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HISTORY OF HUMAN IN-VITRO FERTILIZATION (IVF) AND ASSISTED REPRODUCTION TECHNIQUES (ART)

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Abstract:

In 1970, Patrick Steptoe developed in vitro fertilisation to treat fallopian tube injury or obstruction in females who were infertile. This important development in embryo research has made it possible for a lot more people to become pregnant and as a consequence, their chances of becoming pregnant have considerably risen. In vitro fertilization occurs when sperm & eggs are fertilized outside the body; the term "in vitro" is derived from Latin word for "in glass." After the announcement in 1978 that the world's first test tube baby had been born in United Kingdom (UK), IVF has attracted the attention of the public worldwide, including India, which is a leading country in the field of assisted reproductive technology. Dr. Subhas Mukhopadhyay was a pioneer in the area of IVF in India and is credited for creating Durga or Kanupriya Agarwal, the first and second test tube babies ever born in India, 67 days after the birth of the first IVF child in the UK on October 3, 1978 in Kolkata. The globe now has access to a broad variety of assisted reproductive technologies, and IVF procedures have changed significantly since their inception. IVF and andrology laboratory technology and clinical procedures have advanced to the point that they have transformed into a medical treatment that is well organised, methodical, secure, easily accessible, and reasonably priced. As of today, more than 5 million babies as a result of IVF have been born. The embryo grading and association with successful outcome in women under assisted reproduction (ART). IVF & ART is a golden tool for infertile couple for achieving their desire of child and completing their family.

Keywords: IVF, ART (Assisted Reproductive Technology), Infertility, Embryo Development, Embryo Transfer (ET) and Vitrification.

Introduction: -

Infertility affects a millions of the couples all over the world. Approximately 10-15% of couples have impaired fertility as results of childlessness. There is about 10-15 percent of reproductive age population concerned with infertility due to various explained and unexplained reasons. The infertility problems exert both the direct and indirect effect on the medical, social, psychological and cultural perspectives of the lives of the infertile couples. The condition of infertility is characterized by the inabilities of an individual to contribution biologically to origination. Barrenness can likewise allude to a lady's powerlessness to convey pregnancies to term. The cause of infertility can be attributed to many biological factors, some of which can be overcome through medical treatment. In a couple, infertility can be described

due to problems either in one partner (husband or wife) not necessarily both. Infertility can be divided into primary and secondary infertility. It is vital to remember that primary infertility refers to couples who have never been able to conceive, while secondary infertility refers to couples who are experiencing problems conceiving after having once conceived (and either carrying the pregnancy to term or having miscarried). Subfertility may occur in couples who have unsuccessfully tried to conceive for a year or more.

Causes of infertility can be endometriosis or polycystic ovarian syndrome. A global increase in prevalence of infertility has been estimated on the basis of data in 2004 which had suggested that more than 186 million of women worldwide experience problem in conceiving. According to AIIMS's 2004 reports on infertility, 6 – 8 % of Indian couple faces the similar problem in the reproductive age group. Approximately, one in seven (14.2%) couples has prevalence infertility worldwide. Irrespective of any country level of development, incidences of infertility among the population is somewhat similar. According to WHO, every 1 in the 4 couple is suffering from infertility in the developing countries. A conservative estimate indicates that 25 percent of the Indian population (250 million individuals) are attempting to become parents at any given time. WHO data suggests that nearly 13 – 19 millions couples are suffering from infertility in the country at any given time. Research scientists and doctors from private enterprises had carried out small studies that estimate the prevalence of infertility in India to be 15 % and according to the Human Reproductive Research Centre's Report 2004, half of the cases are caused by the male factor. Initially, the major cause of Infertility was often thought to be associated with the females, but the fact in so many cases it is because of male problem such include poor sperm morphology, reduced sperm motility, and low sperm concentration and some cases were seen poor sperm survival. Some case was reported of severe oligozoospermia and higher sperm DNA fragmentation they also cause of infertility.

