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From Lab to Life: Review of Revolutionizing Conception through IVF

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ABSTRACT

In Vitro Fertilization is a one Assisted Reproductive Technology (ART) commonly referred to as IVF. IVF is the process of fertilization by manually combining an egg and sperm in a laboratory dish, and then transferring the embryo to the uterus. It involves various stages of hormone treatments, monitoring ovulatory process, egg retrieval, fertilization in artificial fluid medium, embryo culture, embryo transfer- guided by skilled medical professionals to optimize success rate. The world's first baby conceived through in vitro fertilization (IVF) was Louise Brown. She was born on July 25, 1978, at Oldham General Hospital in England. Louise's birth was a groundbreaking event in medical history, marking the successful application of assisted reproductive technology to achieve conception outside of the human body. The IVF procedure was developed by Dr. Robert G. Edwards, a physiologist, and Dr. Patrick Steptoe, a gynecologist, after years of research and experimentation. Louise Brown's birth revolutionized fertility treatment options, offering new hope to couples struggling with infertility worldwide. Robert G. Edwards was awarded the Nobel Prize in Physiology or Medicine in 2010. IVF is used to treat infertility due to various factors such as blocked fallopian tubes ovulation disorders endometriosis uterine fibroids , male infertility issues (no or low sperm count) , genetic disorders or other reproductive health conditions. It is complex process that help many couples to achieve pregnancy when other methods have failed.

Key words: IVF (In Vitro Fertilization), ovum retrieval, hCG (human chorionic gonadotropin), ICSI (intracytoplasmic sperm injection), OHSS (ovarian hyper stimulation syndrome)

INTRODUCTION

IVF is the most amazing procedure of the present time which has brought gold in medical science including biological sciences. It is like a wonderful method of giving birth to infertile couple by waving a magic wand over their heads. IVF is increasingly applied worldwide, with a delivery rate per started cycle of around 22% and close to 250 000 children born according to the most recent global registry involving in the year of 2002 1**.** IFV is considered to be one of the most efficacious treatments for infertility nowadays 2**.** Primarily developed to help infertile couples, clinically indications for IVF have expeditiously expanded to include: fertility preservation in addition to medical and genetically conditions. Although access to and use of IVF varies worldwide, practice now accounts for over concept 5% of all new-borns in some European countries where IVF more affordable and/or covered up by insurance 3. IVF is a process of fertilization occurred by manually combining an ovum with sperm in a laboratory petridish, after that transferring this embryo into the uterus. The term 'in vitro' means outer side. A living creatures as oocytes fully grow in vivo condition in the ovary and embryos grow in the uterus of pregnant woman, whereas oocytes are fertilized in a petri dish 4**.**

Robert Edwards, Father of IVF was won Nobel Prize in the field of Medicine for his ground-breaking work in the development of in vitro fertilization in 2010 5 **.** Lesley and Peter Brown, parents of first test tube baby, have been decided in November 1977 to undergo an innovative procedure called IVF that appeared hopeful for infertile couples. And the rest is history. They gave birth to Louise Brown on July 25, 1978. They took this decision because Lesley had complications of blocked fallopian tubes, a cause of infertility. In the year of 1978, the world witnessed the birth of the first "test tube baby". This achievement is considered a milestone not only in reproductive science but also in the history of technological evolution of mankind 5**.**

The first IVF baby, Louise Joy Brown, was born at Oldham General Hospital at the year of 1978. Louise's parents, Lesley and John Brown, had been trying to conceive for 9 years. Edwards and Steptoe published this ground-breaking work in a letter to The Lancet 6.

THE FOREMOST PROCEDURAL STRATEGY OF IVF

This procedure at first developed as a method to overcome bilateral fallopian tube hindrance 1. The fundamental steps in the vitro laboratory sequentially given below:

1. Recognition and separation of sperms and ovums

2. Fertilization of two gamets

3. Culture of embryo

4. Transferring of selected embryo to women's uterus

5. Cryopreservation of leftover embryos and gametes 7.

A. Stimulation of ovary by GnRH

IVF cycle begins with ovarian stimulation. Various protocols have been utilized, from without stimulation to various levels of ovarian stimulation. Medicine such as clomiphene citrate, letrozole, and exogenous gonadotropins (FSH and luteinizing hormone (LH)) are used to stimulate ovary 4.

