

REVIEW ARTICLE

Sexual and Reproductive Health in HIV Serodiscordant Couples

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Abstract

Serodiscordant couples are a significant source of new HIV infection in sub-Saharan Africa. The prevention of HIV transmission to the uninfected partner should be an integral part of their health care. Serodiscordant couples desire pregnancy, treatment for infertility, effective family planning services, sexual health screening, and so on. This paper reviews the sexual and reproductive health needs of heterosexual serodiscordant couples, based on current evidence and recommendations. *Afr J Reprod Health 2013 (Special Edition); 17[4]: 99-106*.

Keywords: HIV, Serodiscordant couple, Conception, Contraception, infertility

Résumé

Les couples sérodiscordants sont une source importante de nouvelles infections du VIH en Afrique sub-saharienne. La prévention de la transmission du VIH au partenaire non infecté doit être une partie intégrante de leurs soins de santé. Les couples sérodiscordants désirent une grossesse, le traitement de la stérilité, des services de planification familiale efficaces, le dépistage de la santé sexuelle et ainsi de suite. Ce document passe en revue les besoins en matière de santé sexuelle et reproductive des couples hétérosexuels sérodiscordants, fondées sur des preuves et des recommandations en vigueur. *Afr J Reprod Health 2013 (Special Edition); 17[4]: 99-106*.

Mots-clés: VIH, couple sérodiscordants, conception, contraception, l'infertilité

Introduction

The human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) have continued to be a major health challenge worldwide. HIV infection started as a recognized niche infection in California men who were described as “homosexual”¹. The report of the first AIDS cases in California² in 1981 prompted additional case reports in other US cities^{1,3} and in Europe^{4,5}, among men who have sex with men. HIV infection has now become a global epidemic and the mode of spread predominantly through heterosexual intercourse, mother-to-child transmission (MTCT), and transmission by unsafe medical and cultural practices. According to Joint United Nations Programme on HIV/AIDS (UNAIDS), about 34 million people were living with HIV at the end of 2011 and about 69% of them lived in sub-Saharan Africa⁶.

Sub-Saharan Africa has the highest prevalence and incidence of HIV infection worldwide, mostly attributed to heterosexual transmission⁷. In this region, at least half of the people living with HIV in stable relationships have an HIV-negative partner⁸, that is, one partner is HIV-positive and the other HIV-negative (serodiscordant relationship). Several studies have shown a high prevalence of HIV serodiscordance among heterosexual couples in Africa⁹⁻¹¹. The proportion of serodiscordant relationship may be up to 75% in countries with low prevalence (<10%) of the infection⁸. Population-based estimate of serodiscordance ranges from 2% (in Rwanda) to 13% (in Zimbabwe and Lesotho)⁷. Among HIV-positive pregnant women attending antenatal clinic in Nigeria, 7.7% to 78.8% of them had HIV-negative partners¹⁰. Evidence suggests that men and women are equally likely to be an index (HIV-positive) partner in a serodiscordant couple¹². The

HIV-negative partners of serodiscordant couples are at an extremely high risk of becoming infected. HIV-negative women may become infected twice as fast as men, possibly due increased biological susceptibility¹¹.

Serodiscordant couples are an important source of new HIV infections in sub-Saharan Africa. In Zambia, DNA sequencing revealed that 87% of new infections in the negative partner were acquired from the HIV-positive partner¹³. A study conducted at 14 sites in Southern and Eastern Africa found that 64% of seroconversions could be linked by viral sequencing to the HIV-positive partner in long-term relationship¹⁴. Also, mode of transmission analysis conducted during 2007-2008 in Kenya, Lesotho, Mozambique, Rwanda and Uganda suggested that the proportion of HIV infection arising from transmission within serodiscordant couples ranges from 10% in Kenya to 56% in Rwanda¹⁵.

Like the general population, serodiscordant couples have reproductive health needs such as desire for conception, treatment for subfertility/infertility, need for effective contraception, and rights to health care and so on. This paper reviews the sexual and reproductive health needs of heterosexual serodiscordant couples, and the management of these health issues based on available evidence and current recommendations.

Risk of HIV Transmission in Serodiscordant Couples

Studies conducted in Africa among heterosexual serodiscordant couples showed that HIV transmission from HIV-positive to HIV-negative partners was 20 – 25% per year, irrespective of whether the man or woman was the index partner¹⁶⁻¹⁸. This rate is based on a coital frequency of two to three times per week and a risk of transmission on the order of one in 500 for each contact^{19,20}. Some other authors have quoted the risk of sexual transmission of HIV from male-to-female as 0.1-0.3% per act of intercourse and female-to-male as 0.03-0.09 per act of intercourse, provided the couples are not participating in any other forms of high-risk activities²¹.

