A Nomogram Model for Predicting Clinical Pregnancy after Fresh IVF/ICSI-ET in Patients with Infertility and Endometriosis

Xiaoju Wan[1], Yiguo Wan[2], Min Yu[1], Zhiqing Zhang[1], Zhihui Huang[1] and Jun Tan[1]

[1]*Reproductive Medicine Centre, Jiangxi Provincial Maternal and Child Health Hospital, Nanchang, China*
[2]*Fuzhou Medical College, Nanchang University, Fuzhou, Jiangxi, China*

ABSTRACT

Objective: To determine the clinical and embryo laboratory factors that affect the clinical pregnancy rate of infertile patients with endometriosis (EMs), and establish a model for predicting clinical pregnancy.

Study Design: An observational study.

Place and Duration of the Study: Reproductive Medicine Centre, Jiangxi Provincial Maternal and Child Health Hospital, China, from January 2016 to December 2023.

Methodology: Inclusion criteria were EMs patients diagnosed and treated through laparoscopic surgery, aged 22 - 37 years, who did not undergo surgery within 3 months before oocyte retrieval, and received fresh embryo transfer; and the causes of infertility included male factors, tubal infertility, intrauterine adhesions, and others. The exclusion criteria were EMs patients with combined uterine adenomyosis, chromosomal abnormalities, abnormal uterine structure, endocrine diseases, cardiovascular diseases and autoimmune diseases. The research variables included clinical and embryonic factors that affect clinical pregnancy rates, such as age, duration of infertility, type of infertility, and sex hormone levels. The outcome variable was the clinical pregnancy rate.

Results: The clinical pregnancy rate was 61.84%. This predictive model was built on the basis of the number of high-quality cleavage embryos, number of embryos transferred, progesterone on HCG day, infertility duration, female age, number of oocytes retrieved, and body mass index showing good calibration and discriminatory abilities, with the area under the curve of receiver operating characteristic curve of 0.641 (95% CI = 0.599 - 0.684) for training set and 0.583 (95% CI = 0.515 - 0.650) for testing set. The Hosmer-Lemeshow test showed no significant difference ($p > 0.05$) between the predicted and the true clinical pregnancy probabilities. The clinical decision curve analysis showed that both the training and testing sets achieved maximum net benefit within a threshold probability range of 0.4 - 0.8, indicating good clinical efficacy within this threshold probability range.

Conclusion: The model for predicting clinical pregnancy in patients with EMs after fresh IVF/ICSI-ET had high accuracy, and can provide useful guidance for clinical doctors and individual adjuvant treatment of patients.

Key Words: *Endometriosis, Predictive model, Clinical pregnancy, Nomogram, In vitro fertilisation.*

How to cite this article: Wan X, Wan Y, Yu M, Zhang Z, Huang Z, Tan J. A Nomogram Model for Predicting Clinical Pregnancy after Fresh IVF/ICSI-ET in Patients with Infertility and Endometriosis. *J Coll Physicians Surg Pak* 2024; **34(12)**:1429-1435.

INTRODUCTION

Endometriosis (EMs) is a common chronic inflammatory and hormone-dependent gynaecological disease.[1] Around 2 - 10% of women of childbearing age worldwide are affected by EMs. EMs is a common cause of infertility, with approximately 30 - 40% of EMs patients experience infertility and about 25 to 50% of infertile patients have EMs. The factors that lead to infertility are EMs itself or in combination with other factors.[2] EMs has adverse effects on both natural and assisted conception.[3] It is generally believed that the pregnancy outcomes of EMs patients are often suboptimal.

Correspondence to: Dr. Xiaoju Wan, Reproductive Medicine Centre, Jiangxi Provincial Maternal and Child Health Hospital, Nanchang, China
E-mail: 1392312903@qq.com

Received: April 18, 2024; Revised: September 12, 2024; Accepted: October 22, 2024
DOI: https://doi.org/10.29271/jcpsp.2024.12.1429

For EMs patients with infertility, assisted reproduction technology (ART) is increasingly being used.[4] EMs not only lead to a decrease in oocyte quality and fertilisation rate in patients but also increase the risk of miscarriage and may be associated with obstetric and foetal complications.[5] EMs patients acquire fewer MII oocytes and available embryos, resulting in a lower cumulative clinical pregnancy rate.[6] Even milder forms of EMs can affect fertilisation and implantation rates.[7] Even after surgical removal of endometriosis, EMs patients who received *in vitro* fertilisation (IVF) treatment, had a pregnancy rate of only 30%, lower than the control group.[8] Therefore, EMs patients undergoing ART deserve more attention to alleviate their anxiety and improve results. Reproductive doctors are urgently concerned about how to predict and enhance the ovarian responsiveness of EMs patients during ovulation induction.

Nomograms are statistical predictive models that incorporate independent influencing factors to estimate the clinical outcomes of individual patients.[9] Multiple nomogram-prediction

models have been established for different purposes in ART treatment, and their advantages in clinical practice have been demonstrated.[10-12] However, there are a few clinical pregnancy prediction models for EMs patients who receive ART treatment after surgery. The aim of this study was to develop a model for predicting the probability of clinical pregnancy in EMs patients after surgery undergoing IVF or intracytoplasmic sperm injection (ICSI) and fresh embryo transfer (fresh IVF/ICSI-ET).