There are two methods of gonadotropin-releasing hormone (GnRH) mediated natural and mild cycle of IVF. In natural cycle of IVF is performed using no medication for ovarian hyperstimulation. On the other hands drugs for ovulation suppression may still be used with gonadotropinreleasing hormone (GnRH) antagonist protocol, as a result cycle in starts from natural mechanisms 8.

Generally in IVF, the oocyte is collected before the mid-cycle LH surge occurs, or a GnRH antagonist (GnRHant) is used to prevent the release of LH. When the main follicle reaches a mature size, hCG is used as a replacement for the LH surge. Natural cycle IVF is not commonly performed because of the lower clinical pregnancy rate 9.

Retrieval of ovum is performed between 34 to 36 hours after injection of human chorionic gonadotropin (hCG) 4.

The ova are extract from the woman using a transvaginal procedure- using by an ultrasound-guided needle piercing vaginal wall to reach the ovaries. In this method, high quality ova can be obtained and follicular fluid sent to embryologist, so that they can collect the ova 10.

B. Preparation of gametes

At first sperm and ovum are examined in the laboratory. If high quality sperm and ovum are combined – a successful pregnancy is possible. From seminal fluid inactive cells, abnormal cells, immotile cells are rejected by sperm washing method for combination with ovum.

If semen is being given by a sperm donor, usually have been prepared for treatment before frozen, quarantined and thawed to make it ready for use 11. Now a day's automated sperms analyser are used in routine IVF 12.

C. Union of sperm and ovum in IVF

Normally Sperm and ova are placed in incubators located in the laboratory for fertilization. On the other hand when lower probability of fertilization was found, intracytoplasmic sperm injection (ICSI) may be done. The ova are monitored to confirm that fertilization and cell division are taking place and it was considered embryos after successful fertilization 10. ICSI has become main process of

insemination in human clinical IVF, the importance of meticulous microfluidic push/pull cumulus-oocyte-complex cumulus cell removal has been shown to yield good visualization of the oocyte cytoplasm 14.

D. Culture of embryo

Microfluidics technology has been strongly used to culture mammalian pre-implantation embryos from the zygote to the blastocyst stage both individually 15-20.

E. Transferring of selected embryo to women's uterus

The selected – healthy embryos are transferred into female's uterus within six days later. Elective one embryo transfer resulted in fewer multiple pregnancies rather than double embryo transfer. Pregnancy and live birth rate every fresh IVF cycle was lower, the cumulative live birth rate associated with single embryo transfer followed by a one frozen and embryo transfer was comparable with that after one cycle of double embryo transfer 21.

The embryos which are decided to be the "best" are transferred to female's uterus by a thin plastic catheter which goes through her vagina and cervix. Several embryos may be passed into the uterus to improve chances of implantation and pregnancy too 13.

Risk associated with IVF

First, risk of ovarian stimulation was observed as ovarian hyper stimulation syndrome (OHSS), especially if human chorionic gonadotropin (hCG) is helped for inducing final oocyte maturation which happens occurrence of swollen, painful ovaries in 30% of patients 22.

OHSS occurs at two stages:

• Early, 1 to 5 days after egg retrieval (as a result of the hCG trigger); and

• Late, 10 to 15 days after retrieval (because of the hCG if pregnancy occurs).

Secondly, during ovum retrieval, there is probability of bleeding, infection. At transvaginal ultrasound aspiration damage occur especially in bowel and bladder. Difficulty in respiration, thoracic infection, nerve damage was observed in some patient during laparoscopic process 23.

Third, major issue of IVF is the risk of multiple births which is directly connected to the practise transferring of multiple embryos. Sometimes, multiple implantation for births are related to elevated risk of miscarriage, obstetrical complications, prematurity, and neonatal morbidity with the potential for life long damage for baby 24. IVF twins are not born earlier or later than naturally conceived twins.

