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Review Article

IN VITRO FERTILIZATION

Abid M*, Rupali, Islam G, Gahlot K, Khan NA

School of Pharmaceutical Sciences IFTM University, Lodhipur Rajput, Moradabad, U.P., India

*Correspondence

Abid M

School of Pharmaceutical Sciences IFTM University,
Lodhipur Rajput, Moradabad, U.P., India

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Abstract

In vitro fertilisation is now established technique for treating some forms of infertility, yet it remains controversial due to its associated undesirable effect to mother as well as to child. The aim of study is to aware the person who is going for IVF treatment about all the procedure, current status in India including success rate, live birth rate and all the relevant negative effects of the treatment to mother including fertility drugs used in the treatment and their side effects on body, ectopic pregnancy, ovarian hyper stimulation syndrome, cervical cancer, increased risk of blood clot. IVF treatment has also a negative impact on child including heart problems, neurological problems, birth defect etc.

Keywords: *In vitro* fertilisation, ovarian hyper stimulating syndrome, fertility etc.

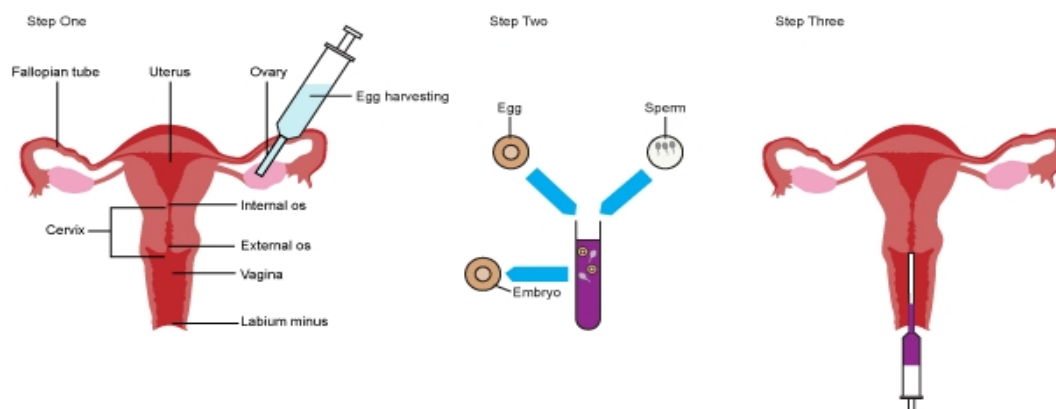
INTRODUCTION

The World Health Organization (WHO) has defined sterility as an illness, if the respective couples have a desire for a child¹. False perceptions are hindering access to new research on IVF². IVF is a technique to solve the female infertility in the woman which is due to the suffering of fallopian tube or there is difficulty in fertilisation by *in vivo* process. IVF is a major treatment in which an egg is fertilised by sperm outside the body. This method is used when the other fertility treatments have unsuccessful. In this process the woman's ovulation process is checked and the ova or egg is removed from the woman's ovary and then letting sperm fertilise them in a fluid medium in a laboratory. Then the fertilised egg that is known as zygote is relocated to the woman's uterus. Louise Brown was born as a result of natural cycle IVF. Robert G. Edwards, the physiologist who developed the treatment, was awarded the Nobel Prize in Physiology or Medicine in 2010³.

Method

In this process after the natural ovulation the content from the woman's fallopian tube or uterus are removed and mixed with a viscous fluid consisting of secretion of accessory gland with sperm and then the content is reinserting into the uterus. The IVF procedure is organized in five steps:

1. Super ovulation: The woman is given fertility medications in order to produce more than one egg per month as she usually does.
2. Egg Retrieval: Collection of eggs from follicle.
3. Insemination: The sperm is mixed with the egg in a propitious environment or they inject the sperm directly into the egg.
4. Embryo formation: After the egg is fertilized it becomes an embryo. After another 5 days the embryo's cells start dividing.
5. Transferring the embryo in the woman's uterus: A tube which contains the embryo is inserted in the vagina, through cervix and into the uterus⁴.



