

## Can Endometriosis Affect the Clinical Outcomes in Patients Undergoing IVF-ET ?

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목적 : 본 연구는 자궁내막증, stage III-IV  
 연구기간 : 1998년 9월 ~ 2001년 9월  
 연구대상 : 자궁내막증, stage III-IV  
 27명, 34명  
 40명, 56명  
 Student's *t*-test, Chi-square test,  $p < 0.05$   
 결과 : 자궁내막증, stage III-IV  
 (10.3 ± 6.6 vs 11.7 ± 5.1), (7.4 ± 4.7 vs 7.7 ± 4.9),  
 (70.2 ± 32.4% vs 73.7 ± 20.0%), Good embryo quality rate (8 (G1+G2) 2PN ) (32.6% vs 32.4%)  
 (4.6 ± 1.4 vs 4.8 ± 1.1)  
 30.7%, 42.8%  
 8.8 ± 4.9, 7.7 ± 3.9, 11.3 ± 7.0, 11.7 ± 5.1  
 stage III IV (66.2 ± 30.0% vs 73.7 ± 20.0%).  
 Good quality embryo rate (GQER) stage III-IV 22.0% 32.4%  
 (p=0.15, Chi-square test).  
 4.7 ± 1.5, 4.8 ± 1.1 가  
 25.0% (8/32), 42.8% (24/56) stage III-IV  
 (p=0.06, Chi-square test),  
 가

**Key Words:** Endometriosis, Good quality embryo rate, IVF-ET

Endometriosis is a common and enigmatic disease that has been linked to decreased fertility.

The relationship between endometriosis and infertility is still debated.

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In vitro fertilization and embryo transfer (IVF-ET) has become a recognized treatment of endometriosis-associated infertility. Using IVF-ET, it is possible to bypass the suspected deteriorated pelvic condition or disturbed function. However, the results from IVF-ET cycles also are controversial. Some investigators have reported high success rates with IVF treatment.<sup>1-2</sup> Other investigators, however, reported a poor outcome of IVF in patients with endometriosis compared with tubal-factor infertility.<sup>3-5</sup> Many investigators also reported that endometriosis can not impact PR and IR in IVF cycles.<sup>6-9</sup> The role of IVF treatment according to stage by stage endometriosis are also controversial.<sup>4</sup>

The purpose of this retrospective analysis to compared the impact of endometrisis on IVF and its outcomes between a group of patients who had stage III and IV endometriosis and a corresponding group with tubal factor infertility.

## MATERIALS AND METHODS

We reviewed the medical records of 91 patients diagnosed with endometriosis who were undergoing 131 cycles of IVF procedures in our unit between September 1998 and December 2001. Of these patients, 27 patients of 34 cycles with stage III and IV endometriosis included, categorized according to the revised classification of the American Fertility Society. Meanwhile, they were compared with an age-matched control group (56 cycles, 40 patients) with only tubal factor infertility.

Controlled ovarian stimulation was performed with long protocol of GnRH agonist (Lucrin Sub Q, Abbott) and Pure FSH (Metrodine HP, Serono) and hMG (Pergonal, Serono). When at least two follicles reached 18 mm or more in diameter, 10,000 IU of hCG (Profasi, Serono) was administered. Transvaginal ultrasound-guided oocyte re-

**Table 1.** Comparison between all stages of EMS and tubal factor

	Endometriosis (n=131)	Control (n=56)
Age	31.6 ±3.3	32.6 ±3.6
Total cycle	1.6 ±1.0	1.3 ±0.6
No. of oocyte retrieval	10.3 ±6.6	11.7 ±5.1
Mature oocytes	7.4 ±4.7	7.7 ±3.9
FR (%)	70.2 ±32.4	73.7 ±20.0
GQER (%)	32.6 ±29.1	32.4 ±24.7
No. of ET	4.6 ±1.4	4.8 ±1.1
PR Per ET (%)	31 (40/129)	42.8 (24/56)

NS

GQER: good quality embro rate (8 cell (GI+GII)/2PN)

trieval was performed 36 hours after hCG administration. Oocyte were suspended and inseminated in P1 medium, supplemented with 10% SSS. ET was performed after 72 hours at the eight cell stage. Good quality embryo rate (GQER) defined as a number of 8 cell grade I and II divided by number of 2PN.

Statistical analysis was conducted using  $\chi^2$  test, Student's *t*-test. The results are presented as mean ± SD.

## RESULTS

Table 1 compares the IVF outcome in patients with all stage of endometriosis and those who had tubal factor infertility. The age of patients, number of total IVF cycle were not significantly different between the groups. Similarly, the number of oocytes retrieval, and number of embryos transferred in each group were comparable. The pregnancy rates were comparable in women with endometriosis patients and with tubal factor patients.

