Fertility Management in HIV

INTEREST Workshop, 16 Dakar May 2013
Vivian Black, Director Clinical Programmes
Wits Reproductive Health & HIV Institute
What to consider

• Does HIV affect fertility success?
• Does HIV affect fertility desire?
• Avoiding un-intended pregnancies
• Does a desire for fertility affect ‘HIV risk’ behaviour?
• Managing conception among the HIV affected couple – a missing PMTCT prong
• Resource considerations
Fertility success

• Demographic Health Surveys conducted across 13 countries compared fertility rates among HIV infected and uninfected women
• Controlled for age, employment, education, behaviour
• Looked at number of births in the last year and last 5 years

## Fertility success

<table>
<thead>
<tr>
<th>Positive HIV status</th>
<th>Number of births last year OLS (1)</th>
<th>Number of births last year OLS (2)</th>
<th>Number of births last year OLS (3)</th>
<th>Number of births last 5 years OLS (4)</th>
<th>Number of births last 5 years OLS (5)</th>
<th>Number of births last 5 years OLS (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>– 0.043*</td>
<td>– 0.042*</td>
<td>– 0.032*</td>
<td>– 0.177*</td>
<td>– 0.176*</td>
<td>– 0.145*</td>
</tr>
<tr>
<td></td>
<td>(0.007)</td>
<td>(0.007)</td>
<td>(0.007)</td>
<td>(0.015)</td>
<td>(0.015)</td>
<td>(0.014)</td>
</tr>
<tr>
<td></td>
<td>(0.010)</td>
<td>(0.010)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>64,056</td>
<td>64,056</td>
<td>64,056</td>
<td>64,056</td>
<td>64,056</td>
<td>64,056</td>
</tr>
<tr>
<td>Mean HIV-Positive</td>
<td>0.127</td>
<td>0.127</td>
<td>0.127</td>
<td>0.616</td>
<td>0.616</td>
<td>0.616</td>
</tr>
<tr>
<td>Mean HIV-Negative</td>
<td>0.167</td>
<td>0.167</td>
<td>0.167</td>
<td>0.722</td>
<td>0.722</td>
<td>0.722</td>
</tr>
</tbody>
</table>
Fertility success

• Found that HIV disease significantly lowers an infected woman’s fertility.
• Being infected with HIV reduces ‘births last year’ by 20–25 %, depending on whether we control for marital status.
• Impact is small
• For example, in Lesotho, with an HIV prevalence of 26.4%, the total fertility rate would be 0.15–0.3 (4-8%) children higher in the absence of HIV

Reasons for reduced fertility

- Women who are infected may be widowed, separated, or divorced, (associated lower birth rates).
- Lower fecundity or the individual may be too sick to be sexually active.
- Higher rates of miscarriage and stillbirth
- Co-infection with other sexually transmitted infections with resultant tubal disease
- Menstrual dysfunctions
- Weight loss leading to amenorrhoea

Zaba and Gregson 1998; Fabiani et al. 2006
Taulo F et al 2009 AIDS Behv
Fertility intentions
Fertility intentions
The Fertility Intentions & Incidence Study

• Among 850 HIV+ women (18 – 35 years) on ART in Johannesburg

• Conducted in 4 PEPFAR supported ART sites in inner city Johannesburg, September 2009 – March 2011

• 18-month clinical cohort study investigating
  – Fertility intentions amongst 850 women on ART
  – Contraceptive use, method preference and barriers
  – Incidence of planned and unplanned pregnancies
  – Hormonal contraceptive failures
  – Issues related to ART regimens and pregnancy

Schwartz, S et al AIDS Behav 2011
Fertility intentions

At baseline

- 12% of the women were actively trying to conceive
- 36% had intentions to conceive within the next 12 months.
- 75% indicated that they had plans of conceiving at some point in the future
- partner cohabitation/marital status and number of children with current partner are strong predictors of current fertility intentions

Schwartz, S et al AIDS Behav 2011
Results: Contraceptive Use amongst those *not* trying to conceive (n=748)

- HC: 32%
- Consistent Condoms: 54%
- Dual Use: 15%
- Unmet Need: 29%

Schwartz, S et al AIDS Behav 2011
Patient-provider communication

“What is it, boy? Want to go outside?”
Enrolment and follow up

907 Consented for enrollment

- 57 Were not enrolled
  - 38 Tested pregnant at time of consent
  - 14 ≥ 36 years
  - 4 Not receiving regular care at study site
  - 1 Sterilized

850 Enrolled for follow-up

28 No follow-up visits

822 Had ≥ 1 follow-up visit

670 No recorded pregnancies
  - 6 confirmed deaths
  - 1 sterilization

161 Incident pregnancies
  - 170 Total pregnancies
    - 7 women with two pregnancies
    - 1 woman with three pregnancies