Fourth, other problems babies can face include cerebral palsy, retinopathy of prematurity (eye problems that result from early delivery), and chronic lung disease. No one knows how much multiple pregnancies affect neurological or behavioural development, even when none of the other problems occur.

Achievement rates of IVF

IVF pass rate in our country falls between 30-35 %, as computed by the Obstetrics and Gynaecology department under the guidance of Dr**.** Alka Kriplani of one of the best hospitals of India, situated in New Delhi, known as All India Institute of Medical Sciences (AIIMS). During a well treatment, the success rates elevated up to 40%. The resulting calculations of success rates by (AIIMS) are mostly similar with other nations as the number being high for females under 35 years of age 25.

Other than AIIMS, many private clinics in India likely to claim about their success rates being 2 to 20 times higher. They have specified the 70 – 80% success rates for females under the age of 35 and 40–50% chance for over 40 years of age 25.

Due to advancement in reproductive technology, the IVF success rates are substantially better today than they were just a few years ago (Table 1 and 2).

Table 1: The most current data available in the United States a 2009 summary was compiled by the ,"American Society for Reproductive Medicine" which reported the average national IVF success rates per age group using non-donor ova 26.

Ages of Patients	< 35	35-37	38-40	41-42
Pregancy rate %	47.6	38.9	30.1	20.5
Live Birth rate%	41.4	31.7	22.3	12.6

Table 2: The live birth rates using donor ova are also given by the," Society for Assisted Reproductive Technology' is given below including all age groups of patients using either fresh or thawed eggs 26.

S.No.	Fresh donor egg embryos	Thawed donor egg embryos
Live birth rate	55.1	33.8

Factors affected in IVF

Body mass index (BMI) over 27 causes 33% decrease live birth rate and pregnant females who are obese have higher rates of miscarriage, gestational diabetes, hypertension, thromboembolism during the time of delivery, as a result an increased risk of fetal congenital abnormality 27**.**

Alcohol, caffeine and smoking decrease the chances of a successful IVF assisted live birth 34% and approx. 30% increases the risk of miscarriage in pregnancy 28.

The number and quality of embryos transferred in the during IVF treatment, an autoimmune disease may also play a vital role in decreasing success rates of IVF by interfering with actual implantation of the embryo in uterus after transfer 29.

Unsung hero of India's IVF

In 1978 India's first IVF baby was born less than three months after the world's first 'test tube' infant came into the world. Bengali physician Subhash Mukhopadhyay, also known as Subhash Mukherjee, pioneered it. But nobody believed him. Dr. Mukherjee is credited as the 'creator' of India's first test-tube baby, Kanupriya Agarwal, nicknamed 'Durga' on 3 October 1978. Durga born during the Durga Puja festival in West Bengal, at Calcutta's Belleview Clinic. His achievements were recognised only after India's second physician to succeed in IVF, Dr TC Anand Kumar, reviewed Mukherjee's notes in 1986. More tragic is the doctor dying from suicide in 1981, reportedly writing, "I can't wait every day for a heart attack to kill me." Indian's actual second IVF baby Harsha Chawda Shah was born in Mumbai on 16 August 1986 by TC Anand Kumar 30-31.

Conclusion

Infertility is a worldwide health issue. Near about 9.3–16.7% of the females of childbearing age suffered from infertility problem 29.

Since in the year of 1978 its clinical introduction, in vitro fertilization (IVF) has reconsider the capability of the human species to produce offspring. Initially developed to treat the infertile couple, clinical indications for IVF have since quickly spread to include medical and genetic conditions and fertility preservation 7**.** Many regimens and adjuvant therapeutic procedure for infertility have been discovered and studied. In vitro fertilization/intracytoplasmic sperm injection and embryo transfer in uterus has been a common technique and has provided pregnancy options for many infertile couples 34.

Overall IVF is a versatile and effective reproductive technology that provides hope and solution for many couples struggling with infertility or genetic conditions affecting fertility.

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