The following matter is to be taken into consideration

- Patient should be aware about drugs and the IVF procedure Fertility medication or hormones are prescribed to encourage the follicle production before IVF procedure patient must aware about those fertility hormones or drugs and associated side effects using in IVF treatment.
- Patient should aware how fertilisation takes place process either has been performed naturally or by using ICSI and resultant effects
- Patient should aware about risk with an IVF procedure such as great pain called as ovarian hyper stimulation and side effect of anaesthesia that is nausea and occasionally bleeding.
- Patient should aware about the success rate of IVF process⁵.

Drugs used in IVF and Their Effects

In IVF procedures medicines are generally used to prepare body for treatment so that increase the probability of more healthy eggs is released from ovaries but have serious side effects also on both child and mother both. They are

- Increased rate of multiple birth
- Increased incidence of miscarriage
- Burning flashes, vomiting
- Headache or blurred vision
- Depression and mood swings
- Ovarian cysts and pelvic discomfort from overstimulation of the ovaries

Medicines are generally used are Clomiphene citrate, Follicle Stimulating, Bromocriptine, Cabergoline and Gonadotropins-Releasing Hormone etc⁶.

Possible Risk Associated with IVF Treatment

Multiple pregnancies

Multiple pregnancies are a greater risk appears in IVF which carries important risks to both the mother and the infants as compared to singleton pregnancies. Due to multiple pregnancies Medical complications are increased and include an increased high blood pressure (pre-eclampsia) and ante partum haemorrhage (bleeding before the onset of labour). There is also a risk of growth retardation in infants and greater risk of premature birth in twins⁷.

Maternal risks related with multiple pregnancy

- Miscarriage
- Haemorrhage
- Pregnancy induced high blood pressure
- Diabetes
- Anaemia
- Polyhydramnios (excessive amounts of amniotic fluid that surrounds the foetus)
- Prolonged hospitalization resulting in higher cost of medical care⁸.

Increases blood clot

Pulmonary embolism is a leading cause of maternal death. The study, published on bmj.com, took data from 23,500 women who had IVF and 117,000 women with natural pregnancies and found that:

- 4.2 % out of every 1,000 women who had IVF suffered blood clots

- Pulmonary embolism occurred in 8 women out of every 10,000 who have IVF
- Compared with six out of 10,000 who get pregnant naturally⁹.

Ectopic Pregnancy

In-Vitro Fertilisation (IVF) and Intrauterine Insemination (IUI) have increased risk of ectopic pregnancy. Ectopic pregnancy occur when the substantial embryo implants somewhere outside the woman's womb. When the embryo grows outside the woman's womb the life threatening situation may occur for both mother and foetus. According to National Health Service data, 95 per cent of ectopic pregnancies results due to the embryo remains in the fallopian tube - even though ectopic pregnancy can occur in the cervix (the neck of the womb), the ovary and the abdominal cavity. Due to this affected organ will rupture and cause severe haemorrhage generally, an embryo cannot survive an ectopic pregnancy and therefore treatment always requires the removal of the embryo¹⁰.

Neurological Problems in Kids

Low birth weight, premature birth and minor problems with brain progress have all been co-related with fertility treatments, which include IVF as well as complicated insemination techniques. In the latest study investigating the association, published online in the journal Archives of Disease in Childhood, researchers report that the latter may be largely responsible for the neurological differences documented among children born via fertility treatments¹¹.

Safety Precautions after IVF

Women should take proper safety precautions to avoid complications after undergoing IVF. Following your doctor's guidance after IVF treatment is also a must. Read on to know about essential safety measures after IVF. If you have undergone IVF you need to take proper safety measures so that it increases the chances of IVF becoming successful. Here are some safety precautions which you should take after your IVF¹².