METHODOLOGY

This retrospective observational analysis was conducted on the clinical and embryonic data of 1,243 individuals with endometriosis who underwent fresh IVF/ICSI-ET treatment at the Reproductive Medicine Centre of Jiangxi Maternal and Child Health Hospital, Jiangxi, China, from January 2016 to December 2023. The Hospital's Ethics Committee approved this study with partial exemption from informed consent (Approval Number.: SZYX-202402) and all of the patients provided informed consent.

All EMs patients were diagnosed and treated by laparoscopic surgery. During laparoscopic examination, any visible lesions were destroyed, ablated, or excised. Inclusion criteria were EMs patients treated and diagnosed through laparoscopic surgery, aged 22-37 years, those patients who did not undergo surgery within 3 months before oocyte retrieval, patients who received fresh IVF/ICSI-ET, or the causes of infertility included male factors, tubal infertility, intrauterine adhesions, and others. Exclusion criteria were EMs patients combined uterine adenomyosis, chromosomal abnormalities, abnormal uterine structure, endocrine diseases (polycystic ovary syndrome, thyroid dysfunction, diabetes, etc.), cardiovascular diseases, autoimmune diseases (systemic lupus erythematosus, connective tissue disease, etc.). Ultimately, 980 (79%) patients met the criteria for inclusion in the study. Subsequently, in order to develop a nomogram predictive model and validate it, 980 patients included in the study were divided into a training set (n = 686) and a testing set (n = 294) in a 7:3 ratio.

In order to promote ovulation, all patients received appropriate ovulation induction treatment according to their personal conditions. The first-line treatment options for EMs include prolonged regimens, microstimulation regimens, antagonist regimens, and long regimens. Regularly, transvaginal ultrasound and serum hormone level detection (estradiol (E_2), luteinising hormone (LH), follicle-stimulating hormone (FSH), progesterone (P), and anti-mullerian hormone (AMH), etc.) were used to monitor follicle growth during the cycle. When the diameter of dominant follicles was ≥19mm or at least 3 follicles had a diameter of ≥17.5 mm, subcutaneous injection of 250 ug of human chorionic gonadotropin (HCG) was given that evening, and oocyte aspiration was performed after 36-40 hour. The IVF embryo procedure was performed in the embryology laboratory according to the centre's standard operating procedures. At present, embryo scoring standards are mainly based on morphological indicators. Day 3 cleavage embryos with 2PN fertilisation, 7 - 10 blastomere, uniform size, and fragmentation degree 0-20% were classified as high-quality cleavage embryos. The evaluation of blastocysts was based on three aspects: The degree of expansion of the blastocyst cavity, the number of inner cell clusters, and the number of trophoblast cells. Fresh D3/D4/D5/D6 embryos can all be transferred, and the number of transferred embryos varied from one to two according to the doctor's advice and the patient's request. After 12 days of embryo transfer, the authors conducted blood tests for HCG and HCG-positive patients underwent ultrasound examinations to observe clinical pregnancy indicators, such as gestational sacs and foetal heartbeat after 5 weeks of the transfer.

Statistical analysis was conducted using R 3.34. The normality of variances in the data was analysed by Shapiro-Wilk's test. The mean ± standard deviation was represented for normally distributed measurement data, the median [Q1, Q3] was represented for measured data with abnormal distribution, and the count data was represented by numbers and percentages. ANOVA or t-test was used for normal distribution data, Kruskal-Wallis test and BH correction were used for non-normal distribution data, and Chi-square test or Fisher's exact test was used for categorical data. In order to screen factors influencing clinical pregnancy, a univariate logistic regression analysis was conducted first, and those with lower p-values ($p < 0.2$) were selected and included in the multivariate logistic regression analysis model. In addition, a nomogram for the predicted model was established. The area under the curve (AUC) of the receiver operating characteristic curve (ROC), Hosmer-Lemeshow test (HL test), and clinical decision curve analysis (DCA) were used to evaluate the performance of the predicted model. A value of $p < 0.05$ was considered statistically significant.

RESULTS

This study included 980 patients, of whom 606 achieved clinical pregnancy, with a statistical clinical pregnancy rate of 61.84%, while 374 patients experienced either non-implantation or biochemical pregnancy. The general clinical and laboratory characteristics are listed in Table I and the data were well-balanced between the two sets except for basal LH.

Univariate logistic regression analysis showed a significant correlation between AMH, number of oocytes retrieved, number of normal fertilisation, number of MII oocyte, number of high-quality cleavage embryos, and number of embryos transferred with clinical pregnancy in the training set. Univariate logistic regression analysis demonstrated that infertility duration (OR = 1.43, 95% CI = 1.03 - 2.00, p = 0.034), P on HCG-day (OR = 0.59, 95% CI = 0.36 - 0.99, p = 0.044), and number of high--quality cleavage embryos (OR = 1.16, 95% CI = 1.03 - 1.30, p = 0.014), number of embryos transferred (OR = 0.57, 95% CI = 0.40-0.80, p = 0.001) were independent influencing factors of clinical pregnancy in EMs patients after surgery undergoing fresh IVF/ICSI-ET. The independent protective factors related to clinical pregnancy were the number of high-quality cleavage embryos and the number of embryos transplanted. The independent risk factors associated with a decreased clinical pregnancy rate were P on HCG day and infertility duration (Table II).

