AI POWERED IVF TREATMENT - A REVIEW

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Abstract: This review article provides a succinct overview of some of the basic aspects of AI and machine learning, most popular AI algorithms, applications, potential limitations and challenges. A number of databases were checked in order to locate articles that used artificial intelligence algorithms on reproductive data. Most of the presented algorithms have attained an acceptable level of precision, highlighting the promise of a variety of AI methodologies. The evaluation of these investigations, however, points to the necessity of conducting more systematic research to verify the presented models and their algorithms. It won't be long before AI is widely used in assisted-reproduction clinics.

Keywords: Artificial intelligence, Machine learning, IVF, Prediction models.

Introduction:

The field of Assisted Reproductive Technology (ART) has grown exponentially since the late 1970s. The birth of Louise Brown in June 1978 was a milestone for the in vitro fertilization (IVF) technique.This event established the successful path that ART would follow. Since that time, approximately six million babies have been born through ART [1]. Infertility is defined as failure to establish a clinical pregnancy after 12 months of regular, unprotected sexual intercourse. It is estimated that infertility affects as many as 186 million people [2], both males and females, or between 8 and 12% of all couples of reproductive ages worldwide [3].

As per WHO**,** Infertility is the third most prevalent problem behind cancer and heart disease. One in six Indian couples and millions of people struggle with infertility, according to the Indian Society of Assisted Reproduction (ISAR).About 48.5 million couples experience infertility worldwide. Today, infertility is rapidly becoming an epidemic. As a result, people have started using assistive reproductive techniques like IVF and other fertility treatments. The global IVF market is set to reach around $36 billion by 2026, per an industry report.

In vitro fertilisation, also known as IVF, is the most popular type of assisted reproductive technology used to treat people who are having trouble getting pregnant. IVF involves mixing eggs and sperm outside the body, in a laboratory.IVF can be provided as a "donor cycle IVF" or a "self cycle IVF," depending, following a thorough examination of a woman.In self-cycle IVF, a couple's own gametes are used, while in donor cycle IVF, either sperms or eggs from a donor are used. However, you should be aware that the kid born through a donor cycle will not receive the DNA from its biological parents.

Embryo evaluation is one of the key factors contributing to a successful pregnancy. It is normally done by a skilled embryologist, who examines each embryo under a microscope and assigns it a grade. The grading enables the fertility centre to choose the embryo with the best chance of leading to a successful pregnancy. This visual assessment is limited to what can be seen with the naked eye down a microscope.

The term AI was first coined by John McCarthy at the Dartmouth Summer Research Project on Artificial Intelligence in 1955. Artificial intelligence (AI) is described as the capacity of machines to learn and exhibit intelligence, which stands in contrast to the inherent intelligence exhibited by humans and other animals. Deep learning is an AI technology that enables computers to detect and categorise images for use in medical imaging. The AI "trains" on prior instances of those images in order to discover intricate patterns and attributesspecific to the type of image. After being trained, AI

can identify and categorise brand-new, undiscovered images.AI has mastered the ability to distinguish between the morphological traits of a viable and non-viable embryo, even those that are imperceptible to the naked eye.

This support technology now provides additional evidence in addition to the visual evaluation of the embryologist in order to rank the most viable embryos. The next significant advancement in IVF treatment is the prediction of human embryo viability utilising cutting- edge artificial intelligence, as this technique offers higher success rates and uniform embryo assessment across the nation's fertility clinics.

The use of AI has primarily been concentrated on optimising IVF treatment in the form of selecting and predicting the sperm cell to improve the success rate of treatment, evaluating the quality of embryos and oocytes to establish ART prediction models and predict the outcome, and defining good noninvasive markers to increase implantation rate and improve ART treatment effectiveness.

By offering automatic categorization of the sperm, embryo, and oocytes, an integrated AI component with image analysis will boost recognition efficiency, reduce errors, and achieve minimal manual classification effort. The quantity and quality of data, which have a substantial impact on the effectiveness, applicability, and generalizability of the trained model, are the primary sources of the current studies' shortcomings.

