KARBALA JOURNAL OF MEDICINE

Review

# Artificial Intelligence Role in Improving in Vitro Fertilization and Embryology

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**Article information:**
**Received:** 2024-07-24
**Accepted**: 2024-09-23
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https://doi.org/10.70863/karbalajm.v17i2.2128

## Abstract

For the past decade, the success rate of *in vitro* fertilization (IVF) has been constant. Many studies aim to enhance the existing success rate of IVF, which is around 30%. Artificial intelligence (AI) has the liability to improve medical results. Embryo evaluation and choice represent the total manifestation of the IVF procedure. The goal is to choose the best embryos from a wide pool of fertilized oocytes, as many may not be viable owing to aberrant development or chromosomal abnormalities. This essay explores whether AI has the ability to improve fertility results in IVF.
**Key Words:** Artificial intelligence, deep learning, oocyte, *in vitro* fertilization

## Introduction

Infertility is characterized by the inability to generate pregnancy following 12 months of regular, sexual activity that is unprotected. Infertility is projected to afflict up to 186 million people, both males and females, or 8 to 12% of all couples of reproductive age globally [1]. Following the delivery of the initial infant using *in vitro* fertilization (IVF) in 1978, the field of assisted reproductive technology (ART) has expanded dramatically. For nearly four decades, ART has helped infertile couples conceive. IVF procedures are complex and require close supervision, with doctors and experts in embryology making a range of critical decisions before and during the course of the procedure. While some of these decisions have a strong scientific basis, numerous are very biased and can vary greatly depending on practical experience, with an unavoidable non-reproducible influence on clinical outcomes, hence the expression "ART is an art" [2]. With global fertility declining, many families and individuals are resorting to assisted reproductive technologies to help them conceive. Unfortunately, IVF success rates are only around 20-30%, causing significant emotional and financial burdens for individuals hoping to conceive [3]. During IVF treatment, one of the most important predictors of successful pregnancy is embryo functionality, and the embryo selection process is critical for ensuring that expectant moms have the shortest time to conception. There is a great need to improve how embryos are selected for implantation into the uterus during the IVF procedure [4].

Artificial intelligence (AI) is a powerful technical advancement that gives a computer the capacity to engage in cognitive tasks like perception, reasoning, learning, and interaction. Three technology developments—algorithm progress, extensive information, and increased computational power and storage at low cost—have acquired a sufficient level of maturity and integration to enable artificial intelligence (AI) to quickly expand into society by eliminating commercial problems [5]. AI is becoming more and more popular in human reproductive and embryology. The growing body of data in the reproductive health field continuously drives advancements in applications for artificial intelligence exhibit in (Figure1). The best clinical practice for infertility patients is to base their decisions on medical data analysis, notwithstanding certain possible drawbacks [6]. Numerous developments in *in vitro* fertilization (IVF) have transpired such as the implementation of single embryo transfer, prolonged embryo culture at physiological oxygen, and customized ovarian stimulation. But for a lot of infertile people, the IVF path to parenting is a drawn-out, emotionally and financially taxing one. Some patients will not become pregnant after IVF. Improving the existing ~30% success rate of IVF is the main focus of a lot of research [7].

