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# Critical Review of Assisted Reproductive Technology and the Nigerian Invitro Fertilisation Situation

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## Abstract

Invitro fertilisation (IVF) technique involves a process of hormonal monitoring and hormonal stimulation of a woman's ovulatory process, for the purpose of removal of an ovum or ova (egg or eggs) from the woman's ovaries. It also includes the assessment of semen quality suitable enough to fertilise the ovum or ova in a liquid medium in a laboratory. The fertilised egg (zygote) undergoes embryo culture for 2–6 days before transfer to the same or another woman's uterus. There are other complex molecular aspects of IVF known as the preimplantation genetic diagnosis (PGD) which is carried out to rule out presence of genetic disorders, as well as egg donation or surrogacy compatibility. The IVF process is a multimillion naira/dollar medical technology. Unlike the simpler process of artificial insemination -- in which sperm is placed in the uterus and conception happens otherwise normally -- IVF involves combining eggs and sperm outside the body in a laboratory. Once an embryo or embryos form, they are then placed in the uterus. IVF is a complex and expensive procedure; only a few couples with infertility seek it out either as a result of religion, culture, ignorance, fear, cost or stigmatisation. The Nigerian IVF system is still an emerging domain, with most of the activities of the IVF technology providers still highly confidential making it difficult to ascertain the challenges, successes and failures of the Nigerian IVF system.

## Keywords

Invitro Fertilisation, Assisted, Reproduction, Sperm, Egg, Nigeria

## 1. Introduction

Invitro fertilisation (IVF) is a system of fertilisation where an egg is combined with sperm outside the body, invitro ("in glass"). It involves monitoring and stimulating a woman's ovulatory process, removing an ovum or ova (egg or eggs) from the woman's ovaries and letting sperm fertilise them in a liquid in a laboratory. The fertilised egg (zygote) undergoes embryo culture for 2–6 days, and is then transferred to the same or another woman's uterus, with the intention of establishing a successful pregnancy. IVF is a type of assisted reproductive technology used for infertility treatment and gestational surrogacy, in which a fertilised egg is implanted into a surrogate's uterus and the resulting child, is genetically unrelated to the surrogate. Some countries banned or otherwise regulate the availability of IVF treatment, giving rise to fertility tourism. Restrictions on availability of IVF include costs and age to carry a healthy pregnancy to term. IVF is mostly attempted if less invasive or expensive options have failed or are unlikely to work [1]. A colloquial term for babies conceived as the result of IVF, "test tube babies", refers to the tube-shaped containers of glass or plastic resin, called *test tubes that* are commonly used in the laboratories. However, IVF is usually performed in the shallower containers called Petri dishes. One IVF method, autologous endometrial co culture, is actually performed on organic material, but is still considered IVF [2].

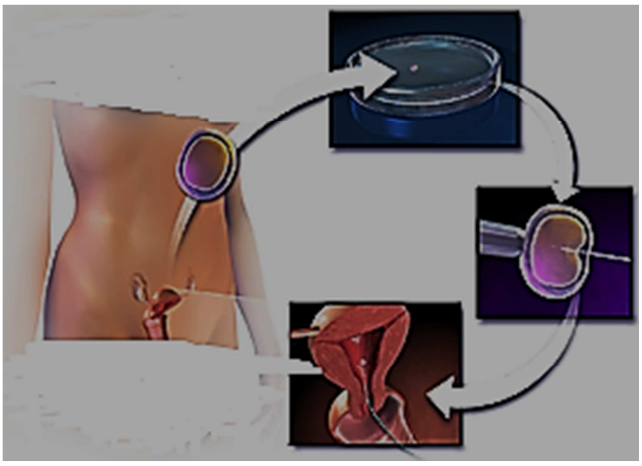

***Figure 1.*** *Schematic of Invitro fertilisation cycle [1].*

### 1.1. History of IVF

It was recorded that in 1977, Steptoe and Edwards successfully did a pioneering conception which led to the birth of first baby conceived by IVF, named Louise Brown on 25 July 1978, in Oldham General Hospital, Greater Manchester, UK. The second documented successful birth occurred in India just 67 days after Louise Brown was born [3]. Louise Brown was born as a result of natural cycle IVF where no stimulation was made. Robert G. Edwards was awarded the Nobel Prize in Physiology or Medicine in 2010, the physiologist who co-developed the treatment together with Patrick Steptoe; Steptoe was not eligible for consideration as the Nobel Prize is not awarded posthumously. With egg donation and IVF, women who are past their reproductive years or have reached menopause can still become pregnant. Adriana Iliescu held the record as the oldest woman to give birth using IVF and donated egg, when she gave birth in 2004 at the age of 66, a record passed in 2006. After the IVF treatment many couples are able to get pregnant without any fertility treatments. In 2012 it was estimated that five million children had been born worldwide using IVF and other assisted reproduction techniques.

In Nigeria, the first successful case of IVF led to the birth of '*Olushina Eghosa Oluwaremilekun'* who was born to the family of one Pius and Stella Oni after five years of research by Osato Giwa-Osagie, an obstetrician and gynecologist and Oladapo Ashiru, an endocrinologist. Pius and Stella Oni were childless for 9 years after marriage in 1980, which is a cultural challenge characterized by stigmatization in Nigeria [4].