The models frequently use small amounts of retrospective data from a single source. Additionally, most research isolates the application of algorithms for classification and prediction without integrating the results of the analysis..Only a few semi-automatic AI applications in reproductive medicine exist at the moment.Further research is required in the areas of automated AI-assisted reproduction, individualised diagnosis, and treatment, as well as remote medical expert systems.[4].

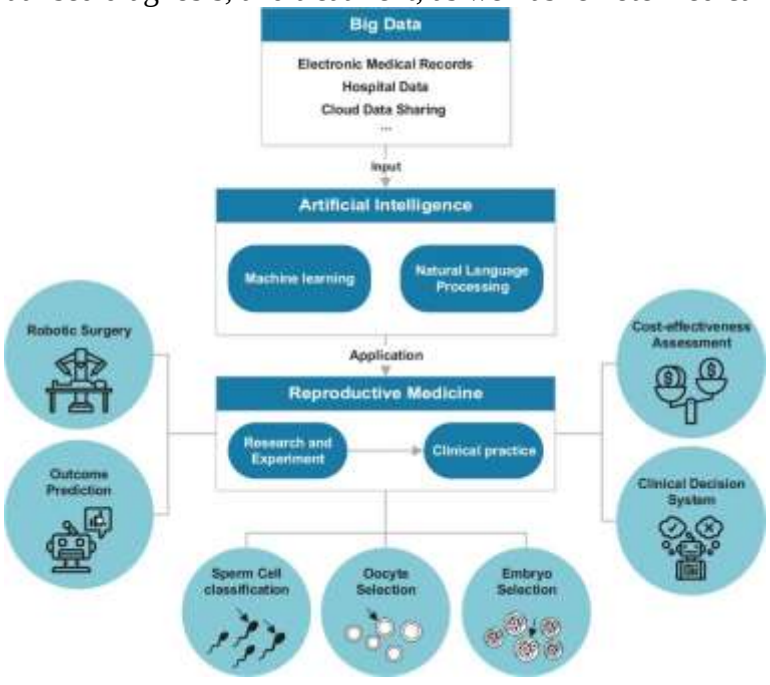

Figure 1
The role of artificial intelligence in Reproductive Medicine. Big data include electronic medical records (EMRs) and other data. EMRs can capture data from various ways and the data is analyzed using AI such as machine learning and natural language processing (NLP). AI has been used in the many aspects of reproduction, from research and experiment to clinical practice. This schematic reviews the seven main applications of AI in reproductive medicine.
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Role of AI in reproductive medicine:

There are three major categories of AI methods widely used in medical applications: machine learning (ML), natural language processing (NLP) and robotic surgery. The ML method attempts to cluster the features of patients and predict the outcome of diseases by analyzing structured data such as medical imaging and genetic data [5].The NLP method extracts and processes meaningful information from unstructured clinical data, such as electronic medical records (EMRs), to complement the structured data[6][7].NLP converts the raw data into structured data that the machine can read and analyzes it using ML techniques.

