canada, cannot detect HIV if there are less than 40 copies of HIV per ml of blood, while tests used in other parts of the world have higher limits of detection.)

Also, not all people living with HIV who take HIV treatment and have an undetectable viral load in the blood also have an undetectable viral load in their other bodily fluids. Research suggests that of those people living with HIV who have an undetectable blood viral load, 5 to 48% can have detectable virus in their semen, vaginal fluid and rectal fluid.[3,4,5]

Although previous research has demonstrated that treatment can reduce the risk of HIV transmission in heterosexual couples, it is unclear exactly what the HIV transmission risk is when a person's blood viral load is undetectable. A recent systematic review[6] of the literature was conducted by Dr. Mona Loutfy, one of Canada's leading infectious disease specialists, and colleagues to gain a better understanding of this risk.

Systematic review

The authors searched for published studies that followed serodiscordant heterosexual or same-sex couples over time. The main purpose of the review was to find studies that met the following criteria:

- the HIV-positive partner was on antiretroviral treatment
- the number of HIV infections in the HIV-negative partner was recorded
- if HIV transmission occurred, the HIV-positive partner's blood viral load was measured close to the time of transmission

The authors identified only three studies that fit all of their criteria. These studies followed a total of 222 heterosexual couples from Brazil, Spain and Uganda.

An additional three studies were identified that fit all of their criteria but did not measure the viral load of the HIV-positive partner near the time of HIV transmission, including the HPTN 052 randomized controlled trial. These

studies enrolled a total of 1,304 couples on treatment.

Overall, these six studies contained 2,975 person-years follow up of treated couples. This is the equivalent of following 2,975 couples for one year. The vast majority of these couples were heterosexual and only a small number were same-sex couples (3% of the couples in the HPTN 052 study were same-sex).

Number of HIV transmissions and HIV transmission risk

In the three studies where viral load was measured, no HIV transmissions occurred among couples where the HIV-positive partner was on treatment and the viral load was undetectable.

In the additional three studies, for which viral load was not measured, a total of four transmissions occurred. However, it is not known if the viral load of the HIV-positive partner was detectable or undetectable at the time of transmission. All of these HIV transmissions occurred shortly after the HIV-positive partner started treatment; therefore, the viral load was likely declining but still detectable when transmission occurred.

In these six studies, the definition of undetectable viral load ranged from less than 50 copies per ml to less than 500.

The lack of HIV transmissions in these studies does **not** mean there is no risk of HIV transmission when the viral load is undetectable. Using data from all six studies (but excluding the four HIV transmissions that occurred in the additional three studies), the authors calculated that when the viral load is undetectable, there may be a 1% risk of HIV transmission per 10 years of relationship and sexual activity.

Limitations of the study findings

There are several factors—other than viral load—that can influence the risk of HIV transmission between serodiscordant couples and may partly explain the lack of HIV transmissions observed in this review. As a result, the authors of the systematic review listed several caveats to their findings, including the lack of data on:

1. Extent of condom use

Condoms are an effective method of preventing the transmission of HIV and many STIs and couples in these studies may have been using condoms often. For example, in the HPTN 052 study, 96% of the couples reported using condoms every time they had sex. Although people often say they use condoms more than they actually do, condom use may have played an important role in keeping the number of HIV transmissions low in these studies.

2. Same-sex couples and type of sexual intercourse

The vast majority of the couples enrolled in the studies were heterosexual and were (likely) having mostly vaginal sex. Therefore, it is unclear how much these findings apply to same-sex couples and other couples who mostly have anal sex. Some researchers think the risk of HIV transmission when undetectable may be higher for anal sex compared to vaginal sex.

3. Rates of sexually transmitted infections (STIs)

STIs are known to increase the risk of HIV-positive people transmitting HIV and HIV-negative partners becoming infected. STIs may increase the risk of HIV transmission even when a person's viral load is undetectable. However, most of the studies reviewed did not provide data on STIs other than HIV; therefore, the review could not evaluate their impact.

In general, the risk of having STIs is lower among stable heterosexual couples (particularly those who are monogamous) than among people in casual relationships. Also, in some studies, such as the HPTN 052 study, participants were provided with regular STI testing and treatment which can help to further reduce the rate of STIs. A low number of STIs among couples in these studies may have decreased the risk of HIV transmission.

Conclusion

This systematic review supports previous research showing that treatment can significantly reduce the risk of HIV transmission among heterosexual couples. The authors concluded: "Our findings suggest minimal risk of sexual HIV

transmission for heterosexual serodiscordant couples when the HIV-positive partner has full viral suppression on cART with caveats regarding information on sexual intercourse type, STIs, and condom use. These findings have implications when counseling heterosexual serodiscordant couples on sexual and reproductive health."

Research is ongoing to gain a better understanding of the risk of HIV transmission (a) when the HIV-positive partner's viral load is undetectable and condoms are not used and (b) in same-sex serodiscordant couples where the HIV-positive partner is taking ART.

—James Wilton

RESOURCE:

Understanding Risk: A Conversation

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Produced By:

555 Richmond Street West, Suite 505
Toronto, Ontario M5V 3B1 Canada
Phone: 416.203.7122
Toll-free: 1.800.263.1638
Fax: 416.203.8284
www.catie.ca
Charitable registration number: 13225 8740 RR

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