IVF technology in Nigeria has been deployed in several cases such as overcoming female infertility due to problems with the fallopian tubes, making in-vivo fertilisation difficult. It has also assisted in male infertility, in those cases where there is a defect in sperm quality; in such situations intracytoplasmic sperm injection (ICSI) may be used, where a sperm cell is injected directly into the egg cell. This is used when sperm has difficulty penetrating the egg, and in these cases the partner's or a donor's sperm may be used [1]. IVF has been deployed in cases of unexplained infertility for women that have not conceived after 2 years of regular unprotected sexual intercourse, although married females in Nigeria above the age of 35 years have been observed to procure IVF less than two years of regular unprotected sexual intercourse.

IVF is also considered suitable in cases where any of its expansions is of interest, that is, a procedure that is usually not necessary for the IVF procedure itself, but would be virtually impossible or technically difficult to perform without concomitantly performing methods of IVF. Such expansions include preimplantation genetic diagnosis (PGD) to rule out presence of genetic disorders, as well as egg donation or surrogacy where the woman providing the egg isn't the same who will carry the pregnancy to term [2], although it is not a well-known documented practice in Nigeria.

### 1.2. General Biomarkers That Affect the Pregnancy Chances of IVF Include

High Antral follicle count and higher levels of Anti-Müllerian hormone could result in higher chances of pregnancy [5], as well as of live birth after IVF, even after adjusting for age [6]. Factors of semen quality for the sperm provider [7] could increase the chances of a successful IVF outcome. A study has shown that women with ovary-specific FMR1 genotypes including *het-norm/low* have significantly decreased pregnancy chances in IVF [8].

Progesterone elevation (PE) on the day of induction of final maturation is associated with lower pregnancy rates in IVF cycles in women undergoing ovarian stimulation using GnRH analogues and gonadotropins. At this time, compared to a progesterone level below 0.8 ng/ml, a level between 0.8 and 1.1 ng/ml confers an odds ratio of pregnancy of approximately 0.8, and a level between 1.2 and 3.0 ng/ml confers an odds ratio of pregnancy of between 0.6 and 0.7. On the other hand, progesterone elevation does not seem to confer a decreased chance of pregnancy in frozen–thawed cycles and cycles with egg donation [9].

The characteristics of cells from the cumulus oophorus and the *membrana granulosa*, which are easily aspirated during oocyte retrieval, these cells which are closely associated with the oocyte and share the same micro environment, and the rate of expression of certain genes, are associated with higher or lower pregnancy rate [10].

An endometrial thickness (EMT) of less than 7 mm has been shown to decrease the pregnancy rate by an odds ratio of approximately 0.4 compared to an EMT of over 7 mm. However, such low thickness rarely occurs, and any routine use of this parameter is regarded as not justified [11].

### 1.3. Other Known Determinants of Outcome of IVF Include

Tobacco smoking reduces the chances of IVF producing a live birth by 34% and increases the risk of an IVF pregnancy miscarrying by 30% [12].

A body mass index (BMI) over 27 causes a 33% decrease in likelihood to have a live birth after the first cycle of IVF, compared to those with a BMI between 20 and 27. Also, pregnant women who are obese have higher rates of miscarriage, gestational diabetes, hypertension, thrombo-embolism and problems during delivery, as well as leading to an increased risk of fetal congenital abnormality. Ideal body mass index is 19–30. Salpingectomy or laparoscopic tubal occlusion before IVF treatment increases chances for women with hydrosalpinges. Success with previous pregnancy and/or live birth increases chances [12].

The number of embryos transferred (the fewer the better) in the treatment cycle, Embryo quality and Low alcohol/caffeine intake has been shown to increase success rate. Some studies also suggest the autoimmune disease may also play a role in decreasing IVF success rates by interfering with proper implantation of the embryo after transfer [8]. Aspirin is sometimes prescribed to women for the purpose of increasing the chances of conception by IVF, but as of 2016 there was no evidence to show that it is safe and effective [13-14]. For women, intake of antioxidants (such as N-acetyl-cysteine, melatonin, vitamin A, vitamin C, vitamin E, folic acid, myo-inositol, zinc or selenium) has not been associated with a significantly increased live birth rate or clinical pregnancy rate in IVF according to Cochrane reviews. The review found that oral antioxidants given to men in couples with male factor or unexplained subfertility may improve live birth rates, but more evidence is needed [15].

A Cochrane review in 2015 explained that the result that there is no evidence identified regarding the effect of pre-conception lifestyle advice on the chance of a live birth outcome [15].

## 2. Method

IVF could literarily be performed by collecting the contents from a woman's fallopian tubes or uterus after natural ovulation, mixing it with sperm, and reinserting the fertilised ova into the uterus. However, without additional techniques, the chances of pregnancy would be extremely small [14].

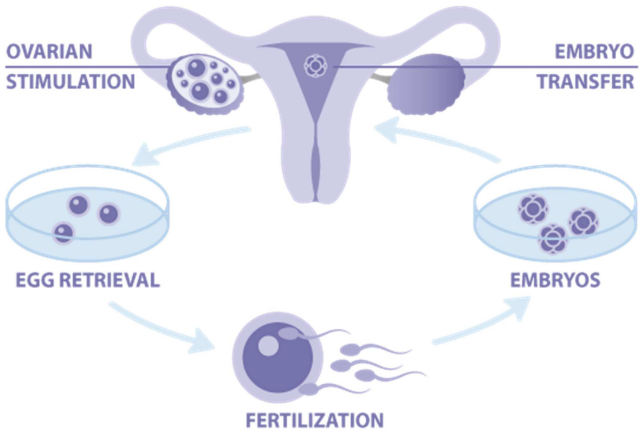


***Figure 2.*** *Schematic diagram of IVF method.*

The additional techniques that are routinely used in IVF include ovarian hyperstimulation to generate multiple eggs or ultrasound-guided transvaginal oocyte retrieval directly from the ovaries; after which the ova and sperm are prepared, as well as culture and selection of resultant embryos before embryo transfer into a uterus [14].