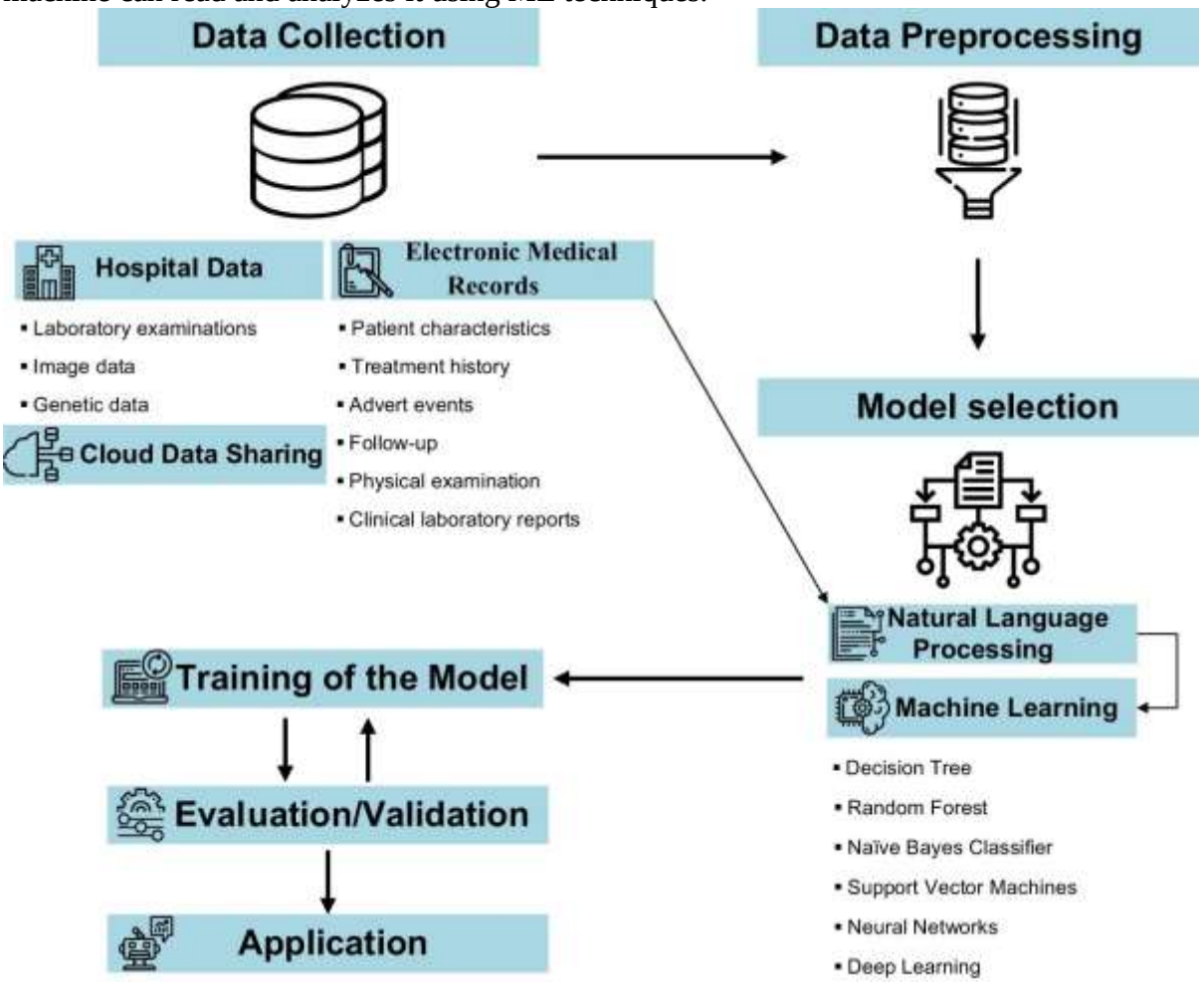

Figure 2

The workflow of artificial intelligence in Reproductive Medicine. This flowchart provides a brief overview of the AI workflow. The first step is the collection of data. The data includes electronic medical records (EMRs), hospital data and cloud data sharing. The second step is data pre-processing. The third step is the selection of the appropriate model. The data is analyzed using artificial intelligence methods such as machine learning and natural language processing (NLP). Then the training dataset is used to train the model. The final steps include the evaluation and validation of the model.

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Fundamentals of Machine learning

Machine learning is a branch of artificial intelligence (AI) and computer science which focuses on the use of data and algorithms to optimize a performance criterion using example data or past

experience. Arthur Samuel, is credited for coining the term, “machine learning”.It explores data in a meaningful, pattern-oriented manner that gives the systems' robustness tomimic a human decision-making capability. Deep learning is a subset of ML that works onthe principles of human neural networks[8]. Humans are susceptible to missing important patterns in the data when conducting extensive analyses with numerous factors.A human's ability to make decisions is aided by the use of ML and DL, which can quickly recognise these patterns and take care of this aspect for you.

Machine learning algorithms can be used to examine patient features, all available information about ovarian hyperstimulation, and the success of a pregnancy in a clinical database.An infertile couple's chances of becoming pregnant can be estimated using the models gained from these procedures.