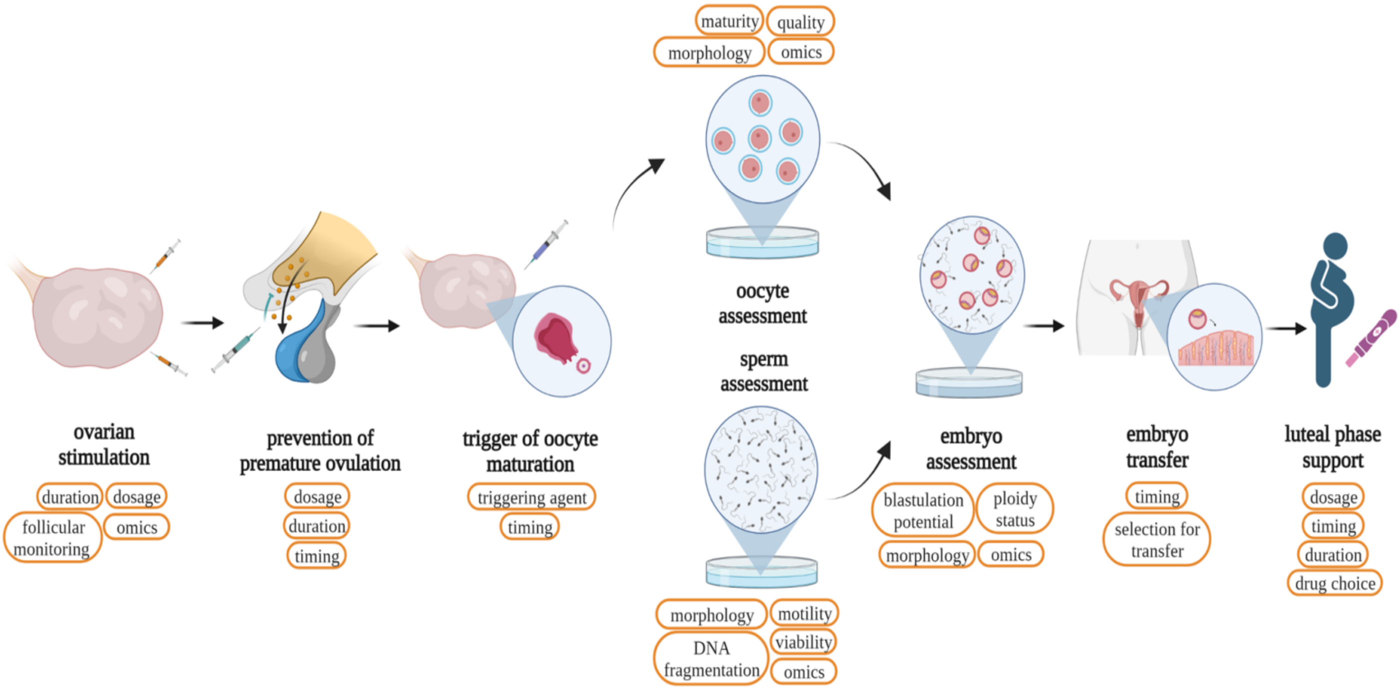


**Figure 1.** Possible applications for artificial intelligence and machine learning approaches in therapeutic and embryological stages of assisted reproductive technology (ART) [6].

Additional developments are expected in fields like as patient-specific treatment regimens, enhanced gamete and embryo choice, endometrium responsiveness, and early pregnancy monitoring. AI has recently acquired popularity for its capacity to predict healthcare outcomes based on frequently collected data for example patient traits, clinical pictures, and blood test findings. As a result, it has been shown to be effective in accurately identifying cancer severity using medical imaging [8]. There is growing acknowledgment that alternative data-driven techniques that take advantage of the enormous amount of ART cycles completed and promote truthful, uniform, and optimal decision-making may result in better outcomes. Large volumes of data gathered during IVF cycles have allowed multidisciplinary specialists to offer artificial intelligence (AI) strategies for driving personalized approaches [9].

In recent years, developing technologies such as time-lapse incubators and preimplantation genetic tests (PGT) have been offered as significant advances in the area, with the promise to produce a more objective approach of selecting embryos with the highest implantation likelihood. However, there is currently insufficient evidence to support the widespread use of these procedures only to improve single embryo transfer live birth rates [10-11]. Machine learning, particularly convolutional neural network technology (CNN), has been applied in conjunction with medical imaging in a wide range of areas over the past ten years [12] , dermatology, radiology and pathology [13-14]. This technique was additionally employed in the embryology laboratory in order to enhance the choice of an embryo with the good implantation criteria, then with the most effective objective of fertility therapy leading to successful delivery of a healthy infant [15].

