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Risk Assessment Of In-Vitro Fertilization, Review Article

Maya Moutaz Albezreh[1*], Aminah Mohamedhafiz Mohmedfouad[2], Shda Fahad Khalil[3], Ali Eid A Alharbi[4], Ghadah Abdullah Aljateli[5], Eman Hasan Alaradi[6], Abdullah Saad Almunyif[7], Ayman Omur Alotaibi[8], Zina Abdulkareem Alzahidy[9], Ahmed Abdullah Alnakhli[10], Qahtani, Mohsen Ahmed M[11], Kariri, Mohammed Aqeel A[12]

[1]Consultant of obstetrician and Gynecologist at Health plus, Jeddah, KSA. Email: Drmaya.bezreh@hotmail.com
[2]Maternity and children's hospital, Najran, KSA. Email: aminahhafz2010@gmail.com
[3]General physician, East Jeddah general hospital, Jeddah, Saudi Arabia. Email: Shada_Khalil@outlook.com
[4]Pharma, Work in Al Dawaa pharmacies. Email: Ali1998official@gmail.com
[5]Inter, Unaizah Collage of Medicine, KSA. Email: Ghadaaljutayli@gmail.com
[6]Misr University for Science and technology. Email: eman.alaradi1997@gmail.com
[7]GP, MOH, Riyadh, KSA. Email: Almonif97@gmail.com
[8]Epidemiology technician, King Abdulaziz Hospital, Makkah, KSA. Email: AyoAlotaibi@moh.gov.sa
[9]Obstetrics and Gynecology resident- health plus, Jeddah, KSA. Email: Zina.alzahidy@hotmail.com
[10]ICU resident, Medina general hospital, King salmon bin Abdulaziz medical city, KSA. Email: Alnakhli9@outlook.com
[11] Laboratory specialist, Najran Armed Forces Hospital, KSA. Email: Moh07sen@hotmail.com
[12] Laboratory specialist, Najran Armed Forces Hospital, KSA. Email: momo07191@hotmail.com

***Corresponding Author:** Maya Moutaz Albezreh*
Consultant of obstetrician and Gynecologist at Health plus, Jeddah, KSA, Email: Drmaya.bezreh@hotmail.com

Abstract

Since its remarkable inception in 1978, IVF has garnered significant public interest. Currently, assisted reproductive technology is widely accessible in most developed countries, and the methods employed have significantly evolved since its inception. Advancements in laboratory technology and clinical practice have enabled IVF to develop into a medical process that is highly efficient, safe, easily accessible, and comparatively affordable. Over 2 million children conceived by IVF have been born so far, and it is probable that ongoing improvements will increase its attractiveness and suitability. There has been a rising interest in the topic of risk assessment in IVF in recent years, with a significant amount of research focused on detecting and reducing the potential dangers linked to the operation. This review article seeks to offer a thorough and all-encompassing analysis of the present understanding of risk assessments in IVF, encompassing the diverse range of risks and complications linked to the operation.

Keywords: IVF, ART, risks, laboratory errors, risk factors.

Introduction:

Assisted reproductive technology (ART) refers to fertility treatments that include manipulating eggs or embryos outside of a female's body to increase the chances of successful pregnancies and the birth of healthy offspring. The current ART methods include in vitro fertilization, with or without intracytoplasmic sperm injection. In vitro fertilization (IVF) is a widely used assisted reproductive technology that has helped millions of couples worldwide to achieve their dream of having a child. However, like any medical procedure, IVF carries certain risks and potential complications that need to be carefully considered and managed. In recent years, there has been increasing interest in the field of risk assessment in IVF, with a growing body of research aimed at identifying and mitigating the potential risks associated with the procedure. This review article aims to provide a comprehensive overview of the current state of knowledge regarding risk assessments in IVF, including the various risks and complications associated with the procedure [1].