The major female infertility problems are composed of damage of fallopian tubes (30 %), endometriosis (5 %), ovulatory problems (20 %), and uterine pathology (2 %). Up to 30% couples which are having unknown reason for infertility comes under unexplained infertility. Besides these major conditions, there are other many conditions of infertility which can be described as Sexually transmitted disease (STD), genital tuberculosis and pelvic infections and cervical cancer, unsafe abortions. Similar infertility conditions have been estimated in UK where infertility affects one in seven couples in the United Kingdom (UK). In UK, male share roughly half of fertility problems with the woman. But 20% of infertility patients have unidentified infertility causes, which is a quite high percentage. 25% of infertile couples in Britain have male factor infertility to blame, 25% have ovulation issues, 25% have female tubal difficulties, and 25% have additional causes of infertility for which there is no known cure. Nearly, 20 % of couples are having infertility problems in the US. Over the last 30 years, Infertility has emerged a major concern across the world. Due to modern and busy seclude, people now opting the marriage at later age and it is a well-known fact that fertility has the tendency to decrease with the increasing in the age, mostly in women.

It's a most fundamental aspect of human nature to desire children and to complete their family. Treatments of infertility by using assisted reproductive technology also called ART techniques have a great relevance in human being. Intrauterine insemination, in vitro fertilisation, intracytoplasmic sperm

injection, intra-morphologically selected sperm injection (IMSI), physiological intracytoplasmic sperm injection (PICSI), TESA-ICSI, frozen oocyte ICSI, embryo biopsy for PGS/PGD, gamete intrafallopian transfer, and zygote intrafallopian transfer are all examples of ART techniques. These are all very old techniques. This paper review will be help in my research study is concerned only with the patients worked up for IVF/ICSI procedure to know the possible role of grading of zygote, grading of embryo, morphology of embryo and selection of good quality of embryo for embryo transfer in respect of positive pregnancy outcomes.

The History of IVF -The Milestones

In 18th centuries scientist does not understand the role of semen and egg in pregnancy. In mid-1800's scientist found that pregnancy caused by mixing of egg and sperm. Dr. Sims performed a IUI with husband sperm in New York and one was success but miscarriage of the pregnancy. It was Dr. William Pancoast who perform Ist donor insemination in Philadelphia in 1884, using the sperms from the medical students voted "best looking," without obtaining the patient's consent. Now a days it is not acceptable without consent. There were many research studies on fertility hormones in the 1900s. In Massachusetts, the Ist infertility clinic was established in 1926 [1]. In 1934 from Harvard University Picus and Enzmann publish a paper that considering the chance off mammalian egg can developed by invitro techniques. Approximately 800 oocytes were recovered from women in 1948, 135 of which were exposed to spermatozoa in vitro [2]. After incubation for four hours in a carrel flask, newly-ovulated eggs were fertilized, thus opening the door to assisted reproduction. In 1961, oocytes were retrieved by laparoscopy and explained by Palmer from France In 1965, with the help of Georgeanna and Howard Jones, a research team at the Johns Hopkins Hospital in the USA tried to fertilise human oocytes in vitro. [3].

In 1973, Professors Carl Wood and John Leeton of Monash University reported the first IVF pregnancy that ultimately ended in an early miscarriage [4]. World's first B2 culture medium was developed in 1976 by Y. Menezo, known as 'the French medium'. In rabbits, sheep, and humans, this medium reflects follicular, tubal, & uterine environments. Steptoe and Edwards implanted a human embryo into a woman the same year [5] while it was in the late morula/early blastocyst stage. On July 25, 1978, Patrick Steptoe and Robert Edwards produced the first IVF child in Oldham, England [6]. Clomiphene citrate was introduced in Melbourne in 1978 by Lopata. Pez et al [8] used ultrasound to track follicle growth in 1979 [9]. It was published by Hackeloer BJ in 1977 that ultrasound could identify growing follicles [10]. The birth of a test tube baby Australia became the second country to announce in 1980. Culture medium was also introduced in 1980 [11]. Howard of the United States in 1981 using hMG, delivered the 1st IVF baby [12]. A fixed foot-controlled aspiration pressure control was introduced by Wood [13]. hMG and Clomiphene Citrate were also introduced in 1981 [14]. Additionally, the Clamart group developed an assay for measuring LH in France in the same year [15]. First IVF births were achieved by Frydman and Testart in 1982 in Clamart, France, and in Sweden in 1983 [16]. Twin pregnancies were reported in Austria in 1982 [17]. A special hormone formula and donor eggs allowed the IVF team to achieve the first pregnancy without ovaries in Australia [18]. Victor Gomel reported the first in vitro fertilisation (IVF) kids in Canada in 1983, Christopher Chen

