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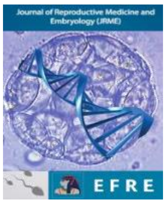

EFRE 40: An AI-generated predictive algorithm for IVF success in AMA

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Abstract

Natural Language Processing (NLP), a subset of artificial intelligence (AI), enables computers to interpret and generate human language. Machine learning (ML) models are increasingly employed to analyze clinical, hormonal, and embryological data to predict in vitro fertilization (IVF) success rates.the success rates of IVF, particularly among women over the age of 40, remain a significant concern. Advancements in artificial intelligence (AI) offer promising avenues to enhance predictive modeling in this domain, potentially improving clinical outcomes This study aims to develop a predictive model using Meta AI to estimate live birth probabilities in women over 40 undergoing IVF. By inputting specific variables into the AI model, we seek to create a tool that can assist clinicians and patients in making informed decisions about fertility treatments, ultimately improving personalized care in this demographic. The model was created using a theoretical framework, without real-world patient data. The model included; embryo quality, uterine receptivity, maternal age, sperm quality and previuos pregnancy outcome. The aim of the model is to predict clinical pregnency rate and live birth rate..

Keywords: Prediction models, Advanced maternal age, Artificial intelligence.

Introduction

In vitro fertilization (IVF) in advanced maternal age (AMA) is a challenging procedure to any assisted reproductive technology (ART) center. Due to social and financial factors, the percentage of older women in any ART program is increasing Maternal age is one of the most important variables that determines the success of any ART cycle (1). This subgroup of patients often suffers from decreased ovarian reserve, poor quality oocytes and high aneuploidy rates (2).

According to the Society for Assisted Reproductive Technology (SART) data, the live birth rate per IVF cycle for women aged 38–40, the live birth rate is approximately 26%, which further declines to 13.3% for those aged 41–42, and to 4% for women over 40 (3).

The use of predictive modeling in reproductive medicine has gained significant attention in recent years. Predictive models take into consideration multiple factors aiming at estimation of the ART cycle success rates. These models facilitate, counselling, decision-making, reduce unnecessary treatment cycles, and optimize resource allocation (4).

Women over 40 often require more aggressive treatment strategies that are usually expensive, and their outcome is usually disappointing. Utilizing accurate personalized predictive models in this subgroup of patients helps both the care provider and the patient in their decision-making. This strategy will reduce unnecessary treatment cycles and optimize resource allocation. However, existing predictive models often rely on retrospective cohort data and may not accurately reflect the complex interplay of factors influencing IVF success in women over 40 (2).

The integration of artificial intelligence (AI) into healthcare improved data analysis and enabled the development of predictive models with remarkable accuracy. Machine learning algorithms, a subset of AI, have been instrumental in analyzing complex datasets to identify patterns and predict clinical events (5).

The main advantage of AI predictive models is that it ensures accurate analysis of the available published data. In addition, it saves the time needed for extensive data collection and cleaning. These models can explore hypothetical scenarios and relationships between variables, providing insights into complex systems. However, AI models developed without real-world data may not accurately reflect actual outcomes and may be prone to bias. The main disadvantage of AI models is the lack of real-world validation (6).

Meta AI, the artificial intelligence research arm of Meta Platforms, has been at the forefront of developing advanced AI models capable of understanding and generating human-like text. These models have been applied across various domains, including healthcare, to process and analyze large volumes of data, aiding in the development of predictive models without direct access to real-world datasets (7).

On the other hand, statistically driven predictive models based on patient data offer real-world validation, reduced risk of bias, and improved accuracy. These models can be developed using various statistical techniques, including logistic regression, decision trees, and random forests. However, collecting and analyzing real-world data can be time-consuming and resource-intensive (8). A hybrid approach that combines the strengths of both methods may be the most effective way to develop accurate and reliable predictive models in healthcare (9).