One of the primary concerns in IVF is the risk of ovarian hyperstimulation syndrome (OHSS), which is a potentially serious complication that can occur as a result of the hormonal stimulation used to induce the development of multiple follicles in the ovaries. OHSS can lead to fluid accumulation in the abdomen and chest, as well as electrolyte imbalances and other systemic complications. Risk assessment for OHSS involves careful monitoring of hormone levels and ultrasound imaging to assess the number and size of developing follicles, as well as the patient's individual risk factors for developing the syndrome. Strategies for managing the risk of OHSS include adjusting the dosage of hormonal stimulation, using alternative protocols for ovarian stimulation, and closely monitoring patients at high risk for the syndrome [2].

Yet another important risk in IVF is the potential for multiple gestations, which can increase the risk of complications for both the mother and the infants. Multiple gestations are more likely to occur in IVF due to the transfer of multiple embryos to increase the chances of a successful pregnancy. Risk assessment for multiple gestations involves careful consideration of the number of embryos to transfer based on the patient's age, reproductive history, and other relevant factors. Strategies for managing the risk of multiple gestations include the use of elective single embryo transfer (eSET) in appropriate candidates, as well as the use of preimplantation genetic testing to identify the embryos with the highest potential for implantation and development [3,4].

In addition to these specific risks, there are also general medical risks associated with IVF, such as the potential for infection, bleeding, and anesthesia-related complications during the egg retrieval and embryo transfer procedures. Risk assessment for these general medical risks involves careful preoperative evaluation of the patient's overall health and the use of appropriate infection control and anesthesia protocols. Strategies for managing these risks include the use of prophylactic antibiotics, careful surgical technique, and close monitoring of the patient's vital signs during and after the procedures [5].

In recent years, there has been growing interest in the use of predictive modeling and personalized risk assessment tools in IVF. Predictive modeling involves the use of statistical and computational methods to identify the factors that are most predictive of the outcome of IVF, such as the likelihood of pregnancy, live birth, and various complications. Personalized risk assessment tools aim to provide individualized risk estimates for patients based on their specific demographic, clinical, and laboratory characteristics. These tools can help to guide clinical decision-making and counseling for patients undergoing IVF, as well as to identify patients who may benefit from additional interventions to minimize their risks [6].

Overall, the field of risk assessment in IVF is rapidly evolving, with ongoing research aimed at improving our understanding of the various risks and complications associated with the procedure, as well as the development of new tools and strategies for managing and minimizing these risks. By carefully assessing and managing the risks associated with IVF, healthcare providers can help to optimize the safety and success of the procedure for their patients. This review article provides a comprehensive overview of the current state of knowledge in this important and rapidly evolving field, with the aim of informing and guiding future research and clinical practice in IVF [7].

Understanding In Vitro Fertilization (IVF):

ART refers to techniques that involve manipulating oocytes outside the body, with IVF being the most prevalent method. The word 'in vitro' refers to processes that occur outside of a living creature. In the case of oocytes, they naturally mature inside the ovary, while embryos develop into pregnancy within the uterus. However, in the context of fertilization, oocytes are artificially fertilized in a petri dish. Robert Edwards and Patrick Steptoe documented the inaugural successful birth resulting from IVF in July 1978 in England. Dr/Edwards was subsequently awarded the Nobel Prize in Medicine in 2010 for this accomplishment [8].

During the process of in vitro fertilization, mature eggs are retrieved from the ovaries and then fertilized by

sperm in a laboratory setting. Subsequently, a medical intervention is performed to implant one or more fertilized eggs, referred to as embryos, into the uterus, the organ responsible for the development of newborns. The duration of one complete cycle of IVF typically spans from 2 to 3 weeks. Occasionally, these procedures are divided into distinct segments, which can result in a lengthier duration for the overall process [9].

