The Supply Chain of Reproductive Biotechnology Increases the Chances of Successfully Conceiving in Women

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Abstract:

Reproductive biotechnology Supply chain has changed the way the world repopulates. Those who have been diagnosed as infertile have opportunities through reproductive technology to have a child. Invitro fertilization has been marked as one of the most sufficient assisted reproductive technologies. Many infertile couples seek this treatment to increase their chances of conceiving. With any treatment comes the possibility of poor outcomes. This paper is to explore the factors that can alter the success rate of in-vitro fertilization. With conception women already have challenging times, with reproductive technology it gives women an option to have a better success rate of conception. Elective oocyte freezing, fertility preservation, and preimplantation genetic screening of embryos to stop transmission of severe genetic abnormalities are further justifications for using assisted reproductive technology. With recent studies, it is shown that with assisted reproductive technology is constantly advancing with new methods to ensure that women are able to have a high success rate with their conception. It is shown throughout this review, that reproductive technology has advanced, and will be an option to women to have a high success rate with conceiving.

Keywords: In-vitro Fertilization (IVF), Advanced maternal, embryo, racial disparity, clinical birth rate (CBR).

1. Background

In a previous study conducted on Danish women using Assisted Reproduction Technology (ART). Assisted reproduction technology (ART) has a minor but rapidly increasing influence on childbearing trends in advance societies [28]. Sobotka and their colleagues state that, the spread of ART has also led to rise in the number of women having children at extremely late childbearing ages, in some cases after menopause, and has repeatedly set new record-high childbearing ages [28]. The rising proportion of births conceived through assisted reproduction, coupled with a long-term trend toward later childbearing,
indicates ART is likely to become more important for future fertility trends in many low-fertility countries [28]. Assisted reproduction technology can partly offset the negative effect of delayed childbearing on aggregate fertility rates among women below age 40 [28]. Sobotka et al. studied a previous study conducted in 2004 and they state that, for women who postpone their first attempt to achieve pregnancy from age 30 to age 35, the use in vitro fertilization (IVF) can make up for half of the births “lost” due to age-related declines in conception rate [28]. In order to complete their study, the team linked births and population records that were given to them form the Danish National Board of Health on IVF treatments. The team states that their study suggests that the continuation of stable fertility will be partly sustained by a rise in the use of assisted reproduction [28]. With the research conducted by Sobotka and their colleagues, they were able to find that, the projected proportion of children born as a result of ART treatment shows a substantial increase from 2.1 percent among women born in 1965 to 4-5 percent among women born in 1978, with an estimated net effect of ART (as compared with the hypothetical situation where no ART treatment is available) on the order of 3-4 percent (2008). The team finds that the spread of ART is attractable to the combination of several facts: continuing easy accessibility of ART treatments and public awareness about this option, rising infertility linked to the continue postponement of childbearing, and more frequent use of ART among both younger infertile women and mothers trying to have another child [28].

In another study conducted by Bergh and their colleagues they studied genetics and assisted reproduction technology. In the years of development of in vitro fertilization (IVF) and more, methods to study the human genome have also advanced enabling the identification of a growing number of individual genes and thereby the molecular genetic etiology of many inherited diseases [1]. Similar to the research team before, Bergh and their colleagues find that, when treating these patients, the new assisted reproductive technology (ART) methods have potentially enabled the inheritance of infertility and certain other genetic conditions to the offspring [1]. The developments in ART and genetics have resulted in advanced knowledge of the genetic etiology in infertility. Moreover, genetic testing methods are increasingly exploited in ART and vice versa [1]. The team found that preimplantation genetic diagnosis (PGD) is a perfect example of using assisted reproductive technology (ART). They also found that Aneuploidy screening (AS) can improve IVF results. PGD is an option if termination of a pregnancy is not acceptable for the couples. In these situations, the patient needs IVF treatment in order to perform PGD regardless of normal fertility. PGD is particularly suitable when a couple need IVF or ICSI treatment for infertility and there is a risk of genetic disease in the offspring, a situation that arises in chromosome translocations associated with male infertility [1].