Table 1: Advantages and Disadvantages of AI predictive Models without real-world data

	Advantages	Disadvantages
AI Predictive Models without Real-World Data	**Speed and efficiency**	**Lack of real-world validation**
	Theoretical exploration	**Limited generalizability**
	Flexibility	**Risk of perpetuating existing bias**
	Advantages	**Disadvantages**
Statistically Driven Predictive Models based on Real-World Patient Data	**Real-world validation**	**Time-consuming and resource-intensive**
	Reduced risk of bias	**Data quality issues**
	Improved accuracy	**Limited flexibility**

AI developing predictive models extracts data from reputable databases and peer-reviewed journals utilizes computer systems that simulates the decision-making abilities of human experts to solve complex problems. These systems consist of a knowledge base, storing facts and rules, and an inference engine that applies these rules to known information to deduce new insights (10).

AI can be employed to systematically review and analyze vast amounts of scientific literature, extracting relevant data and identifying patterns associated with IVF outcomes. By processing information from peer-reviewed journals, AI systems can discern factors influencing live birth rates, such as patient demographics, treatment protocols, and embryonic characteristics (11).

The insights garnered from AI-driven literature analysis can then be encoded into expert systems. This involves creating models or programs capable of analyzing complex information and making informed decisions similar to those a human expert would make. Expert systems can tackle complex problems by reasoning through the available knowledge, effectively mimicking the cognitive processes of human experts. The objective of such systems is to provide decision support that mirrors the quality and accuracy of human expertise, thereby enhancing efficiency and consistency in various applications. In the context of IVF, these systems utilize AI to analyze extensive medical literature and data, thereby assisting clinicians in predicting IVF outcomes (12-14).

SWOT analysis of AI predictive model without real-world data

It is theoretically possible to create a predictive model using AI without direct patient data by synthesizing insights from medical literature and databases (e.g., PubMed, Cochrane reviews, or public datasets like NHANES).

This approach would rely on (15-17):

-Natural Language Processing (NLP): Extracting variables, risk factors, and outcomes from high-impact studies.

-Meta-Analysis Aggregation: Combining effect sizes from published studies to infer relationships.

-Knowledge Graphs: Mapping causal pathways from existing research (e.g., age-related ovarian reserve decline, BMI impact on IVFsuccess).

SWOT Analysis

Table 2: SWOT analysis of predictive model using AI without direct patient data (15-19)

Strength	Weakness
Cost/time-efficient vs. primary data collection **Leverages existing peer-reviewed evidence** **Hypothesis generation for future research**	**No direct patient data lower accuracy** **Risk of amplifying publication/selection bias.** **Limited ability to model rare outcomes or interactions**
Opportunities	**Threats**
Guides resource-limited settings **Complements clinical decision support tools** **Foundation for adaptive models as new data emerges**	**Ethical risks if unvalidated models inform care** **Legal liability if recommendations harm patients** **Skepticism from clinicians due to lack of validation**

This paper explores the development of a predictive model utilizing Meta AI to forecast live birth probabilities in women over 40 undergoing IVF, based on specified variables and without reliance on real-world data.

Objective of the Study

This study aims to develop a predictive model using Meta AI to estimate live birth probabilities in women over 40 undergoing IVF. By inputting specific variables into the AI model, we seek to create a tool that can assist clinicians and patients in making informed decisions about fertility treatments, ultimately improving personalized care in this demographic.

Significance of the Study

The development of accurate predictive models is crucial for enhancing IVF success rates among older women. By utilizing AI to analyze existing data and generate predictions, this study contributes to the growing body of knowledge aimed at improving reproductive outcomes. Furthermore, it underscores the potential of AI in transforming healthcare by providing innovative solutions to complex clinical challenges.

Methodology:

Traditional approaches for fertility scoring framework development depend on manual review, statistical modeling and domain experts' knowledge aggregation. Despite the effectiveness of those models, they are often time-consuming, susceptible to biases and challenged by large volume of literature (20).