Table I: Comparison of clinical indicators in the training set and testing set.

	Testing set (n = 294)	Training set (n = 686)	p-value
Female age (year)*	30.0 [27.0;32.0]	30.0 [28.0;33.0]	0.546
Male age (year)*	31.0 [29.0;35.0]	31.0 [29.0;34.0]	0.273
Type of infertility, n (%)**			0.346
Secondary	135 (45.9%)	291 (42.4%)	
Primary	159 (54.1%)	395 (57.6%)	
Infertility duration (year), n (%)**			0.243
≤2	126 (42.9%)	265 (38.6%)	
>2	168 (57.1%)	421 (61.4%)	
BMI (kg/m^2)*	20.8 [19.4;22.3]	20.8 [19.5;22.7]	0.688
Basal FSH (IU/L)*	6.25 [5.22;7.30]	6.30 [5.32;7.59]	0.368
Basal E2 (pg/mL)*	36.4 [27.8;49.8]	35.6 [27.1;46.5]	0.126
Basal LH (IU/L)*	3.69 [2.72;5.38]	4.01 [2.99;5.50]	0.045
AMH (μg/L)*	2.42 [1.52;3.53]	2.32 [1.48;3.67]	0.941
Protocol, n (%)**			0.975
Other	15 (5.10%)	37 (5.39%)	
Prolonged	279 (94.9%)	649 (94.6%)	
Total dose of Gn*	2120 [1650;2644]	2100 [1575;2700]	0.597
Dosing days of Gn*	11.0 [10.0;12.0]	11.0 [10.0;12.0]	0.566
Endometrial thickness on HCG day(mm)*	11.6 [10.1;13.2]	11.6 [9.72;13.6]	0.612
E^2 on HCG-day (pg/mL)*	1652 [1150;2279]	1670 [1122;2336]	0.997
LH on HCG-day (IU/L)*	1.08 [0.72;1.56]	1.13 [0.72;1.63]	0.567
P on HCG-day (ng/mL)*	0.60 [0.39;0.86]	0.59 [0.40;0.85]	0.854
Number of oocytes retrieved*	10.0 [7.00;13.0]	10.0 [7.00;13.0]	0.822
Number of normal fertilisation*	7.00 [4.00;9.00]	6.00 [4.00;9.00]	0.526
Number of MII oocytes*	8.00 [5.00;11.0]	8.00 [5.00;10.8]	0.873
Number of high-quality cleavage embryos*	2.00 [1.00;3.00]	1.00 [1.00;3.00]	0.292
Stage of transferred embryos, n (%)**			0.404
Cleavage	234 (79.6%)	529 (77.1%)	
Blastocyst	60 (20.4%)	157 (22.9%)	
Number of embryos transferred, n (%)**			0.419
Two	206 (70.1%)	461 (67.2%)	
One	88 (29.9%)	225 (32.8%)	
Fertilisation, n (%)**			0.691
IVh	243 (82.7%)	558 (81.3%)	
ICSI	51 (17.3%)	128 (18.7%)	

**non-normal distribution data were subjected to Kruskal-Wallis test, BH correction, and **categorical data were subjected to Chi-square test.*

Table II: Univariate and multivariate analysis of factors influencing clinical pregnancy.