claimed the first IVF triplets in 1984, and Victor Gomel reported the first human pregnancy after the cryopreservation, thawing, and transfer of an eight-celled embryo in 1985.[19].

During the review of IVF research's & practice, Govt. of Victoria passed the Infertility in 1984 [20]. California produced the 1st surrogacy embryos transfer baby in 1984 [20]. It has been reported that abnormal spermatozoa produce healthy offspring [21]. Melbourne delivered the world's 1st IVF quadruplet in 1984. Human pregnancy first reported through IVF in 1985 [22]. Human tubal fluid mimicked in vivo environments of embryos in 1985 [23]. In 1986 TSSS guided needle-guided transvaginals follicle aspirations [24]. After IVF with donated oocytes, a patient without ovarian failure became pregnant in 1986 [25]. In 1986, frozen human eggs produced twins. A single sperm micro-injected under the ZPF human oocytes in 1987. The result of an epididymal sperm aspiration in 1988, MESA was created for men as congenital vas deferens absence. NUS used sub-zonal sperm injection (SUZI) for the first time. Human spermatozoa were microinjected into human oocytes in preclinical studies. Several significant events occurred in 1989, including the 1st reports on sexing with DNA amplification and the 1st reports at biopsy of preimplantation embryos. A laser technique was used in 1989 to apply gametes or embryos in ART. In 1990, cleavage-stage embryos were vitrified and successfully delivered [25]. The Assist hatching in human embryos was the 1st reported in 1950 by Cohen J [26] investigated the follicle synchronization & cycle scheduling using combined oral contraceptives. According to Fishel et al. [27], twins were born after subzonal insemination. According to a 1991 reports, IVM in unstipulated cycles led to pregnancy [28].

According to Hurely VA, et al. [29], a catheter was used for embryo transfer. Using recombinant human FSH, IVF & embryos transfer was successful in 1992. To rupture the zona pellucida and encourage natural hatching, assisted zona hatching is performed in IVF. A first pregnancy has been reported following ICSI in Brussels. In that same year, Tan SL et al. published the first study on cumulative conceptions & live birth rate after IVF through on patient's ages & causes of infertility. 1993 was the first second-term pregnancy after ICSI in Sweden. A 1993 study found that men without vas deference can pass on cystic fibrosis mutations to their children. A TESE study was reported by Silber SJ et al. In 1994, the first IVM was born after transvaginal ultrasound-guided oocyte collection. For IVF highly purified FSH was developed in 1994. TESE and ICSI were confirmed in 1995 in non-obstructive azoospermians. The combination of IVM oocytes with ICSI and assisted hatching produced a blastocyst in 1995 [30]. In 1995, aneuploidy testing was conducted for the first time [31]. According to Dmitri Dozortsev [32], the activation of oocytes during ICSI is caused by a heat-sensitive, non-species-specific cytosolic sperm component. One of the largest studies on urinary FSH and rec-FSH was conducted in vitro fertilization [33]. Cryopreserved testicular sperm was used in 1996 to achieve the first pregnancy following IVF-ICSI [34]. The Casper groups made the first observation that pre-implantation fragmentation involves programmed cell death in Jurisicova [35].