IVF is a very efficient form of reproductive treatment that entails the manipulation of eggs or embryos and sperm. Collectively, these techniques are referred to as assisted reproductive technology. IVF can be performed utilizing the gametes of the couple themselves. Alternatively, it may encompass the utilization of eggs, sperm, or embryos obtained from either a recognized or unidentified source. Occasionally, a gestational carrier, who undergoes the implantation of an embryo in her uterus, may be employed. The likelihood of achieving a successful pregnancy and delivering a healthy baby through IVF is contingent upon various factors, including your age and the underlying cause of your infertility. In addition, IVF necessitates undergoing procedures that are time-consuming, costly, and intrusive. Placing many embryos in the uterus might lead to a multiple pregnancy. This phenomenon is referred to as a multiple pregnancy. Consulting with your healthcare team will provide you with a comprehensive understanding of the mechanics of IVF, the associated dangers, and whether it is a suitable option for you [10,11].

IVF is a medical procedure used to address infertility or genetic disorders. Prior to undergoing IVF as a means of addressing infertility, it is advisable for you and your spouse to explore alternative treatment options that entail less or no invasive procedures. For instance, fertility medications can enhance the production of eggs in the ovaries. Intrauterine insemination is a process that involves the direct placement of sperm into the uterus around the time of ovulation, which is when an egg is released from the ovary [5].

IVF is occasionally recommended as a primary intervention for infertility in individuals who are 40 years old or older. It is also feasible if you possess specific health issues. IVF may be a viable choice if either you or your spouse possesses the following conditions: 1) Fallopian tube injury or obstruction: Ova are transported from the ovaries to the uterus via the fallopian tubes. If both fallopian tubes become damaged or obstructed, it becomes difficult for an egg to undergo fertilization or for an embryo to successfully navigate to the uterus. 2) Ovulation disorders: In cases when ovulation fails to occur or happens infrequently, there is a reduced number of eggs available for fertilization by sperm.3) Endometriosis is a medical disorder characterized by the growth of tissue resembling the lining of the uterus outside of the uterus. Endometriosis commonly impacts the ovaries, uterus, and fallopian tubes. 4) Uterine fibroids: Fibroids are benign neoplasms that develop in the uterus. Frequently, they are non-malignant. They are prevalent among individuals in their thirties and forties. Fibroids can impede the process of implantation, making it difficult for a fertilized egg to connect to the uterine lining [5, 12]. 5) Tubal ligation is a surgical procedure that permanently prevents conception by cutting or blocking the fallopian tubes. If you desire to achieve pregnancy following tubal ligation, IVF may be a viable option. If you are unwilling or unable to undergo surgical intervention to reverse tubal ligation, this could be considered as an alternative. 6) Sperm-related problems: Diminished sperm count or atypical alterations in their motility, size, or morphology can impede the process of fertilization between sperm and an egg. If medical examinations detect abnormalities in sperm, it may be necessary to consult an infertility specialist in order to determine if there are remediable disorders or other health-related concerns. 7) Unexplained infertility: This refers to cases of unexplained infertility, where medical examinations are unable to identify the underlying cause of a person's inability to conceive.8) A hereditary condition characterized by an abnormality in the genetic material. If you or your partner has a heightened chance of transmitting a hereditary illness to your offspring, your medical professionals may suggest undergoing IVF as a potential solution. The term used for this procedure is pre-implantation genetic testing. Following the collection and fertilization of the eggs, they undergo a thorough examination to identify any specific genetic abnormalities. However, not all of these illnesses can be identified. Embryos that exhibit no discernible genetic abnormalities can be implanted into the uterus. 9) The motivation to maintain fertility as a result of cancer or other medical issues. Medical interventions for cancer, such as radiation therapy or chemotherapy, have the potential to negatively impact reproductive capacity. If you are preparing to commence cancer treatment, IVF may offer a viable option for preserving your ability to have a child in the future. Ova can be extracted from the ovaries and cryopreserved for future utilization. Alternatively, the eggs can be fertilized and cryopreserved as embryos for potential future utilization [5,12,13].

Individuals who lack a functional uterus or face significant health hazards during pregnancy may choose for IVF with the assistance of a surrogate to bear the pregnancy. The individual is referred to as a gestational carrier. In this scenario, the eggs undergo fertilization with sperm, and subsequently, the resulting embryos are transferred to the uterus of the gestational carrier [14].