	Fail (n = 262)	Pregnancy (n = 424)	OR (univariable)	OR (multivariable)
Female age(year)	30.0 ± 3.6	30.1 ± 3.4	1.01 (0.97-1.06, p = 0.660)	
Male age (year)	31.5 ± 4.3	31.9 ± 4.6	1.02 (0.99-1.06, p = 0.253)	
Type of infertility, n (%)				
Secondary	106 (40.5%)	185 (43.6%)		
Primary	156 (59.5%)	239 (56.4%)	0.88 (0.64-1.20, p = 0.414)	
Infertility duration (year), n (%)				
≤2	112 (42.7%)	153 (36.1%)		
>2	150 (57.3%)	271 (63.9%)	1.32 (0.97-1.81, p = 0.082)	1.43 (1.03-2.00, p = 0.034)
BMI (kg/m^2)	21.0 ± 2.5	21.3 ± 2.7	1.05 (0.99-1.12, p = 0.096)	1.05 (0.99-1.12, p = 0.127)
Basal FSH (IU/L)	6.6 ± 2.4	6.7 ± 2.2	1.01 (0.95-1.08, p = 0.711)	
Basal E2 (pg/mL)	37.6 ± 16.6	38.0 ± 15.9	1.00 (0.99-1.01, p = 0.754)	
Basal LH (IU/L)	4.4 ± 3.1	4.8 ± 3.0	1.04 (0.99-1.10, p = 0.133)	1.06 (1.00-1.13, p = 0.058)
AMH (μg/L)	2.6 ± 1.7	2.9 ± 1.7	1.10 (1.00-1.21, p = 0.047)	1.00 (0.90-1.12, p = 0.971)
Protocol, n (%)				
Other	17 (6.5%)	20 (4.7%)		
Prolonged	245 (93.5%)	404 (95.3%)	1.40 (0.72-2.73, p = 0.320)	
Total dose of Gn	2279.8 ± 884.0	2222.2 ± 930.9	1.00 (1.00-1.00, p = 0.422)	
Dosing days of Gn	10.8 ± 1.9	10.9 ± 2.2	1.03 (0.96-1.11, p = 0.432)	
Endometrial thickness on HCG day (mm)	11.8 ± 2.8	11.7 ± 2.6	0.99 (0.93-1.05, p = 0.720)	
E^2 on HCG-day (pg/mL)	1767.8 ± 1037.4	1894.1 ± 972.4	1.00 (1.00-1.00, p = 0.108)	1.00 (1.00-1.00, p = 0.784)
LH on HCG-day (IU/L)	1.5 ± 2.0	1.6 ± 5.1	1.00 (0.97-1.04, p = 0.844)	
P on HCG-day (ng/mL)	0.7 ± 0.4	0.6 ± 0.3	0.75 (0.48-1.15, p = 0.188)	0.59 (0.36-0.99, p = 0.044)
Number of oocytes retrieved	9.6 ± 4.7	10.8 ± 4.3	1.06 (1.02-1.10, p = 0.001)	1.03 (0.95-1.12, p = 0.443)
Number of normal Fertilisation	6.1 ± 3.6	7.2 ± 3.6	1.10 (1.05-1.15, p <0.001)	1.04 (0.93-1.17, p = 0.498)
Number of MII oocytes	7.4 ± 4.0	8.5 ± 3.9	1.08 (1.04-1.13, p <0.001)	1.00 (0.88-1.13, p = 0.969)
Number of high-quality cleavage embryos	1.5 ± 1.6	2.0 ± 1.7	1.20 (1.09-1.32, p <0.001)	1.16 (1.03-1.30, p = 0.014)
Stage of transferred embryos, n (%)				
Cleavage	203 (77.5%)	326 (76.9%)		
Blastocyst	59 (22.5%)	98 (23.1%)	1.03 (0.72-1.49, p = 0.857)	
Number of embryos transferred, n (%)				
Two	163 (62.2%)	298 (70.3%)		
One	99 (37.8%)	126 (29.7%)	0.70 (0.50-0.96, p = 0.029)	0.57 (0.40-0.80, p = 0.001)
Fertilisation, n (%)				
IVF	204 (77.9%)	354 (83.5%)		
ICSI	58 (22.1%)	70 (16.5%)	0.70 (0.47-1.03, p = 0.067)	0.71 (0.47-1.07, p = 0.102)

