Introduction

In vitro fertilization (IVF) is a method of assisted reproduction in which the man's sperm and the woman's egg are combined in a laboratory dish, where fertilization occurs. Normally, an egg and sperm are fertilized inside a woman's body. If the fertilized egg attaches to the lining of the womb and continues to grow, a baby is born about 9 months later. This process is called natural or unassisted conception**(Tsen et al., 2009) .**

The first successful live birth following in-vitro fertilization (IVF) of a human oocyte was performed in 1978 by Steptoe and Edwards with the birth of Lousie Brown, the first test tube baby, at Oldham General Hospital, Oldham, England through a planned caesarean section. She weighed 5 pounds, 12 ounces (2.608 kg) at birth.

IVF is a major treatment for infertility . The process involves ovulation enhancement (stimulating the development of more than one egg in a cycle), egg harvest, fertilization , embryo culture, and embryo transfer **(Trout et al., 2003) .**

During ovulation enhancement , fertility drugs are given to the woman to boost her egg production. Normally, a woman produces one egg per month. Fertility drugs tell the ovaries to produce several eggs. During this step, the woman will have regular transvaginal ultrasounds to examine the ovaries and blood tests to check hormone levels **(Klonoff et al.,2004).**

A minor surgery, called follicular aspiration, is done to remove the eggs from the woman's body. The surgery is normally done as an outpatient procedure in the doctor's office. The woman will be given medicines so she does not feel pain during the procedure. Using ultrasound images as a guide, the health care provider inserts a thin needle through the vagina and into the ovary and sacs (follicles) containing the eggs. The needle is connected to a suction device, which pulls the eggs and fluid out of each follicle, one at a time. The procedure is repeated for the other ovary. The woman may have some cramping after the surgery, but it usually goes away within a day. In rare cases, a pelvic laparoscopy may be needed to remove the eggs **(Tsen et al.,2004).**

The man's sperm is placed together with the best quality eggs and stored in an environmentally controlled chamber. The mixing of the sperm and egg is called insemination. The sperm usually enters (fertilizes) an egg a

few hours after insemination. If the doctor thinks the chance of fertilization is low, the laboratory staff may directly inject the sperm into the egg. This is called intracytoplasmic sperm injection (ICSI). Many fertility programs routinely do ICSI on some of the eggs even if everything is normal **(McGee et al., 2000).**

Embryos are placed into the woman's womb 3 - 5 days after egg retrieval and fertilization. The procedure is done in the doctor's office while the woman is awake. The doctor inserts a thin tube (catheter) containing the embryos into the woman's vagina, through the cervix, and up into the womb. If an embryo sticks to (implants) in the lining of the womb and grows, pregnancy results **(Barnes et al., 2002).**

Other transfer options include zygote intrafallopian transfer (ZIFT) , pronuclear stage tubal transfer (PROST), and tubal embryo transfer (TET). Although fertilization is confirmed before embryo transfer, all of these techniques require TUGOR to aspirate the follicular fluid and laparoscopically guided transfer into the fallopian tube 24 to 48 hours after fertilization. Similar pregnancy rates , and the need for two different procedures and anesthetics, have led to a marked decline in the performance of these techniques **(Lee et al.,2005).**

Risks of egg retrieval include reactions to anesthesia, bleeding, infection, and damage to structures surrounding the ovaries, including the bowel and bladder **(Elkington et al., 2003).**

Pain management is considered to be a fundamental aspect of in vitro fertilization (IVF) oocyte retrieval procedures that are performed transvaginally under ultrasound guidance. The pain during such procedures is the result of a needle passing through the posterior vagina, the peritoneum, and into the ovary **(Robert et al., 2002).**

Anesthesiologists face a special challenge to follow the anesthesia technique allay concern the patient with adequate analgesia for pain and avoid any adverse effect on the product of a successful pregnancy.

Most patients are healthy and young, but show anxiety, tension and some mental disorders, which related not to fertility. It is especially important to the anesthesiologist because the patient understands the concern and take appropriate measures to calm him down.

