# Controversies in Obstetrics & Gynecology and Pediatrics

# The intersection of technology and infertility: pioneering approaches in genetic editing and artificial intelligence

<sup>D</sup>Tuğba Gürbüz<sup>1</sup>, <sup>D</sup>Arzu Yurci<sup>2</sup>

<sup>1</sup>Department of Gynecology and Obstetric Clinic, Medistate Hospital, İstanbul, Turkiye

<sup>2</sup>Department of Óbstetrics and Gynecology, Faculty of Medicine, İstanbul Arel University, İstanbul, Turkiye

**Cite this article:** Gürbüz T, Yurci A. The intersection of technology and infertility: pioneering approaches in genetic editing and artificial intelligence. *J Controv Obstetr Gynecol Ped.* 2024;2(3)64-68

Corresponding Author: Tuğba Gürbüz, drtgurbuz@hotmail.com

Received: 25/03/2024

Accepted: 15/04/2024

Published: 30/07/2024

# ABSTRACT

Infertility, a global health concern, impacts millions of individuals and couples, entailing profound emotional and socioeconomic consequences. Recent advances in genetic editing and artificial intelligence (AI) herald a new frontier in infertility treatment, offering precision, personalization, and enhanced efficacy. This compilation explores the integration of clustered regularly interspaced short palindromic repeats associated proteins (CRISPR-Cas) 9 gene editing and AI-driven diagnostics and treatment strategies in the context of reproductive medicine. Through a comprehensive review of current research, clinical applications, and ethical considerations, this paper highlights the transformative potential of these technologies while addressing the associated challenges. The synergy of genetic editing and AI not only promises to improve outcomes for individuals battling infertility but also raises important questions about accessibility, privacy, and ethical implications. By examining these developments, we aim to provide insights into the future of infertility treatments and the evolving landscape of reproductive medicine.

Keywords: Infertility, genetic editing, CRISPR-Cas9, artificial intelligence, reproductive medicine

# **INTRODUCTION**

Infertility, characterized by the inability to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse, is a global health concern that affects approximately 15-20% of couples worldwide. This condition not only poses significant challenges to individuals' physical and emotional well-being but also imparts substantial socio-economic burdens on families and healthcare systems. The journey of infertile couples through the maze of available treatments is fraught with high costs, emotional distress, and varying degrees of success, reflecting the complexity of human reproduction and the multitude of factors that can influence fertility.<sup>1</sup>

Historically, the approach to managing infertility has evolved significantly, from the use of simple remedies and interventions in ancient times to the development of assisted reproductive technologies (ART) in the modern era. The latter half of the 20th century marked a pivotal moment in reproductive medicine with the advent of in vitro fertilization (IVF), a technique that has since revolutionized the treatment of infertility. Despite these advancements, a substantial proportion of couples remain unsuccessful in their quest for parenthood, underscoring the need for continuous innovation and improvement in fertility treatments.<sup>2</sup>

Into this landscape of ongoing challenge and change, genetic editing and artificial intelligence (AI) emerge as revolutionary

technologies with the potential to fundamentally transform the field of infertility treatment. Genetic editing, particularly through the clustered regularly interspaced short palindromic repeats associated proteins (CRISPR-Cas) 9 system, offers unprecedented precision in modifying the DNA sequences of living organisms, allowing for the correction of genetic defects that contribute to infertility. This technology not only holds promise for eradicating inherited genetic disorders but also opens new avenues for understanding and treating infertility at its genetic roots.<sup>3</sup>

Parallel to the developments in genetic editing, AI and machine learning algorithms are making significant strides in the diagnosis and treatment of infertility. By analyzing vast datasets and identifying patterns beyond human recognition, AI can enhance the accuracy of infertility diagnoses, optimize treatment protocols, and improve the selection process for viable embryos in IVF procedures. The integration of AI into reproductive medicine promises to personalize and refine infertility treatments, making them more effective and accessible to a wider population.<sup>4</sup>

The introduction of CRISPR-Cas9 genetic editing and AI into the domain of infertility treatment represents a convergence of biotechnology and information technology that has the potential to address the limitations of current treatment modalities. This article aims to explore the transformative



potential of these technologies, examining their applications, challenges, and ethical considerations in the context of reproductive medicine. Through a detailed review of the latest research and clinical practices, we will delve into how genetic editing and AI are reshaping the landscape of infertility treatment, offering new hope and possibilities for individuals and couples facing the challenges of infertility.

