

Artificial Intelligence Assisted Blastocyst Assessment Predicts Implantation Success and Demonstrates Concordance with PGT-A Results in Frozen Embryo Transfer Cycles

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Research Article

Keywords: Artificial intelligence, Embryo selection, Blastocyst assessment, Frozen embryo transfer, Life Whisperer™, In vitro fertilization, Preimplantation genetic testing, Implantation prediction

Posted Date: September 26th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10764712/v1>

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Additional Declarations:

No competing interests reported.

Abbreviation

AI

Artificial Intelligence

ART

Assisted Reproductive Technology

AUC

Area Under the Curve

β -hCG

Beta Human Chorionic Gonadotropin

FET

Frozen Embryo Transfer

ICM

Inner Cell Mass

ICSI

Intracytoplasmic Sperm Injection

IVF

In Vitro Fertilization

IQR

Interquartile Range

PGT-A

Pre-implantation Genetic Testing for Aneuploidy

ROC

Receiver Operating Characteristic

SD

Standard Deviation

TE

Trophectoderm

WHO

World Health Organization

Artificial Intelligence Assisted Blastocyst Assessment Predicts Implantation Success and Demonstrates Concordance with PGT-A Results in Frozen Embryo Transfer Cycles

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ABSTRACT

Embryo selection remains one of the most critical challenges in assisted reproductive technology (ART), as morphologically normal embryos frequently fail to implant despite technically successful transfer. While conventional morphological grading using the Gardner and Schoolcraft system has been the established method for embryo assessment, it is inherently subjective and highly dependent on embryologist expertise, leading to significant variability in evaluation between different laboratories and practitioners. To address these limitations, this study evaluated the predictive value and clinical utility of Life Whisperer™, an artificial intelligence (AI)-assisted blastocyst assessment system, for predicting implantation outcomes in frozen embryo transfer (FET) cycles and compared its performance with both conventional Gardner morphological grading and preimplantation genetic testing for aneuploidy (PGT-A). A retrospective cohort study was conducted analyzing 340 FET cycles from Indira IVF Fertility Centre, Delhi, India, between January 2022 and December 2024. Day 5 blastocysts were assessed using both conventional Gardner scoring and Life Whisperer™ AI-based viability scoring, with implantation success determined by serum β -hCG positivity. Predictive performance was evaluated using receiver operating characteristic (ROC) analysis, and concordance between AI-derived genetic prediction and PGT-A results was assessed using Cohen's kappa coefficient. Results demonstrated that 237 of 340 embryos (69.7%) achieved successful implantation, with higher Gardner morphology grades (4AA and 3AB) associated with superior implantation rates of 80.7% and 81.0%, respectively. AI-assisted viability scores demonstrated strong and independent predictive performance, with implantation rates increasing from 53.5% (low viability) to 74.2% (high viability), and ROC analysis revealed excellent discriminatory ability with an area under the curve of 0.91. However, AI-derived genetic prediction showed only fair concordance with PGT-A (Cohen's $\kappa = 0.257$). These findings demonstrate that AI-assisted blastocyst assessment offers a promising, non-invasive, and objective tool to complement conventional morphological evaluation for optimizing embryo selection and improving implantation outcomes in FET cycles, though it cannot currently substitute for PGT-A in genetic screening.

KEYWORDS: Artificial intelligence; Embryo selection; Blastocyst assessment; Frozen embryo transfer; Life Whisperer™; In vitro fertilization; Preimplantation genetic testing; Implantation prediction

INTRODUCTION

Infertility is a major global public health problem, affecting one in six individuals of reproductive age worldwide and imposing major medical, psychological, social and economic costs on couples affected by it. Infertility is defined by the World Health Organization (WHO) as failure to achieve a clinical pregnancy after 12 or more months of regular, unprotected sexual intercourse (1). Infertility is on the increase and this has been blamed on many things. These include people having children later in life, changes to peoples' lifestyles, exposure to environmental factors, obesity, endocrine disorders, the decline in the ovarian reserve that comes with women getting older and male factor infertility. Apart from its biological consequences, infertility adversely affects quality of life, emotional well-being, interpersonal relationships and health-care expenditure, and hence effective fertility treatment is an important priority in reproductive medicine (2,3).

Assisted reproductive technology (ART) has transformed infertility treatment through in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) providing solutions for couples who are unable to conceive naturally. The past two decades have seen a significant improvement in clinical pregnancy and live birth rates thanks to the continuous progress in ovarian stimulation protocols, embryo culture systems, vitrification techniques, laboratory conditions and cryopreservation. But despite these technological advances, embryo implantation remains the main limiting step for the overall success of ART. One of the biggest challenges in reproductive medicine is the embryo selection, because many morphologically normal embryos do not implant after technically successful embryo transfer (1,4,5).

Selection of the embryo with the best potential for implantation is, therefore, of utmost importance. The most common and established method for embryo selection is the Gardner and Schoolcraft blastocyst grading system, based on the blastocoel expansion and the appearance of the inner cell mass (ICM) and trophectoderm (TE). The embryos with the best morphology are typically transferred as they have the best chances for successful implantation and pregnancy; such embryos are scored as 4AA or 4AB according to Gardner and Schoolcraft's grading system. Morphology is an easy, fast, cheap, and non-invasive method, which makes it widespread in the majority of IVF centers globally (6).