Anesthetic techniques in day case surgery should provide smooth and fast effect of anesthesia, satisfactory and quick recovery and return to a state of pre-operative functional complete with soothing the pain after the operation and minimal side effects such as nausea and vomiting after surgery.

Drug, which is important for patient comfort and gynecologist to increase retrieved eggs, plays an important role in the successful output.
Anesthetic tools should be short-acting with fewer side effects. Should not be offended by the oocyte and its existence. The goal is a shorter exposure to less toxic agent.

In case general anesthesia is required, the anesthetic drugs should be used cautiously and efforts should be made to reduce the anesthetic duration. The preferred modality of peri-operative care should be invidualized as per the requirement of the patient.

Conscious sedation is suitable for cooperative females (**Kwan , et al. , 2005) .**

A paracervical block technique can be used for pain relief during oocyte retrieval in IVF. The local anesthetic is deposited in the vaginal wall and between the vaginal wall and the peritoneal surface near the ovary using ultrasound guidance
(Cerne , et al. , 2006) .

Electric acupuncture needle appears effective alternative to anesthesia fashionable while oocyte retrival for external fertilization (**Gejervall , et al. , 2005) .**

In Vitro Fertilization Techniques

In Vitro Fertilization is done to help a woman to be pregnant , it is most often performed to overcome infertility.
Infertility, defined as the inability to conceive after 1 year of unprotected intercourse , is a common condition with psychological , medical and economic implications.
Infertility may be primary (no previous pregnancies) or secondary (previous pregnancy, irrespective of outcome). There are various causes leading to difficulty in conceiving, and very often several causes can be identified at the same time.
Infertility may be due to problems in the woman, man, or both.

FEMALE INFERTILITY:

Ovulation dysfunction is usually indicated by amenorrhoea, oligomenorrhoea or polymenorrhoea, accounting for 21% of cases of infertility.

The ovulatory cycle, under the control of the endocrine system, is necessary for reproduction. It is commonly divided into three phases: the follicular phase (days 1 through 13), ovulation, and the luteal phase (days 14 through 28) . It is also occasionally misclassified using the uterine cycle: menstruation, proliferative phase, and secretory phase . Menstrual cycles are counted from the first day of menstrual bleeding **(Greenberg et al.,2007)**

Stimulated by gradually increasing amounts of estrogen in the follicular phase, discharges of blood (menses) slow then stop, and the lining of the uterus thickens. Follicles in the ovary begin developing under the influence of a complex interplay of hormones, and after several days one or occasionally two become dominant (non-dominant follicles atrophy and die). Approximately mid-cycle, 24–36 hours after the Luteinizing Hormone (LH) surges, the dominant follicle releases an ovum, or egg in an event called ovulation. After ovulation, the egg only lives for 24 hours or less without fertilization while the remains of the dominant follicle in the ovary become a corpus luteum , this body has a primary function of producing large amounts of progesterone. Under the influence of progesterone, the endometrium (uterine lining) changes to prepare for potential implantation of an embryo to establish a pregnancy. If

implantation does not occur within approximately two weeks, the corpus luteum will involute, causing sharp drops in levels of both progesterone and estrogen. These hormone drops cause the uterus to shed its lining and egg in a process termed menstruation **(Lentz et al., 2012).**

Female infertility may be caused by: **(Legro RS et al., 2007)**

Structural anomalies : Müllerian agenesis , Vaginal septum , Imperforate hymen
Chromosomal anomalies : Turner's syndrome , XY gonadal dysgenesis
Ovarian causes : Premature ovarian failure (normal chromosomes)
Hypothalamic causes (hypogonadotrophic hypogonadism) : Systemic and chronic illness
Weight loss
Intense exercise
Genetic (e.g. Kallmann's syndrome)
Idiopathic
Pituitary causes : Hyperprolactinaemia , Hypopituitarism
Hypothalamic/pituitary damage :
Tumours , (hypogonadism) Cranial irradiation , Head injuries
Delayed puberty : Constitutional or secondary
Systemic causes :
Chronic debilitating illness
Weight loss
Endocrine disorders