Machine learning method can be divided into supervised learning, unsupervised learning and reinforcement learning [9]. Currently, supervised learning is widely used in almost all AI applications in reproductive medicine. This algorithm uses labeled training data to develop models that can predict a known output. In clinical practice, it requires a dataset with features and labeled outcomes; however, the main drawback is that it requires data that must be labeled by humans, which is time consuming. Unsupervised learning focuses on the hidden structures and relationships in a dataset and requires only the input features in the training data. Since the output labels are not necessary, it can be used to predict unknown results. Reinforcement learning focuses on continuously improving the accuracy of the algorithm through trial and error. It consists of agents that interact with a specific context, wherein the agent uses the reward feedback in determining appropriate behavior and maximizing the reward[10][11][12] .Currently, reinforcement learning is mainly used for medical image processing[13], personalized medicine[14][15] and robotic surgery [16]

Large-scale data collection and powerful processing power are necessary for machine learning.Processing massive data is made possible by the quick development of graphics processing units (GPUs).In the near future, AI and machine learning can significantly advance the development of reproductive medicine due to the progressive development of hardware and software (algorithms).We will provide a brief overview of some algorithmswith instances of their use.

Supervised learning

The Supervised Machine Learning algorithm can be broadly classified into Regression and Classification Algorithms. In Regression algorithms, we have predicted the output for continuous values, but to predict the categorical values, we need Classification algorithms. The Classification algorithm is a Supervised Learning technique that is used to identify the category of new observations on the basis of training data. In Classification, a program learnsfrom the given dataset or observations and then classifies new observation into a number of classes or groups.

Image analysis and ART prediction have both been successfully accomplished using supervised learning techniques. The algorithms decision tree, random forest, support vector machines (SVMs), and naive Bayes classifier have all been utilised.

Decision tree algorithm : Decision Tree algorithm falls under the category of supervised learning. They are highly interpretable machine learning models that allow us to stratify or segment data They can be used to solve both regression and classification problems. Decision tree uses the tree representation to solve the problem in which each leaf node corresponds to aclass label and attributes are represented on the internal node of the tree. They allow us to continuously split data based on specific parameters until a final decision is made. The main advantage of DT is that it can express rules so clinicians can understand and use the algorithm inthe dataset efficiently[17].The DT model generated rules that were simple to understand and offered more useful information for clinical

decision-making. This model has low training errors and fits the training data well, however it is unable to reliably predict test data or new samples.

Random Forest algorithm : Random Forest is a popular machine learning algorithm that belongs to the supervised learning technique. It can be used for both Classification and Regression problems in ML. It is based on the concept of ensemble learning, which is a process of *combining* multiple classifiers to solve a complex problem and to improve the performance of the model.Random Forest is a classifier that contains a number of decision trees on various subsets of the given dataset and takes the average to improve the predictive accuracy of that dataset." Instead of relying on one decision tree, the random forest takes the prediction from each tree and based on the majority votes of predictions, and it predicts the final output.The greater number of trees in the forest leads to higher accuracy and prevents the problem of overfitting. Several data mining techniques were used to predict the implantation outcome of IVF and intracytoplasmic sperm injection (ICSI). [18]

Support Vector Machine algorithm : Support Vector Machine is one of the most popular Supervised Learning algorithms, which is used for Classification as well as Regression problems. However, primarily, it is used for Classification problems in Machine learning.The goal of the SVM algorithm is to create the best line or decision boundary that can segregate n-dimensional space into classes so that we can easily put the new data point in the correct category in the future. This best decision boundary is called a hyperplane.SVM chooses the extreme points/vectors that help in creating the hyperplane. These extreme cases are called as support vectors, and hence algorithm is termed as Support Vector Machine. SVMs can also be applied to the evaluation of embryos.One of the most important aspects of optimising IVF procedures is the accurate measurement of embryo viability.Automated image analysis of embryos can increase the selection process' objectivity.An ideal classifier for evaluating embryos may be an SVM that performs a classification task by figuring out a separation rule between two sets of feature values. A method was proposed for image segmentation, which could upgrade automatically using SVMs classifiers, to provide a semi-automatic grading of human blastocysts. These investigators obtained an accuracy, ranging from 67 to 92% for human embryo development classification, indicating that automated evaluation tools of embryos based on SVMs are feasible and promising and more work in this area is required. [19]

