

***In Vitro* Fertilization and Endometriosis (Endo). Our Experience**

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Received: April 07, 2020; **Published:** August 31, 2020

Abstract

Endometriosis affects severely those women who suffer it. Pelvic pain and infertility are the two main symptoms of the disease. Our objective is to report our experience with IVF/ICSI in endometriosis patients. In a retrospective cohort study, at a private fertility center, we studied ninety-two endo subjects, of an overall IVF clientele of 660 patients selected in this span of time. Procedures were performed under general anesthesia in an outpatient basis. Average age was similar between both groups (37/endo vs. 38/gen. pop.), the number of oocytes harvested was 6 and 7, and average mature oocytes # was equal: 5. Fertilization was higher in endo (5 oocytes vs. 4), embryo transfer was similar (67 vs. 72.8%) ($p = 0.44$), "freeze all" was similar (20 vs. 20.3%) and lack of embryos for transfer was of 2% and 3% respectively. No oocytes were retrieved, or no fertilization occurred, in 0.7% vs. 3.4% ($p = 0.08$). Cryopreservation of "excess" embryos for fresh transfer was of 45% vs. 41.8%. Blastocysts were reached in 49 vs. 51% of the cases. Early pregnancy rates were of 33.33 vs. 34% respectively.

Keywords: *Endometriosis; In Vitro Fertilization; IVF/ICSI*

Introduction

Endometriosis affects severely those women who suffer it. Pelvic pain and infertility are the two main symptoms of the disease.

The World Consensus for the Current Management of Endometriosis [1], of which one of us was responsible for the Chapter on *In Vitro* Fertilization (IVF), includes the following statements, among others that apply to this publication: "Although IVF may be less effective for endometriosis than for other causes of infertility, it should be considered for use to improve the success rate above expectant management", with strong evidence back up; "GnRH analogue administered for 3 - 6 months prior to IVF/Intracytoplasmic Sperm Injection (ICSI) in women with endometriosis increases the clinical pregnancy rate", also with strong value as medical evidence; that "There is insufficient evidence to support the use of the combined Oral Contraceptive Pills (OCP) prior to IVF/ICSI", in this case with weak evidence; "There is no evidence that surgical removal of endometriosis or surgical treatment of endometriomas (by aspiration or cystectomy) improves success rates through IVF, a statement based in weak evidence: but clearly state that "Ovarian response might be reduced in some women who have undergone surgery for endometriomas", and that "Since endometriomas may damage the ovary, and since complications can arise in women with endometriomas undergoing ART, laparoscopic ovarian cystectomy may sometimes be recommended for women with endometriomas larger than 3 cm diameter, both recommendations also based on weak evidence.

There is a generalized concept on the poor results of IVF/ICSI in patients with endometriosis. On the contrary, Fujimoto [2] in a recent publication found that in his treated population, endometriosis prevalence among Asian women was larger than among Caucasians (15.7

vs. 5.8%, $p < 0.01$), but that at the time of IVF, the quality and quantity of oocytes and embryos, as well as the fertilization rates, did not relate to endometriosis, in a population where endometriosis was diagnosed in 9.5% of participants; 3.5% of them with endometriomas.

A French group [3] found significant differences in the quantity of oocytes obtained (8.37 ± 7.01 vs. 10.13 ± 6.53 $p < 0.001$), the transfer rate (81.4% vs. 86.1%, $p = 0.045$), Specially the number of cycles with embryos frozen (48.9% vs. 57.3%, $p < 0.01$) were lower. They also refer an altered response to stimulation (70.7% vs. 81.0%, $p < 0.001$) and of course, lesser quality embryo cohort (45% vs. 52%, $p = 0.003$).

This would reinforce the general knowledge that endometriosis is detrimental at the time of IVF, however for these investigators, “the implantation and delivery rates per transfer were not distorted in the cases of endometriosis, either in the total group or in any subgroup” (29.2% vs. 29.5%). This challenges the idea that orthotopic endometrium of patients with endometriosis would not be ideal for embryo implantation.

Said all this, we would like to share some preliminary data of a pilot ongoing study on IVF in patients with endometriosis including. All procedures performed during the years 2018 and 2019 are included in this communication.

Objectives of the Study

To report our experience with IVF in endometriosis patients.

Design

Retrospective cohort study.

Setting

Private fertility center.

Materials and Methods

Ninety-two subjects were included in this retrospective cohort study, of an overall IVF clientele of 660 patients selected in this span of time. Ovodonation, for example, was excluded. Due to the characteristics of this review, no previous evaluation of the study was requested to an external ethics committee. It does not alter treatment given to our patients, who remain anonymous. It will not modify previously proposed treatments or any conduct whatsoever for this group of patients, who will continue to be treated aside from the conclusions provided in the present publication.