MALE INFERTILITY:

Male infertility may be due to:
A decrease in sperm count
Sperm being blocked from being released
Sperm that do not work properly

Male infertility can be caused by: **(Lobo et al., 2007)**

Environmental pollutants
Being in high heat for prolonged periods
Birth defects
Heavy use of alcohol, marijuana, or cocaine
Too little or too much hormones
Impotence

Infection
Older age
Cancer treatments, including chemotherapy and radiation
Scarring from sexually transmitted diseases, injury, or surgery
Surgery to prevent pregnancy (vasectomy), or failure of vasectomy reversal
Retrograde ejaculation
Smoking
Use of certain drugs, such as cimetidine, spironolactone .

Several advanced sperm selection methods have been developed with the objective of improving sperm preparation protocols used during ART. These methods aim at isolating mature, structurally intact and non-apoptotic spermatozoa with high DNA integrity **(Aitken et al.,2007) .**

Sperm quantity will be measured, as the number of sperm in the ejaculate. A few days of abstinence is the best way to achieve optimal numbers.

Quality of sperm

It will take as long as 3 month to improve sperm quality. This is because it takes about 72 days for sperm to mature from stem cells to fully-functioning sperm.

Lifestyle

· Minimize excessive heat
· Limit alcohol & caffeine
· Quit smoking
· Consider stress-reduction techniques including exercise and time with friends
· Maintain a healthy BMI through exercise
· Eat well, including red meat in your diet

Medications
Medications such as Sudafed, HCG, clomiphene, letrozole, and FSH preparations have a role in treating male factor subfertility, though in most circumstances they are of limited value at best.

It is important to maximize sperm quantity and quality, but once all has been done, some male factor subfertility may still remain.

Perhaps pregnancy will be possible through intercourse alone, but we should also be able to increase pregnancy rates substantially through intrauterine inseminations (IUI) or in vitro fertilization with intracytoplasmic sperm injection (IVF/ICSI).
(Klonoff-Cohen 2005)

Due to the costs of the procedure, IVF is generally attempted only after less expensive options have failed.

The most commonly used method of assisted reproduction usually proceeds in three steps:
1- Ovulation induction in which a woman is treated with hormones to make her eggs mature.
2- Harvest or retrieval of mature egg cells (oocytes) from the ovaries after treatment for their maturation . The egg cells are then mixed with sperm cells in a laboratory dish.
3-After a few days in the laboratory, fertilized eggs are transferred into the uterus for further development. Two to four embryos are transferred per cycle .

IVF typically involves the collection of multiple eggs and then fertilization in the laboratory normally happens as a result of the sperm simply being combined with the egg. Intra-Cytoplasmic Sperm Injection (ICSI), to achieve fertilization if the sperm are unable to do it in the usual way, and the embryos are typically grown for about three, four, or perhaps five days and then put back inside the uterus. This is the basic assistive reproductive technology upon which all of the others are based **(Vallerand et al., 2003)**.

In vitro fertilization (IVF) is a four-stage procedure:

- Stage1- Ovarian stimulation and monitoring.
- Stage2- Egg (oocyte) retrieval.
- Stage3- Fertilization.
- Stage4- Embryo transfer **(Gougeon et al., 2004).**

Stage 1: Ovarian Stimulation and Monitoring

Various hormonal medications are used to stimulate the ovaries to develop as many ovarian follicles as possible. In addition to multiple follicle development, these medications are also used to control the timing of ovulation for egg recovery . The physician may refer to this part of treatment as controlled ovarian hyperstimulation or superovulation. Ovarian stimulation involves the use of follicle- stimulating hormone (FSH), the hormone necessary for multiple oocyte development. FSH is available in the form of 'Fostimon, Gonal F'. Other drugs currently in use include: clomiphene citrate (Clomid, Serophene) , human menopausal gonadotropin (hMG) , Puregon', and a gonadotropin releasing hormone (GnRH) analog called leupralide , progesterone in the form of 'Prontogest, Cyclogest' , human chorionic gonadotropin (hCG) in the form of 'Chorimon'. Most of these drugs may be used alone or in a combination with others
(Barnes et al., 2002)