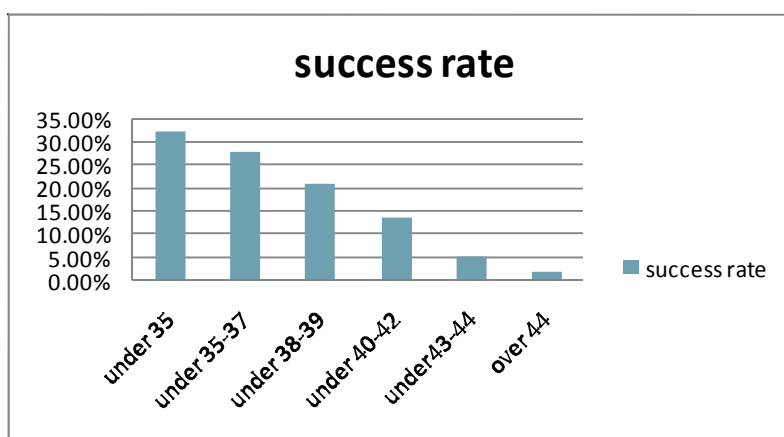
- Avoid vigorous activities which involves forceful bodily movement
- Avoid heavy workout and exercises
- Keep away from smoking
- Try to avoid the caffeine as much as possible
- Avoid indulging yourself in a sexual intercourse
- Avoid lifting heavy weights
- Avoid involving yourself in the activities like aerobics
- Avoid consuming alcohol or alcoholic products and drinks
- Do not take sunbaths and avoid swimming
- Stay away from tough household work.

IVF - Chance of Success

According to NHS (National Health Service) data in 2010, the percentage IVF treatments that resulted in a live birth (the success rate) were¹³:

- 32.2 % for women under 35
- 27.7 % for women aged 35-37
- 20.8 % for women aged 38-39
- 13.6 % for women aged 40-42

- 5 % for women aged 43-44
- 1.9 % for women aged over 44



Success rate of *in vitro* fertilization according to National Health Service data in 2010 in India

IVF Influencing Factors

Age

While younger women have higher chances of IVF success.

Previous pregnancy

If women were pregnant previously with the same partner that's currently undergoing IVF treatment, there is a greater probability of IVF success. Factors such as a history of recurrent miscarriage or a different partner may reduce the chances of IVF success.

Type of fertility problems

Very important to know the IVF success factors are dependent on ovulation. Ovarian dysfunction, like high FSH levels which indicate a low ovarian reserve, may reduce the chances of IVF success. Factors that may lower pregnancy rates and reduce success with IVF include needing large amounts of ovulation stimulation drugs. When both partners are infertile with lower chances for IVF success, factors such as the length of time you have been infertile is important to consider. The chances of IVF success decrease with the amount of time a couple has been infertile¹⁴.

IVF Scenario in India

In India there is an unprecedented and unregulated growth of ART clinics providing IVF procedures over the years within the frame work of medical tourism. IVF is the latest addition. Low cost, easy access and easy availability and economical prices of. India is estimated to be doing currently 80000 cycles per year. To be more precise it is estimated that 70000 to 85000 Ova pick up and 90000 to 95000 as embryo transfer and it is expected that the growth of IVF in India is growing at the rate of 10-15 % every year. The estimated number of clinics in India is almost 500 and going up every day and with such high growth and potential in IVF segment has attracted close consideration of the Government. Also easy availability of Surrogate mother, gamete donors have made India a favoured destination for various IVF procedures especially Surrogacy. The resulting surge of the ART Industry in the country has posed a number of ethical, legal, social and moral dilemmas and the Government is working towards bringing regulation in form of all ART regulation

bill and rules-2008 which is drafted by Ministry of Health and Family welfare and the Indian Council of Medical Research¹⁵.

IVF Baby's Birth Problems

There many problems associated with IVF baby's birth. These are malformed limb or organ, congenital abnormality, problems in musculoskeletal malformations, genitals, and the digestive and neurological systems¹⁶. The risk of a premature birth is roughly doubled, according to Dutch researchers and there may be a slight rise in the risk of death after birth. There was partial evidence of a three times increased risk of having a very premature baby born prior to 32 weeks gestation. There was also a higher risk that IVF babies would be "small for dates" - that is, not weighing as much as would normally be expected for a baby born after a similar-length pregnancy¹⁷.

Who Needs IVF?

For some situation, such as tubal factor, Fallopian Tube Damage/Tubal Factor, Male Factor Infertility, Endometriosis, Unexplained infertility and genetic problem¹⁸.