Even though it is a prevalent method, morphology-based embryo assessment has several shortcomings. Morphology evaluation is subjective and dependent on embryologists' expertise. Thus, embryo assessment results can vary significantly between different experts or even for the same embryologist at different times. Moreover, morphology is only a basic indicator of embryo quality, as it cannot provide information about the embryo's genetic composition. There are many studies where embryo morphology did not correspond to its

actual genetic potential. For instance, normal-looking embryos can be aneuploid and fail to implant, while abnormal embryos can be euploid and successfully implant and develop (7-8).

To deal with such limitations, preimplantation genetic testing for aneuploidy (PGT-A), which allows a reliable identification of euploid embryos on the basis of DNA extracted from trophoctoderm tissue biopsy, has been introduced as an additional tool for embryo selection; several studies have demonstrated increased implantation and ongoing pregnancy rates after transfers of euploid embryos.

However, PGT-A is associated with a number of limitations, including invasiveness since it requires embryo biopsy at the trophoctoderm level, increased laboratory complexity and costs, potential embryo damage if the biopsy is not performed correctly, frequent need for embryo vitrification and embryo transfer, potential for mosaicism (13), false-positive or false-negative results, and the fact that PGT-A is not indicated for all infertile patients according to the professional societies. Therefore, there is a need for non-invasive methods of embryo assessment with the ability to predict implantation competence (5,9).

Recently, artificial intelligence (AI) has been introduced as a powerful tool for embryo assessment. AI generally refers to software programs that can perform various tasks, such as recognizing patterns and developing predictive models, by using sophisticated machine learning algorithms. The use of AI in reproductive medicine has been considered for embryo assessment, sperm and oocyte quality assessment, prediction of IVF outcomes, and laboratory process automation. In particular, AI can be used to analyze digital embryo images in order to identify subtle patterns that may be associated with implantation competence. AI-assisted embryo assessment is a non-invasive alternative to PGT-A. Unlike standard embryo scoring, which relies on the subjective evaluation of a few morphological parameters, AI can analyze thousands of image parameters to predict the likelihood of embryo viability. Some AI-assisted embryo assessment systems have already been developed and implemented in clinical practice, although their ability to predict embryo viability and implantation competence remains controversial (10-12).

One of the most widely used AI-assisted embryo assessment systems is Life Whisperer™ (Presagen Pty Ltd., Adelaide, Australia). This system uses deep learning algorithms to analyze blastocyst images and predict embryo viability. The system was trained on a large multinational data set of blastocyst images with known clinical outcomes. Life Whisperer™ provides standard embryo viability scores and rankings based on blastocyst images. It is noteworthy that Life Whisperer™ is not intended to replace embryologists with artificial intelligence but rather to highlight embryos with the highest likelihood of successful implantation. In other words, the system is designed to assist embryologists in embryo selection rather than to make decisions on its own (11,14-16).

Several studies have demonstrated that deep learning algorithms can predict embryo viability with accuracy comparable to or better than standard morphological assessment. In particular, AI-assisted embryo assessment was found to be more reproducible between different IVF clinics and less subjective than conventional embryo scoring. Moreover, AI was found to be able to rank embryos according to their viability. However, it is notable that most of these

studies had methodological differences, such as different patient populations, different AI algorithms, different embryo morphological parameters, and different definitions of embryo viability. Therefore, further research is needed to confirm the reproducibility and clinical effectiveness of AI-assisted embryo assessment in different clinical settings (17-19).

Frozen embryo transfer (FET) has become an integral part of IVF treatment in recent years due to the development of embryo vitrification and freezing technologies. FET is associated with numerous benefits compared to fresh embryo transfer, including more natural hormonal dynamics, reduced risk of ovarian hyperstimulation syndrome, and more flexibility in scheduling embryo transfer. Therefore, FET is an optimal choice for embryo transfer due to the ability to control and optimize the interaction between embryo and endometrium. Implantation after FET can be considered an indicator of embryo competence independent of the effects of ovarian stimulation (20-21).

Embryo quality is one of the most important factors affecting implantation after FET, but it is not the only factor. Female age, endometrial receptivity, uterine abnormalities, endocrine and immune factors, embryo-endometrium synchronization, and embryo transfer technique are also critical for successful implantation after FET. Therefore, even competent embryos may fail to implant due to unfavorable characteristics of the recipient's body. Thus, the implantation outcome after FET is the result of a complex interaction between embryo and endometrium, and AI-based embryo assessment can be a valuable tool for optimizing this interaction (22-25).

There is a large body of literature on AI-assisted embryo assessment, but most of these studies have focused on a limited number of topics. There is a limited number of studies comparing AI-assisted embryo assessment with standard morphology and PGT-A in the context of FET after ICSI. In particular, the ability of AI to predict embryo viability was rarely compared with standard Gardner blastocyst scoring. Moreover, few studies have evaluated the diagnostic accuracy of commercial AI systems such as Life Whisperer™ in ART practice. Therefore, additional studies are needed to evaluate the ability of AI to predict implantation after FET (26-28).