### 2.1. Ovarian Hyperstimulation

Ovarian hyperstimulation is the stimulation to induce development of multiple follicles of the ovaries. It should start with response prediction by e.g. age, antral follicle count and level of anti-Müllerian hormone. The resulting prediction of e.g. poor or hyper-response to ovarian hyperstimulation determines the protocol and dosage for ovarian hyperstimulation [16].

Ovarian hyperstimulation also includes suppression of spontaneous ovulation, for which two main methods are available: Using a (usually longer) GnRH agonist protocol or a (usually shorter) GnRH antagonist protocol. In a standard long GnRH agonist protocol the day when hyperstimulation treatment is started and the expected day of later oocyte retrieval can be chosen to conform to personal choice, while in a GnRH antagonist protocol it must be adapted to the spontaneous onset of the previous menstruation. On the other hand, the GnRH antagonist protocol has a lower risk of ovarian hyperstimulation syndrome (OHSS), which is a life-threatening complication [16].

For the ovarian hyperstimulation in itself, injectable gonadotropins (usually FSH analogues) are generally used under close monitoring. Such monitoring frequently checks the estradiol level and, by means of gynecologic ultrasonography, follicular growth. Typically approximately 10 days of injections will be necessary [16].

### 2.2. Recent Advancement in Ovarian Hyperstimulation

Some recent researches have shown the potential benefit of using oral letrozole in combination with gonadotropin stimulation in IVF cycles, with particular emphasis on breast cancer patients going through fertility preservation treatment [17-19]. The main aim for letrozole administration is to reduce serum estrogen concentrations during ovarian stimulation in breast cancer patients. These researches revealed that treatment of breast cancer patients with letrozole and gonadotropins during the entire stimulation process greatly decreased estradiol concentrations as expected but, interestingly, also increased the number of mature oocytes for cryopreservation [20]. For now, only breast cancer patients undergoing IVF treatment have been treated with letrozole during the whole stimulation phase so far. Although a recent review has pointed out that this protocol is likely an excellent treatment for normal responders undergoing IVF to lower the dose of gonadotropins required to obtain adequate numbers of oocytes for fertilization and to keep estrogen levels closer to the physiologic range [21].

### 2.3. Natural Cycle IVF

Some IVF methods have been termed *natural cycle IVF* [22].

1. The method for IVF that makes use of no drugs for ovarian hyperstimulation, while drugs for ovulation suppression may still be used.
2. The method for IVF that makes use of ovarian hyperstimulation, including gonadotropins, but with a GnRH antagonist protocol so that the cycle initiates from natural mechanisms.
3. The Frozen embryo transfer; IVF using ovarian hyperstimulation, followed by embryo cryopreservation, followed by embryo transfer in a later, natural, cycle [23].

This method has been used successfully for women to avoid taking ovarian stimulating drugs with its associated side-effects. HFEA has estimated the live birth rate to be approximately 1.3% per IVF cycle using no hyperstimulation drugs for women aged 40–42 years.

The method of IVF referred to as Mild IVF [24] is a method where a small dose of ovarian stimulating drugs are used for a short duration during a woman's natural cycle aimed at producing 2–7 eggs and creating healthy embryos. This method appears to be advancement in the field to reduce complications and side-effects for women and it is aimed at quality, and not quantity of eggs and embryos. One study comparing a mild treatment (mild ovarian stimulation with GnRH antagonist co-treatment combined with single embryo transfer) to a standard treatment (stimulation with a GnRH agonist long-protocol and transfer of two embryos) came to the conclusion that the proportions of cumulative pregnancies that resulted in term live birth after 1 year were 43.4% with mild treatment and 44.7% with standard treatment [25]. Mild IVF can be cheaper than conventional IVF and with a significantly reduced risk of multiple gestation and OHSS [26].

### 2.4. Final Maturation Induction

When the ovarian follicles have reached a level of development, induction of final oocyte maturation is carried out, generally by an injection of human chorionic gonadotropin (hCG). Commonly, this is known as the "trigger shot." HCG acts as an analogue of luteinising hormone, and ovulation would occur between 38 and 40 hours after a single HCG injection [28], but the egg retrieval is performed at a time usually between 34 and 36 hours after hCG injection, that is, just prior to when the follicles would rupture. This proceeds for scheduling the egg retrieval procedure at a time where the eggs are fully mature. HCG injection confers a risk of ovarian hyperstimulation syndrome. Using a GnRH agonist instead of hCG eliminates most of the risk of ovarian hyperstimulation syndrome, but with a reduced delivery rate if the embryos are transferred fresh. This is the reason why many centers freeze all oocytes or embryos following agonist trigger [29].

### 2.5. Egg Retrieval

In this process, eggs are retrieved from the patient using a Transvaginal technique called Transvaginal oocyte retrieval, involving an ultrasound-guided needle piercing the vaginal wall to reach the ovaries. Through this needle follicles can be aspirated, and the follicular fluid is passed to an embryologist to identify ova. It is common to remove between ten and thirty eggs. The retrieval procedure usually takes between 20 and 40 minutes, depending on the number of mature follicles, and is usually done under conscious sedation or general anaesthesia [26].