Of the ninety-two women affected by endometriosis, this disease was the only cause of infertility in 18 of them. Poor ovarian reserve was present in association to endometriosis in 29 of them, 10 women being older than forty years in that group. Tubal and peritoneal factor was associated to endometriosis in 10 patients. Other combined causes of infertility were poor sperm quality (27 of endometriosis patients 'partners), polycystic ovarian syndrome (PCO) in 3 patients (of the endometriosis group), and 3 of them presented abnormal endometrial dating as measured in previous cycle by ERA (all of them over 40 years). In general, although this is not the focus of this presentation, poor ovarian reserve in our general IVF population was linked to age and endometriosis.

Interventions

All 660 patients, including 92 endometriosis cases, were submitted to IVF and/or ICSI procedures during the years 2017 and 2018 at our fertility center, Fertilab, at Buenos Aires, Argentina. All procedures were performed in our own operating room (OR) and Embryology laboratory (EL).

Oocyte retrieval was always carried on under general anesthesia and patients left our premises two hours after the procedures. Eighty of the endometriosis patients 'group were treated by ICSI, and the rest by IVF. At our center the reasons to undergo an ICSI procedure includes severe male factor, use of vitrified oocytes or preimplantation genetic screening (PGS). In some cases, the decision is made by the embryologist considering morphological oocyte quality and clinical history of the patient.

Main outcome measures

As stated in "objectives" our aim was to compare IVF and ICSI results in the endometriosis affected population vs. general population. Using a simple Fisher test we arrived interesting conclusions that will be discussed after presenting our results.

Results

In table 1 we summarize our results. Average age was similar between both groups (37 years among endometriosis patients vs. 38 years in the overall population). Mean number of oocytes harvested was also almost identical: 6 in the endo group and 7 in the general group. The average of mature oocytes was the same for both groups: 5. Incredibly, fertilization was higher in endometriosis patients (5 oocytes) vs the whole group (4 oocytes). The number of patients who reached embryo transfer was slightly higher in the general population (72.8%) than in the endo group (67%), but this was not statistically significant (p = 0.44). In both groups the "freeze all" issue was similar (20 vs. 20,3%). On the other end, lack of embryos for transfer was of 2% and 3% respectively for both groups.

	Results	Results	Fisher's Test
	Endometriosis	General	P
Average age	37	38	p = 1 (ns)
Mean number of harvested oocytes	6	7	p = 1 (ns)
Average of total mature oocytes	5	5	p = 1 (ns)
Fertilization rate	5	4	p = 1 (ns)
% of patients who underwent embryo transfer	67	72,8	p = 0,44 (ns)
% of patients who went to "freeze all" procedure	20	20,3	p = 1 (ns)
% of patients with no embryos for transfer	2	3	p = 1 (ns)
% of patients with no oocytes harvested of no fertilization at all	0,7	3,4	p = 0,08 (ns)
% of patients that froze "excess" embryos after transfer	45	41,8	p = 1 (ns)
% of patients who had blastocyst stage embryos	49	51	p = 0,88 (ns)
% of cases with Beta HCG subunit positive dosages	33,33	34	Ns
n	92	660	

Table 1: Resumes all our results and show that there were no statistically significant differences in both groups.

The number of patients from whom no oocytes were retrieved, or no fertilization occurred was of 0.7% for the endometriosis patients vs. a higher 3.4% for the general population (with a p = 0,08). Although not the objective of this publication, patients 'age surely contributed to these results. At the time of cryopreservation of "excess" embryos for transfer - our limit is two at the same time - the endo group presented this feature in 45% of the cases vs. only 41.8% in the global population. In both groups, blastocysts were reached by around half of the cases (49 vs. 51%).

Although not all cases could be followed till birth due to the fact that many of our patients are referred by non-staff doctors, the incidence of "biochemical" pregnancies (as of positive dosage of Beta HCG subunit)was identical in both groups (33.33 vs. 34%).

In all cases, differences were not statistically significant. Considering the average age of our patients, early pregnancy rates are similar to most publications.

Conclusion

IVF and ICSI in our fertility center were equally profitable for couples where the female partner was affected by endometriosis and general population. This retrospective cohort study is a pilot presentation of an ongoing study to be presented, including results for the year 2019.

Contrary to earlier publications, and agreeing with more recent studies, endometriosis “per se” is not at first glance detrimental when those assisted reproductive techniques are applied. In this publication we intentionally did not segment endometriosis cases by their severity or previous surgical histories. Our purpose was to give a general example of how, modern IVF and ICSI can help those women to achieve pregnancies with identical chances vs. the general population.

In future presentations, where issues such as age, previous number of surgeries and severity of the disease, including a special deep infiltrating endometriosis (DIE) group, we will focus on differences occurring in such divisions. Our present number of cases did not allow us to reach any statistically significant differences that would justify such grouping of patients.

Conflicts of Interest

No conflicts of interest present.

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Volume 9 Issue 9 September 2020

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