HIV-serodiscordant couples sometimes engage in risky sexual behaviour, especially couples who desire pregnancy²²⁻²⁴. HIV transmission in heterosexual serodiscordant couples who are attempting to conceive depends on numerous factors; most important are plasma viral load of the index partner, presence of sexual transmitted infections (STIs), and frequency of intercourse²¹. The viral load of the index partner is the most powerful predictor of HIV transmission²⁵. Studies have shown that there was negligible or no sexual transmission of HIV in serodiscordant couples, where the index partner had an undetectable viral load or a low viral load below a given threshold^{25,26}. The risk of HIV transmission is considerably lower in HIV-infected persons on antiretroviral therapy (ART) with completely suppressed viraemia and long-term undetectable viral load²⁷. Although, viral load in plasma generally correlated well to that in genital secretions; viral shedding in the genital secretion may still occur in fully suppressed HIV-infected persons on ART. The possibility still exists for an HIV-infected partner on ART with long-term undetectable plasma viral load to sexually transmit the virus to an uninfected partner²⁸. The presence of STIs increases viral load substantially in genital secretion, even when the individual is asymptomatic^{29,30}. Both ulcerative and non-ulcerative STIs increase the risk of HIV transmission and acquisition.

Prevention of Sexual Transmission of HIV in Serodiscordant Couples

It is possible for heterosexual serodiscordant couples to remain serodiscordant indefinitely, if preventive programmes are instituted. These interventions include couple HIV testing and counseling, safer sex practices by using condoms consistently and correctly, male circumcision and the use of antiretroviral (ARV) drugs. In HIV counseling and testing programmes where condom use was recommended for prevention, the annual risk of HIV transmission among serodiscordant couples can drop from 20-25% to 3-7%^{7,16,31}. Circumcision of HIV-uninfected male partner reduces the female-to-male transmission of HIV by 38 – 66% over 24 months, assuming adequate

duration of healing (at least 6 weeks) before resuming sexual activity³²⁻³⁴. Male circumcision is recommended as a prevention strategy.

Antiretroviral Drugs in Serodiscordant Couples

The use of ARV drugs for treatment and prophylaxis in an HIV infected partner reduces the risk of HIV transmission to the uninfected partner. In 2010, World Health Organization (WHO) recommended ARV for HIV-infected persons eligible for treatment of their own HIV infection based on clinical and immunologic criteria (WHO clinical stage 3 or 4 and CD4 count of ≤ 350 cells/ μ L)³⁵. The WHO also recommended ART for HIV-infected pregnant women eligible for treatment, and ARV prophylaxis for those HIV-infected pregnant women not eligible for treatment³⁶. In serodiscordant couples, ARV prophylaxis is offered to HIV-infected pregnant women and their infant to reduce the risk of MTCT of HIV throughout the risk period of pregnancy, delivery and breastfeeding.

The current WHO guideline (April 2012) on serodiscordant couples recommends ART for HIV-positive partners with CD4 count of >350 cells/ μ L to reduce the risk of transmission to the uninfected partner³⁷. The HPTN 052 randomized controlled trial found a 96% reduction in HIV transmission in serodiscordant couples, where the HIV-infected partner with a CD4 count between 350 and 550 cells/ μ L had an early initiation of ART. This recent recommendation implies that HIV-infected partners of serodiscordant couples can be offered ART regardless of their CD4 count, to prevent HIV transmission to the uninfected partner.

HIV Pre-Exposure Prophylaxis in Serodiscordant Couples

HIV pre-exposure prophylaxis (PrEP) is the use of ARV drugs by uninfected individuals to prevent HIV infection. PrEP with oral tenofovir (TDF) alone or plus oral emtricitabine (TDF-FTC), have been shown to prevent the acquisition of HIV in an uninfected partner^{38,39}. A randomized controlled trial (RCT) conducted among serodiscordant couples found a 67% reduction in risk of acquiring HIV in uninfected partners who had TDF alone

and a 75% risk reduction in the TDF-FTC group, when compared to placebo⁴⁰. Another RCT conducted among heterosexual men and women showed a 62.6% reduction in risk of acquiring HIV in uninfected partners who had TDF-FTC³⁹. In contrast, a RCT conducted among heterosexual HIV-negative women did not show a significant reduction in the rate of HIV infection in the TDF-FTC group⁴¹.

The expressed concern about PrEP includes acceptability, access, cost and availability of ARV, drug adherence and resistance, and risky sexual behaviours⁴². The need for drug adherence in PrEP should be emphasized, as available data suggest lack of efficacy in couples with low drug adherence^{40,41}. PrEP should be available for serodiscordant couples as a risk reduction strategy to prevent sexual HIV transmission. The combination of ARV prophylaxis in the HIV-infected partner and PrEP in the uninfected partner would further reduce the risk of HIV transmission and acquisition in serodiscordant couples, than either used alone.