Schwartz, S et al AIDS Behav 2011
Incidence of pregnancy in a cohort of South African women August 2009 – March 2011

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Time at Risk</th>
<th>Number of women who conceived</th>
<th>Incidence Rate / 100 PY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unplanned</td>
<td>602.1</td>
<td>97 (60%)</td>
<td>16.1 (13.2-19.7)</td>
</tr>
<tr>
<td>Planned</td>
<td>143.2</td>
<td>64 (40%)</td>
<td>44.7 (35.0-57.1)</td>
</tr>
<tr>
<td>Total</td>
<td>745.2</td>
<td>161</td>
<td>21.6 (18.5-25.2)</td>
</tr>
</tbody>
</table>
Incidence of unplanned pregnancy according to baseline need for contraception

Cumulative Incidence

log-rank $p<0.0001$

Unmet need

Met need

Number at risk

<table>
<thead>
<tr>
<th>Category</th>
<th>At Risk</th>
<th>421</th>
<th>371</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline met need</td>
<td>519</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline unmet need</td>
<td>181</td>
<td>123</td>
<td>113</td>
<td>10</td>
</tr>
</tbody>
</table>

Months since enrollment
Incidence of unplanned pregnancy according to time-varying contraceptive use

- No reliable method
- Condoms only
- HC & HC+condoms

**Number at risk**

<table>
<thead>
<tr>
<th>Method</th>
<th>0</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>No reliable method</td>
<td>76</td>
<td>49</td>
<td>26</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Condoms alone</td>
<td>416</td>
<td>320</td>
<td>301</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>HC &amp; HC+condoms</td>
<td>208</td>
<td>175</td>
<td>157</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

*log-rank p<0.0001*
Outcomes

• 170 pregnancies among 161 women
• 105 (62%) of pregnancies were **unplanned**, of these 38 women elected a termination of pregnancy, 19 had a spontaneous abortion and there was 1 still birth
• 8 pregnancies occurred on hormonal contraception (4.3/100PY)

Special Group: Perinatally Infected Women/Youth

- UK Ireland cohort of 252 women >12 year
- 42 pregnancies among 30 women
- Median age 18 (14-22 years)
- 81% unplanned
- >50% of partners unaware of HIV status
- 36% elected termination of pregnancy
- 33% had detectable VL
- 1/21 infants infected with HIV

Poor uptake of contraception

- Studies of unintended pregnancies in HIV infected women in sSA
  - 84% among PMTCT clients in South Africa
  - 51% among women in Cote d’Ivoire
  - 99% among women in an ART program in Uganda
  - 62% among women on ART in South Africa

- Newly HIV-diagnosed women in Malawi have 46% contraceptive use at 12 months post-diagnosis.

Rochat et al; JAMA 2006
Desgrées-du-Loû et al., Int J STD AIDS 2002
Smart, T. Aidsmap. 2006.
Schwarts, S et, al, al AIDS behav 2011
Perceptions of Contraception

• When choosing contraception women consider side effects, convenience and protection against STIs.
• Condoms often preferred - lack of side effects and protection against STIs.
• Drawbacks to condoms - fear of breakage and need of male participation.
• The pill not liked because of burden of having to remember to take it daily
• Injectable liked for convenience and their secrecy.
• Other methods of contraception (e.g., tubal ligation, the loop) were largely unknown

Laher F et al AIDS Behav 2009
Discontinuation of Contraception

Qualitative research of HIV infected women identified reasons for discontinuation and included:

• Need for follow-up (the pill)
• Side effects
• Changing physical appearance
• Concern about amenorrhea and vaginal wetness
• Interaction with ART
• Fertility desire
WHO Hormonal Contraception and HIV

• Women at high risk of HIV can continue to use all existing hormonal contraceptive methods without restriction.
• Women living with HIV can continue to use all existing hormonal contraceptive methods without restriction.
• Consistent and correct use of condoms, male or female, is critical for prevention of HIV transmission.
• Voluntary use of contraception by HIV-positive women is an important strategy for PMTCT.
Communication: family planning and contraception provision

• Above highlights the need for improved HCW and patient communication

• Integration of contraceptive service provision within ART clinics

• FP integration should address providers’ concerns over condom substitution and patient perceptions
Do you want to conceive?
Different approaches to HIV infected couples

- HIV Infected woman → HIV Uninfected man
- HIV Uninfected woman → HIV Infected man
- HIV Infected woman → HIV Infected man

Remember: adherence is the responsibility of the infected partner and the risk is to the uninfected partner.
Pre-conception counselling

