# Value of Routine Hysteroscopy prior to IVF/ICSI Cycles:
## A Randomized Control Trial

*Thesis*

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|---|---|---|
| **IVF** | **:** | In vitro fertilization |
| **ART** | **:** | assisted reproductive technique |
| **HSG** | **:** | Hysterosalpingography |
| **ICSI** | **:** | Intra-cytoplasmic sperm injection |
| **IUI** | **:** | Intrauterine insemination |
| **GNRH** | **:** | Gonadotropin-releasing hormone |
| **LH** | **:** | Luteinizing hormone |
| **FSH** | **:** | Follicular stimulating hormone |
| **hCG** | **:** | human chorionic gonadotrophin |
| **TVS** | **:** | Trans vaginal sonography |
| **LPS** | **:** | Luteal phase support |
| **PVP** | **:** | polyvinyl pyrrolidone |
| **HIV** | **:** | human immunodeficiency virus |
| **µg** | **:** | Microgram |
| **Mg** | **:** | Milligram |
| **ml** | **:** | Milliliter |
| **SD** | **:** | Standard Deviation |
| **U/S** | **:** | Ultrasonography |
| **wks** | **:** | Weeks |
| **Yrs** | **:** | Years |
| **IUD** | | Intra Uterine Device |
| **BMI** | | Basal Metabolic Index |
| **ROC** | | Receiver-operating characteristic |
| **ET** | | Embryo transfer |
| **IL** | | Interleukin |
| **MIP 1B** | | Macrophage Inflammatory Protein 1beta |

# Introduction

In vitro fertilization (IVF) is a technical process in which retrieved oocytes are fertilized outside the body. The developing embryos grow in a laboratory environment and are subsequently transferred into the woman's uterus. The IVF technique was first introduced as a treatment for infertility in 1978 and success rates have steadily increased in the subsequent decades ***(Bing and Ouellette, 2009).***

The uterine cavity plays a vital role in successful assisted reproduction (ART). Abnormalities in the cavity, such as adhesions, polyps, congenital anomalies and fibroids act not only as deterrents to implantation of embryos, but may also result in spontaneous miscarriage ***(Valle 1980; Kirsop et al., 1991; Varasteh et al., 1999).***

Hysteroscopy is the direct visual examination of the canal of the cervix and the interior of the uterus using thin, lighted and flexible tube called hysteroscope inserted through the vagina, offers great assistance for the interpretation of the uncertain findings from other diagnostic methods and increase the precision and accuracy in the diagnosis of the intrauterine abnormalities ***(Ceci et al., 2004).*** Hysteroscopic findings can be applied toward both diagnosis and therapy in a variety of cases ***(Serden et al., 2000; Isaacson and Keith et al., 2002***).

Historically and till today, most of the clinicians prefer HSG as a first line approach to evaluate the intrauterine pathology in infertile patients, but it has been proven to have certain drawbacks. Studies by Wang et al. and Golan et al. reported HSG has a false positive rate of 15.6% and false negative rate of 35.4 % ***(Golan et al., 1996).***

Hysteroscopic evaluation of uterine cavity for women with infertility has recently become a routine procedure. Hysteroscopy also offers great assistance for the interpretation of uncertain handing from other diagnostic methods. Further, it enables direct visualization of the cervical canal and uterine cavity, and increases the precision and accuracy in the diagnosis of intrauterine conditions. The main objective of the study is to assess the improvement in pregnancy outcome in patients scheduled to undergo IVF/other ART procedures by diagnosing and treating intra uterine abnormalities using hysteroscopy. ***(Wang et al., 1996, Cunha et al., 2001).***

# Aim of the Work

To assess the improvement in pregnancy Rate in patients undergoing IVF/ICSI by inducing endometrial injury using hysteroscopy.

# In vitro Fertilization "I.V.F "

• The first and still the most common form of (ART) is in vitro fertilization, which involves a sequence of highly coordinated steps beginning with controlled ovarian hyperstimulation with exogenous gonadotrophines, followed by retrieval of oocytes from the ovaries under transvaginal ultrasound guidance, fertilization in the laboratory and transcervical transfer of the embryos into the uterus ***(Speroff, 2005)***.

## • Indications of I.V.F:

- IVF was first developed as a mean to overcome infertility resulting from irreparable tubal diseases, but it is now applied much more broadly for the treatment of almost all causes of infertility.
- IVF is most certainly indicated when the method offers the means to overcome one or more specific obstacles not otherwise, amenable to the treatment of the following conditions:

**(1) Tubal factors**:

In cases of severe tubal obstruction as in cases of distal and proximal tubal obstruction and also cases of bilateral tubal obstruction, where I.V.F is the best and most logical treatment, because success rates achieved with surgery are extremely poor ***(Patton et al., 1987).***

**(2) Endometriosis:**

***(a) Mild and minimal endometriosis:***

- In young asymptomatic women with suspected minimal or mild endometriosis and no other infertility factor treatment include surgical treatment, empiric treatment with clomiphene and IUI and last choice IVF.
- In old women or those with other coexisting infertility factor or failed other forms, IVF is the best overall choice.