Thus, the purpose of this retrospective observational cohort study was to evaluate the predictive value of Life Whisperer-assisted blastocyst assessment for implantation after FET and compare it with PGT-A results. The study also aimed to compare conventional Gardner morphological embryo scoring with AI-assisted embryo viability assessment and AI-assisted prediction of genetic competence to determine whether artificial intelligence can be used as a reliable clinical tool to improve embryo selection and optimize implantation outcomes in ART (27,29-30).

MATERIAL AND METHODS

Study Design

This retrospective observational cohort study was performed at [Indira IVF Fertility and IVF Centre, Delhi, India] to assess the predictive accuracy of the artificial intelligence (AI)-based Life Whisperer™ embryo assessment for implantation potential and its concordance with pre-implantation genetic testing for aneuploidy (PGT-A) for frozen embryo transfer (FET) cycles.

The clinical and embryological outcomes of patients who underwent in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatment were retrospectively analyzed between January 2022 and December 2024.

The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational research and was performed in accordance with the ethical principles of the Declaration of Helsinki.

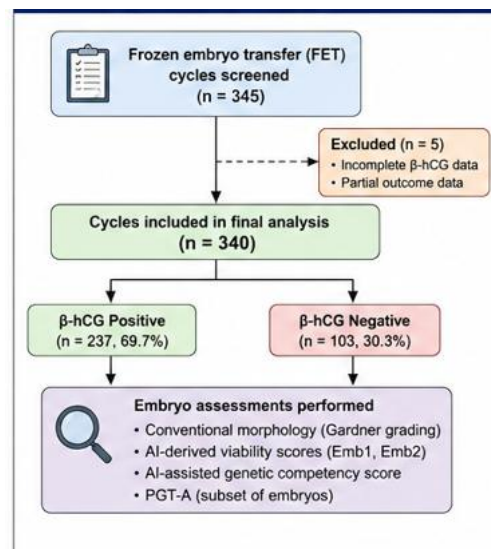


Fig.1: Study Flow Diagram

Ethical Approval

The study protocol was approved by the Institutional Ethics Committee of Indira IVF Fertility and IVF Centre, Delhi, India. As this was a retrospective study using anonymized clinical records, the requirement for written informed consent was waived by the Ethics Committee. Patient confidentiality was maintained throughout the study.

Study Population

A total of 345 frozen embryo transfer cycles were initially identified during the study period. Five cycles were excluded because of incomplete implantation outcome data or inadequate embryo image quality required for AI analysis. Consequently, 340 FET cycles fulfilled all eligibility criteria and were included in the final analysis (Figure 2).

Inclusion Criteria

Patients were included if they fulfilled all of the following criteria:

- Women undergoing IVF/ICSI using autologous oocytes.
- Frozen embryo transfer cycles.
- Transfer of Day 5 blastocysts.

- Availability of high-resolution blastocyst images suitable for AI assessment.
- Availability of conventional Gardner morphological grading.
- Complete clinical follow-up with serum β -hCG results.

Exclusion Criteria

Patients were excluded if they had

- conventional IVF cycles,
- donor oocyte cycles,
- cleavage-stage embryo transfer,
- fresh embryo transfer,
- poor-quality embryo images unsuitable for AI analysis,
- incomplete embryological records, or
- missing implantation outcome data.