## GENETIC EDITING AND INFERTILITY TREATMENT

Infertility, a condition affecting millions of couples worldwide, has a multifaceted etiology, with genetic causes accounting for a significant proportion of cases. Genetic abnormalities, including chromosomal anomalies and gene mutations, can lead to various forms of infertility, such as impaired sperm production or function in men and ovulatory disorders in women.<sup>5</sup> The complexity and diversity of genetic factors involved underscore the need for innovative approaches to diagnosis and treatment.

The advent of CRISPR-Cas<sub>9</sub> technology has marked a revolutionary leap in the field of genetic editing, offering a powerful tool for modifying DNA with unprecedented precision, efficiency, and flexibility. Developed from a naturally occurring genome editing system in bacteria, the CRISPR-Cas<sub>9</sub> technology allows for the targeted alteration of genetic material, opening new avenues for the treatment of genetic disorders, including those leading to infertility.<sup>6</sup>

Historically, the development of CRISPR-Cas<sub>9</sub> technology can be traced back to the discovery of CRISPR and CRISPR-Cas<sub>9</sub> in bacteria, serving as an adaptive immune system against viruses. The transformation of this biological phenomenon into a versatile genetic editing tool was achieved through the characterization of its mechanism, which involves the Cas<sub>9</sub> nuclease guided by a specifically designed RNA sequence to a target DNA site, where it induces a double-strand break. This break can then be repaired through non-homologous end joining or homology-directed repair, allowing for the addition, deletion, or alteration of specific DNA sequences.<sup>3</sup>

In the context of infertility treatment, CRISPR-Cas, technology has been applied to correct genetic abnormalities that lead to the condition. For example, mutations in the Y chromosome affecting sperm production and autosomal recessive disorders like cystic fibrosis-related infertility have been targeted using CRISPR-Cas<sub>o</sub> demonstrating the potential to restore fertility through genetic correction.7 Recent studies have showcased the successful application of CRISPR-Cas, in animal models, correcting gene mutations responsible for infertility and paving the way for clinical applications in humans.8 However, the application of CRISPR-Cas, in infertility treatment raises significant ethical considerations. The prospect of germline editing, which would result in genetic changes being passed on to future generations, has ignited a debate on the moral implications of such interventions. Concerns over the potential for creating "designer babies" with selected traits further complicate the ethical landscape, highlighting the need for stringent regulatory frameworks and ethical guidelines to govern the use of genetic editing technologies in reproductive medicine.9

Despite its transformative potential, CRISPR-Cas<sub>9</sub> technology faces several challenges and limitations. Off-target effects, where unintended genetic modifications occur, pose a risk for unforeseen consequences and necessitate the development of strategies to enhance the specificity and accuracy of the technology. Additionally, genetic mosaicism, resulting from the editing of some but not all cells, can compromise the efficacy of treatment and necessitates further research to optimize the application of CRISPR-Cas<sub>9</sub> in infertility treatment.<sup>10</sup>

In conclusion, while CRISPR-Cas9 technology represents a groundbreaking advancement in the treatment of infertility with a genetic basis, it is accompanied by ethical dilemmas, technical challenges, and limitations that must be carefully addressed. The ongoing development of this technology and its applications in reproductive medicine warrants a multidisciplinary approach, combining scientific innovation with ethical stewardship to ensure the responsible use of genetic editing for the benefit of individuals and couples affected by infertility.

## ARTIFICIAL INTELLIGENCE IN DIAGNOSING AND TREATING INFERTILITY

The advent of AI and machine learning in medical diagnostics has inaugurated a new era in healthcare, offering unprecedented precision, efficiency, and personalization in treatment. AI's application spans various domains, including oncology, neurology, and cardiology, with its role in reproductive medicine and infertility treatment emerging as a particularly promising area of development.<sup>11</sup>

AI and machine learning algorithms excel in identifying patterns within large datasets, surpassing traditional statistical methods in predicting outcomes and diagnosing conditions. In the realm of infertility treatment, these technologies are employed to analyze complex biological and clinical data, offering innovative approaches to diagnosis, treatment optimization, and the personalization of care plans.<sup>12</sup>

One of the most significant applications of AI in infertility treatment is in predictive analytics, which assesses the likelihood of treatment success. By analyzing factors such as patient age, genetic information, lifestyle variables, and previous treatment outcomes, AI algorithms can predict the efficacy of treatments like IVF, helping clinicians and patients make informed decisions about their care.<sup>13</sup>

