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# Predicting peripartum depression using elastic net regression and machine learning: the role of remnant cholesterol

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## Abstract

**Background** Traditional statistical methods have dominated research on peripartum depression (PPD), but innovative approaches may provide deeper insights. This study aims to predict the impact factors of PPD using elastic net regression (ENR) combined with machine learning (ML) model.

**Methods** This longitudinal study was conducted from June 2020 to May 2023, involving healthy pregnant women in the first trimester, followed up until the completion of the assessment in the second trimester. PPD symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS). Features with $p < .05$ from logistic regression were selected and refined using ENR. These features were then used to build six ML models to identify the best-performing one. SHapley Additive exPlanations (SHAP) analysis was employed to enhance model interpretability by visualizing its decision-making process.

**Results** A total of 608 participants were followed, resulting in 384 valid questionnaires. After excluding incomplete or incorrect baseline data, 325 participants were ultimately included in the study. Among these, 130 were classified as having mild depression, and 32 were classified with major depression. Nineteen features were initially identified as being associated with PPD, with 14 retained after ENR refinement. The random forest (RF) model outperformed the other ML models. SHAP analysis identified the top five predictors of PPD: magnesium (Mg), remnant cholesterol (RC), calcium (Ca), mean corpuscular hemoglobin concentration (MCHc), and potassium (K). Mg, Ca, MCHc, and K were negatively correlated with PPD, while RC showed a positive correlation.

**Conclusions** The RF model effectively identified associations between exposure factors and PPD. Mg, Ca, MCHc, and K were found to be protective factors, while RC emerged as a potential risk factor, highlighting its potential as a novel biomarker for PPD.

**Keywords** Peripartum depression, Remnant cholesterol, Elastic net regression, Machine learning, Random forests

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## Introduction

Peripartum depression (PPD) is a major depressive disorder with perinatal onset, encompassing both depression during pregnancy and the postpartum period, as defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition, Text Revision (DSM-5-TR) [1]. The global prevalence of PPD is approximately 11.9% [2], posing significant risks to maternal health and potentially adversely affecting fetal neurodevelopment and behavior by altering hormone and neurotransmitter levels [3, 4]. Identifying risk factors for PPD is therefore essential.

While many studies have explored the factors influencing PPD, such as dietary habits and lipid parameters [5–7], most have employed traditional statistical methods. Newer analytical approaches may offer more accurate identification of PPD risk factors. Analyzing the relationship between PPD and multiple exposures in datasets with high dimensionality and multicollinearity is particularly challenging. Elastic net regression (ENR) addresses this issue by integrating L1 and L2 regularization, facilitating sparse solutions while managing datasets with numerous features and potential collinearity. Furthermore, traditional statistical methods often require extensive data preparation and high-quality, structured datasets, leading to the loss of valuable unstructured data [8]. In contrast, machine learning (ML) algorithms, often considered "black-box" models, require fewer predefined standards and less data preparation, enhancing the ability to analyze large, complex datasets. These methods provide valuable insights for disease diagnosis and the early identification of risk factors.

The research on the relationship between traditional lipid indicators and depression has yielded inconsistent results [9], limiting the clinical application of lipid biomarkers. Remnant cholesterol (RC), also known as triglyceride-rich lipoprotein cholesterol, comprises very low-density lipoprotein, intermediate-density lipoprotein, and chylomicron remnants in both fasting and non-fasting states [10]. Compared to traditional lipid parameters, RC may offer greater pathological significance as a depression biomarker. Its association with inflammation is well-documented; elevated serum levels of RC can permeate arterial walls, where macrophages are involved in foam cell formation [11]. A causal relationship between RC and low-grade chronic inflammation has been established [12], suggesting that RC may contribute to the development and progression of depression through inflammatory mechanisms.

This study aims to construct a predictive model using ENR combined with ML techniques to investigate the association between RC and PPD. Additionally, the SHapley Additive exPlanations (SHAP) technique will be used to quantify the contribution of each exposure factor to PPD prediction, providing a basis for early intervention.

## Materials and methods

### Data sources

This study recruited 608 pregnant women between June 2020 and May 2023. The study protocol was approved by the Ethics Review Committee of the Second Affiliated Hospital of Xinjiang Medical University (Approval Numbers: 20200531-13, KY2023112109). All participants were informed about the study's purpose and significance and provided written informed consent.