Our primary goal should be to integrate AI development with assisted reproductive technology (ART) in order to close the knowledge gap between clinical trials and research. The aimed of this essay whether AI has the ability to improve fertility results in IVF [15].

**Types of Artificial intelligence**

Reproductive specialists may utilize AI to discover the most effective approach for each patient's specific infertility. Machine learning (ML) is the intellectual subject that studies how machines acquire information from data [16]. It emerges using the junction of biostatistics (that help in understanding relationships from information) and software engineering (that depends on effective computing procedures). The computational challenges which can contain millions or billions of information motivate this union of both computer science and mathematics [17]. Computer-based learning can be divided into two categories: supervised learning and unsupervised learning. Supervised learning leads networks to extract outputs that are consistent with a label, whereas unsupervised learning extracts characteristics from the data's underlying structure. However, another divide may be relevant by examining how machine learning enhances medical practice: differentiating between learning tasks that clinicians currently accomplish effectively and acquiring knowledge activities where clinicians experienced unsuccessful outcomes [18]. In opposition to ML, deep learning (DL) enables labels to be connected to input features in a remarkably accommodating way: labels are dependent on intermediate parameters that are functions of other intermediate variables. A deep neural network (DNN) is a mathematical function composed of basic changes known as layers, with the outputs of one layer feeding into the inputs of the next. Deep learning is based on the premise that stacks of transformations can model a wide range of relationships while being trainable [19].

AI is a catch-all phrase for technologies that help to be similar to either animal or human mental processes. Machine learning is the portion of artificial intelligence technology that understands how to process data without specifically programming it. It may anticipate results for various factors that would take too long for humans to do. Deep learning is another subfield of machine learning. It uses artificial neural networks (ANN), which can be the same as the structure of neurons in the brain. Deep neural networks, which comprise multiple layers of neurons, may do every feasible computation if the precise neuron connections are engaged during training. This skill alone has linked deep learning to significant advances in science and technology [20]. Machine learning is described as computer software that learns a particular jobs allover the time and enhances its performance to reach the most important possible result. Machine learning has recently been presented as an automated method for analyzing embryo morphology. This allows the utilization of a deep convolutional neural network. Unlike most previous computer-aided algorithms, certain machine learning techniques applied to embryo evaluation, the reported CNN architecture enables automated embryo selection of features and analysis at the pixel level, with no intervention from an embryologist. These kinds of networks do not rely on human-specified criteria and can build the ability to categorize embryos using iterative learning [21].

Artificial intelligence technologies used in IVF clinics are additionally classified into two types: commercial goods and self-developed in-house solutions. While cloud-based technologies can help IVF clinics with lighter workloads by leveraging data collected by different clinics, but might be unable to maintain accurate forecasts because of intervention from specific clinic practices or conditions. Cloud-based products consist of Embryo Ranking Intelligent Classification Algorithm (ERICA), Intelligent Data Analysis Score (iDA Score), and Life Whisperer. However, using an in-house method may bring some benefits, such as more control and flexibility and its method of operation [22].

**New techniques of Artificial intelligence for assisted reproductive technology:**

Machine learning (ML), robotics, and computer vision are just a few of the expanding branches that fall under the umbrella term artificial intelligence (AI). Primarily, algorithms that use machine learning are able to identify trends in data and make deductions from them, which allow them to create models that customize or enhance ART treatments to achieve a given goal exhibit in (Figure 2) [23]. Historically, supervised, unsupervised, or reinforcement learning frameworks have been used to study algorithms for learning. In supervised learning, input and output labels are applied to data in order to create algorithms that represent the association between each other and can be utilized for predicting results in the presence of novel, unseen inputs. In contrast, models for unsupervised learning are constructed to capture the structure (such as clustering) of data that has no output labels, or is unlabeled, and can be utilized to create or interpret new data [24].