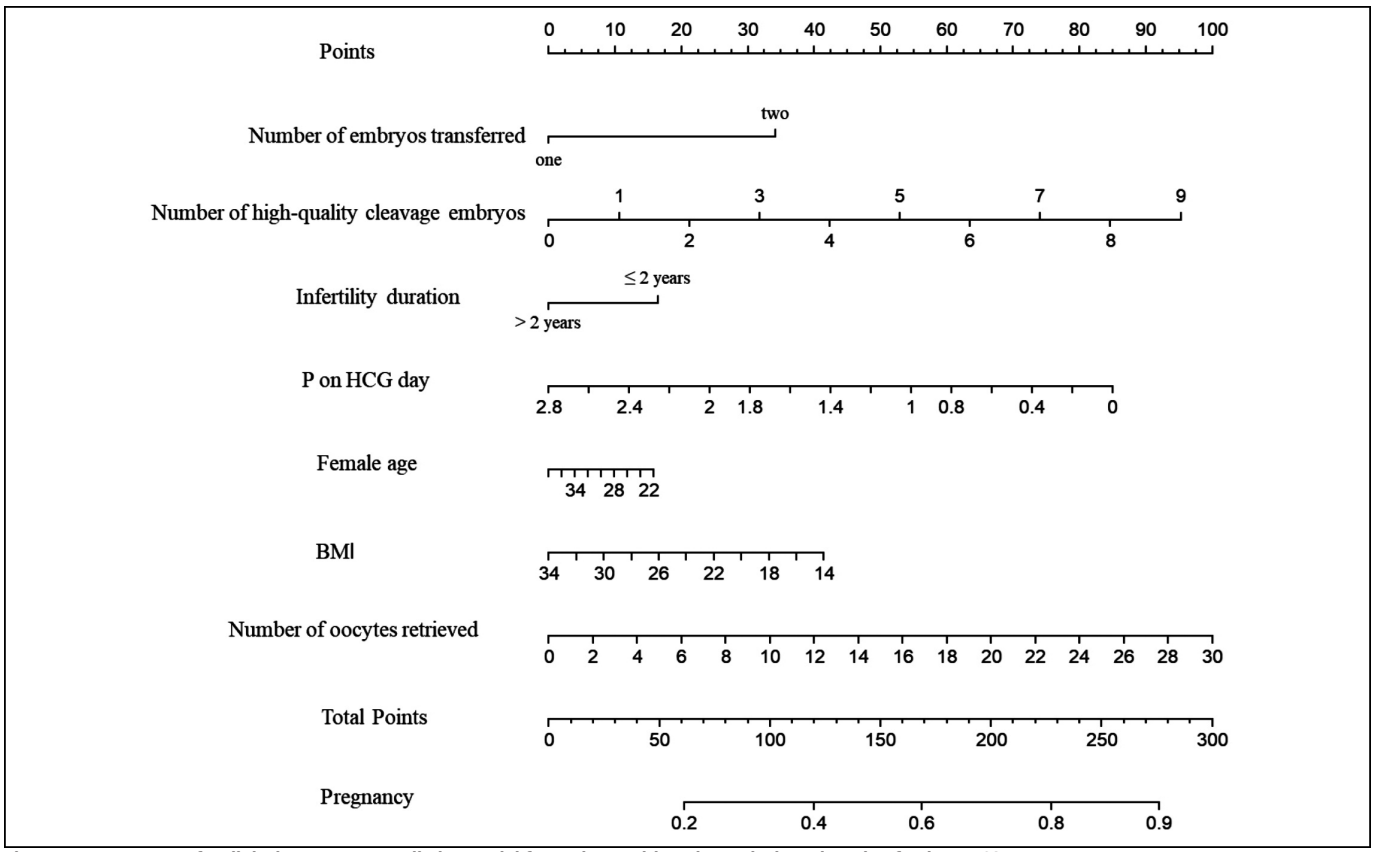

Figure 1: Nomogram of a clinical pregnancy prediction model for patients with endometriosis undergoing fresh IVF/ICSI-ET.

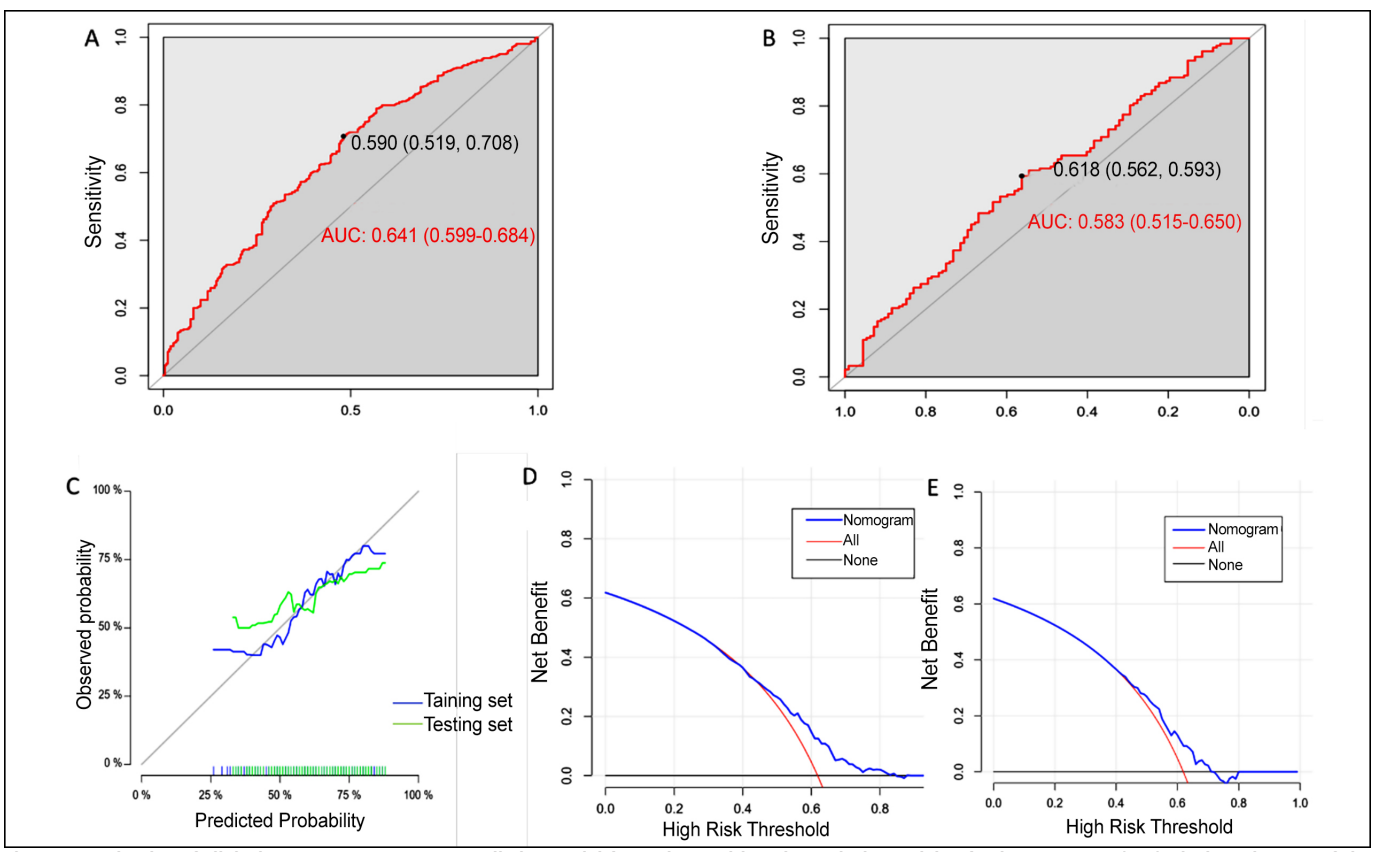

Figure 2: Evaluation of clinical pregnancy nomogram prediction model for patients with endometriosis receiving fresh IVF/ICSI-ET. (A,B) Displays the ROC of the training and testing set, respectively, (C) The calibration curve for the training and testing set. (D,E) Shows the DCA of the training and testing set, respectively.