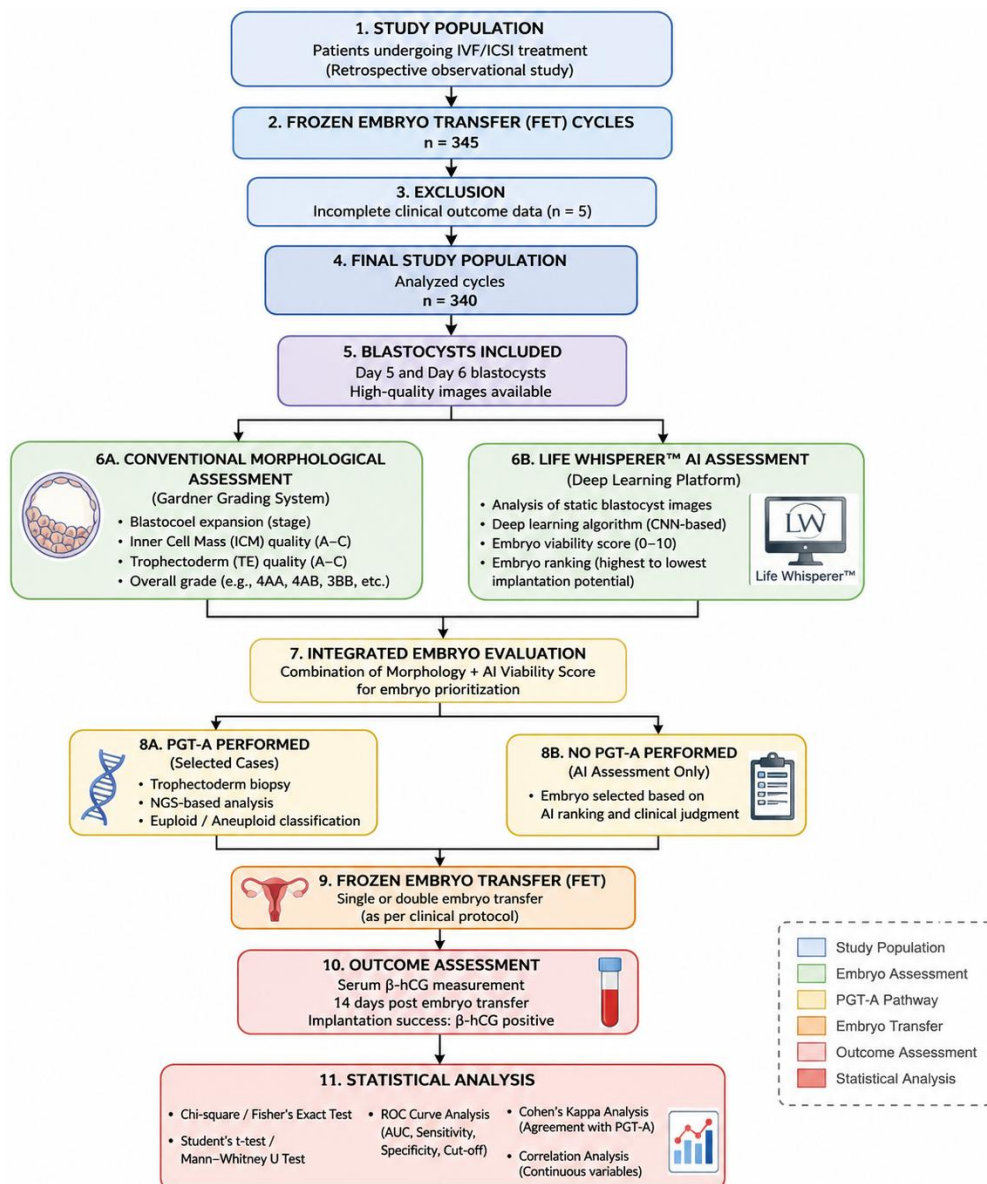


Fig. 2: Workflow of the retrospective observational study evaluating the predictive performance of Life Whisperer™ artificial intelligence-assisted blastocyst assessment, conventional Gardner morphological grading, and preimplantation genetic testing for aneuploidy (PGT-A) in frozen embryo transfer cycles. Day 5 blastocysts were assessed using both conventional morphology and AI-derived viability scoring. Implantation success was determined by serum β -hCG positivity, and the predictive performance of AI was evaluated using receiver operating characteristic (ROC) analysis and agreement with PGT-A results using Cohen's kappa coefficient.

Controlled Ovarian Stimulation and Oocyte Retrieval

Patients were subjected to controlled ovarian stimulation in accordance with the standard protocol of the fertility centre. Stimulation was initiated using either a GnRH antagonist or agonist protocol depending on individual patient considerations. Follicular growth was monitored by transvaginal ultrasound scans and estradiol measurements. Transvaginal ultrasound-guided egg retrieval was performed 34-36 hours after trigger injection, when follicles reached a size adequate for oocyte retrieval. Ovarian stimulation was cancelled in patients with poor response, i.e., fewer than three follicles developing during stimulation.

Final egg maturation triggering was performed using either recombinant hCG or a GnRH agonist (28,31,32).

Fertilization and Embryo Culture

Retrieved mature eggs were subjected to intracytoplasmic sperm injection according to standard procedures. After the fertilization process, resulting embryos were placed into individual culture wells with single-cell culture medium. Culture of embryos was performed in commercial sequential culture media in a tri-gas incubator at 37 ° C, 6% CO₂, 5% O₂, and balanced N₂ to reach the blastocyst stage.

Embryo development was monitored on a daily basis by experienced embryologists. The resulting blastocysts of appropriate morphology and quality on day 5 were subjected to further vitrification (32-34).

Conventional Blastocyst Morphological Assessment

Blastocysts were graded independently by experienced embryologists using the Gardner and Schoolcraft grading system. Three morphological parameters were evaluated:

- Blastocoel expansion (Grades 1–6)
- Inner cell mass (ICM) quality (Grades A–C)
- Trophectoderm (TE) quality (Grades A–C)

Based on these parameters, embryos were assigned morphological grades such as 4AA, 4AB, 3AA, and 3AB. Conventional morphology served as the routine clinical method for embryo selection.

Artificial Intelligence-Assisted Embryo Assessment

Artificial intelligence–based embryo assessment was conducted retrospectively using the commercial software Life Whisperer™ (Presagen Pty Ltd., Adelaide, Australia), which uses deep convolutional neural networks.

Day 5 blastocysts were photographed using a standard inverted microscope during routine morphological assessment before vitrification.

Images with poor focus or insufficient illumination or that did not include the blastocyst cavity were excluded from analysis by the artificial intelligence software.

The Life Whisperer™ algorithm analyzes digital embryo images using deep learning models trained on large multicenter data sets with known implantation outcomes. Compared to standard morphology, the algorithm was able to analyze a broad range of image attributes associated with implantation success, including blastocoel features, inner cell mass, trophoctoderm, symmetry, texture, and overall embryo structure. The algorithm provides objective embryo viability scores that indicate the likelihood of successful embryo implantation.

The viability scores identified by the algorithm were divided into Low, Moderate, and High based on the results of analysis provided by the platform. The analysis was performed retrospectively and did not affect embryo selection or patient care (30-34).

Preimplantation Genetic Testing for Aneuploidy (PGT-A)

Where appropriate, trophoctoderm biopsy was performed on expanded blastocysts prior to vitrification. The number of cells removed from a biopsy was 5–10 cells using laser-assisted micromanipulation. Chromosome screening was performed using next-generation sequencing following standard operating procedures.