- **Gametes (Oocytes and Sperm)**

The primary method of evaluating human embryonic oocytes in a therapeutic context is to examine the morphology of the oocyte cumulus complexes. Selection of competent oocytes may depend on using machine learning (ML) on oocyte pictures prior to intracytoplasmic sperm injection (ICSI) and evaluating oocyte behaviors during ICSI. Finding noninvasive procedure to assess oocyte quality could additionally be helpful for studies on non-invasive oocyte production techniques such direct somatic cell reprogramming, nuclear cloning, and oocyte *in vitro* maturation. Artificial intelligence (AI) techniques have already been used in some early attempts to assess human oocytes and normal fertilization, evaluate embryo development up to the blastocyst (BL) stage, and use static oocyte pictures to examine implantation possibilities [25].

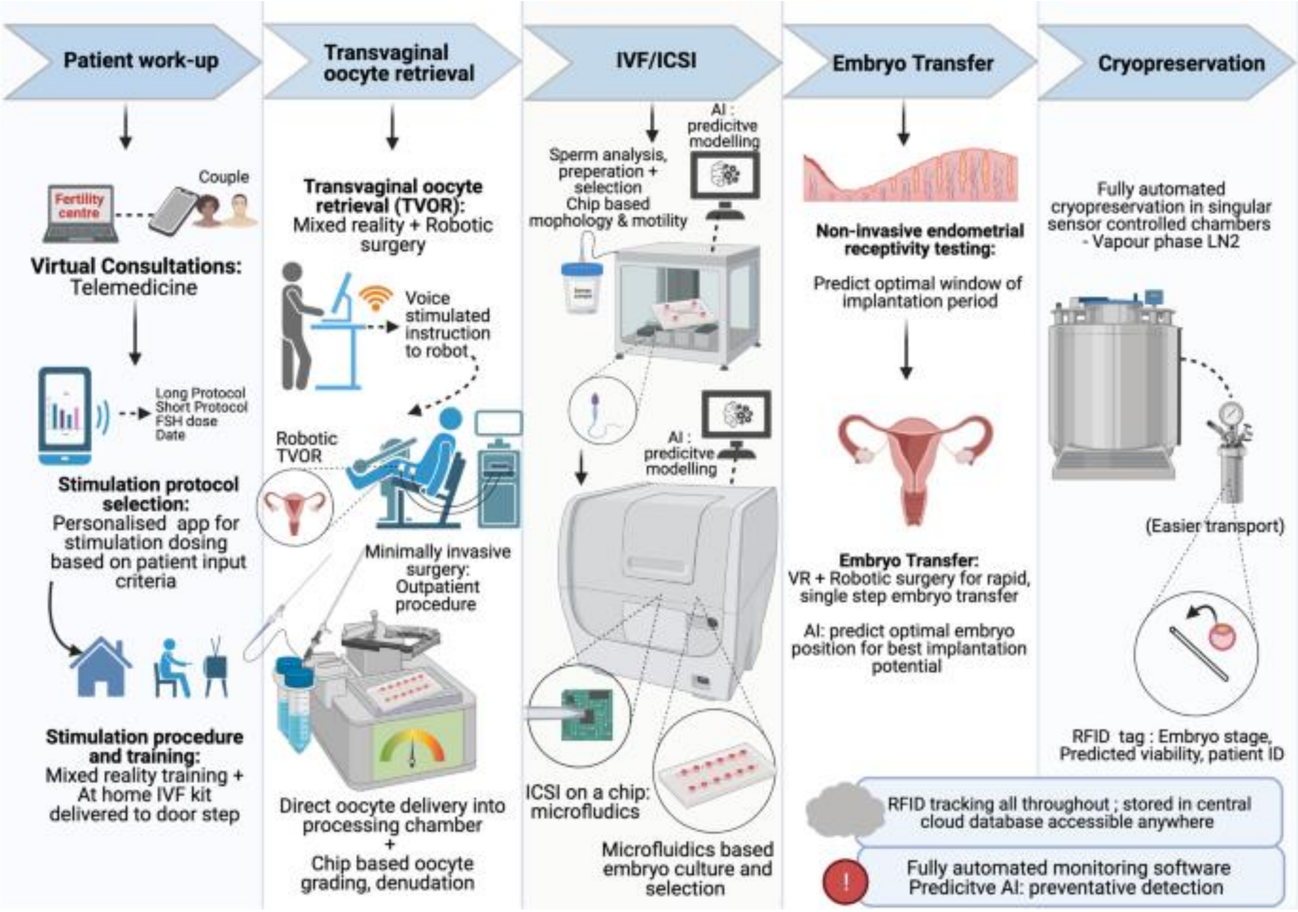


**Figure 2.** New techniques of Artificial intelligence for assisted reproductive technology: Automation in ART [23]

Artificial intelligence is additionally used in semen analysis, sperm choosing, and assessments of the structure of sperm and DNA integrity. Since finding these "precious" cells usually takes many hours for embryologists, sperm cells in microsurgical testicular samples of patients with severe male factor infertility are a prominent target for medicinal AI application. Additionally, to properly distinguish sperm from other tissue cells throughout the development of such a system, a vast amount of sperm pictures will be needed for machine learning. AI techniques are created to accurately forecast male factor infertility as the probability of sperm extraction in azoospermic patients [26].

- **Embryo Evaluation**

The present areas of interest for AI applications in embryology are as follows: grading of embryos (mostly in the BL stage), automatic annotation of embryo development (cell stages and cell cycles), and embryo selection for implantation [27].

**Automatic Annotation**

The subjective and human-made nature of morphokinetic annotations is one of the possibly confusing variables that can impact AI protocols. For the best automatic annotation, AI models that can identify aberrant cytokinetic (direct divisions 1-3) and karyokinetic (nuclear) anomalies will need to be developed. The majority of machine learning techniques for selecting and evaluating embryos have relied on "computer vision