In 1996, Casper [36] employed the hypo-osmotic swelling test to choose the immotile sperms for ICSI for the first time. In 1997, oocyte cytoplasm was transferred to a recipient [37]. The birth of babies as frozen oocyte after ICSI was performed on cryopreserved human oocytes in 1997 [38]. The first reports on

cytoplasmic transfers in [39]. The GIFT through a falloposcopic delivery system (FDS) was confirmed in 1997. Agrawal reported a pregnancy after taking three recombinant gonadotropins. By introducing a sequential media & blastocyst transfers, Gardner greatly supported a single embryo transfer. Pregnancies various embryo culture & blastocyst transfer were reported in 1998 by Jones GM et al. GV eggs and donor eggs were reported to have been used in 1998 by Tucker et al. Also confirmed that immature oocytes could be cryopreserved and subsequently matured in vitro. PGD for sickle cell anaemia confirmed a pregnancy in 1999.

Human oocyte vitrification was reported as resulting in a birth in 1999 [40]. Having successfully air-transported oocytes, McGill Reproductive Center reported 1st IVF/ICSI pregnancy & live birth are introducing the concepts of air-transport IVF programs in larger countries through scattered population / remote areas far from fertility centers. Oktay and Karlikaya reported ovarian tissue transplants in 2000 [41]. By developing a chemically defined protein-free embryo culture medium, the first group of babies was born by fertilizing egg collected & inseminates with spermatozoa prepare in the equivalences free protein medium of conventional IVF & ICSI [42]. A patient with PCOS was born in 2001 using cryopreserved embryos derived from unstimulated IVM oocytes [43]. Using PESA-retrieved spermatozoa in IVM oocytes, the McGill group reported ongoing twin pregnancies [44]. A moribund man's sperm was retrieved in 2001[45]. A birth was reported in 2002 after blastocyst biopsy and PGD analysis [46]. CGH and PBT were used for the 1st time in PGD in aneuploidy [47]. In 2003, oocyte vitrification and embryo transfer resulted in live births [48]. FSH agonist FSH-CTP was used to induce ovarian stimulation [49]. A normal baby was delivered after microsurgical enucleating of tri-pronuclear human zygote [50]. A combination of IVM and TESE resulted in pregnancy and delivery in 2004 [51].

The orthotropic transplantations of cryopreserve ovarian tissue led to the successful delivery of a baby [52]. The 1st preimplantations HLA matching in stem-cell transplantations to a sibling was reported [53]. In cancer patients, IVM and oocyte vitrification can preserve fertility. The PGD of Retinoblastoma confirmed pregnancy [54]. A possible infertility therapy that combines natural cycles and IVM has been examined [55]. The pregnancies & live birth in 2005 were confirmed using trophectoderm biopsy (TB) & preimplantation genetic testing (PGT) [56]. The first child was born after preimplantation genetic testing for beta-thalassaemia and trophectoderm biopsy [57]. In embryos produced from natural cycle IVF paired with IVM in 2006, a first birth was verified through PGD for aneuploidy screening [58]. In 2007, Maria Infertility Hospital Seoul (MIHS), Korea and McGill Reproductive Centre, Canada reported confirming deliveries following the transfers of human blastocyst derive from in VMO [59]. IVF Mild Treatment Strategy was introduced. The entire ovary can be cryopreserved using an innovative multi-gradient freezing technique. It has been shown that thawing the ovary does not damage the vascular walls or intima. First North American IVM eggs donation pregnancy at McGill Reproductive Centre. Live births can be identified by DNA fingerprinting, and biopsied trophectoderm can be differentiated from non-viable blastocysts by gene expression profiles. The first healthy twins have been born after bilateral ovariectomy and cryopreservation. After conducting polar body array comparative genomics hybridizations, Simons Fishel

and his collaborators at CARE Fertility in Nottingham announced a live birth in 2009. The HMC in Jerusalem's reported that a viable pregnancy was achieved following in vitro fertilization and embryo implantation in a woman with defective BRCA2 genes [60].