Table 2 compares the outcome in patients with minimal to mild (stage III) endometriosis and those who had moderate to severe endometriosis (stage III-IV). although stage III-IV patients appe-

**Table 2.** Comparison between stage I-II and stage III-IV endometriosis

	Endometriosis stage I-II (n=97)	Endometriosis stage II-IV (n=34)
Age	31.6 ±3.5	31.1 ±2.8
Total cycle	1.6 ±1.0	1.8 ±1.0
No. of oocyte retrieval	10.0 ±6.4	11.3 ±7.0
Mature oocytes	6.9 ±4.5	8.8 ±4.9*
FR (%)	71.6 ±33.2	66.2 ±30.0
No. of ET	4.5 ±1.4	4.7 ±1.5
GQER (%)	36.4 ±30.0	21.6 ±20.0 <sup>†</sup>
PR Per ET (%)	33.3 (32/96)	25.0 (8/32)

\*p=0.04, <sup>†</sup>p=0.01

ared to have significantly higher number of mature oocytes, the GQER was significantly lower in stage III-IV. The pregnancy rate, however, was not significantly different between the groups.

Table 3 compares the IVF outcome in patients with stage III-IV endometriosis and those who had tubal factor infertility. The data showed a reduced GQER and pregnancy rate among patients with stage III-IV compared with tubal factor patients (p=0.04). But there was no significant statistical difference in pregnancy rate (p=0.06, ?<sup>2</sup>).

## DISCUSSION

The association between endometriosis and infertility has been extensively reported. Much of the controversy exists because in many cases there is no clear mechanism by which endometriosis might be causing infertility.

IVF-ET has become a common technique to help women with endometriosis-associated infertility.<sup>6</sup> Some investigators reported a poor outcome of IVF in patient with endometriosis compared with tubal infertility.<sup>3-5</sup> However, other authors reported that pregnancy rates were comparable in women with or without endometriosis.<sup>6-9</sup> The

**Table 3.** Comparison between stage III-IV endometriosis and tubal factor

	Endometriosis stage III-IV (n=34)	Tubal factor (n=56)
Age	31.1 ±2.8	32.6 ±3.6
No. of oocyte retrieval	11.3 ±7.0	11.7 ±5.1
Mature oocytes	8.8 ±4.9	7.7 ±3.9
FR (%)	66.2 ±30.0	73.7 ±20.0
GQER (%)	22.0 ±20.1	32.4 ±24.7*
No. of ET	4.7 ±1.5	4.8 ±1.1
PR Per ET (%)	25.0 (8/32)	42.8 (24/56) <sup>†</sup>

\*p=0.04, <sup>†</sup>p=0.06

impact of endometriosis stage on IVF-ET was also controversial. Azem et al (1999)<sup>4</sup> reported that patients with advanced endometriosis have poorer outcome. However, Olivennes et al (1995)<sup>6</sup> reported that PRs were comparable between women who had endometriosis and those who did not. Dmowski et al (1995)<sup>7</sup> reported that IVF success rates were comparable in women with and without endometriosis regardless of the stage of the endometriosis.

Our study shows that the number of oocyte retrieved and fertilization, good quality embryo rate and pregnancy rate were similar to patients with tubal factor. Our results did not find a significant difference between pregnancy rates and the stage of endometriosis. But interestingly, GQERs were significantly decreased in patients with stage III-IV endometriosis, the PRs were similar to patients with stage I-II endometriosis. Our study, however, shows that patients with moderate to severe endometriosis have a tendency toward lower pregnancy rate than patients with tubal infertility. (p=0.06)

In patients with endometriosis, we find that the number of oocytes retrieved and fertilization rates were similar to patients with tubal factor, the embryo quality was significantly decreased in patients

with moderate to severe endometriosis.

Good quality embryo may be another consequence of alterations within the oocyte. Endometriotic lesions produce different cytokines such as IL-1 $\beta$ , IL-6, TNF- $\alpha$ . We have recently carried out a pilot study on the effect of endometriosis on IVF outcomes on the basis of the measurement of estradiol, progesterone, IL-1 $\beta$ , IL-6, VEGF in follicular fluid of patients with endometriosis undergoing IVF. It has been indicated that there was a significant increase of IL-1 $\beta$  level in follicular fluid of patients with severe endometriosis (not published). The present study, however, gives no indication of abnormal folliculogenesis and lower fertilization rate. A previous study by Brizek et al (1995)<sup>10</sup> reported that patients with endometriosis have increased incidence of aberrant morphological phenotypes. They also indicated that although the effects of endometriosis may not be seen in terms of follicular development or oocyte quality at the time of aspiration, toxic exposure most likely occurs during folliculogenesis resulting in the aberrant embryo morphology. Additional supports for their reports found in Shulman et al (1993)<sup>11</sup> and Simon et al (1994)<sup>12</sup> studies. However, Bergendal et al (1998)<sup>13</sup> indicated that once the oocyte is fertilized, it seems that the embryo has a normal chance of implantation, leading to similar pregnancy rates.

The present study has its limitation in being not only retrospective, but also the number of cases was small, and a few had also ever undergone pelvicoscopic cystectomy and fulguration.

In conclusion, the presence of endometriosis may not affect clinical outcomes in patients undergoing IVF-ET when all stages of endometriosis were pooled. There might be, however, an unfavorable outcome of IVF-ET in patients with moderate to severe endometriosis because it might be affecting embryo quality by toxic exposure during folliculogenesis.

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