Decreased pregnancy rate after in-vitro fertilization in HIV-infected women

Selimova Fatima¹, Perminova Svetlana¹, Mityurina Elena¹,
Kozyrina Nadezhda², Abubakirov Aydar¹

¹Department Of Preservation And Restoration Of Reproductive Function Research Center for Obstetrics, Gynecology and Perinatology named after academician V.I. Kulakov', Moscow, Russia

²Specialized research laboratory for AIDS epidemiology Central Research Institute of Epidemiology, Moscow, Russia

The goal of the study was to evaluate clinical and laboratory characteristics and efficacy of ART in female HIV-infected patients.

Thirty-eight HIV-infected female patients (main group) and 56 HIV-seronegative women (control group) were enrolled into a prospective case-control study. Seventy-four in vitro fertilization (IVF) cycles, including 44 treatment cycles and 30 cryocycles, were conducted in the main group. The respective numbers of cycles in the control group were 59 and 30. Stimulation of superovulation was performed according to long IVF protocols and GnRH-antagonist-based protocols using recombinant FSH and hMG. While preparing the endometrium in cryocycles, natural estrogen- and micronized progesterone-containing medications were used. The infectious status of the patients was assessed based on the data on the disease stage, viral load, CD4+ count and the duration of ARV therapy. The patients in both groups were comparable in respect of age (median age - 34 and 32 years; $p=0.160$). The duration of HIV-infection was 10 years (interquartile range 6-13 years); most of the patients had the third subclinical stage of the disease (68.4%).

The patients with stages 4a (23.6%), 4b (5.3%) or 4c (2.6%) were in the remission period of the disease. All females were receiving combination ARV therapy, including 37 patients receiving NRTI in combination with PI and one patient was receiving NRTI + NNRTI. Median duration of therapy was 4 years (2 - 6.2 years). Viral load before initiation of the IVF program was undetectable in 100% cases. Median CD4+ count was 625.5 cells/ μ L (412.7 - 815.5). The patients in the main and control group were comparable in respect of duration and the factor of infertility - both groups had tubal-peritoneal factor as the most prevalent infertility cause (39.5 and 30.4%, $p=0.467$). Most HIV-infected women had secondary infertility (76.3% and 35.7%; $p=0.0001$).

The most frequent types of gynecologic pathology in HIV-infected females were cervix disorders (28.9%) and chronic salpingoophoritis (28.9%), which was comparable to the control group. However, complicated forms of uterine appendages inflammatory disorders were observed only in the main group (7.9%). History of sexually transmitted infection (syphilis, chlamydia infection) was reported in 11 (28.9%) and 3 (5.3%) of HIV-infected females and women without HIV-infection, respectively ($p=0.001$). History of pelvic surgery was reported in 27 (71%) and 31 (55.4%) of HIV-infected females in the main group and women in the control group, respectively ($p=0.036$). In both groups, the most prevalent type of surgery was tubectomy, and its frequency was higher in HIV-infected women (47.3% versus 30.4%, $p=0.046$).

The frequency of ovarian surgery was comparable in both groups (13.1 versus 14.2%, $p=0.429$). AMH concentration was significantly lower (1.86 ng/mL versus 3.2 ng/mL; $p=0.024$), while FSH levels were statistically significantly higher (7.9 IU/L and 6.3 IU/L; $p=0.013$) in HIV-infected females compared to HIV-seronegative patients. Analysis of the parameters of IVF stimulation cycles did not reveal any significant differences in the initial or total doses of gonadotropins or duration of stimulation in both groups. However, lower number of oocytes (8.86 ± 1.1 vs 12.9 ± 0.8 ; $p=0.001$), mature oocytes (7.45 ± 0.9 vs 10.1 ± 0.6 ; $p=0.003$), zygotes (5.88 ± 0.7 vs 8.4 ± 0.001 ; $p=0.001$), cleavage stage embryos (5.55 ± 0.6 vs 8.1 ± 0.4 ; $p=0.001$) and blastocysts (2.68 ± 0.5 vs 4.4 ± 0.4 ; $p=0.009$) were recovered from HIV-infected patients compared to control group. Selective embryo transfer was conducted on the third or fifth days of culture in both groups. Lower frequency of clinical pregnancy was revealed in HIV-infected females compared to HIV-seronegative women both during treatment cycles of ART (13.8% vs 40.4%; $p=0.014$) and cryocycles (20% vs 53.6%; $p=0.008$).

Parameters	Study group (n=94)		
	HIV + (n=38)	HIV - (n=56)	p
IVF /ICSI	44	59	
Frozen embryo cycles	30	30	
Initial dose of administered gonadotrophins (IU), (M $\pm$ m)	203,2 $\pm$ 9,6	201,1 $\pm$ 5,0	0,071
Total dose of administered gonadotrophins (IU), (M $\pm$ m)	1997,04 $\pm$ 145,2	1929 $\pm$ 66,3	0,335
Number of days of stimulation, days (M $\pm$ m)	9,8 $\pm$ 0,1	9,33 $\pm$ 0,3	0,122
Number of oocytes, (M $\pm$ m)	8,86 $\pm$ 1,1	12,9 $\pm$ 0,8	0,001
Number of mature oocytes (M II), (M $\pm$ m)	7,45 $\pm$ 0,9	10,1 $\pm$ 0,6	0,003
Number of zygotes (2PN), (M $\pm$ m)	5,88 $\pm$ 0,7	8,4 $\pm$ 0,5	0,001
Abnormal fertilization ($\geq$ 3PN)	0,17 $\pm$ 0,05	0,08 $\pm$ 0,03	0,212
Cleavage stage embryos, (M $\pm$ m)	5,55 $\pm$ 0,66	8,1 $\pm$ 0,4	0,001
Number of blastocysts, (M $\pm$ m)	2,68 $\pm$ 0,5	4,4 $\pm$ 0,4	0,009
Number of frozen embryos, (M $\pm$ m)	1,49 $\pm$ 0,3	2,6 $\pm$ 0,3	0,008
IVF/ICSI			
Chemical pregnancy rate	17,2% (5/29)	44,2% (23/52)	0,015
Clinical pregnancy rate	13,8% (4/29)	40,4% (21/52)	0,014
Frozen embryo transfer:			
Chemical pregnancy rate	30% (9/30)	55,2% (16/30)	0,049
Clinical pregnancy rate	20% (6/30)	53,6% (15/52)	0,008

Lower efficacy of ART programs was demonstrated in HIV-infected women, which can be either due to the influence of the infection itself on the reproductive function, or the effects of ARV therapy, as well as the effects of other factors, which require further research.