Common Risks Associated with IVF:
IVF increases the likelihood of specific health issues. From immediate to more extended periods, these dangers encompass:

Anxiety and stress: IVF can have a significant impact on the body, psyche, and financial resources. Assistance from counselors, family, and friends can provide valuable support to both you and your spouse as you navigate the challenges and fluctuations of infertility therapy [16].
Adverse effects arising from the operation to extract eggs: Following the administration of medications to stimulate the development of ovarian sacs, each housing an egg, a procedure is performed to retrieve the eggs. This procedure is referred to as egg retrieval. Ultrasound pictures are utilized to direct a lengthy, slender needle down the vaginal canal and into the sacs, known as follicles, in order to extract the eggs. The needle has the potential to induce hemorrhage, infection, or harm to the gastrointestinal tract, urinary bladder, or a vascular structure. Anesthesia, a type of medication used to induce sleep and alleviate discomfort during medical procedures, is associated with certain risks [16,17].
Ovarian hyperstimulation syndrome: Ovarian inflammation is characterized by the enlargement and discomfort of the ovaries. The condition can be induced by the administration of reproductive medications, such as human chorionic gonadotropin (HCG), to stimulate ovulation [17].
The duration of symptoms often extends for a period of one week: The symptoms encompass minor abdominal discomfort, distension, gastrointestinal distress, emesis, and diarrhea. If you conceive, the duration of your symptoms may persist for a few weeks. Occasionally, certain individuals may experience a more severe manifestation of ovarian hyperstimulation syndrome, which can result in fast weight gain and difficulty breathing [15-17].
Spontaneous abortion: The incidence of miscarriage among individuals who achieve pregnancy by IVF with fresh embryos is comparable to that of individuals who conceive naturally. It ranges from approximately 15% for individuals in their 20s to more than 50% for those in their 40s. The rate increases in correlation with the advancing age of the pregnant individual [5,15].
Ectopic pregnancy refers to a condition when a fertilized egg implants and grows outside of the uterus. Ectopic pregnancy is the implantation of a fertilized egg in tissue outside the uterus, typically occurring in a fallopian tube. The embryo is not viable extracorporeally, and there are no means to sustain the pregnancy. A minority of individuals undergoing IVF may experience an ectopic pregnancy [17].
Pregnancy involving the simultaneous development of more than one fetus: IVF increases the likelihood of multiple pregnancies. Pregnancy with multiple babies is associated with elevated risks of pregnancy-induced hypertension, gestational diabetes, preterm labor and delivery, low birth weight, and congenital abnormalities compared to pregnancy with a single baby [15-17].
Congenital abnormalities: The mother's age is the primary determinant of birth abnormalities, regardless of the method of conception. However, assisted reproductive technologies like as IVF are associated with a slightly elevated risk of infants being born with cardiac abnormalities, gastrointestinal disorders, or other medical illnesses. Further investigation is required to determine whether the increased risk is directly attributed to IVF or another factor [16,17].
Preterm birth and reduced fetal weight: Evidence indicates that IVF marginally increases the likelihood of premature birth or low birth weight in infants.
Malignant neoplasm: Preliminary research indicated a potential association between the usage of medications to induce egg development and the occurrence of a particular form of ovarian tumor. However, recent investigations contradict these conclusions. There is no substantial increase in the incidence of breast, endometrial, cervical, or ovarian cancer following IVF [5,15-17].

Types of errors in IVF laboratory:
It is evident that substantial errors in IVF laboratories are seldom [18]. The IVF laboratories categorize and evaluate errors and non-conformances based on their potential impact on the progress or outcome of a treatment cycle. The gradings encompass the following [19]:

)1(Lowest grade
Minimal grade non-conformances are problems that occur during a treatment cycle but do not cause harm or significantly reduce the chances of success. Alternatively, these concerns may necessitate the rearrangement of a cycle.

)2(Intermediate level

Non-conformances refer to problems that have a detrimental effect on a cycle, diminishing the probability of success in that cycle or the following one, without posing a significant risk of failure or loss of the cycle.

)3(Significant grade
Non-conformances in this category possess the capacity to significantly jeopardize a cycle or result in its failure.