• Disclosure of status
• Reproductive options: including risks, risk reduction, costs and chances of success
• Balance the risk of natural conception with established risk-reduction methods
• Consequences of failure to prevent transmission to partner and child and importance of regular testing
Reduce risk of HIV sexual transmission at an individual level

• Risk per event is low, but not eliminated

• Reduce risk of HIV transmission at an individual level:
  – Viral load
  – Mucosal integrity
  – Frequency of exposure

• Reduce risk of HIV acquisition
  – Post exposure prophylaxis
  – Mucosal integrity
  – Frequency of exposure
  – Circumcision
Minimum pre-conception medical assessment

- Exclude STI’s through syphilis serology and clinical assessment
- Clinically and immunologically should not have AIDS: Medical exam and CD4 cell count
- Those on ART should have an undetectable VL
- Screen for infertility through history
- Pregnancy: RH, haemoglobin
Medical management

- Optimise medical condition
- Treat any current infection
- Treat co-morbid illnesses
- Prevent infections as appropriate
- Determine ovulatory cycle
Fertility and HIV

- The infected partner should ideally be on ARVs and have suppressed viral load
- Pre-exposure prophylaxis for the uninfected partner, not sure of additional benefit if VL suppressed.
Assisted reproduction

• Assisted techniques for discordant couples
  – IUI, IVF, ICSI
  – Sperm washing with VL check

• Most studies have looked at HIV - infected males, but a few have looked at infected women

• Expensive and not routinely available

• Lowest risk of horizontal transmission

Chadwick RJ, Topics in Antiviral Med, 2011
Fertility and HIV

• Self insemination

• Sperm collection with self-insemination at the time of ovulation (avoiding spermicide-containing condoms)
  – Man ejaculates in clean receptacle
  – Semen drawn up into a large syringe (10 - 20ml)
  – Syringe placed about 4 – 6 cm in woman’s vagina in prone position and semen pushed out of the syringe
  – Can be done at home or in clinic.

• No studies published on self insemination
Natural Conception

• The couple practice safe sex for most of the woman’s cycle using condoms.
• Use ovulatory method and have sex without condom on alternate days during ovulation
• Increasingly being accepted for concordantly infected couples, starting to be accepted for discordant couples
• Limited research of natural conception among discordant couples
• Big concern that safe sex messaging will be compromised

Natural Conception

• Extrapolation from studies of HIV discordant couples in stable relationships
• A meta-analysis of 11 cohorts with 5021 couples, there was no horizontal transmission if infected partner was on ART and VL <400
• In Spain, 393 couples followed for 12 years there was not transmission among those on ART
Natural Conception

• In Uganda, 174 discordant couples followed for 4 years linked transmission to VL

<table>
<thead>
<tr>
<th>Transmission/coital act</th>
<th>VL copies/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0001</td>
<td>&lt;1 700</td>
</tr>
<tr>
<td>0.0023</td>
<td>~ 38 500</td>
</tr>
<tr>
<td>0.041</td>
<td>With herpes</td>
</tr>
</tbody>
</table>

• HPTN 052 96% risk of 0.37/100 person years

Gray RH et al Lancet 2010
Natural Conception

- Among 3 studies of natural conception among discordant couples (variable ART use)
- 168 couples – 3 horizontal and 1 vertical infection.
- All horizontal transmissions occurred in pregnancy (months after conception)
Criteria for natural conception

- HIV positive partner on ART for 6 months or longer
- Viral load undetectable on PCR (< 50 copies/ml)
- Perfect adherence to treatment and regular medical follow-up
- Mutually faithful relationship
- No concomitant sexually transmitted infections
- Limited to 6 months during ovulation period only
- Condoms should be used at all other times

Barreiro, Human Reproduction 2007
Unsuccessful

• After attempting 6 ovulation cycles and the couple are unsuccessful in conceiving, consider reduced fertility and risk of continuing naturally may be more harmful than successful
• Council and if appropriate refer for further work-up
• Repeat HIV testing of exposed partner
Successful
• Repeated HIV antibody testing for exposed partners

• If woman seroconverts during pregnancy, provide ART as soon as possible as seroconversion is associated with high rates of mother-to-child transmission

• Test infant at birth and 6 weeks if positive start ART
Important to protect partner after conception

Increased Risk of HIV-1 transmission in pregnancy: Prospective study among Africa serodiscordant couples

- HIV viral load in genital secretions during pregnancy is increased
- Increased risk of transmission of HIV from a pregnant woman to her sexual partner

Mulago NR et al, AIDS 2011
PMTCT

• If woman HIV infected, ideally she was on ART prior to conception. She should continue ART throughout pregnancy.

• If the woman was not on ART, provide ART if feasible (guideline limitations in some settings), else provide PMTCT as per local guidelines.
Thank you