Highly Active Anti-Retroviral Therapy, Pre- Exposure Prophylaxis, and assisted reproductive techniques for the conception of a seronegative baby in HIV sero-discordant couples: A retrospective analysis

Sir,

With the advent of Anti-Retroviral Therapy (ART), HIV infection has now become like any chronic illness and many infected individuals lead a near-normal life. With increasing life expectancy, many desire conceptions. We report our experience of 15 sero-discordant couples who desired to conceive.

Preprocedure, they were subjected to the following procedures:

- Preconceptual counseling explaining the procedure, the safety versus risks, and the efficacy. Positive reinforcement remained essential
- Written informed consent
- Both HIV-infected and uninfected partners were tested for the following infectious diseases and appropriately treated:
  i. Hepatitis B
  ii. Hepatitis C
  iii. Syphilis
  iv. Gonorrhea
  v. Chlamydia trachomatis.
- CD4 count and plasma viral load for the infected partner
- Semen analysis to rule out infertility.

Infected partners were treated with antiretroviral therapy (ART). Infected women were given two nucleoside reverse transcriptase inhibitors (NRTIs) with a protease inhibitor (PI) and infected males were given two NRTIs with one non-NRTIs or PIs or integrase strand-transfer inhibitor. After 4–6 months of follow-up, once viremia was suppressed to undetectable levels and CD4 counts had improved, measures for conception were offered, namely,

- Timed sexual intercourse during the periovulatory period
- If unsuccessful at 3 months, intrauterine insemination (IUI) or finally *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI) was attempted. All the procedures of assisted reproductive techniques included sperm wash.

The uninfected partners were given tenofovir and emtricitabine combination pill for 3 days before and after attempted conception period as preexposure prophylaxis (PrEP).

OUR STUDY RESULTS

Of the 15 HIV-1 infected sero-discordant couples, five had male infected partner (female uninfected), while ten had female infected partner. The median age of males and females was 34 years and 30 years, respectively.

All the individuals in the study tested negative for hepatitis B, hepatitis C, and other sexually transmitted infections (STIs). One individual with tuberculosis received Anti-Koch's treatment (AKT). The most common ART regimen in females was zidovudine, lamivudine, and lopinavir/ritonavir, whereas in males, it was tenofovir, emtricitabine, and nevirapine/efavirenz/darunavir/dolutegravir/raltegravir. As an adverse drug reaction to nevirapine, one patient developed Steven–Johnsons syndrome which was appropriately managed.

Undetectable viremia was obtained in 12 of 15 patients at 6 months (80%), while two took longer period to achieve undetectable levels of virus and one was lost to follow-up. During the antenatal period, all the infected women had persistent undetectable viremia (checked every 3 monthly) throughout the pregnancy except one woman whose viral load increased to 2470 copies/mL at the end of the second trimester. She received the same lopinavir/ritonavir-based therapy with escalated doses: lopinavir 200 mg/ritonavir 50 mg – two tablets 12 hourly was increased to three tablets 12 hourly. As she developed diarrhea, her regimen was shifted to the initial dosage, but was intensified with raltegravir. Her viral load returned to undetectable levels after 3 months. The uninfected partners also underwent a battery of tests for HIV and other STIs every 3 months as abstinence in the marital relationship may lead to high-risk behavior, thereby acquiring STIs.

All couples were offered to first attempt timed periovulatory unprotected sexual intercourse. If conception was unsuccessful after three attempts, assisted reproductive techniques such as IUI and IVF/ICSI were offered. In our study, two couples underwent IUI, two couples chose IVF/ICSI, and the rest attempted through timed sexual intercourse method. A total of 13 couples conceived. One did not conceive till two cycles and then stopped attempting and one was lost to follow-up. PrEP was offered to all uninfected partners. It was taken by 7 of 13 patients and was tolerated well.

Of the 13 couples who conceived, two suffered from an abortion in the 2nd month and 11 delivered an HIV-negative baby (one underwent a miscarriage, then conceived again and delivered). Ten of the 11 couples underwent an elective cesarean section as per our protocol. Nine babies were top fed and two were breastfed. All the 11 babies received prophylaxis with zidovudine/nevirapine.

Thirteen of the 13 HIV uninfected partners remained HIV negative. The conception rate was found to be 13 of 15 (86.7%), and 11 of 15 partners (73.3%) delivered a baby.

Quinn *et al*. from the Rakai Project Study group had noted that the transmission of HIV virus closely correlated with the viral load measure.[1] The benefit of ART in the prevention of transmission was proved in HPTN-052.[2] While all patients had undetectable viremia, additional measures such as PrEP and artificial reproduction techniques were employed as there are few instances of disparity between plasma and genital fluid viral load.[3] The benefit of PrEP and the use of artificial reproduction techniques have been individually shown by various studies.[4,5] Our results are encouraging and are the first reported results from our country.

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Conflicts of interest
There are no conflicts of interest.

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