methods" that make use of visual data, such as time laps microscopic system (TLM) or microscopic images. The preferred approach for processing visual data is CNN. One use for it is automatic cell annotation [28]. Embryo Scope (Vitrolife) and Geri (GeneaBiomedix) are professional timelapse microscopic (TLM) systems that assert to have some degree of machine learning in the assessments software. The technology and effectiveness of each of these manufacturers' systems' achievements have not been made public. Embryologists are able to record the exact moment of each cleavage event during TLM incubation. But because it's a manual procedure, it relies on the accuracy, skill, and competence of each embryologist to discern between aberrant and normal cleavage traits and events [29].

Like any manual task, there is a great deal of intra- and interoperator variability, especially when working in various laboratories. For this reason, AI-based automatic annotations with high accuracy and reliability are crucial, in addition to the goal of standardizing and automating the process [30]. The two most common noninvasive embryo selection procedures are classical embryo morphological evaluation, which is performed predominantly at the BL stage, and the morphokinetic algorithm, that needs sophisticated time-lapse microscopy (TLM). On the other hand, using an in-house method may bring certain advantages, including more influence and versatility over the AI system and its workflow, and additionally having the capacity to test own ideas without necessity of waiting for commercial releases [31]. An effort has been made to automate TLM annotation. Recent studies have shown the effectiveness of automatic, non-human mediated embryo developmental annotation systems, independently from business interest's producers of TLM instruments [32]. These also need to include the capacity to differentiate between nuclear anomalies, such as multinuclear blastomeres, and the morphological characteristics of the embryo. Each characteristic's weight, or relevance, would need to be appropriately allocated and computed in the perfect system. Numerous computerized imaging systems are available that can be integrated with AI systems (mainly using convolutional neural networks (CNN) approaches). It is difficult to use TLM systems to examine cell stages and corresponding division intervals (t times) utilizing automatic detection technology [31].