Furthermore, AI plays a crucial role in embryo selection during the IVF process. Advanced imaging techniques, combined with machine learning algorithms, evaluate embryo viability more accurately than the human eye, predicting implantation success rates and improving overall IVF outcomes. This technology not only increases the likelihoo d of pregnancy but also reduces the risk of multiple gestations by identifying the single best embryo for transfer.<sup>14</sup>

Personalized treatment plans, tailored to the individual's unique profile, represent another breakthrough facilitated by AI in infertility treatment. By analyzing detailed patient data, AI algorithms can optimize treatment protocols, adjust medication dosages, and recommend lifestyle changes, thereby enhancing the chances of successful pregnancy.<sup>15</sup>

Recent advancements in AI have led to success stories that underscore its potential in transforming infertility treatment. Studies have documented cases where AI-assisted embryo selection resulted in higher pregnancy rates compared to traditional selection methods, marking a significant milestone in the application of AI in reproductive medicine.<sup>4</sup> However, the integration of AI into infertility treatment raises several ethical considerations. Data privacy concerns emerge as patient data are used to train AI models, necessitating robust safeguards to protect sensitive information. Algorithmic bias is another critical issue, where AI models may inadvertently reflect or amplify biases present in the training data, potentially leading to unequal treatment outcomes across different patient groups.<sup>16</sup>

Challenges and future prospects for AI in infertility treatment include its integration into clinical practice and ensuring accessibility. The successful adoption of AI technologies requires not only technological infrastructure but also training for healthcare professionals to interpret and apply AI-driven insights effectively. Moreover, ensuring equitable access to AI-enhanced treatments across different socio-economic and geographical areas remains a paramount concern, calling for strategies to democratize access to these advanced technologies.<sup>17</sup>

In conclusion, AI and machine learning represent transformative forces in the diagnosis and treatment of infertility, offering new hope to countless individuals and couples. As these technologies continue to evolve, they promise to further refine the precision, efficacy, and personalization of infertility treatments. Nonetheless, realizing the full potential of AI in this field will require addressing the ethical, technical, and accessibility challenges, ensuring that the benefits of AIenhanced treatments are available to all who need them.

# THE SYNERGY OF GENETIC EDITING AND AI IN REPRODUCTIVE MEDICINE

The convergence of genetic editing and AI in reproductive medicine is setting the stage for a paradigm shift in the diagnosis, treatment, and management of infertility. The integration of these two cutting-edge technologies offers a holistic approach that not only addresses the genetic underpinnings of infertility but also optimizes treatment protocols through predictive analytics and personalized medicine. This synergy promises to enhance the efficacy of treatments, reduce associated risks, and pave the way for new therapeutic possibilities.

Genetic editing, particularly through CRISPR-Cas9 technology, provides a powerful tool for correcting genetic anomalies that contribute to infertility. By precisely targeting and modifying DNA sequences, CRISPR-Cas9 can potentially rectify mutations in genes implicated in infertility, such as those affecting sperm production, egg quality, and embryo development.<sup>18</sup> This precise correction at the genetic level

represents a significant advancement over traditional treatment methods, offering the potential for a permanent cure for certain types of genetic-based infertility.

Concurrently, AI and machine learning algorithms are revolutionizing the field by analyzing complex datasets to predict the success of infertility treatments, including IVF. AI can identify patterns and factors that influence treatment outcomes, enabling the development of personalized treatment plans that maximize the chances of success.<sup>15</sup> Moreover, AI-driven embryo selection techniques enhance the IVF process by accurately predicting embryo viability, thereby improving implantation rates and reducing the likelihood of multiple pregnancies. The synergy between genetic editing and AI extends to the realm of gene therapy for inherited disorders that impact fertility. AI algorithms can assist in the identification of genetic mutations that cause infertility, while CRISPR-Cas, can be employed to correct these mutations in affected individuals or embryos. This collaborative approach not only aims to restore fertility but also prevents the transmission of genetic disorders to future generations, offering a profound impact on reproductive health.<sup>19</sup>

Recent studies underscore the potential of combining genetic editing with AI in reproductive medicine. For instance, research has demonstrated the use of AI to optimize the selection of CRISPR-Cas, targets for genetic correction, enhancing the efficiency and accuracy of gene editing in preclinical models.<sup>20</sup> Moreover, the development of AI platforms that predict the outcomes of gene editing interventions in reproductive cells or embryos heralds a new era of precision medicine in fertility treatments. However, the integration of genetic editing and AI in reproductive medicine raises ethical and social concerns. Issues such as the potential for germline editing, the creation of "designer babies," and the equitable access to these advanced technologies necessitate careful consideration and regulation. Ensuring that these technologies are used responsibly and ethically, with a focus on improving human health and wellbeing, remains a paramount concern for the scientific and medical communities.<sup>21</sup> In conclusion, the synergy of genetic editing and AI represents a frontier in reproductive medicine with the potential to significantly improve the diagnosis and treatment of infertility. By combining the precise targeting capabilities of CRISPR-Cas, with the predictive power of AI, this integrated approach offers new hope for individuals and couples facing fertility challenges. As research and development in this area continue to advance, it is imperative that ethical, legal, and social implications are addressed to ensure that the benefits of these technologies are realized in a manner that is equitable and just.