2. Introduction

In recent years, the idea and use of biotechnology have increased. In the medical field, biotechnology is used to provide treatments for various conditions and disorders. Biotechnology was created by using cells to develop research to further
understand the human body. To be specific, scientists’ study different cells and their behavior to formulate a treatment to fix a particular problem at hand. The example that will be described in this paper is fertility in women. Fertility is the ability of a multicellular organism to reproduce. Through sexual reproduction, fertile beings can reproduce offspring with similar genetic traits to their parents. Although all multicellular organisms, specifically humans, have reproductive organs, all cannot reproduce. When an organism is unable to reproduce, it is said to be infertile. It is possible for some humans not to be genuinely sterile but still have difficulty conceiving. Women can benefit from biotechnology in this area. Biotechnology-based fertility treatment increases a woman's chances of successfully getting pregnant. Across the globe, over 5 million newborns have been a result of reproductive biotechnology [41].

Medical biotechnology has been used to discover and develop recombinant DNA technology, genetic testing, stem cell research, and the HPV vaccine. The medical field is just one area out of many that biotechnology is used. Agriculture, industry, and even animals have ties to biotechnology. Biotechnology is divided into six categories. The main subfields are medical, agricultural, industrial, marine, food, and environmental. Through years of research and study, biotechnology has expanded into these fields. All things relating to biotechnology have the basis of altering DNA or manipulating cells through other means.

One of the branches that biotechnology has impacted is the medical field. Advances in medical biotechnology research have brought about more information on conditions and diseases and treatment processes to resolve said issues [2]. This makes it possible for reproductive technologies to emerge. Reproductive biotechnologies have been developed since the late 1900s. The first instance that made it commonly known was in the 70s, the first live birth through in vitro fertilization [23]. Assisted reproductive technologies, or ART, are how biotechnology connects to infertility. In vitro fertilization is one of the techniques used in ART and through ART, women can conceive while being infertile.

Infertility is the issue that most researchers are trying to combat. Specifically, in humans, infertility is ruled when an individual cannot conceive after a year of unprotected intercourse [22]. Infertility can impact women of different ages, weights, and ethnicities. Eight to twelve percent of couples who wish to conceive face infertility [34]. In Vitro Fertilization specifically combats fertility and can be especially useful in biotechnology.

In-vitro fertilization or IVF is a process where an egg (oocyte) is fertilized outside of the uterus and then transferred back into the individual's body to induce pregnancy potentially” [30]. The egg is fertilized in a Petri dish, hence the term “in vitro.” As stated before, the first successful IVF birth marked the possibility for IVF to be a successful treatment in many infertile women. Since then, IVF has been successful in 50% of cases, specifically in women younger than 35 [10]. The reasoning behind using in-vitro fertilization in women may vary. Some women are incapable of using their eggs, have internal disorders, and have cancer or
other illnesses that lower their chances of conceiving through intercourse [6]. So, if a woman does not produce oocytes (eggs) in quality or a substantial quantity, in vitro fertilization still makes it possible to conceive. Donor eggs can be used, or even eggs that have been cryopreserved.

To explain the cycle of IVF, let us use the patient Mary. Mary has to first go through an ovarian simulation. In most IVF cycles, 10-20 oocytes are recovered through ovarian stimulation. The two common hormones to prompt ovulation are a long luteal GnRH agonist (GnRHa) or a GnRH. [6] Mary would have to undergo taking these hormones so her body can start the process of ovulation. The mature oocytes are retrieved and then fertilized, and in 3 to 5 days, are transferred into our patient Mary. Mary receives the embryos via transabdominal ultrasound guidance into the uterus by a catheter passing through the cervix [6]. This same process would be used if Mary were to receive donor eggs. Once the embryos have been inserted, Mary will have to wait two weeks to confirm whether she is pregnant. This is just one cycle of IVF. Most women must go through multiple cycles to become pregnant successfully.

Although IVF treatment has been proven successful, individuals and a combination of factors can alter the success rate. These factors can be from the individual receiving treatment, the technician administering treatment, or technological factors. The factors that will be explored are of the individual. Maternal age, state of the egg, and the patient's ethnicity are factors that can significantly change the success rate of clinical pregnancy and live birth through IVF.

