

INFERTILITY TREATMENT BY *IN VITRO* FERTILIZATION OR INTRA-CYTOPLASMIC SPERM INJECTIONS IN CHRONIC HIV-1 SERO-DIFFERENT COUPLES : DO WOMEN HIV INFECTION OR INFERTILITY INFLUENCE RESULTS ?



Infectious Diseases Department
Pitié Salpêtrière Hospital, Paris F- 75013 France
Corresponding author : Roland TUBIANA
roland.tubiana@psl.aphp.fr

Roland Tubiana¹, Nadia Prisant², Françoise Marguet¹, Stephanie Dominguez¹, Michele Naouri³, Ouriel Roseblum⁴, Gilles Lefebvre⁵, Daniele Vauthier³,
Anne Geneviève Marcelin³, Catherine Poirot² for the Pitié-Salpêtrière " AMP a Risque Viral " Study Group
1- Infectious Diseases Unit , 2 Genetic, Cytogenetic and Embryology Unit, 3 Obstetric-Gynécology Unit, 4 Psychiatry Unit, 5 Virology Unit
AP-HP, Hôpital La Pitié Salpêtrière, Paris, France

Abstract

Background: ART. The objective was to assess the impact of HIV-1 infection on assisted reproductive treatment (ART) in couples in which a member is infected with HIV-1.

Methods: In a retrospective study, we included 80 HIV-1 sero-different couples who had undergone ART between December 2002 and June 2007. The couples were divided into two groups: Group A1 (n=43) and Group A2 (n=37). Group A1 consisted of couples where the male partner was HIV-1 infected, and Group A2 consisted of couples where the female partner was HIV-1 infected.

Results: In Group A1, 52% (22/43) of couples achieved a pregnancy, compared to 21% (8/37) in Group A2. The difference was statistically significant (p=0.02).

Conclusion: HIV-1 infection in the male partner does not significantly influence the success of ART, while HIV-1 infection in the female partner significantly reduces the success rate.

Background

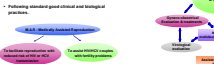
Since 2001, French law allows the use of assisted reproductive treatment (ART) in couples in which a member is infected with HIV-1.

With stringent inclusion criteria coming in addition to the usual inclusion criteria for assisted reproductive treatment (Journal Officiel de la République Française, December 22, 2006).

For HIV sero-different couples, the French legal requirements include stability of the infection, or absence of ongoing disease, defined as a CD4 lymphocyte count > 200/mm³ and a stable viral load, observed for at least 4 months prior to the start of assisted reproductive treatment, as well as an undetectable HIV viral load for at least 2 weeks before the reproductive treatment of the couple.

Couples were followed by a multidisciplinary team including HIV/HCV clinicians, embryologists, gynecologists, virologists and pediatricians, in order to securely handle the situation. Couples were to engage only in safe sexual intercourse.

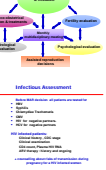
Medically Assisted Reproduction



Family assessment

Partner	Sex	Marital status	Age	Duration of HIV-1 infection	CD4 count	Viral load	Stability of infection	Stability of viral load
Infected partner	Male	Married	34.5	10.5	500	500	10.5	500
Uninfected partner	Female	Married	35.7	10.5	500	500	10.5	500

Infertility Assessment



Technical issues: ART vs HIV-1

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Study objectives

- To describe the outcome of *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI) in HIV-1 sero-different infertile couples, according to :
 - the **gender of the infected partner**
 - the **gender of the partner with an etiology of infertility.**

Comparison between groups were done using exact Fisher test

Inclusion Criteria

- Couples attending the Assisted Reproductive Treatment (ART) program in a context of viral risk in our institution from December 2002 to June 2007
- With one partner infected by HIV-1 (séro-différent couples for HIV-1)
- Fulfilling the French regulatory criteria for HIV infected couples access to Assisted Reproductive Treatment
- With one partner diagnosed with an infertility leading to an indication for *in-vitro* fertilization or intra-cytoplasmic sperm injection

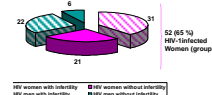
Exclusion Criteria

- HIV-1 sero-different couples without evidence of fertility impairment treated with self or Intra- Uterine insemination (50% in our experience)
- Couples with both partners infected with HIV-1
- Couples with one partner infected or co-infected with HCV (HIV +HCV)

Results

N = 80 HIV-1 exclusive sero-different couples

- 52 HIV-1 infected women :
 - 31/52 (59.6%) with an aetiology of infertility
 - 21/52 (40.4%) without evidence of fertility impairment
- 28 HIV-1 infected men:
 - 22/28 (78.6%) with an aetiology of infertility
 - 6/28 (21.4%) without evidence of fertility impairment
- Gender of infertility
 - 43/80 (53.8%) couples with a male aetiology of infertility
 - 37/80 (46.2%) couples with a female aetiology of infertility



