Editorial

Artificial intelligence in assisted reproductive technology—current scenario and future implications

INTRODUCTION

After the first IVF conception the ensuing four decades have seen improvisations like oocyte and embryo cryopreservation, assisted fertilization, preimplantation genetic testing, and embryo selection technologies to increase fecundity. Innovative semi-automation techniques like time-lapse technology came next. There are still many grey areas and challenging critical issues that limit the success of ART. Artificial intelligence (AI) is the latest cognitive computer application attempting to bring a paradigm shift in ART. Introduced in 1990 in the research area of ART, AI was initially used to predict the outcome of IVF. This was followed by experimentation on more pertinent clinical applications in the field.

To understand how AI can promote the outcome of ART, we need to comprehend the basics of AI, its current applications, limitations, and also the future trends of AI. AI algorithms have been around for a really long time with experimentation going as far back as the 1950s and 1960s. However the AI industry has seen an immense rise in all fields recently and the healthcare industry is no exception. The reasons for this growing adoption can be attributed to the easy availability of compute power in the form of graphical processing units as well as the ever-growing amount of data that are being generated all around us. These two factors have made it possible to run complex algorithms on a huge amount of data and generate results in a timely fashion without breaking the bank.

At this point, it becomes pertinent to answer a basic question which is often raised by many of us. How useful is AI in improving the outcome of ART and does it make the judgement of a clinician or an embryologist redundant. To answer these questions, we need to understand that AI is in no way to be considered as a replacement for healthcare professionals but instead it is to be used as a tool to give more information which can help them to make better decisions. We know the limitations of current practice of IVF. We also know that there is huge data and information available and continuously being generated from all across the globe from IVF cycles. This knowledge and data can be channelized using AI to improve the working of an IVF lab and improve outcome. It is our belief that the application of AI in IVF can be significant. Areas where AI may be used to great advantage in IVF include: embryo evaluation and selection, optimizing the assessment of ovarian reserve parameters, and sperm selection. AI also has tremendous scope in managing the data, its storage, analysis, and in witnessing system to reduce human errors and providing much needed quality assurance. Indeed, AI may be useful in analyzing vast data sets of patient characteristics with diverse infertility treatment outcomes, all with the goal of providing individualized patient-centered treatment. It may also have potential in third-party reproduction, for example, it may improve our ability to match egg donors with recipients based on a variety of attributes including facial similarity.

The three applications of AI that are most widely used in ART are natural language processing (NLP), machine learning (ML), and robotics.

NLP is a section of AI which helps computers in understanding human language, text processing, and for classification. NLP can be used to extract useful information from contents such as electronic medical records (EMRs). NLP processes unstructured clinical data and converts it into structured data which can be further used for analysis and experimentation using other ML techniques. Using NLP one can use the usual prescription slip to identify/quantify the clinical data, which prevents the clinician from writing prescriptions in a particular format. Similarly laboratory data can be automatically prognosticated using techniques from NLP. Even with this flexibility it is hard for NLP systems to be generalized and they might require some customization to accommodate for specific nuances to increase their performance.

ML is a subfield of AI that performs specific tasks without using explicit instructions, but by relying on patterns and inference instead. It builds a mathematical model based on sample data known as the "training data" in order to make decisions or predict the outcome. It is divided into unsupervised learning, supervised learning, and reinforcement learning.

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.

Supervised learning methods use labeled training data to develop models that can predict a known output. Supervised learning is the most widely used form of ML with many applications in reproductive medicine. Some of the techniques that can be classified as supervised approaches are Decision Trees (DT), Random Forest, Support Vector Machines (SVMs) as well as more complex models like neural networks.

Reinforcement learning differs from the supervised learning in that it does not require input/output pairs of data need not be given to the model, instead it focuses on improving the accuracy using trial and error. Applications of RL are fairly limited in the space but it is mainly used for medical image processing and robotic surgery.

AI—CURRENT STATUS IN CLINICAL SCENARIO

Currently in ART the challenge for the clinician is to determine ways in which AI can be used clinically. ML algorithms like DT, SVMs, and neural networks have achieved good results and are promising.

AI finds clinical applicability in automated assessment, selection, and prediction of the sperm, oocyte, embryo in order to predict and improve the success rate of ART. The most critical determinant for the success of IVF is the quality of gametes and embryo, but in the current practice gametes and embryos are graded by embryologists using morphological assessment. Hence there is subjectivity involved in grading the quality depending on the expertise of the embryologist. There is also no single parameter or algorithm to grade or to predict the probability of a pregnancy or to learn the cause of failure. These are some of the problems that AI-based approaches can tackle which would result in optimizing the treatment cycle of ART.

OOCYTE ASSESSMENT

The success of ART is directly dependent upon the quality of oocytes with a current low pregnancy rate of 4.5% per retrieved oocyte. Current oocyte assessment is based on morphology and not the assessment of oocyte developmental competence. Aneuploidies are also missed as aneuploid oocyte may be normal morphologically. Hence it becomes crucial to identify new noninvasive biomarkers to predict oocyte quality and to exclude aneuploidies. AI algorithms appear promising for oocyte selection by quantification of gamete developmental competence. Evaluation of human oocytes from the germinal vesicle (GV) to the metaphase II stage by time-lapse or assesses gene expression through transcriptomics or genomics. Competence of oocytes by calculating the cytoplasmic movement velocities [by using the particle image velocimetry (PIV)], with data analysis by artificial neural network (accuracy of 91.03%) or measuring viscoelastic properties of human zygotes hours after fertilization could reliably predict viability and blastocyst formation, with >90% precision, 95% specificity, and 75% sensitivity.