***(b) Advanced Endometriosis***

After the surgical treatment, the choice between expectant or empirical treatment and IVF should be based on age, the surgical results, and if there is any other coexisting infertility factors. I.V.F is the treatment of choice ***(Speroff, 2005).***

**(3) Male factor of infertility**:

- Poor semen quality is the sole cause of infertility in approximately 20% of the infertile couples and an important contributing factor in another 20-40% of couples with reproductive failure ***(Thonneau et al., 1991), (Schlegel and Giradi, 1997).***
- Many infertile men have medically or surgically correctable disorders that if properly diagnosed and treated can be overcome to allow them to achieve natural conception with their partners ***(Schlegel and Giradi, 1997).***

- When treatment is not possible or fails and insemination with donor sperm is not an acceptable option, IVF and ICSI, using sperm isolated from ejaculate or extracted from the epididymis or testis, offers a realistic hope for success ***(Speroff, 2005)***.

**(4) Unexplained infertility:**

- Which is diagnosed when all of the standard elements of the infertility evaluation yield normal results, the incidence of unexplained infertility ranges from 10% to as high as 30% among infertile populations, depending on diagnostic criteria. ***(Crosignani and Collins, Rubin, 1993)***.
- At a minimum, the diagnosis of the unexplained infertility implies a normal semen analysis, objective evidence of ovulation, a normal uterine cavity, and bilateral tubal patency. ***(Speroff, 2005)***.
- The necessity for a diagnostic laparoscopy in the evaluation of couples with unexplained infertility has been controversial laparoscopy certainly can reveal otherwise undetected tubal factors and endometriosis that merit specific treatment or that could limit the effectiveness of empirical treatments for unexplained infertility ***(Crosignani et al., 1993).***
- Unexplained infertility likely represents either the lower extreme of the normal distribution of reproductive efficiency or abnormalities of sperm or oocyte function fertilization,

implantation or pre-embryo development that cannot be reliably detected by standard methods of evaluation ***(Guzick and Sullivan, 1998).***

- The incidence of unexplained infertility ranges from 10% to as high as 30% among infertile populations depending on diagnostic criteria ***(Crosignani et al., 1993).***
- Subclinical autoimmune diseases: they form a lot of controversies that still surround the possible association between abnormal autoimmune function and female infertility, prominent investigators, as well as authoritative professional organizations, have published statements that deny the value of diagnostic efforts to detect subclinical autoimmune abnormalities in infertile patients ***(Hill et al., 2000)***.
- Yet these opinions are based only on observation that proposed treatments tailed to demonstrate outcome benefits indeed, as previously noted, there is considerable evidence in the literature to suggest such an association, many investigators have reported a clustering of subclinical autoimmune diseases, even before they reach diagnosis. ***(Geva et al., 1997; Gleicher, 1999).***
- The most convincing evidence comes, however from the widely reported observation that women with classical autoimmune diseases, even before they reach diagnosis in

other words at preclinical stages of their impending autoimmune diseases – already demonstrates decreased fecundity ***(Nelson et al., 1993) (Sicman and Black, 1998).***

- Among couples with unexplained infertility IVF is the preferred treatment for some and the treatment of last resort for others, A number of groups have observed a higher incidence of fertilization failure and lower over all pregnancy rates in couples who have already failed treatment with Induction/ IUI suggesting that the abnormalities of fertilization, early embryonic development or implantation might be responsible for unexplained infertility in many couples ***(Gurgont et al., 1995) (Takeuchis et al., 2000).***

**(5) Other Indications of (IVF)**

- Patients recently diagnosed with a cancer or another medical disorder facing imminent treatment (chemotherapy, radiation therapy) that possess a serious threat to their future fertility may be candidates for IVF and cryopreservation, of embryos before the treatment begins, if time and health allow ***(Speroff, 2005).***
- Women with normal ovaries but no functional uterus as a result of a congenital anomaly (mullerian agenesis) advanced disease (multiple myomas; severe intrauterine adhesions), or a previous hysterectomy, and those with medical conditions which pregnancy poses a serious health risk may still be

afforded the opportunity to have their own genetic offspring via IVF with transfer of embryos to the uterus of a gestational surrogate.

- Women with ovulatory disorders (hypogonadotropic hypogonadism, polycystic ovary syndrome) generally can be treated effectively with a variety of ovulation inducing medications. In some anovulatory women treated with exogenous gonadotrophins, ovulation induction proves difficult and consistently result in excessive ovarian stimulation and cycle cancellation due to legitimate concerns about the high associated risks for the ovarian hyperstimulation syndrome and high-order multiple gestation, an alternative to cycle cancellation is to convert the cycle to an attempt at IVF success rates in such converted cycles are comparable to those achieved in intentional IVF cycles, an ovulatory women who ovulate in response to treatment but do not conceive also may ultimately becomes candidates for IVF ***(Wiedemann and Hepp, 1989)***.