# *Effect of Endometrial Injury on implantation in IVF-ET program*

Thesis

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## *ABSTRACT*

Local injury to the endometrium using a pipell endometrial sampler doubles the incidence of successful pregnancies in patients undergoing in vitro fertilization ***(Barash A et al, 2003)***.this study was confirmed by ***(Raziel et al, 2007).***

Local injury to endometriam of IVF patients in controlled ovarian hyperstimulation cycle may increase the incidence of embryo implantation***. (Li R, Hao G, et al, 2009)***

***Aim of the work*** :To review the effect of local injury to the endometrium on the outcome of IVF and embryo transfer

**Patient & Method:**A prospective controlled trial ,a total 60 women in their first invitro fertilization (IVF)cycle were randomized .in 30 patient two small endometrial samples from anterior & posterior walls of the uterus were obtained with a pipelle endometrial sampler on the day before down regulation (group A) and in 30 patients no intervention was done(are used as control) (group B).

-The implantation will be calculated for both groups.

-The results will show whether the endometrial injury will increase implantation in IVF or not.



Key words;

Effect of Endometrial Injury on implantation in IVF-ET program

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# INTRODUCTION

The birth of Louise Brown, the first child born as a result of an in vitro fertilization, galvanized the world in 1978 ***(Steptoe and Edwards, 1978)*.**

In vitro fertilization (IVF) means the fertilization of an oocyte with a sperm outside the body. IVF treatment involves the collection of mature oocytes, their fertilization and cultivation as embryos, and their subsequent transfer to the uterus ***(Rabe et al., 2000).***

In assisted reproductive technology (ART), pregnancy and birth rates following IVF attempts remain low. Indeed, 2 out of 3 IVF cycles fail to result in pregnancy and more than 8 out of 10 transferred embryos fail to implant ***(Kovalevsky and Patrizio, 2005***).

Recent publications have been reporting IVF success rates in terms of cumulative live-birth rate (CLBR) per woman, thus providing a more realistic estimate that becomes applicable to individual couples. In general, CLBR following IVF has been reported between 45 and 55%. Increased maternal age has been shown to significantly reduce these rates, as has preimplantation genetic diagnosis ***(Moragiann et al 2010)***.

The most recent SART IVF success rates, (Society for Assisted Reproductive Technologies). In 2010, live birth

occurred for the following women undergoing IVF with their own fresh embryos:

- 42 percent of women under 35
- 32 percent of women age 35-37
- 22 percent of women age 38-40
- 12 percent of women age 41-42
- 4 percent of women over 42

## Failed IVF -Recurrent implantation failure (RIF)

Failure to achieve a pregnancy following 2–6 IVF cycles, in which more than 10 high-grade embryos were transferred to the uterus, was defined by various clinicians as RIF ***(Tan et al., 2005).*** Today with the tendency of transferring only one or two embryos, the definition of RIF is not apparent. There are two things that determine the success or failure of an IVF cycle:

1. Quality of Embryos
2. Receptivity of Uterus

Implantation failure is thought to result from impairment of embryo development and/or from abnormal uterine receptivity ***( Delphine Haouzi et al., 2012)*** .Inadequate uterine receptivity is responsible for approximately two-thirds of implantation failures, whereas the embryo itself is responsible for only one-third of these failures ***(Simon et al., 1998; Ledee-Bataille et al., 2002).***

## Assumed etiologies for RIF

1. *Defective embryonic development*

Chromosomal abnormalities of the male or female partner, the gametes or the developing embryo may burden embryogenesis. Increased frequency of female chromosomal abnormalities such as transloc**a**tions, mosaics, inversion, deletion and chromosomal breakages, particularl**y** at the centromere region were observed in young women with high-order RIF **(*Tarlatzis et al., 2000; Raziel et al., 2002)***. Increased incidence of sperm chromosomal abnormalities in patients with normal karyotype and RIF was also observed ***(Rubio et al., 2001).***

**2.** ***Decreased endometrial receptivity*:**

RIF might be because of undiagnosed uterine pathology. In 18–27% of women with a normal initial hysteroscopy or hysterosalpingogram, repeated hysteroscopic visualization after RIF revealed uterine abnormalities, mainly hyperplasia, polyps, endometritis, synechiae and leiomyomata ***(Demirol and Gurgan, 2004).***