Limitations of IVF

The limitations that are appropriate to natural fertility also be relevant to IVF treatment. Though IVF can give older women a better chance of getting pregnant than natural fertility, it does not overcome the fall in fertility that is seen when women usually reach their late 30's and early 40's - if a woman's eggs are of poor quality or there are none left, the only option will be to use donor eggs. Success with IVF also relies on a woman responding to the drugs. If she does not respond, the ovaries will only produce one egg as usual, which greatly reduces the chance of success. Generally, IVF will not be useful if a woman has suffered from miscarriages¹⁹.

Reasons IVF Should Always be the Last Option

- Injected fertility drugs can influence women to chromosomal irregularities and are linked to increased risk of uterine cancer, ovarian cancer and fatal abnormalities.

- The Telegraph mentioned on 24 Apr 2012 about a French research which concluded that IVF drugs were linked to childhood cancer.
- The same newspaper had mentioned on 25 Jul 2010 that the risk of women dying during pregnancy increases more than threefold after IVF.
- A recent study from the Netherlands show that overall rate of death in IVF pregnancies was higher than the maternal death rate in the general population (42 mothers' deaths per 100,000 IVF pregnancies compared to 6 deaths per 100,000 pregnancies overall)²⁰.

How to Improve the Success Rate in IVF

There many ways by which we can increase the success rate in IVF technology. These are

- Reducing Stress
- Diet
- Exercise
- Acupuncture²¹
- Preimplantation Genetic Screening etc²².

Alternative to IVF

The three most popular alternatives to IVF include:

- Gamete Interfallopian Transfer (GIFT) – similar to *in vitro* fertilization but fertilization of the egg takes place inside the fallopian tubes. This creates a more “natural” method of conception and is preferred by many couples who have not had success with traditional IVF.
- Zygote Intrafallopian Transfer (ZIFT) – unlike IVF, the fertilized eggs are placed back into the fallopian tubes instead of in the uterus. Women must have healthy fallopian tubes in order to enjoy success with this IVF alternative.
- Tubal Embryo Transfer (TET) – this IVF alternative is almost identical to the ZIFT procedure, but the embryos are transferred back to the woman at a much later stage of development²³.
- Surrogacy is a non-direct medical alternative to traditional IVF treatment. Surrogacy comes in two forms. In the first, Traditional surrogacy a woman agrees to be artificially inseminated with donor sperm and carries the baby to term. The surrogate female is directly related to the baby, its mother.
- Gestational surrogacy involves implantation of both sperm and egg from the patient and their partner into the surrogate and the child is then carried to term. The surrogate is not related to the child as it is direct offspring of the patient and their partner. These methods can be discussed with qualified medical staff²⁴.

Advantages to IVF Alternatives

- May offer higher success rates than traditional IVF procedures
- Some can mimic the natural conception process
- Popular choice by couples who have not been able to conceive for at least a year, or after five to six cycles of ovarian stimulation with intrauterine insemination
- Physician select only the best embryos

Disadvantages of IVF Alternatives

- May not be appropriate for women who have damaged fallopian tubes or tubal blocks

- Some surgery may be required
- Some can increase the chances of having a multiple pregnancy
- Some may increase the risk of miscarriage and preterm labor²³.

CONCLUSION

In Vitro Fertilization are not embedded in one single aim but founded upon several opinion, Taken together, these arguments are all the more compelling to reject IVF as a way of alleviating the problem of infertility due to its resulting side effects to mother as well as to baby. IVF treatment is normally carried out by specialist and well qualified personnel; still having complications which depends on many factors. Despite the fact that the IVF treatment has its share of disadvantages, the treatment has had its fair portion of success rate, moreover, in many cases, it is the only alternative for the couple, affected by infertility. IVF and ICSI intra cytoplasmic sperm injection technologies have reached a generalized level where they are widely known and performed, but still not even the status of genetic risks is clearly known. Furthermore, concerns about the risk to mother including multiple pregnancy, ectopic pregnancy, ovarian cancer, cervical cancer, ovarian hyper stimulating syndrome and have studied also the risk to child including birth defect, neurological problems etc. In India IVF is a developing technique success rate is found to be moderate on the age group of fewer than 35. Although IVF is a developing treatment for infertility still have a various limitations and major side effects so that it should be last choice when all the alternative treatments for infertility are failed.

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