Monitoring Ovarian Stimulation:

The physician will carefully monitor the response of the patient by one or both of the following methods:
* Ultrasound
* Blood estrogen levels

Stage 2: Egg Retrieval

There are two procedures commonly used for egg retrieval:
●Laparoscopy.
●Ultrasound –guided aspiration.

Laparoscopy:

Laparoscopy is a surgical procedure that usually requires general anesthesia. If an egg has not been retrieved , the process is repeated until an egg is recognized and until all the mature follicles have been aspirated.

Ultrasound-Guided Aspiration:

The ultrasound image allows for more accurate aspiration of the egg as the physician can guide a needle into each follicle and withdraw its contents. The needle may also be guided through the abdominal wall or through the bladder into the follicle. The harvested eggs are examined in a laboratory and each is graded for maturity . The maturity of an egg determines when the sperm will be added to it (insemination) . Insemination can be done immediately upon harvest, after several hours , or on the following day **(Zeleznik et al., 2004).**

On the day the eggs are harvested , the partner collects his semen by masturbating . The male , if fertile , refrains from ejaculating for two or three days and then collects semen through masturbation . If scar tissue or other conditions block the natural release of sperm , a sperm aspiration may be performed . Sometimes the man's sperm can be frozen ahead of time .
In western countries, if the male partner is unable to produce viable sperm, donor sperm may be used **(Nick etal., 2006).**

Sperm Retrieval for In Vitro Fertilization

With the improvement in intracytoplasmic sperm injection (ICSI), the options available for retrieval of sperm from the male have increased tremendously. Several methods exist , and most are indicated in men who have an obstruction that cannot be repaired , such as absence of the vas deferens, congenital obstruction, or failed vasectomy reversal **(Richard et al., 2006).**

Sperm may be obtained through testicular biopsy. This procedure, testicular sperm extraction (TESE), can be performed under general anesthesia or a combination of local anesthesia with intravenous sedation. Alternatively, sperm may be obtained form the testicle using needle biopsy or fine needle aspiration **(Linda et al.,2006).**

Microdissection testicular sperm extraction (TESE), performed under general anesthesia and with the use of the operating microscope, may allow the surgeon to identify even tiny islands of sperm production within the testicles. Surgically retrieved sperm may be cryopreserved (frozen and banked) , and used later for in-vitro fertilization (IVF) **(Bart et al., 2006).**

Stage 3 : Fertilization

Once mature eggs have been retrieved , the sperm and egg are placed together in the laboratory and incubated at a temperature identical to that of the woman's body. After about 48 hours, if the eggs have been successfully fertilized and are growing normally , they are ready to be transferred to the uterus. This is called embryo transfer. The trick with IVF is to get the resulting embryo to implant in the uterus , and this depends on both the egg quality and the strength of the embryo that results from that egg , as well as on the uterus. Also it is important to make sure that the uterine cavity is normal and the uterine lining has been properly prepared **(Findlay et al., 2002).**

Stage 4: Embryo Transfer

Embryo transfer is not a complicated procedure and can be performed without anesthesia. The embryos are placed in a catheter and transferred into the uterus. Any embryos that have not been transferred can be frozen (or cryopreserved) and stored for future use. The entire transfer procedure usually takes between 10 and 20 minutes . Some doctors recommend bed rest after the transfer. Each ART center will determine the (optimal) number of embryos for transfer for each patient . If there are any remaining embryos, they can be frozen through a process known as cryopreservation. Frozen embryos can be used at a later time **(Elder et al., 2000).**