)4(Major grade
These non-conformances fall under a rare classification of problems that possess the capacity to cause significant harm to individuals.

Typically, there are two types of errors that may occur in an IVF laboratory:

Active errors
These are high-risk activities that have the potential to immediately jeopardize the well-being of a patient or the functioning of the system. These errors are often unforeseen blunders committed by individuals who closely interact with patients or systems. Active errors can manifest in the following forms:
1- Humans error
Human errors are typically defined as deviations from correct activities and violations of established protocols resulting from impaired cognitive processes such as inattention, memory lapse, negligence, impulsiveness, lack of accountability, and reduced drive [20]. Human errors can be prevented by exercising proper supervision and adhering to set norms throughout the execution of operations [21]. By assessing an operator's talents, knowledge, and adherence to regulations, it is possible to track human errors that are frequently associated with specific behavioral traits. Slips and trips occur due to skill-based human errors resulting from inadequate fine motor coordination and poor whole-body movement, respectively. For example, accidentally dropping plates containing gametes or embryos, or unintentionally misplacing pipettes while working with oocytes or embryos. Human errors stemming from insufficient training can also lead to mistakes in skill execution [22]. In IVF laboratories, human errors that are based on rules can manifest in various ways, including but not limited to, incorrect labeling, documentation errors, unexpected equipment shutdowns during cycles, improper operation of equipment, unintentional omission of an embryo during assessments, improper handling of dishes, inadequate thawing procedures, mishandling of gametes and embryos, and misidentification of samples. The impact of these errors on academic performance could range from insignificant to significant [23].

2- Lack of communication
The team consists of many experts, such as medical professionals, nurses, clinical embryologists, paramedics, and even housekeeping and maintenance people. They work together to achieve a common goal of optimizing patient outcomes [24].

3- Patient-related issues
These difficulties are to the characteristics or symptoms of a patient rather than being under the jurisdiction of the staff, and they have the potential to pose challenges to therapy. Additionally, patient grievances could potentially originate from this [25].

Latent errors
These errors occur as a result of inefficiencies in the system. Examples of factors that might negatively impact work conditions include inadequate personnel levels, excessive supervision of workers, time constraints, inadequate and poorly maintained equipment, protocols that are either erroneous or excessively complex, exhaustion, and burnout. They can be readily identified and effectively prevented [26].
The primary source of system inefficiencies is often attributed to poor and non-strategic decision-making by high-ranking executives (such as IVF clinical and laboratory directors), builders, and designers. They dictate the working conditions for humans. Inadequate judgments made by high-level management, leading to a lack of staff, limited time, poorly maintained equipment, excessive control over employees, implementation of impractical, erroneous, or unnecessarily complex protocols, exhaustion, and burnout, are all factors that can induce hidden errors in the workplace. Likewise, certain non-strategic choices made by designers and builders, such as the implementation of unreliable warning systems and indicators, along with infrastructural building and design flaws, create enduring vulnerabilities in the system's safeguards against errors. These underlying illnesses, like to a ticking time bomb, may remain inactive within the system for an extended

period of time before manifesting explosively [27].

As an illustration, a laboratory director used a regional IVF clinic building and design agent to establish an affordable cryostorage facility. A substandard alarm system was installed to monitor the capacity of the cryotank. In addition, the alarm system utilized the identical power source as the liquid nitrogen autofill system. The continuous operation of this power source is required. Regrettably, a maintenance worker without familiarity with the updated arrangement of this unit entered as usual to clean the lights, mistakenly supposing that the power supply also functioned as a light switch. Consequently, this staff consistently turns off the cleaning switch [28].