3. Methods

Due to the internal and external factors that affect IVF treatment, developments have been made to combat this. Those who have multiple IVF failures can use physical endometrial manipulation. This can be due to embryos failing to implant [12]. Poor IVF outcomes can also be due to endometrial receptivity disorders [9]. A specific study used tubal hydration to achieve this. According to the study, those who underwent this special treatment had higher clinical and live birth rates [3]. Another study used endometrial receptivity analysis (ERA), a molecular diagnostic method. Out of all the women who participated, 69.2% showed clinical pregnancy [16]. Cryopreservation is used for women who want to save their eggs for future use instead of using the eggs they will have in said future. Frozen embryos have an exceedingly high survival rate once thawed. Many verified blastocysts have a 95% survival rate [8]. As stated before, frozen eggs yield better clinical and pregnancy rates for IVF treatment. Some solutions are still being studied, such as assisted hatching. A study done in 1998 found no significant data that supports assisted hatching helping individuals with advanced maternal age obtain clinical pregnancy [18].

One study took a total of 530 cycles of IVF in women and divided them based on the state of the egg. Three hundred fifty-one eggs were used in one group, and 179 frozen-thawed eggs were used in another. All subjects went through controlled ovarian simulation with a follicle-stimulating hormone. For the fresh cycles, the Embryos are evaluated three days after oocyte retrieval and then transferred. For the frozen-thawed embryos, they are cryopreserved on day 3. The clinical
pregnancy rate resulted in 35.9% using fresh embryos and 46.6% using frozen-thawed embryos. The ongoing pregnancy rate is 31.1% using fresh embryos and 39.7% using frozen embryos [24].

4. Main Body

4.1 Age and Effective IVF Treatment

Age can be a limiting factor if IVF treatments are more or less successful. Based on the researched studies, the connection between the age of the Female and the IVF success rate will be determined. The number of oocytes produced, and the quality of the oocytes can be altered by the patient's age [32]. The quality of the oocyte is the result rather than the quantity. A study was done in 1997 to determine whether the age-related decline in fertility is due to degenerative oocytes or aneuploidy [19]. The study took 155 women, ages ranging from 24-44, to undergo 158 cycles of IVF. The women chosen were divided into four groups based on age. After IVF treatment, data were collected on each group and compared. The study concluded that the rate of oocyte chromosome degeneration increased as the age group increased. Group 1, aged less or equal to 34 years, had a rate of 23.7%. Group 2, aged 35-39, had a rate of 52.0%. Group 3, aged more or equal to 40 years, had a rate of 95.8%. Group three, which held the oldest patients out of the study, also had the highest rate of degeneration.

So, for the percentage of advanced-aged patients who successfully conceive through IVF, there seem to be problems due to age later in the pregnancy. Specifically, when it is time for the patient to give birth. A study was done to report the cumulative live birth rate (CLBR) after IVF treatment based on the number of embryos required to achieve a live birth in women 35 and older [39]. The older the woman, the lesser chances of live birth. According to the study, women younger than 42 had a CLBR of 50% after six embryo transfers to reach live birth (ETRL). In women older than 42, the CLBR is half of the former (25%). This establishes the connection between the chances of live birth and advanced age. To be clear, advanced age does not rule out the possibility of having a live birth. Advanced age decreases the possibility. Women of a younger maternal age have higher chances of live birth after successful IVF treatments. In this study, half of the women had a CLBR of 50%, which was way higher than their older counterparts [39]. The lower CLBR for women older than 42 may be connected to producing lesser-quality oocytes.

As a woman ages, her fertility decreases. As stated before, the decline in fertility is the lower number of oocytes produced and the quality of oocytes. Chromosomal aneuploidy, chromosomal errors, fragmentation, and mitochondrial dysfunction all contribute to the lesser quality of oocytes [39]. Based on the results of a study done to discover the impact of maternal aging on human cumulus cell, the oocyte in a female is affected because of mitochondrial and gene expression mishaps in natural aging. The extracellular matrix protein, Versican (VCAN) mRNA expression, is higher in CC from oocytes that produce a live birth.