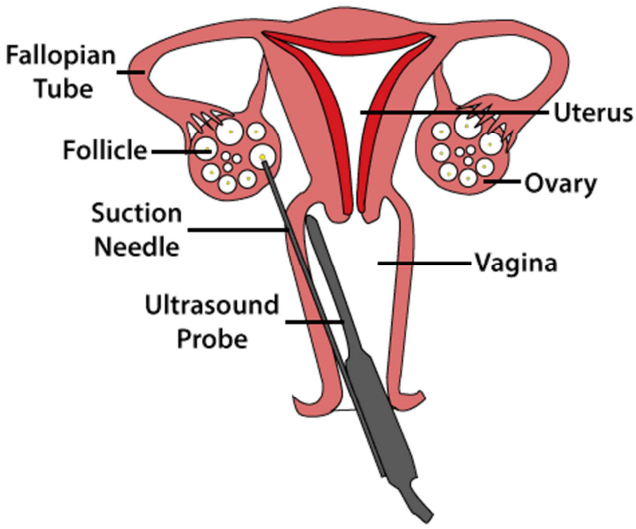


***Figure 3.*** *Transvaginal ovum retrieval [27].*

### 2.6. The Laboratory Aspect of IVF

The Laboratory is the backbone of the Invitro fertilisation process, as more than 50% of the IVF process takes place in the laboratory, although Medical Laboratory Practitioners have not been able to harmonize their functions and potentials in this area as embryologists. There is an urgent need to regulate the Laboratory aspect of embryo culture in addition to the regulation of the Nigerian IVF process in general, so as to avoid un-ethical practices in the laboratory section.

Even before the IVF process, the following tests are required to establish infertility before the IVF process is initiated. These tests include;

#### 2.6.1. Follicle-stimulating Hormone FSH

FSH helps to control a woman's menstrual cycle and the production of eggs. In men, it regulates the production and transportation of sperm. For women, a FSH test is done on the third day of the menstrual cycle and is used to evaluate egg supply. For men, the test is used to determine sperm count [30].

#### 2.6.2. Estradiol

Estradiol is an important form of estrogen. The estradiol test is carried out to measure a woman's ovarian function and to evaluate the quality of the eggs. Like FSH, it is done on

the third day of a woman's menstrual cycle [30].

### 2.6.3. Luteinizing Hormone Level (LH)

In women, LH is linked to ovarian hormone production and egg maturation. In men, it stimulates the hormone testosterone which affects sperm production. An LH test is used to measure a woman's ovarian reserve (egg supply) and a man's sperm count. It is done during a woman's menstrual cycle to see if she is ovulating [30].

### 2.6.4. Serum Progesterone

Progesterone is a female hormone produced by the ovaries during ovulation. It causes the endometrial lining of the uterus to get thicker, making it receptive for a fertilized egg. A serum progesterone test is used to determine if ovulation is occurring. Since progesterone levels increase towards the end of a woman's cycle, the test is done during the luteal phase of the menstrual cycle (just before her period starts) [30].

### 2.6.5. Prolactin

The hormone prolactin is made by the pituitary gland and causes milk production. In women, a prolactin test is done to find out why they are not menstruating, or why they are having infertility problems or abnormal nipple discharge. The test is done in men when there is a lack of sexual desire, difficulty getting an erection, or if there might be a problem with the pituitary gland [30].

### 2.6.6. Androgen

Testosterone is probably the most well-known androgen and it affects the sexual functioning of both men and women. In men, an androgen test is used to find the cause of a low sex drive, the inability to get an erection, or infertility. In women, it is used to determine the cause of irregular periods or a low sex drive [30].

### 2.6.7. Inhibin

The premenopausal ovary loses its ability to secrete the hormone inhibin, which is part of the negative feedback loop. Assay of this hormone may be valuable in assessing ovarian function in older women. Anti Müllerian hormone is another marker of ovarian reserve [30].

### 2.6.8. Thyroid Tests

The thyroid can affect fertility, the ability to become pregnant and maintain a healthy pregnancy, postpartum health, successful breastfeeding, and even the health of your baby.

The thyroid-stimulating hormone (TSH) is tested to detect any problems affecting the thyroid gland. TSH, which is produced by the pituitary gland, is measured first because it is a more sensitive indicator of thyroid function than the thyroid hormone itself [30].

## 2.7. Egg and Sperm Preparation

In the laboratory, the identified eggs are stripped of surrounding cells and prepared for fertilisation. An oocyte selection may be performed prior to fertilisation to select eggs with optimal chances of successful pregnancy.

***Figure 4.*** *Image of oocyte in a petri dish.*

In the meantime, semen is prepared for fertilisation by removing inactive cells and seminal fluid in a process called sperm washing.

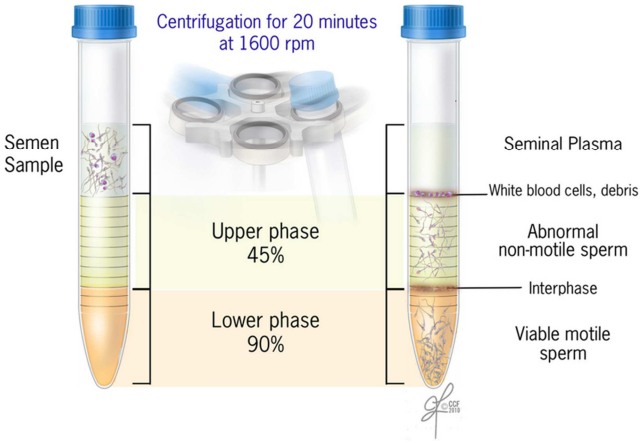


***Figure 5.*** *Seminal fluid processing [26].*

If semen is being provided by a sperm donor, it will usually have been prepared for treatment before being frozen and quarantined, and it will be thawed ready for use [26].

