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## DISCUSSION ON IVF: BOON FOR WHOM?

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*“The difficulty of IVF or of any fertility issues is the hope and the shattered hope, the dream that it might happen this time and then it doesn't happen”*

- Brooke shields

### ABSTRACT

Infertility is the failure to achieve pregnancy after 12 months or more of regular unprotected sex. WHO estimates there are 48 million couples and 186 million individuals live with infertility globally. Increased demand for in vitro fertilization (IVF) due to socio-demographic trends, and supply facilitated by new technologies, converged to transform the way a substantial proportion of humans reproduce. The purpose of this article is to discuss about indications of IVF based on scientific research reviews. Researcher searched online journals through reputed sites such as PUBMED, Google Scholar, Research gate for evidences and institutional sites for current practice of IVF. The categories are IVF and Problems with Fallopian Tube, Problems with ovulation, endometriosis, male infertility and Fertility preservation. Infertility is the major reason for the people to choose IVF. Since there are plenty of reasons for drastic increase of infertility, approach to IVF became new normal among young couple. Outcome of discussion is about early approach to IVF clinic will make the people confident and cost effective compared to treating the problems related to infertility. Some infertility issues are untreatable or need long term follow up. Some prognosis of infertility treatment is better, but natural conception after treatment is still on discussion. But IUI, IVF and ICSI maintains high success rate.

Keywords: In vitro fertilization, IVF, IVF treatment, Infertility, fallopian tube, ovulation, fertility, IUI, ET, ICSI.

### INTRODUCTION

The first In Vitro Fertilization (IVF) baby was born in 1978. Global statistics indicate that approximately 7 million plus successful IVF attempts have been achieved till date. Infertility and tubal factors are holding major among all causes of inability in giving natural birth. This discussion is about IVF is a boon innovation and saves millions of couple who struggles days, months and years from self-psychology and societal pressure. Huge issues may have simple solution. IVF is a simple remedy for such inevitable health issues. There is no meaning in finding the problem with husband or wife. Instead, find solution which is very proximal and affordable at our door step.

The researcher categorized the indications of IVF based on scientific research reviews which published in reputed indexed journals with considerable impact factor. The categories are IVF and Problems with Fallopian Tube, Problems with ovulation, endometriosis, male infertility and Fertility preservation.

#### IVF AND PROBLEMS WITH FALLOPIAN TUBE

The primary indication for IVF is tubal factor (related to the fallopian tubes). If a fallopian tube is blocked or damaged, women may have fertility problems. A blocked or damaged fallopian tube can prevent the sperm from reaching the egg or prevent the egg or fertilized egg (zygote) from moving from the ovary to the uterus to be implanted.

**I Briceaget. al., 2015** published a literature review on Fallopian tubes by reviewing updated free full text literature, 4 major textbooks and around 100 articles centered on tubal infertility, in order to raise the awareness on anatomy and etiology in female infertility. They concluded that the anatomy of the Fallopian tube is complex starting from its embryological development and continuing with its vascular supply and ciliated microstructure, that is the key to the process of egg transport to the site of fertilization. There are many strongly documented causes of tubal infertility: infections (Chlamydia Trachomatis, Gonorrhea, and genital tuberculosis), intrauterine contraceptive devices, endometriosis, and complications after abdominal surgery, etc.<sup>(1)</sup>

**Louise M Hafner, 2015**, studies about Pathogenesis of fallopian tube damage caused by Chlamydia trachomatis infections and resulted as Chlamydia trachomatis is the leading cause of bacterial sexually transmitted disease worldwide resulting in 4-5 million new cases of Chlamydia annually and an estimated 100 million cases per annum. Infections of the lower female genital tract (FGT) frequently are asymptomatic; thus, they often remain undiagnosed or untreated. If infections are either not resolved or left untreated, chlamydia can ascend to the upper FGT and infect the fallopian tubes (FTs) causing salpingitis that may lead to functional damage of the FTs and tubal factor infertility (TFI). If Chlamydia immunopathology can be controlled, it might yield a method of inducing fibrosis and thus provide a means of nonsurgical permanent contraception for women.<sup>(2)</sup>

#### IVF AND PROBLEMS WITH OVULATORY

Women with irregular/absence of ovulation, ovulation disorders, polycystic ovaries can be treated with IVF. If ovulation is infrequent or absent, fewer eggs are available for fertilization. Ovary stimulation with the induction of hormones can stimulate the ovaries to produce more eggs and improve chances of pregnancy through IVF.