THE HISTORY OF IN-VITRO FERTILIZATION IN INDIA:

In India "**Durga**" was reborn on occasion of Mahashtami puja / Durga Ashtami on 15 October 2003. Dr. Subhas Mukhopadhyay created Durga on October 3rd, 1978 in Kolkata, eventually being known by the name of Kanupriya Agarwal. 67 days after the birth of the first test tube baby in the United Kingdom, Durga, the second test tube baby in the world and the first in India, was born. It was at that time that India's scientific community and government did not recognize his prestigious IVF work, and he was not permitted to present his work at international conferences. As a result of rejection and non-acknowledgement from the Indian scientific community & the Indian government, Dr. Mukhopadhyay committed suicide. A film based on his life, EK Doctor (1991), was awarded a national award. At an event hosted by the ICMR in honour of Hope Fertility Clinic and Inter Academy Biomedical Science Forum, Bangalore, on October 3rd, the scientific community awarded Dr. Mukhopadhyay what was due. Anand Kumar was another famous infertility specialist who later acknowledged Dr. Mukhopadhyay's hard work and achievement. He was the first gynecologist in India to deliver the 1st test tube baby in 1986 until now. As a result of his efforts, Dr. Mukhopadhyay was acknowledged for his achievements. Dr. T. C. Anand was responsible for collecting and examining Dr. Mukhopadhyay's documents, as well as disseminating them to other scientists. The sole surviving member of Mukhopadhyay's IVF team who was standing in front of his invention Durga at the moment, Sunit Mukherjee, was subsequently recognised by the state government. The Indian Council of Medical Research and the "National Academy of Medical Sciences" were founded as a consequence of his services. have included his name and scientific research as part of the Artificial Reproductive Technique Bill, and Dr. Mukhopadhyay has been recognized as 'the pioneer of IVF in India' without hesitation. In contrast to his British counterparts, Dr Mukhopadhyay did not publish his IVF research in a scientific journal. Dr Mukhopadhyay developed certain innovative technique, such as embryo verification and thawing in IVF work [62].

Conclusion

ART has made it possible for couples to have children since Louise Brown's birth. IVF has been more effective and widely accessible as a result of important advancements in the first ten years. With the development of technology, treatments for male infertility like as ICSI, MESA, and TESE become available. With the development of PGD, it is now possible for couples with sex-related illnesses and a variety of genetic abnormalities to have children who are clear of the problem. The effectiveness of ART that use PGD for aneuploidy screening is still being worked on. And last, increasing the effectiveness of ovarian tissue transplantation and oocyte cryopreservation would hopefully provide women who must postpone having children more alternatives.

Although ART has made significant scientific strides over the last three decades, significant work still needs to be done to monitor the long-term effects of its technologies since the oldest kid born via IVF is

just twenty-seven years old. Additionally, there is limited information on the results of numerous methods, including PGD, oocyte cryopreservation and vitrification, ICSI, and in vitro maturation. The continual monitoring of uncommon problems of ART that may only appear over time requires heightened awareness of possible health hazards resulting from ovulation induction drugs, in vitro culture settings, and oocyte/embryo modifications. True connections between ART and uncommon illnesses may be found with the use of periodic meta-analyses that pool well-conducted research with sample size and statistical power restrictions. It will be easier to do research on IVF-related birth malformations and imprinting diseases if national ART birth registries are meticulously maintained and more international data are accessible.

In conclusion, few medical specialties have seen the widespread expansion and consistent advances that doctors and their infertility patients have seen. However, there is mounting evidence that infants born via the use of ART may have more perinatal difficulties than children born naturally and that our understanding of the long-term health impacts of ART is still lacking. Therefore, it is essential for all doctors and scientists working on these patients to keep a sharp eye out for any possible problems. As assisted reproductive technology (ART) enters its third decade, it is important to appropriately employ both new and current technologies to assist infertile couples in achieving their objectives while upholding the principle of "first, do no harm." [63].

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