## 2.8. Co-incubation

The sperm and the egg are incubated together at a ratio of about 75,000:1 in a culture media in order for the actual fertilisation to take place. A review in 2013 came to the result that duration of this co-incubation of about 1 to 4 hours results in significantly higher pregnancy rates than 16 to 24 hours. In most cases, the egg will be fertilised during co-incubation and will show two pro-nuclei. In certain situations, such as low sperm count or motility, a single sperm may be injected directly into the egg using intracytoplasmic sperm injection (ICSI). The fertilised egg is passed to a special growth medium and left for about 48 hours until the egg consists of six to eight cells. In gamete intra-fallopian transfer, eggs are removed from the woman and placed in one of the fallopian tubes, along with the man's sperm. This allows fertilisation to take place inside the woman's body. Therefore, this variation is actually an in vivo fertilisation, not in vitro [31]. The most commonly used environmental conditions for human IVF incubators are 5% $CO_2$ in air, 37°C, and 100% relative humidity. $CO_2$ Incubators are the most important equipment for the IVF because the eggs harvested from the ovaries of the patients for fertilization spend most of the time outside the body that is in the incubator. Because

this unit gives the special environment conditions of the body like 37°C (body temperature) and 5-7% $CO_2$ maintain the physiological pH value of the cultural medium used and offer the best conditions for optimal oocyte and embryo development. $CO_2$ is used to regulate the pH level, thus pH is measured and maintained by monitoring and adjusting the concentration of $CO_2$. $CO_2$ and pH has an inverse relationship; as the concentration of $CO_2$ increases, pH level decreases.

## 2.9. Embryo Culture

The main durations of embryo culture are until cleavage stage (day two to four after co-incubation) or the blastocyst stage (day five or six after co-incubation) [32].


***Figure 6.*** *Schematic diagram of embryo culture stages [31].*

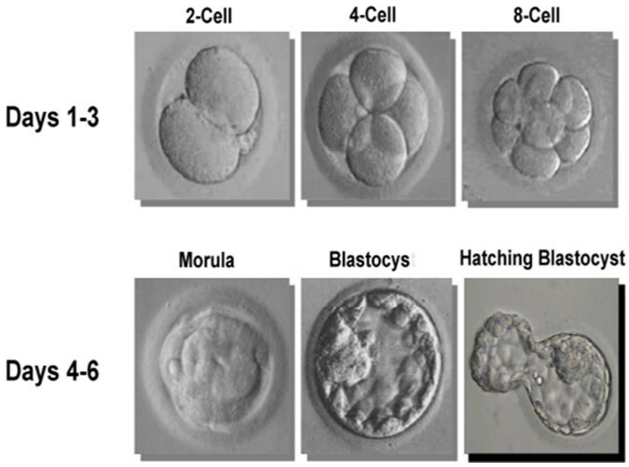


***Figure 7.*** *Microscope image of embryo culture stages [15].*

Embryo culture until the blastocyst stage confers a significant increase in live birth rate per embryo transfer, but also confers a decreased number of embryos available for transfer and embryo cryopreservation, so the cumulative clinical pregnancy rates are increased with cleavage stage transfer. Transfer day two instead of day three after fertilisation has no differences in live birth rate [15]. There are significantly higher odds of preterm birth (odds ratio 1.3) and congenital anomalies (odds ratio 1.3) among births having from embryos cultured until the blastocyst stage compared with cleavage stage [32].

### 2.9.1. Embryo Selection

From various reviews, it was observed that laboratories have developed grading methods to judge oocyte and embryo quality. In order to optimize pregnancy rates, there is significant evidence that a morphological scoring system is the best strategy for the selection of embryos [33]. From the onset of the first time-lapse microscopy system for IVF was approved for clinical use, morphokinetic scoring systems has shown to improve to pregnancy rates further [34]. However, when all different types of time-lapse embryo imaging devices, with or without morphokinetic scoring systems, are compared against conventional embryo assessment for IVF, there is insufficient evidence of a difference in live-birth, pregnancy, stillbirth or miscarriage to choose between them [35].

### 2.9.2. Preimplantation Genetic Screening or Diagnosis

Preimplantation genetic screening (PGS) or preimplantation genetic diagnosis (PGD) has been suggested to be able to be used in IVF to select an embryo that appears to have the greatest chances for successful pregnancy. However, a systematic review and meta-analysis of existing randomised controlled trials came to the result that there is no evidence of a beneficial effect of PGS with cleavage-stage biopsy as measured by live birth rate. On the contrary, for women of advanced maternal age, PGS with cleavage-stage biopsy significantly lowers the live birth rate. Technical drawbacks, such as the invasiveness of the biopsy, and non-representative samples because of mosaicism are the major underlying factors for inefficacy of PGS [36].

Patients who can benefit from PGS/PGD include:

1. Couples who have a family history of inherited disease
2. Couples who want to use gender selection to prevent a gender-linked disease
3. Couples who already have a child with an incurable

disease and need compatible cells from a second healthy child to cure the first, resulting in a "saviour sibling" that matches the sick child in HLA type [37].

PGS screens for numeral chromosomal abnormalities while PGD diagnosis the specific molecular defect of the inherited disease. In both PGS and PGD, individual cells from a pre-embryo, or preferably trophectoderm cells biopsied from a blastocyst, are analysed during the IVF process. Before the transfer of a pre-embryo back to a woman's uterus, one or two cells are removed from the pre-embryos (8-cell stage), or preferably from a blastocyst. These cells are then evaluated for normality.

Typically within one to two days, following completion of the evaluation, only the normal pre-embryos are transferred back to the woman's uterus. Alternatively, a blastocyst can be cryopreserved via vitrification and transferred at a later date to the uterus. In addition, PGS can significantly reduce the risk of multiple pregnancies because fewer embryos, ideally just one, are needed for implantation [36].