Naive Bayes Classifier algorithm : Naïve Bayes algorithm is a supervised learning algorithm, which is based on **Bayes theorem** and used for solving classification problems. It is mainly used in *text classification* that includes a high-dimensional training dataset. It is a fast machine learning models that can make quick predictions.**It is a probabilistic classifier, which means it predicts on the basis of the probability of an object**. Naïve Bayes classifier can predict the implantation outcome of individual embryos in an IVF cycle by providing decision support based on the number of embryos transferred. By using morphological variables of individual embryos, higher accuracy rates could be obtainedregarding human implantation prediction.[20]

Challenges of implementing of AI in practice

The best techniques to use AI in clinical work provide a considerable issue in the reproductive realm.According to the authors, modern machine learning algorithms like deep learning are still in their infancy and haven't been well studied.As a result, they claimed that the majority of these machine-learning algorithms, a class of AI that shows the most potential for IVF, have ethical and legal dangers and liability difficulties, which may lead to distrust of patients and physicians[21].

In another review published in 2020, authors expressed “seemingly similar parameters can vary between clinics. For example, if one clinic captures blastocyst images at 110 hours, another clinic might capture them just before freezing — a time that may vary based on embryo development speed and current workload in the laboratory.” “AI requires calibration, and there is currently no agreement

on how to compare performances of various AI models for optimal methods. According to Hariton, another challenge in bringing AI to more practices is the current regulatory process[22].

ML algorithms, such as deep learning, require a significant amount of data for training; it may perform poorly if the data is insufficient. Selection bias from sample collection can result in poor performance of ML models in a clinical setting [23]. The efficient use of the high-quality data is also emphasised, along with the significance of data collecting and sharing.The majority of current AI research focuses on predicting ART outcomes as well as image analysis of sperm cells and embryos. Doctors may save a tonne of time and effort by using machine learning to tackle easy and repetitive chores.In the meantime, clinicians shoulduse the outcomes to inform their clinical work rather than blindly following the predictions ofthe ML models.

Future of AI in IVF treatment

The benefits of AI research are enormous.Much work needs to be done to integrate AI into reproductive medicine and IVF processes specifically.AI can assist doctors in accurately and efficiently choosing superior sperm and embryos for ART, as they can now analyse and understand more data with more depth than ever before. Notable developments in big data analytics will produce high-quality evidence. The ongoing development of such datasets is anticipated to offer a wealth of new prospects for reproductive medicine. Data mining is the foundational technique for this effort, and big data is the source of wisdom for the creation of AI medicine.The foundation for further uses of AI, such machine learning, can be laid by gathering a lot of reliable data, analysing it, and integrating it. Additionally, merging medical data from EMRs, medical images, laboratory tests, genetic information, and health records with cutting-edge AI techniques has the potential to alter how medicine is practised.

Big data-based decision support systems represent a substantial advancement in the field of reproductive medicine. Through dynamic programming and reinforcement learning techniques, it may update in real-time, supporting clinicians in making better clinical judgments based on patient clinical data.Develop a large dataset by learning, analysing, and condensing medical information using NLP, and then use deep learning to learn these enormous volumes of data to build models. The models are eventually applied in AI-assisted diagnosis after being continuously enhanced by comparing expert diagnosis.

The effectiveness and impact of ART can be significantly increased by incorporating new technologies for non-subjective sperm and embryo selection, oocyte denudation by mechanical removal of cumulus cells, oocyte positioning, fertilisation, embryo culture, and monitoring of embryo development into an automated device[24].Therefore, more infertility couples will benefit from AI advancement.

Conclusion:

In this study, we reviewed the fundamentals of artificial intelligence (AI) and machine learning, examined its applications in reproductive medicine, and briefed about the current and upcoming trends in AI. The use of AI in the medical industry will expand as big data becomes more widely available and precision medicine advances. Despite a number ofdrawbacks, modern AI technologies are ideally suited to tackle specific problems across a range of therapeutic disciplines.