Older women show a lower VCAN expression, thus explaining why the quality of the oocyte determines if a live birth is
possible [20]. Like any other cell, the mitochondrion is how a cell obtains energy by producing ATP. Oocytes also use ATP to conduct their required functions. In aging women, there is "increased mitochondrial damage and a decrease in…ATP production" [20]. This mitochondrial damage is due to mitochondrial deletions, specifically Mitochondrial DNA (mtDNA). These deletions also occur in other aging cells, not just oocytes or granulosa cells. Tissues such as cardiac [14] and skeletal [21] can experience deletion. A study explored these deletions in granulosa cells between younger women and women of advanced reproductive age undergoing IVF treatments [25]. Twelve women older than 38 and 12 younger than 34 granulosa cells were studied for mtDNA deletions. As these women underwent IVF, their cells were analyzed using a polymerase chain reaction analysis. 7 out of 10 women in the <34 age group exhibited normal mtDNA. The women in the older age group all exhibited mtDNA deletion. In contrast, none of the women in the >38 age group showed normal mtDNA [25]. This study explains that women of advanced maternal age have more difficulty getting pregnant, staying pregnant, and delivering through IVF due to their lower quality of oocytes.

Ultimately, based on the studies explained, age is a relative factor in the success of IVF treatments. Younger women have the best results due to their better quality and quantity of oocytes. This results in a better chance of having a successful live birth. Women of advanced maternal age will often run into the issue of having lower-quality oocytes when using their eggs. I suggest older women use donor eggs for IVF treatment rather than their own. Using their own is possible but risky.

The chances of live birth are low, and the fetus may be damaged because of the lower quality of the oocyte. Resulting in potential health challenges for the child. But the older a woman is the fewer chances of IVF being a successful route to conceiving.

4.2 State of Oocyte

During IVF, mothers can choose between using their eggs or eggs from other individuals. These eggs can either be fresh or frozen eggs that need to be thawed. The frozen eggs can come from donor eggs or the individual. Based on researched clinical trials, using frozen oocytes can increase the outcome of live birth rates and fewer prenatal complications.

One study took a total of 530 cycles of IVF in women and divided them based on the state of the egg. Three hundred fifty-one eggs were used in one group, and 179 frozen-thawed eggs were used in another. All subjects went through controlled ovarian simulation with a follicle-stimulating hormone. For the fresh cycles, the Embryos are evaluated three days after oocyte retrieval and then transferred. For the frozen-thawed embryos, they are cryopreserved on day 3. The clinical pregnancy rate resulted in 35.9% using fresh embryos and 46.6% using frozen-thawed embryos. The ongoing pregnancy rate is 31.1% using fresh embryos and 39.7% using frozen embryos [24].

Though it is not a significant difference, it is still appropriate to state that using frozen embryos yields a better outcome. Another similar study yielded comparable results. A 2017 study examined the outcomes of using fresh vs. frozen embryos during embryo transfer. The study took 179 women subjected to IVF and put them in 2
randomized groups [40]. This particular study measured ongoing pregnancy rates and live birth rates. For this study, the ongoing pregnancy rate was 80% using frozen embryos and 61% using fresh embryos [7]. Like the previous study, the ongoing pregnancy rate was higher for individuals who used frozen rather than fresh embryos. The difference between these two studies is that the 2017 study had more significant results between the two states of embryos, while the other had a less significant difference [40]. Both suggest that using frozen embryos increases the ongoing pregnancy rate, meaning the pregnancy has completed 20 or more weeks of gestation [31].

As stated before, these results are not significant. Nevertheless, it still supports why using frozen embryos is best. Not only is using frozen embryos better for women without certain infertility disorders, but it is also better for women with infertility disorders such as PCOS. Both trials were done on women who do not have polycystic ovary syndrome (PCOS). One study specifically mentioned using individuals who did not have the syndrome [33]. Like the other clinical trials, these yielded related results as well. Another clinical trial especially used women with PCOS. Interestingly this trial also had positive results when using frozen embryos rather than fresh ones, with a live birth rate being 49.3% for frozen embryos and 42.0% for fresh ones [5].