Results: Assisted Reproduction Treatment (80 couples)

- 140 oocyte retrievals (OR) performed
- 90 IVF, 47 IVF-ICSI and 3 combined IVF/ICSI
- Median attempts per couples : 1,71 (1-4)
- 16.4% and 18.8 % pregnancy rate per OR and Embryo-transfer (ET) respective
- 23 clinical pregnancies achieved including :
 - 3 pair of twins
 - 6 miscarriages
- Cumulatively:
 - 28.75 % clinical pregnancy/couples
 - 25 % (twins=2) or 21.3% (twins = 1) take home baby rate (THR)
 - 43.5% of pregnancies occurred on the first IVF or ICSI cycle

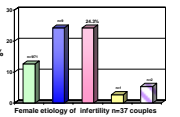
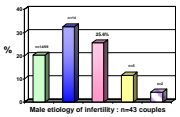
- All sero-negative partners remained negative
- All delivered babies are alive and during their on going follow

Study Population: HIV status and results

Sero-different couples at inclusion	Women HIV-1 (Men HIV+)	Women HIV+ (Men HIV-1)	TOTAL
N	38	42	80
Infertility etiology (%)			
- Female	6 (21.4)	31 (59.6)	37 (46.2)
- Male	22 (78.6)	11 (40.4)	43 (53.8)
Female age [mean]	34.5 (28-44)	35.7 (25-43)	35 (25-44)
HIV-1 partner under HAART (%)	27 (96.5)	47 (90.4)	74 (92.5)
Plasma HIV RNA titer: 50 or 200 copies/ml (%)	27 (96.5)	48 (92.7)	75 (93.8)
CD4 count [mean]	509 (135-1130)	502 (163-1340)	534 (136-1340)
Assisted reproduction technique performed :			
- IVF	22	68	90
- ICSI	23	24	47
- IVF-ICSI	4	3	7
Number of Oocyte Retrieved (OR)	46	95	140
Number of Embryo Transfer (ET)	37	95	122
Clinical pregnancies OR (%)	17.7	15.8	16.4
Clinical pregnancies ET (%)	21.6	17.8	18
% pregnancies after 1-1st ET cycles	25 (29)	63 (66)	43 (37.3)
Clinical pregnancies/couple (%)	8 (28.9)	15 (28.8)	23 (28.7)
Miscarriage	2	4	6
Twin pairs	0	3	3
Children born or ongoing pregnancies (Take Home Baby Rate %)	14 (42.4)	14 (25.9)	28 (25)

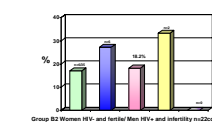
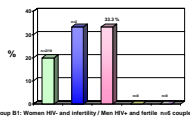
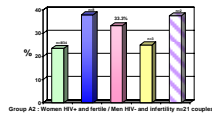
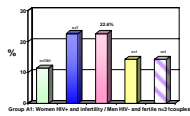
Assisted reproduction treatment outcome according to male or female etiology of infertility

- Pregnancies OR
- Miscarriages / not pregnancies
- Clinical pregnancies couple
- Twin pairs / not pregnancies
- Take Home Baby Rate (%)



Assisted reproduction treatment outcome in 4 sub groups

- Pregnancies OR
- Miscarriages / not pregnancies
- Clinical pregnancies couple
- Twin pairs / not pregnancies
- Take Home Baby Rate (%)



Conclusion

Comparison with matched non infected couples

- To complete the Analysis we formed a control group, selected from our non HIV infected couples, pairing one on one female patient on several criteria (age, etiology of infertility, rank of attempt and IVF or ICSI) with our HIV-1 infected female patients (group A).

	Control group Men HIV-1 Women HIV-	Women HIV+ Men HIV-1 Group A
Number of couples	82	52
Mean female age (years)	35	35
Twin rate	1.6	1.7
Infertility etiology (%)		
- Female pathology	57	59
- Male factor	25	6.6
Number of Oocyte Retrieved (OR)	155	155
Number of Transfer (ET)	89	85
Clinical pregnancies OR (%)	12.9	15.8
Clinical pregnancies ET (%)	13.9	17.6
Children born or ongoing pregnancies (Take Home Baby Rate %)	13 (28.3)	14 (26.9)

- Among this population of sero-different couples for HIV-1 starting an assisted reproductive treatment program with an indication of *In-vitro* fertilization or intra-cytoplasmic sperm injections and efficiently treated with cART for the majority of infected partners (88% HIV-RNA Bloq):

- We found no significant difference in term of efficacy of the reproductive treatment (Take Home Baby Rate) when considering either:
 - The gender of the HIV-1 infected partner or
 - The gender of the infertile partner

- The lack of difference with HIV negative couples is an important issue in the controversial topic of HIV/HAART influence on the ovarian reserve in HIV infected women.

- These data suggest the importance of comprehensive care of both HIV infection and access to parenthood for HIV sero-different couples