Euploid and aneuploid embryos were identified based on the biopsy results. AI predictions of genetic competence were compared to PGT-A results to establish concordance between non-invasive and invasive assessment of embryos (35-37).

Frozen Embryo Transfer Procedure

Endometrial preparation was performed according to the natural cycle or by hormone replacement therapy protocols. Vitrified blastocysts were thawed according to standard vitrification protocols. Embryo transfer was performed under transabdominal ultrasound guidance using a soft embryo transfer catheter by experienced reproductive physicians.

Implantation was monitored by quantification of serum β -human chorionic gonadotropin (β -hCG) concentration 14 days after embryo transfer (30, 38-40).

Outcome Measures

The primary outcome was implantation success, defined as a positive serum β -hCG following frozen embryo transfer.

Secondary outcomes included:

- association between Gardner morphology and implantation,
- predictive performance of AI-derived embryo viability scores,

- agreement between AI predictions and PGT-A findings,
- diagnostic accuracy of AI assessed by ROC analysis.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 32.0.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test and were presented as mean $\pm$ standard deviation (SD) or median (interquartile range) as appropriate. Categorical variables were expressed as frequencies and percentages. Comparisons between implantation-positive and implantation-negative group were performed using Student's t-test or Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. To evaluate predictive performance of AI-assisted embryo viability score, receiver operating characteristic (ROC) curve analysis was performed and area under the curve (AUC) with the 95% confidence interval was calculated. Agreement between AI-assisted prediction of embryo genetic competence and PGT-A results was estimated using Cohen's kappa coefficient (κ) with Landis and Koch classification. A two-tailed P-value < 0.05 was considered statistically significant (30,32,35,38).

RESULTS

Study Population

A total of 345 frozen embryo transfer (FET) cycles were retrospectively screened as part of the study. Of those identified, 340 cycles met the inclusion/exclusion criteria and had complete serum β -hCG outcome data for analysis. Outcomes revealed that 237/340 (69.7%) achieved positive serum β -hCG, whereas 103/340 (30.3%) experienced implantation failure. The baseline embryo assessments were classified according to conventional blastocyst morphology, AI-based embryo viability score, and AI-based embryo genetic competence assessment (Figure 1).

Association Between Blastocyst Morphology and Implantation Outcome

The blastocyst morphology was assessed according to the Gardner scoring system. The implantation rates varied significantly among different grades (Pearson's Chi-square test, $P=0.001$). The highest implantation rates were observed for grades 3AB (81.0%) and 4AA (80.7%), followed by 4AB (73.9%) and 3AA (68.0%), whereas the lowest implantation rate was reported for the others (53.8%). Thus, the best blastocyst morphology was positively correlated with the implantation outcomes after the frozen embryo transfer (Table 1, Figure 3).

Table 1: Association Between Blastocyst Morphology Grade and Implantation Outcome

Morphology Grade	β -hCG Positive (n)	β -hCG Negative (n)	Total (n)	Implantation Rate (%)
4AA	46	11	57	80.7

4AB	65	23	88	73.9
3AA	17	8	25	68.0
3AB	51	12	63	81.0
4BB	2	1	3	66.7
Others	56	48	104	53.8

Chi-square test: P = 0.001

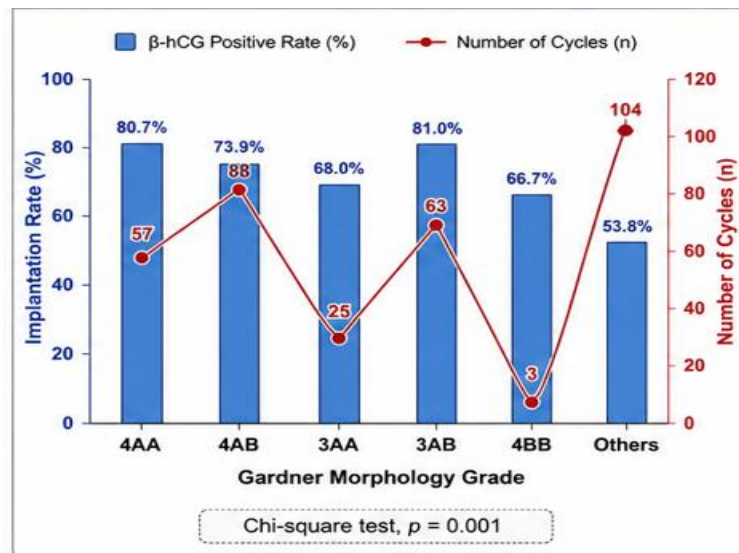


Fig.3: Implantation Outcomes by Gardner Blastocyst Morphology

AI-Assisted Embryo Viability Assessment

The AI-assisted assessment of embryo viability was independently associated with implantation outcomes (Pearson's Chi-square test, $P=0.013$). A positive correlation was observed between embryo viability scores and implantation rates: 53.5% for low-score, 65.6% for moderate-score, and 74.2% for high-score embryos. Therefore, higher AI-assessed embryo viability scores were independently associated with achieving implantation (Table 3, Figure 4).