4.3 Racial Disparities in IVF treatment

Assisted reproductive technology practices such as IVF have medical factors that can affect the success of said treatment. As previously discussed, age, state of the oocyte, and use of growth hormones impact whether or not IVF is effective. Another factor that affects the IVF treatment of the individual is race. Most of the women studied in the stated clinical trials are white. The outcomes of these studies apply to white women, specifically White women who can afford the cost of treatment, not minorities. However, there have been recent studies that explicitly explore these disparities and put an emphasis on minority subjects.

A study done in 2000 concluded that white women have better IVF outcomes than black women. The pool of minority women in this trial was small (37 women), which may be a factor in the lower percentages. After 121 cycles of IVF, white women had a pregnancy rate of 42.2% while black women who had undergone 47 cycles had a lower rate of 23.4% [27]. Another study in 2007 presented lower results for black women. A live birth rate of 26.3% for white women and 18.7% for black women [26].

The studies show a pattern; black women have lower rates during IVF. Low birth and pregnancy rates are the main outcomes for minority women who undergo IVF. A more recent clinical trial generated comparable results to support this conclusion further. This study had 40,545 patients. A bigger pool yields more accurate results. This study also was inclusive of Hispanic/Latino and Asian women. Even with the bigger pool and more ethnicities implemented, black women still had the lowest clinical pregnancy rate of 45% [13]. Factors such as body mass index and
tubal occlusion may contribute to these low percentages [17].

A pool of white, black, and Asian women underwent a study to explore racial disparities in frozen embryo transfers. There were significant differences in the live birth rate between the three groups. White women had the highest percentage, at 52.36%. Asian women had a percentage of 44.19%. Black women had the lowest percentage, 25.81% [15]. Even using frozen embryos, proven to yield better results, black women still have lower rates than other ethnicities. If a black woman were to obtain pregnancy through IVF, they are five times more likely to have a preterm birth [36].

4.4 Supply Chain/ RFID

In a recent study by Zhan and their colleagues, the environmental exposure that emerges alternatives of per and polyfluoralkyl substances in women diagnosed with fertility. A broad family of synthetic aliphatic hydrocarbons with at least one carbon atom called per- and polyfluoroalkyl substances (PFAS) are created when all hydrogen atoms on the carbon chain are switched out for fluorine atoms [38]. In women of reproductive age, polycystic ovarian syndrome (PCOS) is a prevalent endocrine condition [38]. It accounts for 80% of female anovulatory infertility and is one of the most frequent causes of infertility [38]. Endocrine-disrupting chemicals (EDCs) may be one of the most significant environmental drivers of PCOS, despite the fact that its etiology is still being researched [38]. Telomerization and electrochemical fluorination techniques, which frequently entail the scission and restructuring of carbon chains, are the main methods for producing PFAS [38].

Tariq and their colleagues authored their research on how leveraging technology and supply chain will improve family planning coordination. This research was based in Pakistan [29]. In low- and middle-income countries, there were an estimated 214 million women of reproductive age who did not have access to contraception in 2017, despite advances in the usage of contraceptives [29]. Reproductive health has long placed a high priority on reducing the unmet need for modern contraception by expanding access to and availability of contraceptives [29]. Provincial departments of population welfare were transferred to provincial administrative supervision and administrative independence from the Ministry of Population and Welfare in 2010 [29]. The processes that go into getting a product from the supplier to the client are included in supply chain management. Ineffective distribution systems and a lack of institutionalized LMISs have been cited as major obstacles to efficient contraception supply chains in low- and middle-income countries [29]. For instance, the very intricate "pull-based" supply chain system in Morocco required unnecessary stages and depended on the accuracy of 900 untrained midwives at service delivery locations to provide forecasts for contraception [29]. Prior to the launch of the contraceptive coordination management information system (cLMIS) in Pakistan, surveys and data from service delivery points revealed significant disparities in the reported clientele [29]. To help with better policy decisions, this cLMIS gathers, arranges, and publishes data as well
as produces analytics [29]. The technology enables nonprofit organizations and the public sector to see all contraceptive health goods' supply chains [29]. The cLMIS eliminated paper-based reporting and improved data reconciliation between health systems at the level of health facilities [29]. Over the past ten years, with USAID's assistance, the Pakistani FP supply chain has grown from $5 million to almost $20 million in annual spending [29]. By giving decision-makers the data, they need to make fast, strategic decisions, this expansion has been sped up [29]. Technology-driven data visibility alone cannot bring about significant change; data analysis and utilization for regular and strategic choices as well as ongoing quality improvement are necessary [29].