It is challenging to employ TLM systems to investigate cell phases and associated division intervals (t times) with automatic detection technology. Initially, the system must detect an embryo in the culture, as well as construct an automated zone of interest. Segmentation or a cascade classifier can be utilized to achieve this. According to a recent study from our group, automatic cell annotation using the Inception V3 CNN model eliminates the requirement for region-specific preprocessing. We believe the AI algorithm conducts embryo segmentation inside. Up to the eighth cell stage, we achieved 100% accuracy among mice study and 93.9% accuracy on human [33].

- **Embryo Grading**

A recent research investigation used a system built on deep learning and developed with an evolutionary algorithm (CNNg) and demonstrated its capacity to discern between different euploid blastocysts based on their implantability. The study discovered that artificial intelligence-based approaches offer a significant probability of increasing IVF rates of success, with considerably more accurate alignment with real implantation results for embryos with higher implantation scores. Furthermore, a simpler deep learning model was found to be more accurate in grading cleavage embryos (at day 3). However, this study used a simpler dataset and had limited resource constraints, such as an image capture procedure that caused varying color hues and blockage [34]. The BL stage is beneficial for evaluation because it has been shown to have a good connection with implantation. Unfortunately, there are several different grading systems. Especially with the commonly utilized "Gardner" technique, deviations and aberrations have grown common [31].

The key problem in using deep learning to improve accuracy is the need for a big dataset to train the automated grading model. Despite there are plenty of resources accessible for analysis of medical images, very few are provided for ART. The only publicly available human embryology dataset, specifically at the blastocyst stage, was donated by and used as ground truth (GT) in various investigations. Image resolution effects the outcome of deep learning-based vision processing. To obtain adequate effectiveness for object categorization, for example, high-resolution images or video are necessary, which increases the amount of data that must be processed, saved, and delivered [35]. A recent research investigation of ten experts in embryology found a substantial level of heterogeneity in categorizing human embryos suitable for biopsies and freezing. In contrast, educated AI-based algorithms outperformed human assessment and selection [36]. One of the most difficult components of this job is ensuring that the training data is of excellent quality and that the machine understands efficiently. For example, the computer learns from a training set of embryo pictures that have been examined and assessed by embryologists (human engagement) [35].

It would be truly great if ML happens without human intervention. Earlier chances to overcome this issue relied on picture segmentation to distinguish between the ICM and the TE. This necessitated the employment of two separate focal pictures, one on the ICM and the other on the TE. The system applied "basic" ML approaches (support vector machine) to two-dimensional BL pictures. Although these approaches needed human participation, they are the first step toward BL grade uniformity and automation [37]. The automatic evaluation of the BL is potentially a promising approach for animal research [38]. The time-lapse monitoring device is a significant technological advancement in the field of assisted reproductive technology, since it allows for ongoing embryo observation without removing the embryo from the incubators for frequent inspections of embryonic growth. TLM data provide raw photos and videos containing valuable knowledge that can be employed in AI technology to support in embryo selection. This information is used in AI models designed to annotate morphokinetic events, detect blastocyst morphology, and select embryos with higher blastocyst quality. Other algorithms have been developed to predict clinical outcomes such as clinical pregnancy and implantability [38].