It has been observed that additional methods of embryo profiling, such as methods of making comprehensive analyses of up to entire genomes, transcriptomes, proteomes and metabolomes which may be used to score embryos by comparing the patterns with ones that have previously been found among embryos in successful versus unsuccessful pregnancies.

## 3. Extensions of IVF

### 3.1. Intracytoplasmic Sperm Injection (*ICSI*)

Intracytoplasmic sperm injection (*ICSI*) is where a single sperm is injected directly into an egg. Its main usage as an expansion of IVF is to overcome male infertility problems, although it may also be used where eggs cannot easily be penetrated by sperm, and occasionally in conjunction with sperm donation. It can be used in teratozoospermia, since once the egg is fertilised abnormal sperm morphology does not appear to influence blastocyst development or blastocyst morphology [38].

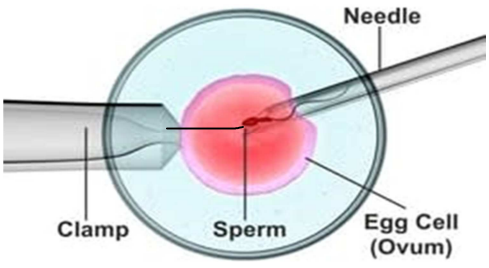


***Figure 8.*** *Schematic description of Intracytoplasmic sperm injection (ICSI).*

### 3.2. Assisted Zona Hatching (AZH)

This can be performed shortly before the embryo is transferred to the uterus. A small opening is made in the outer layer surrounding the egg in order to help the embryo hatch out and aid in the implantation process of the growing embryo [38].

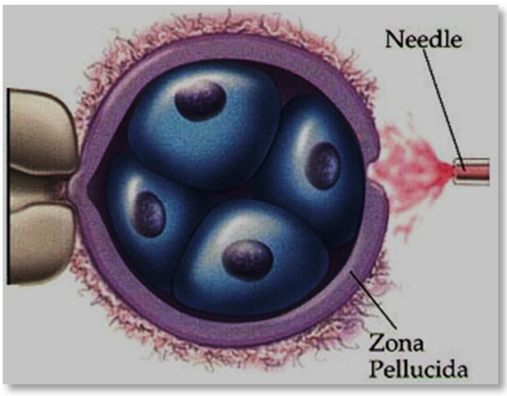


***Figure 9.*** *Assisted zona hatching (AZH) [37].*

In egg donation and embryo donation, the resultant embryo after fertilisation is inserted in another woman than the one providing the eggs. These are resources for women with no eggs due to surgery, chemotherapy, or genetic causes; or with poor egg quality, previously unsuccessful IVF cycles or advanced maternal age. In the egg donor process, eggs are retrieved from a donor's ovaries, fertilised in the laboratory with the sperm from the recipient's partner, and the resulting healthy embryos are returned to the recipient's uterus and in some cases to a surrogate. Although surrogacy is not a popular practice in Nigeria because of lack of public acceptance, chances exist that it is being practiced in the West African country.

In oocyte selection, the oocytes with optimal chances of live birth can be chosen. It can also be used as a means of preimplantation genetic screening.

Embryo splitting can be used for twinning to increase the number of available embryos [39].

Cytoplasmic transfer is where the cytoplasm from a donor egg is injected into an egg with compromised mitochondria. The resulting egg is then fertilised with sperm and implanted in a womb, usually that of the woman who provided the recipient egg and nuclear DNA. Cytoplasmic transfer was created to aid women who experience infertility due to deficient or damaged mitochondria, contained within an egg's cytoplasm [40].

### 3.3. Embryo Transfer

Although this process of Embryo transfer is not carried out by the Laboratory expert (embryologist), Embryos are graded by the Laboratory expert based on the number of cells, evenness of growth and degree of fragmentation. The number to be transferred depends on the number available, the age of the woman and other health and diagnostic factors. In countries such as Canada, the UK, Australia and New Zealand, a maximum of two embryos are transferred except in unusual circumstances. In the UK and according to HFEA regulations, a woman over 40 may have up to three embryos transferred, whereas in the USA, younger women may have many embryos transferred based on individual fertility diagnosis [15]. Unfortunately, there is no publicly available regulation guiding the fixed number of embryos that can be

transferred in Nigeria. Most clinics and country regulatory bodies seek to minimise the risk of pregnancies carrying multiples, as it is not uncommon for more implantations to take than desired. The embryos judged to be the "best" are transferred to the patient's uterus through a thin, plastic catheter, which goes through her vagina and cervix. From participants' interaction in Nigeria, more than one embryo may be passed into the uterus to improve chances of implantation and pregnancy.

### 3.4. Recent Breakthrough in Preimplantation Screening (mtDNA Screening)

A recent research outcome of a scientist Prof Dagan Wells has the potential of elevating the success rate of IVF treatment to 80 per cent globally according to fertility experts. He observed that the levels of a particular type of DNA in a developing embryo are a crucial factor in whether a pregnancy will be successful and a simple test can be used to select the most viable embryos. This development has the potential to revolutionize the success rate of fertility treatment, which currently stands at about 35-40 per cent of IVF cycles resulting in a pregnancy. The new technique focuses on mitochondria, the part of the cell that is its main energy provider and plays a key role during the development of an embryo. They observed that some embryos have excessive levels of mitochondrial DNA (mtDNA) and will consequently not produce a viable pregnancy [41].