Safer Conception in Serodiscordant Couples

The desire for child bearing among serodiscordant couples may lead to attempt at natural conceptions through unsafe sex practices, regardless of safer contraception guidelines. Serodiscordant couples who wish to achieve pregnancy should ideally have preconception care and counseling.

Preconception Counseling and Care

Comprehensive preconception counseling should provide the couple and individual partners with information on the available safer conception options⁴³. Safer conception eliminates or reduces the risk of HIV transmission to the uninfected partner and/or the unborn child. Information on the benefit, success rate and inherent risks of each option should be provided. The couple should be counseled on risk-free and risk-reduction reproductive methods. Preventive counseling should be offered to serodiscordant couples, particularly information on safer sex practices and condom use. The counseling should also emphasize early initiation of ART for an HIV-infected partner to prevent HIV transmission to an

uninfected partner. The risk of MTCT of HIV in infected female partner and the available strategies for prevention should also be discussed. HIV-positive partners on treatment should achieve maximal viral suppression before attempting conception. Screening and prompt treatment of STIs should be offered to HIV serodiscordant couples during preconception care.

Options for Safer Conception

The options available for safe conception in a serodiscordant couple depend on the gender of the index partner.

HIV infected female and HIV uninfected male

Artificial insemination

Artificial insemination with partner's semen is considered a risk free method of achieving pregnancy in serodiscordant couple, when the male partner is uninfected⁴³. Timed, self, vaginal insemination during the woman's fertile period is a low-technology method for achieving conception.

Timed unprotected intercourse

Timed unprotected intercourse during the peri-ovulatory period is risk reduction method, especially in HIV-infected women on ART with undetectable viral load^{44,45}. Sero-discordant couples are educated on the woman's fertile period and are encouraged to limit unprotected sexual intercourse to the fertile period. This method decreases the number of unprotected sexual intercourse while optimizing the couple's chance of conception. Provision of ART to HIV-infected female partner can significantly decrease the risk of HIV transmission to the HIV-negative male partner^{27,37}.

Periconception pre-exposure prophylaxis

PrEP for the HIV-negative male partner may be combined with timed unprotected intercourse to achieve pregnancy. The provision of PrEP for the HIV-negative male partner prevents acquisition of HIV³⁷. This risk reduction method can be offered to sero-discordant couple, especially where the HIV-infected female partner on ART has undetectable viral load⁴⁶.

Assisted reproductive techniques

Assisted reproductive techniques such in-vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) can also prevent horizontal transmission of HIV infection to the uninfected male partner. This method of conception is also indicated in sero-discordant couples with additional fertility issues like bilateral tubal blockage or male factor infertility.

HIV infected male and HIV uninfected female

Sperm wash/preparation

Sperm wash of the infected male partner's semen combined with intrauterine insemination (IUI) or assisted reproductive technique is an established, safe and effective risk-reduction method of achieving conception⁴⁷. This is indicated when donor sperm from an HIV-uninfected male is unacceptable.

Donor sperm

Artificial insemination or assisted reproductive technique with sperm from an HIV-negative donor eliminates the risk of HIV transmission to the uninfected female partner in a sero-discordant couple.

Periconception preexposure prophylaxis

PrEP for HIV-negative female partner in sero-discordant couple can also prevent acquisition of HIV³⁷. This method may be combined with timed unprotected sexual intercourse, as a risk-reduction method. However, available data is mixed and inconsistent to recommend this method of conception for HIV-uninfected females in sero-discordant couples³⁹⁻⁴¹.

Treatment of Infertility

HIV sero-discordant couples with infertility should be offered similar evaluation and treatment options like HIV-negative couples. Infertility treatment in sero-discordant couples should be based on the identified causes of infertility and the management tailored to their specific needs. Treatment should be offered in the appropriate environment, to prevent cross-contamination of samples and HIV

transmission to HIV-negative individuals and health workers⁴³. Guidelines and recommendations on laboratory and patient care have been established to minimize this potential risk.

Pregnancy and Childbirth

Counseling for the prevention of mother to child transmission (PMTCT) of HIV should be offered to all HIV-sero-discordant and sero-concordant couples. Recent evidence suggests that the risk of HIV transmission, to the uninfected partner in sero-discordant couples, doubles during pregnancy⁴⁸. HIV-negative pregnant women in sero-discordant relationships should be adequately counseled to prevent seroconversion during pregnancy. The high viral load (acute viraemia) at the time of sero-conversion substantially increases the risk of MTCT of HIV^{49,50}. HIV-negative pregnant women in sero-discordant relationships should be offered a repeat HIV-testing (retesting) during the third trimester, preferably between 28 and 36 weeks⁵¹. In the antenatal clinic setting, there is need to emphasize couple's HIV counseling and testing, and male partner involvement.