References:

1. Ledford H. IVF at 40: revisiting the revolution in assisted reproduction. Nature. 2018. 10.1038/d41586-018-05792-9.
2. Inhorn MC, Patrizio P. Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. Hum Reprod Update. 2014;21:411–426.]
3. Vander Borght M, Wyns C. Fertility and infertility: definition and epidemiology. ClinBiochem.

2018;62:2–10.
4. Renjie Wang et al, Artificial intelligence in reproductive medicine,Reproduction, 2019 10; 158(4): R139-R154.
5. Darcy AM, Louie AK & Roberts LW2016 Machine learning and the profession ofmedicine. JAMA 315 551–552.
6. Nadkarni PM, Ohno-Machado L & Chapman WW 2011 Natural language processing: an introduction. Journal of the American Medical Informatics Association 18 544–551.
7. Mehta N & Devarakonda MV 2018 Machine learning, natural language programming, and electronic health records: the next step in the artificial intelligence journey? Journal of Allergy and Clinical Immunology 141 2019.e1–2021.e1.
8. Goodfellow, I. *et al. Deep Learning* 151–161 (The MIT Press, Cambridge, 2016).
9. Jordan MI & Mitchell TM 2015 Machine learning: trends, perspectives, and prospects. *Science* 255–260.
10. Mnih V, Kavukcuoglu K, Silver D, Rusu AA, Veness J, Bellemare MG, Graves A, Riedmiller M, Fidjeland AK, Ostrovski G, ***et al***. 2015 Human-level control through deepreinforcement learning. *Nature* 529–533.
11. Krittanawong C, Zhang H, Wang Z, Aydar M & Kitai T 2017 Artificial intelligence inprecision cardiovascular medicine. *Journal of the American College of Cardiology* 2657–2664.
12. Senders JT, Zaki MM, Karhade AV, Chang B, Gormley WB, Broekman ML, Smith TR & Arnaout O 2018 An introduction and overview of machine learning in neurosurgical care.*Acta Neurochirurgica* 29–38.
13. Wang L, Lekadir K, Lee SL, Merrifield R & Yang GZ 2013 A general framework forcontext-specific image segmentation using reinforcement learning. *IEEE Transactions onMedical Imaging* 943–956.
14. Tseng KK, Li Y, Hsu CY, Huang HN, Zhao M & Ding M 2013 Computer-assisted system with multiple feature fused support vector machine for sperm morphology diagnosis.*BioMed Research International* 687607.
15. Tao Y, Wang L & Almirall D 2018 Tree-based reinforcement learning for estimatingoptimal dynamic treatment regimes. *Annals of Applied Statistics* 1914–1938.
16. Baek D, Hwang M, Kim H, Kwon DS & Ieee 2018 *Path Planning for Automation of Surgery Robot based on Probabilistic Roadmap and Reinforcement Learning*. New York,NY: Ieee Publications.
17. Sahoo AJ & Kumar Y 2014 Seminal quality prediction using data mining methods.Technology and Health Care 22 531–545.
18. Hafiz P, Nematollahi M, Boostani R & Namavar Jahromi B 2017 Predicting implantation outcome of in vitro fertilization and intracytoplasmic sperm injection using data mining techniques. International Journal of Fertility and Sterility 11 184–190.
19. Santos Filho E, Noble JA, Poli M, Griffiths T, Emerson G & Wells D 2012 A method forsemi-automatic grading of human blastocyst microscope images. Human Reproduction 27 2641–2648.
20. Uyar A, Bener A & Ciray HN 2015 Predictive modeling of implantation outcome in an invitro fertilization setting: an application of machine learning methods. Medical Decision Making 35 714–725.
21. Wang R, et al. *Reproduction*. 2019;doi:10.1530/REP-18-0523.
22. Curchoe CL, et al. *Fertil Steril*. 2020;doi:10.1016/j.fertnstert.2020.10.040.
23. Senders JT, Zaki MM, Karhade AV, Chang B, Gormley WB, Broekman ML, Smith TR & Arnaout O 2018 An introduction and overview of machine learning in neurosurgical care.*Acta Neurochirurgica* 29–38.
24. Meseguer M, Kruhne U & Laursen S2012 Full in vitro fertilization laboratory mechanization: toward robotic assisted reproduction Fertility and Sterility 97 1277–1286.