A nomogram containing significant influencing factors was established based on the results of multivariate logistic regression analyses to predict the probability of clinical pregnancy in EMs patients after surgery undergoing fresh IVF/ICSI-ET. Although female age, number of oocytes retrieved, and body mass index (BMI) were not statistically significant with clinical pregnancy, they were still included in the predictive model due to their clinical relevance. A total score of the nomogram was calculated using the number of high-quality cleavage embryos, number of embryos transferred, P on HCG day, infertility duration, female age, number of oocytes retrieved, and BMI, as shown in Figure 1.

To evaluate the discriminatory ability of the constructed nomogram, AUC and calibration curves were used. The AUC were 0.641 (95% CI = 0.599-0.684) and 0.583 (95% CI = 0.515 - 0.650) in the training and testing sets, indicating a fair performance (Figure 2). The calibration curves displayed proximity to the 45-degree diagonal reference line in both training and testing sets, indicating that the actual clinical pregnancy was close to the predicted clinical pregnancy on the nomogram (Figure 2). Moreover, the p-value of the HL test for both the training (R^2 = 4.159, p = 0.842 >0.05) and testing set (R^2 = 5.633, p = 0.688 >0.05) were greater than 0.05, indicating that the model can accurately predict the clinical pregnancy probability of EMs patients after surgery undergoing fresh IVF/ICSI-ET. In the training (R^2 = 4.159, p = 0.842) and testing set (R^2 = 5.633, p = 0.688), HL test showed no significant difference between the predicted and the true clinical pregnancy probabilities (p >0.05).

To analyse the clinical efficacy of the model DCA was used. The results indicated that within the threshold probability range of 0.4 to 0.8, both the training and testing sets achieved the maximum benefits. DCA showed that the predictive model was far from extreme curves, and had a high net profit, indicating that the constructed clinical pregnancy nomogram prediction model was safe, reliable, and highly practical (Figure 2).

DISCUSSION

The research on the prediction model of fresh embryo transfer pregnancy outcomes in infertile patients with EMs has not been fully developed, and currently only a few are available for reference. A study used machine learning to construct a model for predicting the clinical pregnancy rate of fresh embryo transfer in patients with endometriosis.[11] However, the sample size of the study was relatively small. Another study used multiple logistic regression analysis to construct a model for predicting the clinical pregnancy rate of fresh embryo transfer in patients with endometriosis.[12] The model included multiple factors such as female age, ASRM stage, duration from surgery to *in vitro* fertilisation, number of antral follicles, AMH level, ovulation induction protocol, number of retrieved eggs, number of high-quality cleavage embryos, and number of transferred embryos.

This study constructed a nomogram model through univariate and multivariate logistic regression analysis, incorporating the following variables: Number of high-quality cleavage embryos, number of embryos transferred, P on HCG day, infertility duration, female age, number of oocytes retrieved, and BMI, aimed at predicting the probability of clinical pregnancy in EMs women receiving fresh IVF/ICSI-ET treatment after surgery. The AUC of the training set for this prediction model is 0.641, and the AUC of the testing set is 0.583. Although the model's discrimination is average, its calibration and clinical practicality perform well. The performance of the model may be affected by the amount of data included in the study. The inclusion of data in this study is limited by strict inclusion criteria. Endometriosis cases combined with other infertility factors were excluded and endometriosis was analysed as the only infertility factor. All included patients received surgical treatment for endometriosis before ART.

At present, the quality of embryos is mainly judged by observing their morphology under a microscope, which is the main criterion for selecting embryos for transplantation. Embryo morphology is closely related to implantation potential.[13] Studies have shown a significant correlation between embryo quality and IVF-ET outcomes, with high-quality embryo transfer leading to a higher chance of successful pregnancy.[10,14] Recent studies demonstrated that Day-3 embryo cell number needed to be considered when Day-5 single blastocyst was transferred.[15] Based on the study's multivariate analysis, the number of high-quality cleavage embryos was independently associated with clinical pregnancy (OR = 1.16, 95% CI 1.03-1.30, p = 0.014), which was in agreement with previous reports.

Nowadays, selective single blastocyst transplantation is becoming increasingly popular in order to diminish the rate of multiple pregnancies. However, according to statistics from 2016 to 2023, the study centre mainly transferred cleavage-stage embryos rather than blastocysts for fresh embryo transfer. A study compared single-cleavage embryo transfer with double-cleavage embryo transfer and found that the live birth rate of single-cleavage embryo transfer was lower than that of double-cleavage embryo transfer.[16] This study's results showed that in a single fresh IVF/ICSI-ET cycle, the clinical pregnancy rate of single-embryo transfer was lower than that of double-embryo transfer (one *vs*. two, OR = 0.57, 95% CI 0.40-0.80, p = 0.001), which was consistent with previous study.[17] Therefore, young EMs patients can improve their clinical pregnancy rate by obtaining good-quality embryos and increasing the number of transplanted embryos, which provides them with confidence in seeking ART-assisted pregnancy.