EMBRYO ASSESSMENT

This presents a similar problem to oocyte assessment as the current assessment of embryos is subjective. Embryologists select the embryos based on morphology or dynamic development of karyogamy and cytokinesis. This subjective evaluation of embryos is dependent on the expertise of the embryologist. A precise selection of embryo will increase the practice of SET reducing the incidence of multiple pregnancy and the associated risks of pre-eclampsia and maternal hemorrhage. AI helps in automated image analysis of embryos objectivity assessment and grade the human blastocysts by morphological assessment. Current studies appear promising with an accuracy of 67–92% based on implementations using SVMs. Assessment of embryos is done by SVM algorithms to quantify and grade the inner cell mass (ICM) and trophectoderm (TE) quality. Blastocysts are assessed by fractal dimension and mean thickness of TE and ICM image texture description. AI algorithms also permit greater manipulation of digitized image of the embryo by optimization of the microscope for better contrast resolution and better demarcation of boundaries for better image and Retinex algorithm to improve the input images with greater accuracy to grade blastocysts by analyzing TE in an automated method appear to be promising. Other applications have detected non-viable embryos with aberrant transcriptomes in RNA-sequential data.

AI-based processes also enable the embryologist to perform sperm selection and semen analysis for assessment of morphology of the sperm and sperm kinetics subjectively. AI models help diagnose and predict chromosomal abnormalities using simple parameters like height, total testicular volume, follicle-stimulating hormone, luteinizing hormone, total testosterone, and ejaculate volume with 95% accuracy.

Robotic surgery in minimally invasive surgery (MIS) has improvised traditional laparoscopy by providing three-dimensional visualization, greater precision, fine instruments, and shorter learning curves. It also gives better perioperative outcomes and safety thereby optimizing patient's reproductive outcomes. Surgeries currently done by robotic surgeries are uterine leiomyomas, adenomyosis, endometriosis, DIE, adnexal masses, sterilization reversal, and fertility preservation techniques. In adenomyosis, robotic surgery has an advantage as it can do meticulous suturing in multiple layers and provide a 3D vision to help discern the boundaries between the myometrial lesions and surrounding healthy myometrium for corrective surgery of adenomyosis. Robotic surgery can reduce blood loss, postoperative pain, and hospital stay and shorten convalescence but there is a hike in cost with longer operating time. However, since most studies available in literature are observational or retrospective studies more RCTs are required.

Prediction of IVF outcome using AI can help clinicians to tailor personalized treatment to couples to improve the pregnancy outcome of ART. Such prognostication may help in reducing cost, plan treatment, and help in counselling of patient .

The limitations of current studies are that the quality and quantity of data derived in most studies are small, single in source, and retrospective. There is a lack of large-scale randomized controlled trials to test the validity of the algorithms and optimize the use of limited research resources.

Since in certain domains AI technology has equaled or excelled human performance, there is an apprehension that AI may replace clinicians. As of date AI is mere tool to supplement the clinician by handling simple and repetitive tasks, saving time and effort for clinicians. Clinicians still have to weigh certain facts before amalgamating AI into clinical practice. If approved for clinical application, the use of AI to select better embryos with greater fecundity potential might save time and effort by processing and interpreting more data and with precision and is cost effective.

ML models lack transparency and unfortunately have a black box nature associated with them. This lack of transparency poses ethical and legal risks. What if the embryo selection suggested by AI algorithm erred and selected a wrong or an aberrant embryo and implanted leading to anomalies in the fetus. In this unexpected and unfortunate situation who will bear the brunt of wrath—the clinician, institute, or the AI? Another dilemma and ethical challenge to be considered is that can/should AI be allowed/train currently trained to "select" embryos with better genetic "make-up" or "design" embryos with the "best genes"? As the use of AI in ART moves rapidly from research to clinical use, it becomes imperative to address the potential ethical, legal, and organizational challenges that might arise and create a formal framework to navigate around these issues.[1-4]

CONCLUSION

The applications of AI in ART have the potential to bring the next paradigm shift. Despite the current limitations, today AI can address certain clinical challenges which are of prognostic importance and can be used as an auxiliary tool. For better adoption industry wide there is a huge need to change the black box nature of AI algorithms into a more transparent process as in its current state it lacks interpretability. This lack of interpretability becomes a huge limitation as application of critical decisions generated by the algorithms to the treatment of a patient requires the clinician to know how those results are derived.

In future, the applications of AI techniques and their amalgamation in clinical practice of ART have the potential to improve fertility rate and address the grey areas like implantation. It is however important to lay down guidelines, policies, and recommendations for the integration of AI technologies in ART practice in order to ensure ethical practice.

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SUGGESTED FURTHER READING

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