It would be fascinating to investigate how AI techniques are utilized to assess and select TE cells for embryo, as well as compare them to chromosomal results. Multiple efforts already attempted to imitate BL morphological classification with automated systems. The attempts to anticipate ICM and TE grades is automatically based on static or TLM pictures. One way includes using TLM BL data rated by embryologists on the ICM and TE [38-39]. Despite an AI system could assess static photos; its main use will involve working with TLM films (stacked images) of developing embryos. There is some debate over whether static photographs or videos should be used to evaluate embryos. On the contrary, it appears natural that films would reveal more information about embryo development, leading to more accurate choosing. On the contrary, it seems that analyzing a single embryo image at key time points appears to be adequate for accurately determining developmental potential [27, 40]. Furthermore, most neural network-based classifiers in models that use deep learning cannot adjust adequately to diverse imaging systems and are limited to the technologies used to obtain training data. Although CNN-based algorithms offer an alternative to current embryo scoring methods, their effectiveness is restricted by several factors, including the dataset used in training and the technique used to train these kinds of systems. Furthermore, the usage of RNNs and GANs remains restricted and more investigations areneeds to be done to use transfer learning systems, particularly on unsupervised medical data sets [40].

**Assisted reproductive technology software**

Considering its various advantages, the proposed fertility therapy software might end up playing a key role in the growth and increased productivity of reproductive clinics. It helps in the entire IVF treatment process, from the patient's first session to the last summary of their discharge, all of which is monitored, recorded, reviewed, and automated [41-42].

- **Anti-Müllerian Hormone and Ovarian Reserve**

It is a crucial step in assisted reproductive technology operations because it anticipates the ovarian reaction to hormonal stimulation and helps construct patient profiles. AMH, a dimeric glycoprotein from the TGF-β family, is secreted by granulosa cells of developing follicles during sexual differentiation. AMH concentrations represent the functional reserve of ovaries, which diminishes dramatically with age [43]. It is critical for ART since it assesses the ovaries' response to stimulation. Antral follicle count (AFC) or antral microhyperchus (AMH) as ovarian reserve tests (ORT) have been used to determine an individualized gonadotropin dose in order to optimize the advantages and dangers of stimulating the ovaries for IVF [43].

- **Automatic measurement of follicular diameter using 3D ultrasound.**

The ultrasonography follicular counting (antral follicle count, AFC) is an important method for monitoring ovarian reserve since the anticipated amount of FSH-sensitive follicles is predictive of the number of oocytes recovered in IVF cycles and may serve as the basis for personalized ovarian stimulation therapy. Recent developments in ultrasound technology have led to higher image resolution and quality [44]. The treatment success is better when using follicular volume, which is derived through automatic measures of follicular growth, in conjunction with volume-based criteria for hCG triggering, as opposed to traditional monitoring that uses follicular diameter. The AI ART program is capable of conducting a thorough analysis of all data by using 3D ultrasound and automatic follicular diameter measures to track the cycle and trigger hCG [45].

- **Oocyte selection and evaluation**

In order to decrease the number of embryos created and wasted—which is crucial in nations that forbid the use of surplus embryos—as well as the number of embryos needed for trophectoderm (TE) biopsy and PGT, non-invasive AI techniques for assessing oocyte competency may develop into a significant selection and prediction tool. It may also be used to predict the likelihood of an IVF cycle's success. For psycho-social reasons, intended parents may find it quite beneficial to have a tool that objectively evaluates the quality of the oocytes and the possibility of fertilization afterward in the event of donor ovarian cycles. Estimation and selecting AI systems might also be beneficial for experimental and research processes such as somatic cell nuclear transfer and reprogramming, *in vitro* gametogenesis (IVG), and oocyte maturation (IVM) [46].

When reproduction is accomplished naturally or with the use of ART, a significant factor in its effectiveness is the general quality of the oocytes. The projected pregnancy rate per recovered oocyte as of right now is 4.5%. In non-invasive methods to predict the developmental potential of human oocytes, viscoelastic properties of human zygotes determined nondestructively throughout hours of fertilization have been demonstrated to be an accurate indicator of viability and blastocyst formation. AI methods for time-lapse photography analysis of human oocytes or transcriptomics studies or genomics analysis of gene expression can be used to optimize ART [47-48].