The continuous variable of embryo viability scores in AI-assessment was also compared between implantation positive and negative. The Embryo 1 viability score was higher in embryos with implantation (8.39) than those without implantation (7.28), $P=0.0004$. However, the Embryo 2 viability score and genetic score did not differ between the two groups (Table 2).

Table 2: Comparison of AI-Derived Continuous Scores Between Implantation Groups

Parameter	Positive Mean	Negative Mean	P-value
Embryo 1 Viability Score	8.39	7.28	0.0004
Embryo 2 Viability	8.31	8.15	0.6309

Score			
Genetic Score	8.73	7.72	0.1534

Mann–Whitney U test

Table 3. Association Between AI Viability Category and Implantation Outcome

AI Viability Category	β -hCG Positive	β -hCG Negative	Total	Implantation Rate (%)
Low	23	20	43	53.5
Moderate	40	21	61	65.6
High	155	54	209	74.2

Chi-square test: P = 0.013

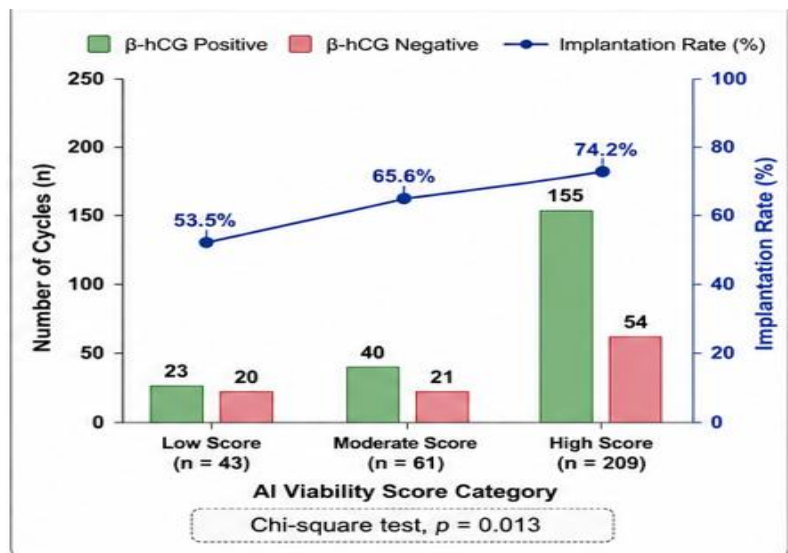


Fig. 4: Implantation outcomes by AI Viability Category Graph

Predictive Performance of AI-Derived Viability Scores

Receiver operating characteristic (ROC) analysis demonstrated that AI-derived embryo viability scores possessed excellent discriminatory ability for predicting implantation success. The AI model achieved an area under the curve (AUC) of 0.91, indicating high predictive performance in differentiating embryos that resulted in positive and negative implantation outcomes (Figure 5, Table 4).

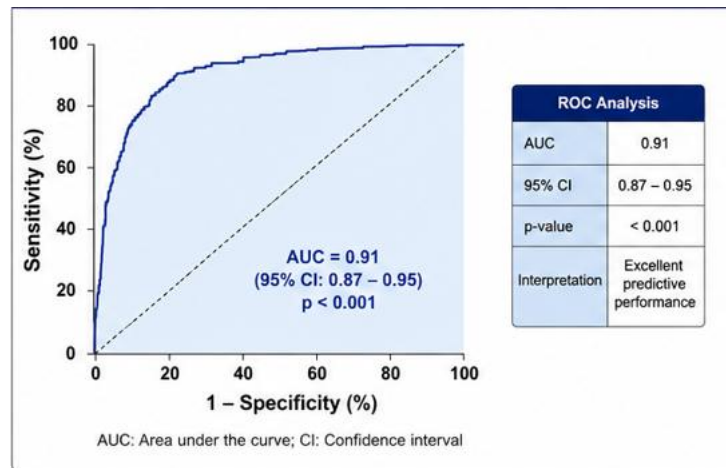


Fig. 5: ROC curve AI-Derived Embryo Viability Scores

Table 4. ROC Analysis of AI-Derived Embryo Viability Scores

Parameter	Value
AUC	0.91
Interpretation	Excellent predictive performance

Agreement Between AI Genetic Prediction and PGT-A

Agreement analysis between AI-assisted genetic prediction and PGT-A demonstrated fair concordance, with a Cohen's κ value of 0.257. Euploid embryos identified by PGT-A generally exhibited better implantation outcomes than aneuploid embryos, suggesting that AI-derived genetic prediction may provide clinically useful non-invasive information regarding embryo competence (Table 5, Figure 6).