**Adam H Balenet. al., 2016**, done an analysis of the evidence to support the development of global WHO guidance on the management of anovulatory infertility in women with polycystic ovary syndrome with the aim to present an evidence base for the management of anovulatory PCOS. Management includes lifestyle changes, bariatric surgery, pharmacotherapy (including clomiphene citrate (CC), aromatase inhibitors, metformin and gonadotropins), as well as laparoscopic surgery. In-vitro fertilization (IVF) was considered as were the risks of ovulation induction and of pregnancy in PCOS. Approximately 80% of women who suffer from anovulatory infertility have PCOS. In addition, they recommended that patients should be informed of the potential side effects of ovulation induction agents and of IVF on the foetus, and of the risks of multiple pregnancy.<sup>(3)</sup>

**Davinia M. White et. al., 2018**, conducted an experimental study on Low-dose gonadotropin induction of ovulation in anovulatory women: still needed in the age of IVF with 364 women with polycystic ovary syndrome (PCOS) and 80 women with hypogonadotrophic hypogonadism (HH). Forty-nine percent of women with PCOS and 65% of those with HH conceived (more than 90% within 6 cycles of treatment) and had at least one pregnancy. Multiple pregnancies (all twins) occurred in only 4% of women with PCOS and 5% of those with HH. These findings emphasise the efficacy and safety of low-dose gonadotropin treatment for both clomiphene-resistant women with PCOS and those with HH. These results highlight the importance of choosing the more physiological approach of gonadotropin induction of ovulation in both groups as the most appropriate treatment, in preference to IVF.<sup>(4)</sup>

## IVF AND ENDOMETRIOSIS

Endometriosis is a condition where the endometrial (uterine) lining grows beyond the uterine boundary often affecting the function of the ovaries, uterus and fallopian tubes. IVF can be performed in women with endometriosis after treating endometriosis conditions.

**Tom Tanbo and Peter Fedorcsak, 2017**, concluded that Endometriosis may impair fertility through multiple pathways, including peritoneal inflammation and endocrine derangements, which interfere with ovarian function and ultimately reduce oocyte competence. Removal of superficial peritoneal foci in minimal/mild endometriosis has been shown to improve fertility modestly, while resection of endometriomas and deep infiltrating lesions has an undocumented effect on fertility. Intrauterine insemination is a simple treatment procedure, but with modest effect. IVF is a successful treatment option with results comparable to other causes of infertility.<sup>(5)</sup>

**Catherine Allaire, 2006**, published a review on endometriosis and infertility based on a MEDLINE search and bibliography review of the relevant literature from 1960 to 2003. The exact nature of the relationship between endometriosis and infertility remains uncertain. Surgical treatment of moderate and severe endometriosis improves the monthly fecundity rate. Surgical ablation of minimal and mild endometriosis seems superior to expectant management. Infertile patients with minimal and mild endometriosis can benefit from using clomiphene citrate and intrauterine insemination (IUI) or gonadotropins and IUI. Ovarian suppression should not be used in asymptomatic patients wishing to become pregnant except in the setting of in vitro fertilization and embryo transfer (IVF/ET). Prolonged suppression with gonadotropin-releasing hormone analogues should be considered for endometriosis patients about to undergo an IVF/ET cycle. IVF seems to be effective in endometriosis patients.<sup>(6)</sup>

**Annie S Leung and Michael H Dahan, 2016**, found answer for “Should we diagnose and treat minimal and mild endometriosis before medically assisted reproduction?”. The treatment of minimal or mild endometriosis prior to assisted reproduction (ranging from intrauterine insemination to in vitro fertilization [IVF]) to improve the likelihood of success is controversial. Ovulation suppression is commonly used in endometriosis to decrease pain, however, there is little evidence to suggest improvements in fertility associated with this technique. Moreover, current evidence is sparse and does not support ovarian suppression prior to intrauterine insemination with or without ovulation induction, while there is some evidence favoring ovarian suppression with gonadotropin releasing hormone agonists prior to IVF to improve pregnancy rates. However, the majority of studies were performed in women with moderate to severe endometriosis. There is currently conflicting evidence regarding surgical ablation or removal of endometriomas prior to IVF, and its outcome on pregnancy rates. This review highlights the paucity of data in the management of endometriosis prior to assisted reproductive technologies and suggests that further studies are needed.<sup>(7)</sup>

## IVF AND MALE FERTILITY

Low sperm count, reduced sperm motility, poor sperm quality, ejaculation issues, erectile problems, blocked ducts, etc are some of the male infertility conditions that can be effectively treated through IVF and other techniques of ART such as microsurgical sperm aspiration and Intra-cytoplasmic Sperm Injection (ICSI).