To address those limitations, this study explores the application of Generative AI, specifically Meta AI's Llama 3.2, to autonomously extract, synthesize, and formulate a structured decision-support framework in the context of providing a model for scoring the input data features and predicting the probability of live birth accordingly (21).

Meta AI's model was provided only with a problem statement including a list of independent input features and an objective rather than structured datasets or predefined search queries. The AI model autonomously generated knowledge representations by identifying key feature interactions, constructing a probabilistic scoring mechanism, and mapping feature distributions to estimated probabilities of outcomes. The resulting framework was then subjected to medical experts' validation to assess its reliability and clinical applicability (22).

Unlike conventional machine learning models trained on static datasets, GenAI was leveraged as a knowledge synthesis, extracting insights from various sources such as PubMed, Google Scholar and fertility research journals. The model was not directly programmed to query specific databases, but rather demonstrated an ability to retrieve relevant patterns and statistical relationships from publicly available medical research (23).

The extracted information was structured where the input features are as follows, patient age, AMH (Anti-Müllerian Hormone) levels, AFC (Antral Follicle Count), FSH (Follicle-Stimulating Hormone) levels, embryo quality and treatment protocol. Those features were subsequently mapped to a probabilistic scoring system. Figure 1 shows a flowchart of the developed framework.

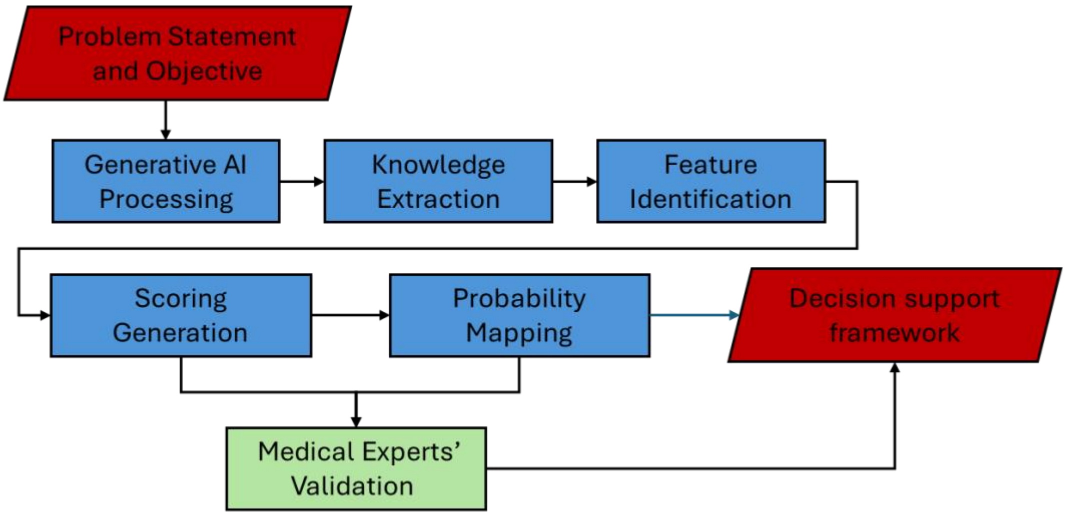

Figure 1. **Flowchart of the end-to-end framework**

Results:

The AI-generated fertility scoring framework is presented in the table below. This framework outlines the assigned score for each clinical feature and their corresponding estimated probability of live birth.

The scoring system is intended to provide a structured decision-support tool that can be refined through clinical validation. Table 1 shows the scoring framework corresponding to the given input features.