An advantage of cryopreservation is that the likelihood of pregnancy may be improved . This is because the future transfer can be performed during a normal ovulatory cycle . After transferring procedure, the patient rests at the fertility center for a few hours before going home . The patient will have a pregnancy test 10-12 days after the transfer procedure **(Stouffer et al., 2003).**

Outcome :

The patient will probably be able to resume normal activities within a few days . Many women find it emotionally difficult to wait the two weeks to learn if an egg has implanted. Even if pregnancy occur ,a miscarriage remains a possibility . If the pregnancy test indicates conception, an

ultrasound will be scheduled for two weeks later to confirm a fetal heartbeat and assess if more than one egg is growing. Pregnant women are referred to an obstetrician for follow-up . If pregnancy did not occur, additional IVF attempts can be scheduled at least one month later . Success rates are influenced by both age and
the cause of infertility **(Bentin-Ley et al., 2000).**

Success Rates for In Vitro Fertilization

The live birth rate for one cycle varies by maternal age: 30% to 35% among women younger than 35 years of age and 25% for those aged 35 to 37 years. The success rate ranges from 6%-10% in those older than 40 years of age. Pregnancy in women older than 44 years of age is rare.
When reviewing statistics for IVF programs, it is important to understand what is actually being reported. A pregnancy rate may include so-called chemical pregnancies, in which the pregnancy test is positive but the pregnancy ends before a viable fetus can be demonstrated by ultrasound. Pregnancy rate is also different from the live birth rate, since it includes all pregnancies that may or may not lead to a live birth. Even live birth rates may vary among different clinics because of selection criteria for patients and the number of embryos typically transferred.
The rate of miscarriages with IVF pregnancies is the same as that with normally conceived pregnancies. Ectopic pregnancy occurs in about 3% to 5% of cases. An ectopic pregnancy is a serious condition that requires emergency medical care. The embryo is growing outside the uterus and does not survive**. (Mastenbroek S et al., 2011)**

Other Assisted Reproduction Techniques

The following procedures have been used as alternatives to IVF but are not discussed in detail in this article:

Gamete intrafallopian transfer (GIFT): Gamate intrafallopian transfer is similar to IVF. It is used when a woman has at least one normal Fallopian tube. Eggs are placed in this tube along with a man's sperm to fertilize there. GIFT allows for the oocyte fertilization in vivo and may be acceptable for couples with religious beliefs that preclude IVF **(David et al., 2002).**

Zygote intrafallopian transfer (ZIFT): Zygote intrafallopian transfer is tubal embryo transfer in which a woman's eggs are taken from her ovaries, fertilized in the laboratory, and put back in the Fallopian tubes rather than the uterus. ZIFT is even less common than GIFT, making up less than 1.5% of assisted reproductive procedures.

Embryo cryopreservation (frozen fertilized egg and sperm) is available when more embryos are created than are transferred to the woman's uterus. These can be transferred during a future cycle. In this case a woman would take medications to prepare her uterus to receive the embryos at the appropriate time **(Shevell T et al., 2011)**

Various anesthetic and analgesic techniques for

In-Vitro Fertilization

In vitro fertilization is an upcoming specialty. Anaesthesia during assisted reproductive technique is generally required during oocyte retrieval, which forms one of the fundamental steps during the entire procedure. Variety of techniques like conscious sedation, general anaesthesia and regional anaesthesia has been tried with none being superior to the other. However irrespective of the technique the key point of anaesthesia for in vitro fertilization is to provide the anaesthetic exposure for least duration so as to avoid its detrimental effects on the embryo cleavage and fertilization .

Role of Anaesthesiologist

1980's witnessed a drastic change from the use of laparoscope to vaginal ultrasound probe for egg retrieval. Although this technique of using Vaginal ultra-sound probe is less invasive and associated with higher pregnancy rates, it forms one of the most stressful and painful components of the entire assisted reproductive treatment**(Ng et al., 2001).**

The ideal method of pain relief would be one that is :

(i) safe, providing adequate pain relief with minimal side effects and complications.
(ii) easy to administer and monitor.
(iii) short acting and easily reversible.
(iv) without deleterious effects on oocytes and embryos.