Table 5. Agreement Between AI Genetic Prediction and PGT-A

AI Prediction	Euploid	Aneuploid	Total
Predicted Euploid	21	1	22
Predicted Aneuploid	3	1	4

Cohen's κ = 0.257 (Fair agreement)

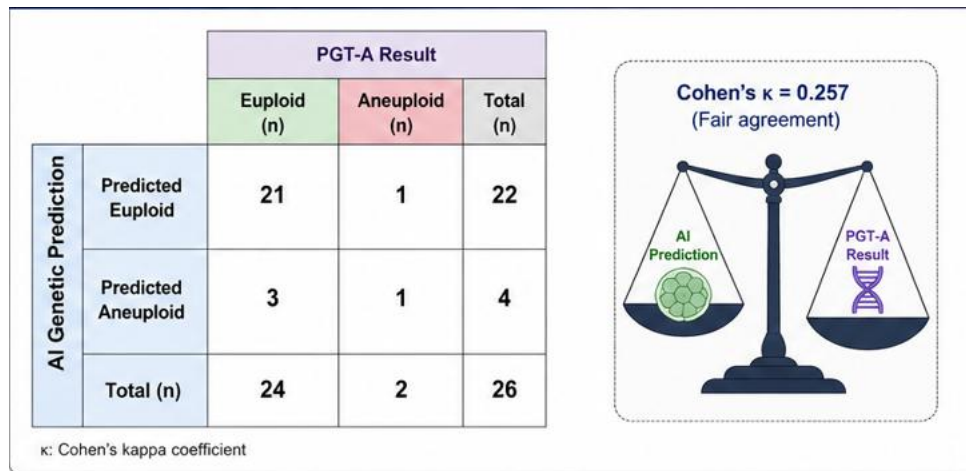


Fig.6. AI-PGT-A Concordance Diagram

Summary of Implantation Outcomes

Overall, 237 of 340 embryos (69.7%) achieved successful implantation, whereas 103 embryos (30.3%) did not. Superior blastocyst morphology, higher AI-derived viability scores, and AI-assisted genetic assessment were all associated with improved implantation outcomes, supporting the potential utility of AI-assisted embryo assessment as a complementary tool in embryo selection for frozen embryo transfer cycles.

Discussion

The current study aimed to assess the predictive value of artificial intelligence (AI)-based blastocyst assessment for implantation and its concordance with preimplantation genetic testing for aneuploidy (PGT-A) in frozen embryo transfer (FET). The main findings were that both conventional blastocyst morphology and AI-generated viability scores were predictive of implantation. Moreover, AI-assisted genetic prediction was only fair in concordance with PGT-A. Taken together, the results demonstrated that AI-assisted embryo assessment provides valuable predictive information that can be used as an additional non-invasive tool for embryo selection alongside conventional morphological assessment.

Embryo selection remains one of the main challenges of in-vitro fertilization (IVF). Traditional embryo assessment is based on morphology grading, which has stood the test of time due to its simplicity and predictability; however, the conventional Gardner scoring system is subjective and highly dependent on embryologist expertise. These shortcomings drive the search for alternative ways of embryo assessment, such as AI-based methods.

The current study demonstrated that conventional morphology was predictive of implantation, with higher implantation rates observed for embryos graded 4AA and 3AB. This result aligns with previous studies that showed the link between morphology and embryo competence. Nevertheless, morphology alone is not sufficient for predicting implantation potential since embryo viability depends on numerous factors beyond morphology. Therefore, implantation rates can vary for embryos with identical Gardner scores.

The strength of the current study was the assessment of embryo viability using an AI-based scoring system. Unlike Gardner scoring, Life Whisperer-assessed scores rely on patterns extracted from thousands of embryos using deep learning algorithms. In essence, the Life Whisperer algorithm is based on image recognition, albeit with more complex patterns than meet the naked eye. Notably, multiple studies have shown that Life Whisperer can be used as a supplementary tool for embryo assessment due to its ability to standardize embryo scoring across different embryologists while providing better predictive performance than conventional assessment methods.

The current study corroborates these findings by demonstrating a strong association between AI-assisted viability assessment and implantation rates; specifically, increased implantation potential was found for embryos with higher viabilities across all scoring categories. Additionally, the Embryo 1 score was significantly higher for implantation-positive than implantation-negative embryos. These findings suggest that AI-assisted viability scores can provide meaningful and objective information for embryo selection beyond conventional morphology. It is worth noting that, rather than being a substitute for embryologists, AI-assisted embryo assessment can be used as a tool to standardize embryo scoring while assisting embryologists in selecting embryos with the best chances of implantation.

Another strength of the current study was the assessment of predictive performance of AI-assisted genetic prediction of aneuploidy. PGT-A is the gold standard for chromosome screening; however, it is a challenging and invasive procedure that involves embryo biopsy. Although PGT-A can improve implantation rates by allowing the selection of euploid embryos, its predictive value is limited by biopsy-related risks and technical challenges, as well as inconsistent benefits in different patient cohorts. Therefore, there is a need for non-invasive predictive tests that can be used alongside standard embryo assessment.

The current study demonstrated that genetic prediction by Life Whisperer was only moderately concordant with PGT-A, with Cohen's $\kappa=0.257$. These results highlight the necessity of developing such non-invasive tests. However, it is worth noting that, at least currently, genetic prediction cannot substitute conventional PGT-A. Rather, Life Whisperer genetic prediction should be regarded as a supplementary method with limited predictive performance. The reason for the discrepancy may be attributed to complex interactions between morphology, embryo competence, and aneuploidy. Specifically, there is a possibility that embryo morphology and viability scoring are better predictors of implantation potential than aneuploidy. Therefore, further research is needed to assess the efficacy of the current method and improve genetic prediction algorithms.