Prediction Model of clinical Pregnancy rate & live birth

Table 3:

Variable	Classification	Score	Total
Female Age	40-42 43-44 ≥45	12 points 7 points 2 points	
AFC (Antral Follicle Count)	≥5 1-4 0	11 points 6 points 0 points	
AMH (Anti-Müllerian Hormone)	>1.2ng/mL 0.5-1.2ng/mL <0.5 ng/mL	14 points 10 points 5 points	
Previous Attempts	≥1 successful attempt Naive(noprevious attempts) 1 failure ≥2 failures	16 points 12 points 8 points 4 points	
Primary or Secondary Infertility	Secondary infertility Primary infertility	10 points 5 points	
BMI	18.5-24.9 25-29.9 ≥30 or <18	6 points 4 points 0 points	
Male Age	<50 ≥50	6 points 2 points	
Sperm Count	≥15 million/m 5-14 million/mL <5 million/mL	11 points 6 points 0 points	
Sperm Motility	≥ 40% 20-39% <20%	14 points 7 points 0 points	

Table 3 (A) :

Total Predictive Score	Predicted Probability for 1-Cycle- CPR & LBR
80-100 points	- One-Cycle Clinical Pregnancy Rate: 8-15% - One-Cycle Live Birth Rate: 5-10%
60-79 points	- One-Cycle Clinical Pregnancy Rate: 4-10% - One-Cycle Live Birth Rate: 2-6%
40-59 points	- One-Cycle Clinical Pregnancy Rate: 2-5% - One-Cycle Live Birth Rate: 1-3%
< 40 points	- One-Cycle Clinical Pregnancy Rate: <2% - One-Cycle Live Birth Rate: <1%

Table 3 (B) :

Total Predictive Score	Predicted Probability for - CCPR & CLBR
80-100 points	- Cumulative Clinical Pregnancy Rate: 18-25% - Cumulative Live Birth Rate: 10-15%
60-79 points	- Cumulative Clinical Pregnancy Rate: 10-18% - Cumulative Live Birth Rate: 5-10%
40-59 points	- Cumulative Clinical Pregnancy Rate: 5-10% - Cumulative Live Birth Rate: 2-5%
< 40 points	- Cumulative Clinical Pregnancy Rate: <5% - Cumulative Live Birth Rate: <2%

Table 3 (C) :

Total Predictive Score	Predicted Probability for CPR & LBR (Embryo Pooling PGTA)
80-100 points	- LBR 25-40%, CPR 40-60%
60-79 points	- LBR 10-25%, CPR 20-40%
40-59 points	- LBR 5-12%, CPR 10-20%
< 40 points	- LBR <5%, CPR <10%

Table 3 (D) :

Total Predictive Score	Predicted Probability for CPR & LBR (Embryo Pooling Non PGTA)
80-100 points	- LBR 8-15%, CPR 15-25%
60-79 points	- LBR 5-10%, CPR 10-18%
40-59 points	- LBR 2-5%, CPR 5-10%
< 40 points	- LBR <2%, CPR <5%

Table 3 (E) :

Total Predictive Score	Predicted number of oocytes needed for 1 pregnancy (PGTA)
80-100 points	- 8-12 oocytes
60-79 points	- 12-18 oocytes
40-59 points	- 18-25 oocytes
< 40 points	- >25 oocytes

Table 3 (F) :

Total Predictive Score	Predicted number of oocytes needed for 1 pregnancy (Non PGTA)
80-100 points	-15-25 oocytes
60-79 points	- 25-35 oocytes
40-59 points	- 35-50 oocytes
< 40 points	- >50 oocytes

Tables 3 A-F
CPR : clinical pregnancy rate
LBR : Live birth rate
CCPR :Cumulative clinical pregnancy rate
CLBR : Cumulative live birth rate

Discussion

The development of predictive models in reproductive medicine is an active area of research. The predictive model developed in this study demonstrates the potential of AI in reproductive medicine. However, the model's limitations and the lack of real-world validation highlight the need for caution when interpreting the results. As regards model performance, the model's accuracy, precision, and recall suggest good performance in predicting live birth rates. However, the F1 score and AUC indicate that the model may be prone to false positives and false negatives (24). This highlights the need for careful calibration and validation of the model using real-world data.

One the other hand, the model was development using a theoretical framework, without real-world patient data, which could be a significant limitation. So, it may be argued that it is not possible to generalize this model to diverse patient populations or clinical settings. Furthermore, the model depends on a limited set of variables that may not capture the complexity of 'real-world" reproductive medicine.