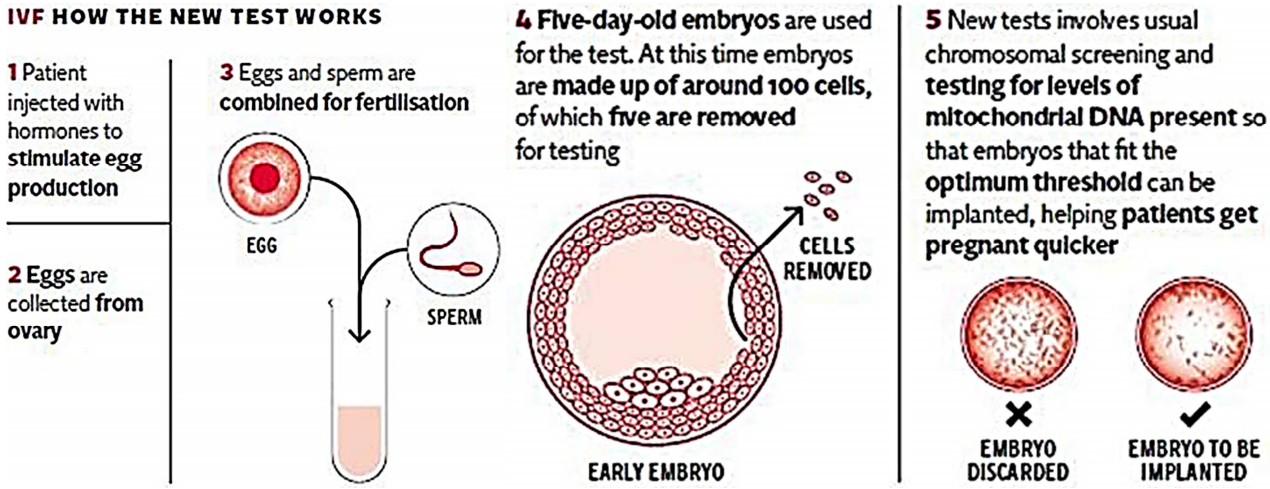


***Figure 10.*** *IVF process for mitochondrial DNA testing as described by Knapton, [40].*

It involves embryos known as blastocyst that have been grown in the laboratory until they are five days old. At this time, embryos are made up of around 100 cells, of which five are removed for testing. In this design, Scientists first test to see if the embryos are chromosomally abnormal - a flaw which affects about half of all embryos. A significant number of embryos have unusually high levels of mitochondrial DNA and have too much of it. Having mtDNA above a certain threshold seems incompatible with implantation of an embryo [42]. It is still unclear why the embryos produce too much mtDNA. But the new technique allows scientists to pinpoint embryos with levels of mtDNA below a certain threshold and implant those, resulting in the very high success rates seen in the New York trial. When available the new test will cost just £200.

### 3.5. Relative Medication

Luteal support is the administration of medication, generally progesterone, progestins or GnRH agonists, to increase the success rate of implantation and early embryogenesis, thereby complementing and/or supporting the function of the corpus luteum. A recent study found out that HCG or progesterone given during the luteal phase may be associated with higher rates of live birth or ongoing pregnancy, although the evidence is not enough to make a conclusion. Co-treatment with GnRH agonists appears to improve outcomes [43], by a live birth rate RD of +16% (95% confidence interval +10 to +22%) [44]. Although growth hormone or aspirin is commonly used as adjunctive medication in IVF no evidence of overall benefit has been observed.

## 4. The Nigerian IVF Practice

The introduction of in-vitro fertilization (IVF) has been a major breakthrough in the health study of conception and reproduction globally. Although IVF is no longer a strange topic in Nigeria the giant of Africa has not been able to print her name among the nations known for research-based innovation in IVF, although some Nigerians in Diaspora may have been involved in major innovative research.

### 4.1. Cost Implication of IVF in Nigeria

Infertility is the biggest treat to marriages especially in a continent like Africa where children are seen as the finishing touches to a marriage. In countries in Africa it is a national health problem affecting 10-32% of couples on the average [45]. Studies in Nigeria have shown the prevalence rate of infertility to be about 25%, with 1 in 4 women of child-bearing age having challenges in conception. In Nigeria more

centres continue to emanate to make sure that the dire needs of searching couples are attended to resulting in a lucrative industry in Nigeria were the average cost ranges from N870,000 to N1,760,000. The number of cycles is a vital factor that is considered when calculating the cost of IVF treatment in Nigeria. For example, at a reputable IVF centre in the country, the cost depends on the number of cycle, as the price can get to as much as N3,600,000 (about ten thousand US dollars) with multiple cycles [46].

## 4.2. The Challenges of the IVF Process in Nigeria

### 4.2.1. Exploitation

The activities of IVF centres in Nigeria are shrouded in so much secrecy, with poor documentation of patient outcomes, implantation failures, and the exact financial implication of procuring IVF. This has been fueled largely by the presence of little or virtually no regulation. Ola [46] and Osazuwa [48] agreed that there is a despicable lack of regulation for IVF in the country which makes couples seeking the treatment defenseless in the face of all sorts of exploitative practices. Because IVF is usually a last resort for couples with reproductive challenges it makes them vulnerable to possible irregularities and malpractices. Hence, an overwhelming need for IVF regulation.

### 4.2.2. Moral Pitfalls

Because of the improper or absence of effective regulation, it can be difficult to ascertain the competency of those who claim to give the specialised treatment, or whether those involved in the IVF laboratory are actually qualified to do so. Though there are documented researchers in the line of medical care who have dedicated time and resources towards IVF specialisation, the likelihood of persons without proper specialisation in IVF exploiting unsuspecting couples exists [45].