- **Semen analysis and sperm selection**

Semen analysis is the first test that infertile couples have to undergo. In manual sperm analysis, significant interlaboratory variations have been seen, especially when working with tests that have wide ranges of normal outcomes. Comparing the efficacy of a computer-aided sperm analysis (CASA) technology against a manual approach produced results that were similar. Morphology, motility, concentration, and vitality are the four variables being studied. Rather than being just "black boxes" that produce cold, bare data without any human participation, CASA systems are helpful instruments that offer faster and more accurate findings for the essential parameters in routine sperm testing. CASA devices with AI ART is a technology to facilitate sperm selection for ART [49].

- **Choosing an embryo**

Accurate determination of embryo survivability is critical for increasing pregnancy rates and improving IVF procedures. The use of automated morphological studies of embryos or blastocysts in conjunction with AI is a promising development. Time-lapse microscopy (TLM) is a technique used in embryology labs to improve embryo selection. This objective, non-invasive study of embryos has enabled a fresh method for forecasting embryo growth and implantation potential [50].

- **Genetic testing before implantation**

Preimplantation genetic testing (PGT) is a popular strategy in both genetic clinics and assisted reproductive technologies, with over one-third of ART institutions now using it. The fact that a large proportion of transplanted euploid embryos do not end up in a clinical pregnancy demonstrates how much effort remains to be performed to recognize embryos with the highest developmental potential. To prevent any possible harm from embryo biopsy procedures, one of the primary concerns will be the development of non-invasive PGT approaches, as well as the automation and optimization of AI ART software [51].

The benefits of adopting AI may include reduced mistake rates in job execution independent of the external environment, the ability to do labor-intensive and boring repetitive tasks, the ability to organize medical information, and logical machine reasoning free from physical or emotional limitations. The high cost of deployment up front, the morality of having a machine take over human decision-making, and the loss of human interaction are some of the obstacles to implementing AI [51]. It is imperative to highlight the fact that human empathy should never be replaced or substituted by a supercomputer. These are difficult problems that call for serious consideration and introspection [51]. However, we think that artificial intelligence (AI) will revolutionize and automate the field of reproductive health, ultimately benefiting both society and infertile patients greatly. AI being used as a tool to help doctors, improving treatment effectiveness and enabling more accurate diagnosis. Instead of replacing doctors of reproductive medicine and embryologists, AI will help them work more efficiently while still providing superior care for their patients.

## Conclusion

Artificial intelligence (AI) has the potential to significantly enhance the field of *in vitro* fertilization (IVF) and embryology. Through the use of advanced algorithms, machine learning, and data analytics, AI can assist reproductive specialists in optimizing treatment protocols, predicting embryo viability more accurately, and identifying factors that contribute to successful pregnancy outcomes. Assisted reproductive technology software offers several advantages to reproductive clinics by providing automated monitoring and recording of IVF treatment processes from start to finish. It utilizes Anti-Müllerian Hormone (AMH) testing to assess ovarian reserve accurately and determine individualized gonadotropin doses for optimal stimulation outcomes. The software also incorporates automated measurement of follicular diameter using 3D ultrasound technology to monitor follicle development accurately. Furthermore, it includes electronic medical record capabilities that streamline documentation processes while ensuring secure storage of patient information. Overall, this software has significant potential in enhancing clinic productivity and improving outcomes in assisted reproductive technology procedures.

As research continues to advance in this area, it is essential for stakeholders such as fertility clinics, researchers, and regulatory bodies to collaborate on ethical considerations and guidelines for incorporating AI into IVF practices. With responsible implementation and ongoing advancements in technology and medical expertise, it is foreseeable that AI will play a pivotal role in further enhancing the efficacy of IVF procedures and revolutionizing approaches to reproductive medicine.

**Funding:** No funding has been received for this study.

**Conflicts of interests:** No conflicts of interests to be declared

**Authors' Contributions:** Conceptualization: S.H.S, Formal analysis and investigation: N.F.H, Writing: S.H.S Resource: N.F.H Supervision: N.F.H and S.H.S

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