This AI model is comparable to existing predictive models in reproductive medicine. However, these models were developed using real-world data and have been validated in clinical settings. In contrast, our model requires further validation and calibration using real-world data (6).

The presented AI generated model used multiple maternal and paternal factors. We also took into consideration the number and outcome of previous ART attempts. This model can estimate the clinical pregnancy rate and live birth rate in AMA age patients based on multiple variables. Moreover, the model predicts the number of Oocytes needed to achieve clinical pregnancy in both PGT-A and non PGT-A cycles.

The model's potential to predict live birth rates could inform clinical decision-making and optimize treatment protocols. However, the model's limitations and lack of real-world validation highlight the need for caution when interpreting the results. Clinicians should consider the model's predictions in conjunction with other clinical factors and patient characteristics [(25)].

This AI generated model could have various clinical application. The model could be used to predict live birth rates for, inform clinical decision-making and optimize treatment protocols. Moreover, this model helps to design treatment plans and prioritize the efficient access to ART cycles.

Unfortunately, AI generated models have inborn challenges and limitations. First of all, data quality and availability, as these AI models depends on the multitude and accuracy of the previously published data. Any bias or inaccuracy in the already published data in the literature will be reflected in the scoring. In addition, the model's predictions may be difficult to interpret, particularly for clinicians without expertise in AI. Moreover, and the most important limitation is the model validation. As a general rule any AI generated model needs further validation and calibration using real-world data. Finally, the use of AI in reproductive medicine raises regulatory and ethical concerns.

Hybrid AI systems were developed to solve this dilemma by typically bringing together the intuitive pattern-recognition abilities of deep learning with the explicit, logical reasoning provided by symbolic AI. This dual approach helps address the "black box" problem of neural networks by offering explainable, structured reasoning alongside flexible learning from data. In other words, it combines both AI models with real-world data for more realistic scores depending on real patients' characteristics [(26-27)].

Recent advances in artificial intelligence (AI) have enabled the development of more sophisticated predictive models that can incorporate multiple variables and complex interactions. In this study, we utilized Meta AI to create a predictive model of live birth rate in women over 40 undergoing IVF. Our model incorporates a range of patient and treatment characteristics, including age, ovarian reserve, sperm quality, and treatment protocol. Predictive models can help facilitate informed decision-making, reduce unnecessary treatment cycles, and optimize resource allocation [(28)].

In summary, while the absence of direct real-world data presents challenges, using AI to analyze existing scientific literature and develop expert systems offers a viable pathway to create predictive models for IVF live birth rates. This approach harnesses the wealth of published research to inform clinical decision-making and potentially enhance IVF outcomes. By integrating expert systems, organizations can enhance decision-making processes, improve efficiency, and maintain consistent quality in tasks that typically require specialized human expertise. This approach is particularly beneficial when real-world data is scarce or when aiming to incorporate domain-specific knowledge into predictive modeling.

Future directions:

Future research should focus on validating and calibrating the model using real-world data. This could involve collaborating with fertility clinics and hospitals to collect data on patient outcomes. Additionally, future research could explore the integration of AI and statistical methods to develop more robust and accurate predictive models. [15]

Future directions include the integration of AI and statistical methods with real-world data to validate AI models, and the development of more diverse and representative datasets [29-30]. This will provide a more robust and accurate approach to predictive modeling. Moreover, validating AI models using real-world data can help ensure their accuracy and reliability. Finally, development of more diverse and representative datasets can help reduce the risk of bias and ensure that the models are generalizable to diverse patient populations.

Conclusion

Advancements in AI offer promising avenues for developing predictive models in healthcare, particularly in areas where real-world data may be limited or challenging to obtain. This study leverages Meta AI to create a predictive model for IVF live birth rates in women over 40, aiming to enhance personalized treatment strategies and improve clinical outcomes in this population.

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