All HIV-positive pregnant women should be offered interventions for the PMTCT of HIV. The core interventions for PMTCT include; voluntary HIV testing and counseling, use of ARV drugs, safer practices during pregnancy, safer delivery practices, and safe infant-feeding practices. The risk of MTCT without intervention is estimated to be 15-30% in non-breastfeeding HIV-infected women, and 20-45% in breastfeeding HIV-infected women. These interventions reduce the risk of MTCT of HIV to less than 2% in non-breastfeeding population and less than 5% in breastfeeding population^{36,52}.

HIV-positive pregnant women eligible for treatment

HIV-infected pregnant women who are eligible for treatment (for their own disease) should be offered daily ART, starting as soon as possible, irrespective of the gestational age during pregnancy, delivery and thereafter³⁶. Their infants should receive daily nevirapine (NVP) or twice

daily Zidovudine (AZT) from birth until 6 weeks of age, irrespective of the mode of feeding³⁶.

HIV-positive pregnant women not eligible for treatment

HIV-infected pregnant woman not eligible for treatment should be provided with ARV prophylaxis, starting at 14 weeks gestation or as soon as possible thereafter³⁶. The available options are: Option A, which involves AZT monotherapy for the mother and infant prophylaxis with either AZT or NVP for 6 weeks after birth, if infant is not breastfeeding. If the infant is breastfeeding, daily NVP is continued for 1 week after the end of breastfeeding³⁶. Option B involves triple ARV prophylaxis for the mother during pregnancy and throughout breastfeeding period, and the infants receive daily NVP or twice daily AZT from birth until 4 to 6 weeks of age, irrespective of the mode of feeding³⁶.

Safer Practices during Pregnancy and Delivery

Basic antenatal care including nutritional supplementation, malaria chemoprophylaxis and routine immunization should be offered to HIV-infected pregnant women. Invasive procedures such as chorionic villus sampling, amniocentesis, cordocentesis, and placement of fetal scalp electrode should be avoided during pregnancy and delivery. In the absence of obstetric indications, the preferred mode of delivery depends on the maternal viral load. HIV-positive women with undetectable viral load or viral load less than 1000 copies/ μ L can be offered vaginal delivery, while planned caesarean section should be offered to those with high viral load^{53,54}. Prolonged labour should be avoided and artificial rupture of fetal membranes should be delayed until delivery is imminent. Routine episiotomy and instrumental vaginal delivery should be avoided. The mother should be counseled and supported on the preferred choice of infant feeding.

Contraception

Correct and consistent use of condoms is strongly recommended in sero-discordant couples, either

alone or with another effective contraceptive method (dual method).

Barrier Contraception

Male (latex or polyurethane) and female condoms are highly effective in preventing sexual transmission of HIV. Cervical cap and diaphragms are not recommended for contraception in sero-discordant couples.

Hormonal Contraception

Combined hormonal contraceptives (such as combined oral contraceptive pills, combined injectable contraceptive, and combined contraceptive patches and vaginal rings) and progestogen-only contraceptives (such as progesterone only pills, implants and injectables) are recommended for both HIV infected and uninfected women in sero-discordant relationship⁵⁵. HIV-positive women on ARV drugs such as protease inhibitors that induce liver enzymes should be educated on the potential of the drugs to reduce the efficacy of certain hormonal contraception such as combined oral pills, patches, vaginal rings, progestogen-only pills and implants. A recent study among sero-discordant couple using progestogen-only injectables (depomedroxyprogesterone acetate) suggested an increased risk of HIV transmission among user⁵⁶. The current WHO (February 2012) review, states there was not enough evidence to suggest that hormonal contraceptives adversely affect HIV or its transmission⁵⁷. The report strongly recommended that HIV-positive women on hormonal contraception should consistently use condoms.

Intrauterine Contraceptive Device

Intrauterine contraceptive devices such as copper intrauterine device and levo-norgestrel intrauterine system may be offered to women in sero-discordant relationship. However, correct and consistent use of condoms should be encouraged to prevent the transmission of HIV and other STIs. Among intrauterine device users, limited evidence shows no increased risk of overall complications or infectious complications when comparing HIV-infected with non-infected women.

Conclusion

Sero-discordant couples are a significant source of new HIV infection in sub-Saharan Africa. In order to achieve zero new HIV infection, governments and other stakeholders (non-governmental organization, policy makers and healthcare providers) responsible for HIV prevention need to focus on the sexual and reproductive health of sero-discordant couples. This population group should be offered high-quality sexual and reproductive healthcare services.

Conflict of interest

The authors declare that they have no conflicts of interest.

Contribution of authors

CCM and OFG conceptualized the review. CCM carried out the literature review and wrote the initial draft manuscript. All authors made critical intellectual contributions to the manuscript and approved the final copy for submission.

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