Because the industry is widely unregulated it is prone to serious abuses in the desire of practitioners to obtain profit. For instance, in 2008, a California physician transferred 12 embryos to a woman who gave birth to octuplets (see Suleman octuplets), several cases of quadruplets, triplets from IVF abound in Nigeria with loud applaud from the health sector and general public with no questions asked, and maternal well being considered, hence many health practitioners are willing to seriously endanger the health and even the lives of these women in order to gain money. The IVF industry can thus be seen as an example of what social scientists are describing as an increasing trend towards a market-driven construction of health, medicine and the human body [49]. The industry has been accused of making unscientific claims, and distorting facts relating to infertility, in particular through widely exaggerated claims about how common infertility is in society, in an attempt to get as many couples as possible and as soon as possible to try treatments (rather than trying to conceive naturally for a longer time). This risks removing infertility from its social context and reducing the experience to a simple biological malfunction, which not only *can* be treated through bio-medical procedures, but *should* be treated by them [50]. Necessary moral pitfalls need to be carefully straightened out to put in motion a national dialogue of all health stakeholders involved which should lead to a regulatory framework.

### 4.2.3. Leftover Embryos or Eggs

There may be leftover embryos or eggs from IVF procedures if the woman for whom they were originally created has successfully carried one or more pregnancies to term. With the woman's or couple's permission, these may be donated to help other women or couples as a means of third party reproduction. In embryo donation, these extra embryos are given to other couples or women for transfer with the goal of producing a successful pregnancy. The resulting child is considered the child of the woman who carries it and gives birth, and not the child of the donor, the same as occurs with egg donation or sperm donation [40]. This aspect of IVF in Nigeria is either widely undeveloped or probably being carried out under questionable circumstances, as little or no information on usage of leftover embryos or eggs as well as third party reproduction activities is available to the public. Other possible alternatives to donating unused embryos could be; destroying them, keeping them frozen indefinitely, or donating them for use in research after thorough ethical considerations.

## 4.3. Religious Point of View in IVF

Africa is a Religious continent, and Nigeria being the most populated African country has a rich religious environment. In the Roman Catholic Church, all kinds of assisted reproductive technology and artificial contraception are opposed, asserting that they separate the procreative goal of marital sex from the goal of uniting married couples. The Catholic Church permits the use of a small number of reproductive technologies and contraceptive methods like natural family planning, which involves charting ovulation times. The church allows other forms of reproductive technologies that allow conception to take place from normative sexual intercourse, such as a fertility lubricant. Pope Benedict XVI had publicly re-emphasized the Catholic Church's opposition to In vitro fertilisation, claiming it replaces love between a husband and wife [51]. The Catechism of the Catholic Church claims that Natural law teaches that reproduction has an "inseparable connection" to sexual union of married couples [52]. In addition, the church opposes IVF because it might cause disposal of embryos; in Catholicism, an embryo is viewed as an individual with a soul that must be treated as a person. The Catholic Church maintains that it is not objectively evil to be infertile, and advocates adoption as an option for such couples who still wish to have children. This religious stand could be a major reason for the absolute discretion and refusal to admit to IVF assistance by faithful, hence blackmailed into silence when exploited by IVF providers. Religious views of Pentecostal Christians in Nigeria and Africa in general is positive, as there is the popular belief that “Children are given by God”

regardless of the role of assisted reproduction technology.

Regarding the response to IVF of Islam, the conclusions of Gad El-Hak Ali Gad El-Hak's ART fatwa include that:

1. IVF of an egg from the wife with the sperm of her husband and the transfer of the fertilised egg back to the uterus of the wife is allowed, provided that the procedure is indicated for a medical reason and is carried out by an expert physician.
2. Since marriage is a contract between the wife and husband during the span of their marriage, no third party should intrude into the marital functions of sex and procreation. This means that a third party donor is not acceptable, whether he or she is providing sperm, eggs, embryos, or a uterus. The use of a third party is tantamount to *zina*, or adultery [53].

### 4.4. Society and Culture

In sub-Saharan Africa largely, people choose to foster their children to infertile women. IVF enables these infertile women to have their own children, which impose new ideals to a culture in which fostering children are seen as both natural and culturally important. Many infertile women are able to earn more respect in their society by taking care of the children of other mothers, and this may be lost if they choose to use IVF instead. As IVF is seen as unnatural, it may even hinder their societal position as opposed to making them equal with fertile women. It is also economically advantageous for infertile women to raise foster children as it gives these children greater ability to access resources that are important for their development and also aids the development of their society at large [54] leading to a reduction in the rate of child labour and out of school children in Nigeria and Africa at large.

## 5. Conclusion

Today, invitro fertilization (IVF) is practically a household word. But not so long ago, it was a mysterious procedure for infertility that produced what were then known as "test-tube babies." Unlike the simpler process of artificial insemination in which sperm is placed in the uterus and conception happens otherwise normally IVF involves combining eggs and sperm outside the body in a laboratory. Once an embryo or embryos form, they are then placed in the uterus. IVF is a complex and expensive procedure; only a few couples with infertility seek it out either as a result of culture, ignorance, fear, cost or stigmatisation. We recommend the immediate Government regulation of IVF in Nigeria in order to minimize unethical practices and exploitation, and also public enlightenment to endear the IVF procedure to the minds of the African populace so as to avoid stigmatisation of those conceived by IVF; When this is done those seeking supportive reproduction such as IVF will be open about their decision in seeking affordable pricing and medical-legal help thereby avoiding exploitation by IVF providers.

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