Although surgery for EMs can improve pain and increase the chances of natural conception compared to expectant treatment,[18] the risk of disease recurrence is high.[19] The authors found that some patients had undergone more than 2 surg-

eries (data not shown). Also, the present study demonstrated a correlation between infertility duration and pregnancy outcomes (≤2 years *vs*. >2 years, OR = 1.43, 95% CI 1.03 - 2.00, p = 0.034). Conversely, with increasing age, the ovarian reserves diminish, and fewer embryos can be obtained.[20] On the other hand, the risk of recurrence of EMs increases with time intervals. Therefore, infertility duration is an important factor affecting fertility and young patients with EMs should obtain pregnancy as early as possible through natural or ART.

P is an essential hormone involved in implantation and pregnancy maintenance processes.[21] Previous studies demonstrated the harmful effects of premature P elevation on endometrial receptivity.[22] Published data pointed out that there was an association between the elevated P level on HCG day and the low rate of top embryo quality.[23] Zhao *et al.* reported that the slight elevation of P level on HCG day may had a negative effect on the clinical pregnancy in gonadotropin-releasing hormone antagonist cycles and a whole embryo freezing strategy was recommended when HCG injection day was p >1.4 ng/ml.[24] This study's result showed a negative effect of elevated P on HCG-day to clinical pregnancy in EMs patients undergoing fresh IVF/ICSI-ET cycle (OR = 0.59, 95% CI 0.36-0.99, p = 0.044), which was in line with the previous study.[25]

This study has several limitations. First, the retrospective nature of the study can lead to selection bias. Second, patients only come from one centre and may be influenced by centre-specific practices. Third, it is best to have external validation of this model before clinical implementation. Fourthly, some important variables were not included in the model due to certain factors.

CONCLUSION

This study confirmed that the number of high-quality cleavage embryos, number of embryos transferred, P on HCG day and infertility duration were the significant independent influence factors of clinical pregnancy and constructed a prediction nomogram model to predict and analyse pregnancy outcomes for patients with EMs who underwent fresh IVF/ICSI-ET after surgery.

ACKNOWLEDGEMENT:
This work was supported by the Scientific Research Project of Jiangxi Provincial Health Commission (No. 202211108).

ETHICAL APPROVAL:
The Ethics Committee on Jiangxi Provincial Maternal and Child Health Hospital approved this retrospective study (Approval Number: SZYX-202402).

PATIENTS' CONSENT:
Written informed consent was obtained from all participants.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
XW: Presented the ideas and was responsible for the organisation and coordination of the trial.
YW: Developed the trial design and wrote the original draft.
MY: Analysed the data.
ZZ: Reviewed and edited the manuscript.
ZH: Designed the write-up, extracted the data.
JT: Revised the manuscript critically.
All authors contributed to the management and administration of the trial and approved the final version of the manuscript to be published.

REFERENCES

1. Reis FM, Santulli P, Marcellin L, Borghese B, Lafay-Pillet MC, Chapron C. Superficial peritoneal endometriosis: Clinical characteristics of 203 confirmed cases and 1292 endometriosis-free controls. *Reprod Sci* 2020; **27(1)**:309-15. doi: 10.1007/s43032-019-00028-1.
2. Tanbo T, Fedorcsak P. Endometriosis-associated infertility: aspects of pathophysiological mechanisms and treatment options. *Acta Obstet Gynecol Scand* 2017; **96(6)**:659-67. doi: 10.1111/aogs.13082.
3. Tsikouras P, Oikonomou E, Bothou A, Chaitidou P, Kyriakou D, Nikolettos K, *et al.* The impact of endometriosis on pregnancy. *J personalized Med* 2024; **14(1)**. doi: 10.3390/jpm 14010126.
4. Sharma S, Roy Choudhury S, Bathwal S, Bhattacharya R, Kalapahar S, Chattopadhyay R, *et al.* Pregnancy and Live birth rates are comparable in young infertile women presenting with severe endometriosis and tubal infertility. *Reproductive Sci* 2020; **27(6)**:1340-9. doi: 10.1007/s43032-020-00158-x.
5. Yang XC, Liu Y, Sun WW, Shi G, Wu Y, Xu C, *et al.* Efficacy of Chinese herbal medicines on pregnancy outcomes in patients with endometriosis in long-term management: A multicenter retrospective cohort study. *Chinese J Integrative Med* 2023; **29(11)**:971-9. doi: 10.1007/s11655-023-3736-z.
6. Li A, Zhang J, Kuang Y, Yu C. Analysis of IVF/ICSI-FET Outcomes in women with advanced endometriosis: Influence on ovarian response and oocyte competence. *Frontiers In Endocrino* 2020; **11**:427. doi: 10.3389/fendo.2020.00427.
7. Horton J, Sterrenburg M, Lane S, Maheshwari A, Li TC, Cheong Y. Reproductive, obstetric, and perinatal outcomes of women with adenomyosis and endometriosis: A systematic review and meta-analysis. *Human Reproduc Update* 2019; **25(5)**:592-632. doi: 10.1093/humupd/dmz012.
8. Rossi AC, Prefumo F. The effects of surgery for endometriosis on pregnancy outcomes following *in vitro* fertilization and embryo transfer: A systematic review and meta-analysis. *Arch Gynecol Obstet* 2016; **294(3)**:647-55. doi: 10. 1007/s00404-016-4136-4.
9. Wu J, Lu L, Chen H, Lin Y, Zhang H, Chen E, *et al*. Prognostic nomogram to predict the overall survival of patients with early-onset colorectal cancer: A population-based analysis. *Int J Colorectal Dis* 2021; **36(9)**:1981-93. doi: 10.1007/s00384-021-03992-w.