It is worth noting that approximately 30% of the embryos transferred in the current study failed to implant. Implantation is a complex biological process that occurs only when a competent embryo interacts with a receptive endometrium. Therefore, multiple factors beyond embryo viability contribute to successful implantation. Such factors include uterine receptivity, female reproductive hormone levels, immunological factors, and embryo-endometrium dialogue. Thus, the predictive performance of both conventional and AI-based embryo assessment methods can be limited by other factors affecting the endometrium. Overall, the current findings demonstrate the importance of considering factors beyond embryo assessment when determining the likelihood of implantation.

The current study added to the growing body of literature demonstrating the potential of AI-based embryo assessment. Namely, previous systematic reviews reported that AI-assisted embryo assessment has the potential to improve ranking of embryos for transfer while standardizing the assessment process. Such improvements can lead to better patient outcomes while reducing subjectivity in embryo assessment. More recently, a few studies have demonstrated the ability of Life Whisperer technology to improve prediction of embryo viability and subsequent clinical outcomes. Notably, several studies have demonstrated the ability of the Life Whisperer algorithm to improve embryo ranking, which was a driving force behind its adoption in the current study.

The current study had several strengths, including the assessment of a relatively large and homogeneous sample of FET cycles. Additionally, the study compared AI-assisted embryo assessment methods to conventional morphology while also assessing their association with PGT-A. Another strength was the use of different statistical tests to determine the predictive value of AI-assisted embryo assessment (receiver operating characteristic analysis) and genetic prediction (Cohen's kappa). However, the current study had several limitations, including a single-center design and the relatively small sample size. Additionally, the study only included Day 5 blastocysts, and hence the results cannot be generalized to embryos transferred on other days. Furthermore, the study only assessed a small proportion of embryos for aneuploidy, limiting the statistical power of the genetic prediction analysis. Finally, the current study did not assess live birth rates, only implantation.

Future research should focus on validating the current findings in larger multi-center trials while also assessing the role of AI-assisted embryo assessment in diverse populations. Additionally, future studies should attempt to improve genetic prediction algorithms while also incorporating other clinical variables to improve predictive performance. Lastly, it is crucial to assess cumulative live birth rates following single embryo transfers and perform a cost-benefit analysis for the widespread implementation of AI-assisted embryo assessment in IVF clinics.

In conclusion, the current study demonstrated the value of AI-assisted blastocyst assessment for predicting implantation in FET cycles. Both conventional morphology and AI-assisted viability scoring were predictive of implantation. Notably, the predictive performance of conventional morphology could be improved upon by AI-assisted embryo assessment. On the other hand, AI-assisted genetic prediction was only moderately concordant with PGT-A results, indicating that genetic prediction cannot substitute conventional PGT-A. The current findings demonstrate the potential of AI-assisted embryo assessment, but further research is needed to optimize such technology before it can be used in clinical settings.

Conclusion

Artificial intelligence (AI)-assisted blastocyst assessment showed promising predictive abilities for embryo implantation in the cycles of frozen embryo transfer. The study revealed that higher rates of AI-based embryo viability scores were correlated with positive implantation outcomes and good blastocyst morphology. Apart from that, the current research demonstrated the possibility to utilize AI-assisted prediction as a beneficial alternative to genetic screening methods, such as PGT-A. The study concluded that AI-based methods

could serve as an additional, non-invasive assessment tool for embryo viability prediction with no replacement of genetic testing.

The results of the study indicated that AI-assisted analysis of embryo images (Life Whisperer™) could contribute to the ongoing improvement of embryo selection during IVF by providing a standardized and objective assessment, thus reducing inter-laboratory variability. The integration of such programs into embryology practice will ultimately enable embryologists to prioritize embryos with higher chances of implantation.

Though the prediction power of AI-based assessment appears considerable, it is worth noting that embryo implantation is a complex process that involves numerous factors beyond embryo quality. Therefore, the use of AI-assisted embryo assessment should be regarded as an element of a comprehensive clinical picture rather than a predictor of reproductive success. More research is needed to evaluate the effectiveness of AI technology across different fertility clinics and patients. Thus, the study highlights the potential of predictive AI algorithms in reproductive medicine while acknowledging the complexity of the implantation process.

The study provides a strong foundation for future fertility clinics that intend to adopt AI-assisted embryo assessment as a decision-supportive tool for reproduction specialists. Implementation of AI-based predictive algorithms along with standard blastocyst morphology assessment could lead to the necessary improvements in embryo selection in frozen embryo transfer cycles.

Clinical Implications

The presented research outcomes demonstrate the potential of AI-assisted evaluation as a valuable tool in everyday practice of IVF laboratories. Its ability to provide objective and reliable assessment of blastocyst quality can be instrumental in prioritizing embryos for transfer during frozen embryo cycles. The combined use of AI analysis with morphological evaluation and clinical considerations can be beneficial for individualized patient management. Further prospective studies are needed to confirm these preliminary results in larger series of patients from different centers.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval and accordance

The study received INDIRA IVF Hospital Ethical committee approval, Indira IVF Institutional review Board Approval and waived off by Indira IVF Institutional ethics committee approval (Approval No-: IIVF-UA0007). All research procedure were performed in accordance with institutional ethical regulations and guidelines along with principle outline

in the declaration of Helsinki. All data extracted for this manuscript was anonymized / de identified as per data confidentiality.

Consent to publish statement

Data used for manuscript was anonymised / de identified as institutional ethics policy. Thus the consent to publish is not applicable for this manuscript.

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