Embryo transfer procedure's associated risk factor:

The quantity of embryos transferred is subject to disagreement and deliberation. Multiple studies provide strong evidence in favor of elective single embryo transfer (eSET), particularly in surrogacy instances, as the most effective strategy for reducing the occurrence of multiple pregnancies and premature birth, both of which are associated with negative outcomes for both mother and baby [29]. The elective single embryo transfer is widely accepted as the most effective procedure linked with the most favorable perinatal and neonatal results. Nevertheless, the inquiry at hand is whether the group of preimplantation embryos created for a surrogacy cycle may undergo extended cultivation to improve the selection of the most optimal individual embryo and facilitate eSET. Prior to implementing this method, it is important to consider the potential hazards that may arise from extended culture. In addition, it has been suggested that preimplantation genetic screening can be utilized to improve and safeguard the eSET method. Nevertheless, it is important to consider an additional layer of intricacy when it comes to managing these embryos. This hypothesis is subject to potential contradiction; therefore, it is crucial for it to undergo a comprehensive examination [30]. However, it is important to note that eSET is not exclusively associated with extended culture or the use of PGS. Time-lapse imaging combined with morphological characteristics has been suggested to greatly improve embryo selection. This technique can help identify aneuploid embryos and prevent any negative impacts on the embryo. Similarly, the objective remains to enable uninterrupted and uninterrupted cultivation of cells while avoiding any disturbance to the cultivation of embryos. Time-lapse technology could help reduce occurrences of epigenetic alterations during the preimplantation phase. Efforts to reduce the intrusiveness of IVF are highly sought after in the field of embryology, and time-lapse imaging is seen as a promising initial step towards achieving this goal [31].

Factors that increase the likelihood of complications during pregnancy and affect the developing fetus:

Contrary to common beliefs, pregnancies resulting from ART cycles, including surrogacy cycles, may be associated with a higher likelihood of perinatal problems. Studies have shown that the perinatal results of gestational surrogacy, when compared to autologous IVF, do not demonstrate a significant increase in the risks of preterm birth, live birth rate, and congenital abnormalities. Furthermore, it was considered that oocyte donation exhibits inadequate fetal immune adaptation to allogeneic antigens. Consequently, gestational surrogacy seems to be linked to a greater likelihood of hypertensive problems compared to autologous IVF. The previous exposure of the embryo to the culture medium in the IVF setup may also lead to perinatal issues, including imbalanced fetal placenta formation, aberrant fetal growth, and metabolic reactions. Elevated systolic blood pressure has been seen in 21-week-old mice who underwent IVF culture. Additionally, rat embryos exposed to this culture method exhibited slight anxiety, altered psychomotor activity, and impaired spatial memory [32].

Some IVF cases choose to utilize the technique of multiple embryo transfer in order to enhance implantation rates. This practice is also utilized and potentially intensified in the instances of surrogacy, leading to the occurrence of numerous pregnancies along with the associated obstetric and perinatal difficulties that may arise as a result. IVF-surrogates have a reduced occurrence of complications in the third trimester, including pregnancy-induced hypertension, placenta praevia and abruption, diabetes mellitus, and hemorrhage. This is true regardless of whether it is a multiple gestation or a singleton, when compared to women who undergo standard IVF. Nevertheless, it is clear that IVF surrogacy involving many pregnancies is linked to a higher likelihood of experiencing preeclampsia, postpartum hemorrhage, hysterectomy, and gestational diabetes. Furthermore, numerous pregnancies are associated with an increased likelihood of experiencing hyperemesis and anemia. Considering the information presented, it is advisable to avoid multiple pregnancies, particularly in surrogate cycles. Therefore, it is strongly suggested to promote the use of eSET [30,33].

Conclusion:

In conclusion, the risk assessment of IVF is a crucial component of the decision-making process for individuals and couples considering fertility treatment. By understanding and evaluating the potential risks associated with IVF, patients can make informed choices about their reproductive health and overall well-being. While IVF offers the possibility of achieving pregnancy for those struggling with infertility, it is important to recognize and mitigate the potential risks, such as multiple pregnancies, ovarian hyperstimulation syndrome, and emotional stress. By working closely with healthcare providers and fertility specialists, patients can navigate the complexities of IVF and make the best decisions for their individual circumstances. It is essential for healthcare professionals to continue researching and monitoring the risks associated with IVF in order to provide the highest standard of care for patients undergoing fertility treatment.

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