### *3- Multifactor causes*

- Endometriosis as a cause for RIF has not been investigated directly; however, all markers of reproductive process, including ovarian response, embryo quality, implantation and pregnancy rates (PRs), are

decreased in endometriosis, especially in severe disease ***(Kuivasaari et al., 2005).*** Several studies have demonstrated an attenuated or dysregulated progesterone response at a molecular level in endometrium from women with endometriosis ***(Burney et al., 2007***). Alteration in the ratio of progesterone receptor (PR)-A to PR-B was suggested as one of the possible mechanisms of progesterone resistance in endometriosis ***(Lee et al., 2009).***

- Leiomyoma: Intramural and submucosal leiomyomas can distort the uterine cavity or obstruct the tubal ostia or cervical canal and, thus, may affect fertility ***(Pritts, 2001)***. Moreover, in the setting of a distorted uterine cavity caused by leiomyomas, significantly lower IVF pregnancy rates were identified ***(Surrey et al., 2001).*** When myomectomies have been performed on women with otherwise unexplained infertility, the subsequent pregnancy rates have been reported to be 40–60% after 1–2 years ***(Campo et al., 2003)***. Recent studies demonstrated that leiomyomas may adversely affect the overlying endometrium and impair endometrial receptivity ***(Matsuzaki et al., 2009; Rackow and Taylor, 2010).***
- Patients with hydrosalpinges have lower implantation and PRs ***(Zeyneloglu et al., 1998).*** Hydrosalpinx fluid is commonly slightly alkaline and may contain cytokines,

prostaglandins or other inflammatory compounds. These compounds may have either direct embryo-toxicity or adversely affect the endometrium ***(Meyer et al., 1997)***. The presence of hydrosalpinx may also reduce the receptivity of the endometrium by decreasing the expression of specific factors. In the presence of hydrosalpinges, the expression of $a_v\beta_3$ integrin is significantly reduced in the window of implantation when compared with fertile controls, and 70% of the patients with hydrosalpinx who underwent salpingectomy demonstrated return of this marker back to normal levels ***(Savaris et al., 2006).*** Similarly, the expression of LIF is lower in the endometrium during the window of implantation in infertile patients with hydrosalpinx, compared with normal fertile patients without hydrosalpinx. Furthermore, if the hydrosalpinges are removed, the LIF expression returns to normal expression in these patients **(*Seli et al*., 2005).**

## *Suggested methods for investigation and treatment of RIF*

### *1. Endometrial stimulation*

Endometrial injury or stimulation may cause a pseudo-decidual reaction that enhances implantation. ***Barash et al***., 2003, performed repeated endometrial biopsies in 45 cases. Pregnancy and live birth rates in the IVF cycle following the

biopsy were doubled. They concluded that local injury to the endometrium increased the incidence of implantation. There is a need for a prospective controlled study to prove the value of this procedure.

## *2. Treatment of thin endometrium*

Endometrial thickness is defined as the minimal distance between the echogenic interfaces of myometrium and endometrium, measured in the plane through the central longitudinal axis of the uterine body. Increased endometrial thickness is associated with improved pregnancy rates in IVF–embryo transfer cycles ***(Zhang et al., 2005)***. The data extracted from the donor oocyte programs suggest that a pregnancy cannot be achieved if the endometrium thickness is below a certain critical cutoff limit. Although there are studies revealing that the thickness of endometrium for a successful implantation can be as thin as 4 mm ***(Check et al., 2003a, b)***; for the majority of the cases, at least 6 mm of endometrial thickness is prerequisite for a successful implantation ***(Alam et al., 1993; Coulam et al., 1994).*** However, no correlation was demonstrated between endometrial histology and endometrial thickness either in spontaneous ovulatory cycles or in IVF patients ***(Sterzik et al., 1997, 2000***). The presence of a thin endometrium did not influence the cumulative PRs in a prospective large cohort studies ***(Geyter et al., 2000)***, particularly when high-quality embryos were transferred ***(Zhang et al., 2005)***. Thin or hyperechogenic endometrium or