*Coexisting illness :

Patients presenting in the IVF clinic needs to be investigated for any co morbid illnesses .

Thyroid can also be a cause of infertility so it becomes mandatory to assess the thyroid function tests and take appropriate anaesthetic precautions .

Some of the patients might be receiving treatment for psychomotor disorders like depression and are on anti depression drugs like Selective serotonin reuptake inhibitors(SSRI), tricyclins or drugs like tragadone, bupropion. It is therefore important to adjust the dosages of anaesthetic agents especially narcotics accordingly .

*** Pain in IVF :**

Pain during oocyte retrieval is caused by the puncture of the vaginal skin and ovarian capsule by the aspirating needle as well as manipulation within the ovary during the entire procedure .

Another factor that could affect perception of pain is the duration of the oocyte retrieval procedure. Multiple-follicle aspiration would entail a lengthier procedure, which could affect pain scores when compared with single-follicle aspiration **(Lok et al., 2002)** .

Evaluating pain experience during oocyte retrieval is difficult since there are so many factors that influence pain, fear of pain, anxiety, type of analgesia, physician's skill and technical factors such as needle diameter and sharpness. These factors have a clear influence on pain threshold .

Very little attention has been paid to the technical aspects, such as needle design and the effect on pain experience .

Multi-centre study was performed to compare the overall pain experience of a reduced designed needle (RN) compared with a thicker standard needle (SN) in Ultrasound-guided transvaginal oocyte retrieval at the Fertility units in Sweden University Hospitals between June and December 2009 **(Wikland et al., 2011)**

The oocyte aspiration was performed under local anaesthesia, either with a needle with a reduced diameter (0.9 mm) for the last 50 mm from the tip (RN) or with a SN (1.4 mm)

It remains unknown whether an even thinner needle might cause less pain when the OPU procedure is performed under local anaesthesia. Reducing the needle diameter too much (<0.8 mm), however, may be a problem with regard to damage to the oocyte . Another problem with a very thin needle is that it may miss the target, thereby making the retrieval

technically more difficult and less efficient. In order to circumvent these problems, a needle has been designed where only the last 50 mm of the needle is reduced in diameter.

Thus, only the part of the needle that penetrates into the tissues is reduced in diameter .

Rating of pain was performed by self-assessment by means of visual analogue scale (VAS) consisting of a line oriented vertically on a paper with a range from 0 mm (no pain) to 100 mm (unbearable pain) .

The overall pain during oocyte aspiration was significantly reduced in the group with the thinner needle when compared with the SN. The reduction in overall pain as measured by self-assessment on a VAS scale was 19%. Furthermore, significantly more patients had less vaginal bleeding than expected. No negative effects were found in relation to the oocyte or the outcome of the treatment .

There were no difference in aspiration time, oocytes recovered, damage to oocytes, fertilization rate, cleavage rate, proportion of good quality embryos, implantation and clinical pregnancy rate between the two groups .

It becomes customary for the anesthetist to provide adequate pain relief to immobilise the patient and eliminate the danger of piercing any vessel during the process of oocyte retrieval . Pain associated with oocyte retrieval is intermittent rather than continuous . The ideal pain relief during oocyte retrieval should be effective and safe, easy to administer and monitor, short acting and readily reversible with a few side effects **(Wilhelm W et al., 2002)**

Factors that may influence the pain are the number of follicles, duration of the oocyte retrieval procedure, the position and mobility of the ovaries. Multiple-follicle aspiration would entail a lengthier procedure, which could affect pain scores when compared with single-follicle aspiration. For alleviating pain of IVF, opioids and benzodiazepines have been used, many of these agents have been detected in the follicular fluid, albeit clear evidence to indicate negative effects on oocytes, oocyte