In this study on identifying bottlenecks in the iron and folic acid supply chain based in India, Wendt et. al. states that, maternal anemia affects more women than prone to preterm birth, low birth weight, inadequate fetal iron reserves, and decreased cognitive development in offspring [35]. In order to combat widespread anemia, the Government of India developed the National Nutritional Anaemia Prophylaxis Programme in 1970, focusing on high-risk groups for iron supplementation [35]. In 1991, the program's reach was broadened to include all pregnant and nursing mothers [35]. Only 10% of women in Bihar, India, claimed to have consumed IFA for at least 100 days during their most recent pregnancy, despite the fact that 80% of women there reported having registered their pregnancies, indicating at least one visit to the antenatal clinic [35]. Obstacles to pregnant women in India and other low-income countries consuming gastrointestinal adverse effects have been reported in middle-income countries [35].

5. Conclusion

While IVF is a great solution to infertility, some factors can impede treatment success. Advanced maternal age, stage of an oocyte, and ethnicity can impact the outcome of IVF treatment. Women of a younger age have a higher chance of successfully having a clinical pregnancy and live birth through IVF. Women of advanced maternal age may not meet the same result. As humans age, our systems begin to undergo changes that affect certain molecular processes. In older women, oocytes begin to malfunction. Genetic codes begin to delete, and the cells continue replicating with this mutation. This results in a lower-quality oocyte that may not be able to support life. If an older woman seeking pregnancy chooses IVF treatment, her chances of clinical pregnancy and live birth are quite low. This is if she uses her egg. Using a donor egg from a younger woman may increase the chances. Regardless, younger women have a better outcome than women of advanced maternal age.

IVF treatment includes the use of an oocyte. Oocytes can come from the individual or a donor. Individuals undergoing IVF can choose either egg to use at their discretion, but the state of the egg affects the treatment outcome. Eggs frozen and thawed for use yield higher percentages for ongoing pregnancy, clinical pregnancies, and live birth rates. On the contrary, fresh eggs produce lower percentage rates. This may be due to the lower risk of ovarian hyperstimulation syndrome [11]. Fresh eggs can increase this risk which, in turn, will
decrease clinical pregnancy rates and increase miscarriage.

Ethnicity plays a part in IVF treatment as well. Caucasian women are more likely to have successful IVF treatment out than races, specifically African American women. Although white women have a higher infertility rate, their chances of conceiving and having a live birth are greater. Researchers have blamed lower IVF outcomes for black women on BMI and certain types of infertility, such as tubal or uterine [4]. However, a bigger issue may be at hand here. In every study researched, there was a common trend with minority women having a lower clinical birth rate and live birth rate. Some studies had a smaller pool of minorities, but others represented 30% of the study population. This makes the data well grounded. There needs to be more research on why minority women have poor IVF outcomes.

This is within the United States. According to a study in 2020, women of African descent in the Caribbean had better IVF outcomes than black women in the United States [37]. This could be due to the quality of treatment. Again, further research needs to be done to conclude why there is such a significant gap.

Biotechnology is the solution to many of these factors. To combat advanced maternal age, there is endometrial manipulation. Cryopreservation makes it possible for frozen eggs to be used. Also, new treatments are being developed to counteract types of infertility. With these advances, success rates for conceiving and having a live birth are bound to increase.

Based on all the analyzed data, a woman of younger maternal age, Caucasian descent, and who used a frozen egg for IVF treatment will yield the best results. This is compared to any other combination of the three factors. Women who do not fit into those categories may have a difficult and longer IVF process that may still have poor outcomes. Individuals who need extra assistance can use biotechnology-driven treatments to increase their chances. To be clear, these factors do not rule out the chances of conceiving through IVF. They limit the chances of a successful outcome.

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