10. Huang FP, Zhang HL, Xie X, Du SR, Yi JS. A model for pregnancy rates after IVF-ET in patients with infertility and endometriosis. *Euro Rev Med Pharmacol Sci* 2022; **26(19)**: 7188-94. doi: 10.26355/eurrev_202210_29908.
11. Pan S, Li Y, Wu Z, Mao Y, Wang C. Establishment of a predictive nomogram for clinical pregnancy rate in patients with endometriosis undergoing fresh embryo transfer. *Nan Fang Yi Ke Da Xue Xue Bao* 2024; **44(7)**:1407-15. doi: 10.12122/j.issn.1673-4254.2024.07.21.
12. Zhu S, Liao X, Jiang W, Sun Y, Chen X, Zheng B. Development and validation of a nomogram model for predicting clinical pregnancy in endometriosis patients undergoing fresh embryo transfer. *BMC Pregnancy Childbirth* 2023; **23(1)**: 764. doi: 10.1186/s12884-023-06082-7.
13. Yu X, Zhao Y, Huang S, Wang Y. Correlation of Blastocyst Quality and Pregnancy Outcome during Freeze - thaw cycle. *J Coll Physic and Surg Pak* 2021; **31(3)**:278-81. doi: 10.29271/jcpsp.2021.03.278.
14. Dashti S, Pejman A, Tabibnejad N, Mortezanasab M. The effect of transferring a poor-quality embryo together with a good-quality embryo on the singleton birth weight: A retrospective cohort study. *Int J Reproductive Biomedicine* 2022; **20(2)**:79-90. doi: 10.18502/ijrm.v20i2.10500.
15. Wang J, Diao Z, Fang J, Zhu L, Xu Z, Lin F, *et al*. The influence of day 3 embryo cell number on the clinical pregnancy and live birth rates of day 5 single blastocyst transfer from frozen embryo transfer cycles. *BMC Pregn Childbirth* 2022; **22(1)**:980. doi: 10.1186/s12884-022-05337-z.
16. Wong KY, Tan HH, Allen JC, Chan J, Ee TX, Chua KH, *et al.* Outcomes and cost analysis of single-embryo transfer *versus* double-embryo transfer. *Women's Health (London, England)* 2023; **19**:17455057231206312. doi: 10.1177/17455057231206312.
17. Zhou Y, Ji H, Zhang M, Zhang J, Li X, Zhang J, *et al.* Single *versus* double blastocyst transfer in first and second frozen-thawed embryo transfer cycle in advance-aged women: A two-center retrospective cohort study. *BMC Women's Health.* 2024; **24(1)**:51. doi: 10.1186/s12905-023-02753-x.
18. Muzii L, C DIT, Galati G, Mattei G, Chine A, Cascialli G, *et al.* Endometriosis-associated infertility: Surgery or IVF? *Minerva Obstetr Gynecol* 2021; **73(2)**:226-32. doi: 10.23736/S2724-606X.20.04765-6.
19. Di Maida F, Lambertini L, Grosso AA, Mari A, Vannuccini S, Capezzuoli T, *et al.* Urinary tract endometriosis: How to predict and prevent recurrence after primary surgical excision. *J Minimally Invasive Gynecol* 2022; **29(10)**:1178-83. doi: 10.1016/j.jmig.2022.07.004.
20. Wasielak-Politowska M, Kordowitzki P. Chromosome segregation in the oocyte: What goes wrong during aging. *Int J Molecul Sci* 2022; **23(5)**. doi: 10.3390/ijms23052880.
21. Cortes-Vazquez A, Escobosa C, Cortes-Algara AL, Moreno-Garcia JD. Novel insights on premature progesterone elevation: A mini-review. *JBRA Assist Reproduc* 2022; **26(3)**: 531-7. doi: 10.5935/1518-0557.20210096.
22. Arvis P, Lehert P, Guivarch-Leveque A. Both high and low HCG day progesterone concentrations negatively affect live birth rates in IVF/ICSI cycles. *Reproduc Biomed Online* 2019; **39(5)**:852-9. doi: 10.1016/j.rbmo.2019.07.001.
23. Huang B, Ren X, Wu L, Zhu L, Xu B, Li Y, *et al.* Elevated progesterone levels on the day of oocyte maturation may affect top quality embryo IVF cycles. *Plos One* 2016; **11(1)**:e0145895. doi: 10.1371/journal.pone.0145895.
24. Zhao J, Hao J, Xu B, Wang Y, Li Y. Effect of slightly elevated progesterone on hCG trigger day on clinical pregnancy rate in GnRH-ant IVF/ICSI cycles. *Reproduc Health* 2022; **19(1)**:66. doi: 10.1186/s12978-022-01371-4.
25. Pitner I, Mikus M, Sprem Goldstajn M, Lagana AS, Chiantera V, Ferrari F, *et al.* Effects of different progesterone levels on reproductive outcomes in assisted reproductive technologies: from molecular basis to treatment strategies. *Gynecological Endocrinol* 2023; **39(1)**:2190806. doi: 10.1080/09513590.2023.2190806.