**Victor Chow and Anthony P Cheung, 2006**, reported about male infertility that, with infertile couples, one third of cases can be due to a male factor. It is important to have a comprehensive yet efficient approach to identifying potential causes for appropriate counseling and treatment. Semen analysis is a common, convenient measure of assessing the male. It should precede any invasive tests of the female. While reference values are important in standardization, the current trend in using sperm morphology alone in predicting male fertility remains problematic. Overreliance on this reference can lead to misdiagnosis and unnecessary invasive treatment with intra-cytoplasmic sperm injection (ICSI). In those who have no identifiable or correctable causes, ICSI provides new hope for couples with male infertility who, in the past, could only choose among therapeutic donor insemination, adoption or voluntary childlessness. With increasing application of these assisted reproductive

technologies, it is important to rule out genetic causes, such as cystic fibrosis, and to provide appropriate genetic counseling before embarking on these invasive and costly procedures.<sup>(8)</sup>

**Herman Tournaye, 2012**, mentioned in his study that, current clinical practice involves extensive use of assisted reproductive techniques (ART). Where specific treatments are not indicated or have failed, ART have become popular adjunctive treatments for alleviating male factor infertility. According to the limited evidence available, intrauterine insemination (IUI) may be considered as a first-line treatment in a couple in which the female partner has a normal fertility status and at least  $1 \times 10^6$  progressively motile spermatozoa are recovered after sperm preparation. If no pregnancy is achieved after 3-6 cycles of IUI, optimized in vitro fertilization (IVF) can be proposed. When less than  $0.5 \times 10^6$  progressively motile spermatozoa are obtained after seminal fluid processing or sperm are recovered surgically from the testis or epididymis, intra-cytoplasmic sperm injection (ICSI) should be performed. Although the outcome of no other ART has ever been scrutinized as much before, no large-scale 'macro-problems' have as yet been observed after ICSI. Yet, ICSI candidates should be rigorously screened before embarking on IVF or ICSI, and thoroughly informed of the limitations of our knowledge on the hereditary aspects of male infertility and the safety aspects of ART.<sup>(9)</sup>

## IVF AND FERTILITY PRESERVATION

Patients who intend to undergo cancer treatment such as chemotherapy or radiotherapy that can affect fertility can choose to preserve fertility via egg/embryo preservation procedures of IVF.

**Benjamin Fisch and Ronit Abir, 2018**, studied in detail and reported that, Until the late 1990s, the only option for fertility preservation and restoration in women with cancer was embryo cryopreservation. The development of other assisted reproductive technologies such as mature oocyte cryopreservation and *in vitro* maturation of oocytes has contributed to fertility preservation. Treatment regimens to obtain mature oocytes/embryos have been modified to overcome various limitations of conventional ovarian stimulation protocols. In the last decades, several centres have begun cryopreserving ovarian samples containing primordial follicles from young patients before anti-cancer therapy. The first live birth following implantation of cryopreserved-thawed ovarian tissue was reported in 2004; since then, the number has risen to more than 130. Nowadays, ovarian tissue cryopreservation can be combined with *in vitro* maturation and vitrification of oocytes. The use of cryopreserved oocytes eliminates the risk posed by ovarian implantation of reseeding the cancer.<sup>(10)</sup>

**Alberto Vaiarelliet. al., 2020**, conducted a systematic review on DuoStim - a reproducible strategy to obtain more oocytes and competent embryos in a short time-frame aimed at fertility preservation and IVF purposes. DuoStim appears among these unconventional stimulation protocols as one of the most promising. It combines two consecutive stimulations in the follicular and luteal phases of the same ovarian cycle, aimed at increasing the number of oocytes retrieved and embryos produced in the short time-frame. This protocol has been suggested for the treatment of all conditions requiring a maximal and urgent exploitation of the ovarian reserve, such as oncological patients and poor responders at an advanced maternal age. At present, data from independent studies have outlined the consistency and reproducibility of this approach, which might also reduce the drop-out between consecutive failed IVF cycles in poor-prognosis patients. However, the protocol must be standardized, and more robust studies and cost-benefit analyses are needed to highlight the true clinical pros and cons deriving from DuoStim implementation in IVF.<sup>(11)</sup>

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