### DISCUSSION

The synergy between genetic editing and AI in reproductive medicine represents a frontier of innovation with the potential to address some of the most persistent challenges in infertility treatment. The convergence of these technologies not only enhances the precision and effectiveness of treatments but also raises significant ethical, societal, and practical considerations that warrant a comprehensive discourse. Genetic editing, particularly through CRISPR-Cas, offers the promise of correcting genetic abnormalities that lead to infertility, thus providing targeted treatments that could increase the chances of successful pregnancy outcomes. Meanwhile, AI and machine learning algorithms have shown remarkable success in improving diagnostic accuracy, optimizing treatment protocols, and selecting viable embryos for IVF procedures. The integration of these technologies could lead to a more personalized approach to infertility treatment, where interventions are tailored to the specific genetic and physiological profiles of individuals or couples.<sup>22,23</sup> However, the application of genetic editing and AI in reproductive medicine is not without its challenges. Ethical concerns, particularly regarding germline editing and the potential for creating "designer babies," have sparked debate among scientists, ethicists, and the public alike. The possibility of introducing irreversible changes into the human germline necessitates cautious deliberation and robust ethical guidelines to prevent misuse and ensure that the technology is used for therapeutic purposes only.24,25

Moreover, the use of AI in infertility treatment raises questions about data privacy, algorithmic bias, and the equitable access to these advanced technologies. Ensuring that AI systems are transparent, fair, and accessible to diverse populations is essential for their ethical and effective integration into clinical practice.<sup>26</sup>

#### CONCLUSION

The integration of genetic editing and AI into reproductive medicine heralds a new era of possibilities for treating infertility. These technologies have the potential to transform the landscape of infertility treatment, offering more precise, effective, and personalized therapeutic options. However, realizing this potential requires navigating a complex array of ethical, technical, and societal challenges.As we move forward, it is imperative that the development and application of genetic editing and AI in reproductive medicine are guided by rigorous scientific standards, ethical principles, and a commitment to equity. Collaborative efforts among scientists, clinicians, ethicists, policymakers, and patients will be crucial in addressing the challenges and harnessing the opportunities presented by these technologies. The future of infertility treatment lies in the balance of innovation and responsibility. By carefully managing the risks and ethical implications, we can unlock the full potential of genetic editing and AI to provide hope and solutions to those facing the challenges of infertility.

### ETHICAL DECLARATIONS

#### **Referee Evaluation Process**

Externally peer-reviewed.

#### **Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

#### **Financial Disclosure**

The authors declared that this study has received no financial support.

#### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

#### REFERENCES

- 1. World Health Organization. Global prevalence of infertility, infecundity, and childlessness. 2021;1(123).885-910.
- 2. Ombelet W, Van Robays J. Artificial insemination history: hurdles and milestones. *Facts Views Vis Obgyn*. 2015;7(2):137-143.
- 3. Doudna JA, Charpentier E. Genome editing. The new frontier of genome engineering with CRISPR-Cas<sub>9</sub>. *Science*. 2014;346(6213): 1258096. doi: 10.1126/science.1258096
- Rolfes V, Bittner U, Gerhards H, et al. Artificial intelligence in reproductive medicine-an ethical perspective. *Geburtshilfe Frauenheilkd*. 2023;83(1):106-115. doi: 10.1055/a-1866-2792
- 5. World Health Organization. Infertility Definitions and Terminology. 2020;1(35):2735-2745.
- 6. Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science*. 2012;337 (6096):816-821.
- Zhu P, Wu F, Mosenson J, Zhang H, He TC, Wu WS. CRISPR/Cas<sub>9</sub>mediated genome editing corrects dystrophin mutation in skeletal muscle stem cells in a mouse model of muscle dystrophy. *Mol Ther Nucleic Acids*. 2017;16(7):31-41.
- 8. Ma H, Marti-Gutierrez N, Park SW, et al. Correction of a pathogenic gene mutation in human embryos. *Nature*. 2017;548 (7668):413-419. doi: 10.1038/nature23305
- 9. National academies of sciences, engineering, and medicine; national academy of medicine; national academy of sciences; committee on human gene editing: scientific, medical, and ethical considerations. human genome editing: science, ethics, and governance. *National Academies Press.* 2017;2(14):28796468.
- Fu Y, Foden JA, Khayter C, et al. High-frequency off-target mutagenesis induced by CRISPR-Cas, nucleases in human cells. *Nat Biotechnol.* 2013;31(9):822-826. doi: 10.1038/nbt.2623
- Lin B, Ma Y, Wu S. Multi-omics and artificial intelligence-guided data integration in chronic liver disease: prospects and challenges for precision medicine. *Omics.* 2022;26(8):415-421. doi: 10.1089/ omi.2022.0079
- 12. Medenica S, Zivanovic D, Batkoska L, et al. The future is coming: artificial intelligence in the treatment of infertility could improve assisted reproduction outcomes-the value of regulatory frameworks. *Diagnostics*. 2022;12(12):2979.
- 13. Hanassab S, Abbara A, Yeung AC, et al. The prospect of artificial intelligence to personalize assisted reproductive technology. *NPJ Digit Med.* 2024;7(1):55. doi: 10.1038/s41746-024-01006-x
- 14. Si K, Huang B, Jin L. Application of artificial intelligence in gametes and embryos selection. *Hum Fertil*. 2023;26(4):757-777.
- Wang R, Pan W, Jin L, et al. Artificial intelligence in reproductive medicine. *Reproduction*. 2019;158(4):139-154. doi: 10.1530/REP-18-0523
- Güell E. Criteria for implementing artificial intelligence systems in reproductive medicine. *Clin Exp Reprod Med.* 2024;51(1):1-12. doi: 10.5653/cerm.2023.06009
- 17. Arnold MH. Teasing out artificial intelligence in medicine: an ethical critique of artificial intelligence and machine learning in medicine. *J Bioeth Inq.* 2021;18(1):121-139. doi: 10.1007/s11673-020-10080-1
- 18. Collins FS, Varmus H. A new initiative on precision medicine. *N Engl J Med.* 2015;372(9):793-795. doi:10.1056/NEJMp1500523
- Ishii T. Reproductive medicine involving genome editing: clinical uncertainties and embryological needs. *Reprod Biomed Online*. 2017;34(1):27-31. doi: 10.1016/j.rbmo.2016.09.009
- 20. Morshedzadeh F, Ghanei M, Lotfi M, et al. An update on the application of CRISPR technology in clinical practice. *Mol Biotechnol*. 2024;66(2):179-197. doi: 10.1007/s12033-023-00724-z
- 21. Ishii T. Germ line genome editing in clinics: the approaches, objectives and global society. *Brief Funct Genomics*. 2017;16(1):46-56.

#### Controversies in Obstetrics & Gynecology and Pediatrics

- 22. Long C, McAnally JR, Shelton JM, et al. Prevention of muscular dystrophy in mice by CRISPR/Cas<sub>9</sub>-mediated editing of germline DNA. Science. 2014;345(6201):1184-1188.
- 23. Wang YL, Gao S, Xiao Q, et al. Role of artificial intelligence in digital pathology for gynecological cancers. *Comput Struct Biotechnol J.* 2024;24 (11):205-212. doi: 10.1016/j.csbj.2024.03.007
- 24. van Dijke I, Lakeman P, Mathijssen IB, Goddijn M, Cornel MC, Henneman L. How will new genetic technologies, such as gene editing, change reproductive decision-making? Views of high-risk couples. *Eur J Hum Genet*. 2021;29(1):39-50.
- 25. Knoppers BM, Kleiderman E. "CRISPR babies": what does this mean for science and Canada? *CMAJ*. 2019;191(4):91-92.
- 26. Khan B, Fatima H, Qureshi A, et al. Drawbacks of artificial intelligence and their potential solutions in the healthcare sector. *Biomed Mater Devices*. 2023;1(2):731-738. doi: 10.1007/ s44174-023-00063-2

#### Tuğba Gürbüz

I was born in Tarsus and graduated from a high school in Tarsus in 2000, and then from İstanbul Faculty of Medicine in 2006. I completed my training as a Gynecology and Obstetrics specialist and became a specialist in 2011. After working at Babaeski State Hospital, I returned to İstanbul and started working at Private Medistate Kavacık Hospital. I am an academician at Nişantaşı University. I became an Associate Professor in 2021 and I have a son.