The inclusion criteria for the study were as follows: (1) age between 20 and 45 years; (2) singleton pregnancy with an estimated gestational age of 6 to 13 weeks; (3) regular prenatal check-ups at the Second Affiliated Hospital of Xinjiang Medical University during pregnancy and completion of the questionnaire. The exclusion criteria included: (1) a history of depression; (2) diagnosis of type 1 or type 2 diabetes before pregnancy; (3) abnormal screening results for hypertension or Down syndrome during pregnancy; (4) diagnosed infectious diseases such as hepatitis B, hepatitis C, syphilis, or others; (5) metabolic diseases such as hyperthyroidism or hypothyroidism; (6) disabilities or organic mental disorders; (7) use of assisted reproductive technologies for conception; (8) missing early pregnancy biochemical data; (9) inability to provide informed consent or poor adherence to the study protocol.

### Study design

This longitudinal study initially collected baseline data and fasting blood biochemical test results from participants in early pregnancy (6–13 weeks of gestation). Participants were then followed up during the second trimester (24–27 weeks of gestation), at which time they completed a depression scale assessment. Prior to the study's initiation, all researchers underwent standardized and rigorous training. Data collection was conducted using electronic questionnaires, and data entry was verified independently by two researchers to ensure accuracy.

### Sample size calculation

The sample size was calculated using PASS 15.0 software. With an estimated average incidence of PPD of 11.9%, the following parameters were set: $\alpha = 0.05$ (two-sided), confidence level $(1\text{-}\alpha) = 0.95$, and power $(1\text{-}\beta) = 0.9$. The calculation yielded a required sample size of 162 participants. Considering a 40% attrition rate due to follow-up requirements, a minimum of 227 participants was determined to be necessary for the study.

### Questionnaire quality

Depression during the second trimester was assessed using the Edinburgh Postnatal Depression Scale (EPDS), a 10-item instrument with each item scored from 0 to 3. Higher total scores (maximum of 30) indicate more

severe depressive symptoms. Based on clinical research and experience, EPDS scores are typically categorized as follows:

- Normal: 0–9 points.
- Mild depression: 10–12 points.
- Moderate to severe depressive symptoms: 13–30 points [13].

For this study, an EPDS score of ≥ 10 was used as the cut-off for a positive depression screening result, consistent with the sensitivity (92%) and specificity (77%) reported in a recent meta-analysis [14]. The Chinese version of the EPDS has demonstrated high reliability and validity, with a Cronbach's α of 0.87 [15].

### RC calculation

The RC value is obtained by subtracting the sum of high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) from total cholesterol (TC) [16].

### Statistical analysis

To enhance statistical power and facilitate analysis, EPDS scores were categorized into three groups for univariate and differential analyses. For model development, EPDS was treated as a binary variable, with a threshold of EPDS ≥ 10 indicating a positive depression screen. Continuous variables were summarized as mean ± SD for normally distributed data or as median (interquartile range) for skewed distributions. Categorical variables were reported as frequencies and percentages.

Initially, logistic regression was used to examine the association between each feature and EPDS scores. Features with $p < .05$ in univariate analysis were included in the ENR model for further selection. The ENR model was constructed using RGui software (version 4.4.0) with the *glmnetUtils* package, and its performance was evaluated using the area under the curve (AUC) metric. Clinically, an AUC value between 0.7 and 1.0 is indicative of strong model discrimination, reliability, and validity [17].

After ENR model selection, the filtered dataset was divided into training (80%, $n = 260$) and testing (20%, $n = 65$) sets using JASP software (version 0.18.3.0) (available at https://jasp-stats.org/download/). Six ML models were employed to identify depression based on exposure features:

1. Random forest (RF).
2. Adaptive boosting (AdaBoost).
3. Support vector machine (SVM).
4. Decision tree (DT).
5. K-nearest neighbors (KNN).
6. Linear discriminant (LD).

The training dataset was used to develop each of the six ML models. Model performance was evaluated using a combination of metrics, including:

- AUC [18].
- Accuracy.
- Precision.
- Recall.
- False positive rate (FPR).
- F1 score.
- Negative predictive value (NPV).
- True negative rate.
- False negative rate.

To interpret feature importance and visualize the decision-making process of the selected model, the SHAP tool was utilized within RGui software (version 4.4.0).

## Results

### Descriptive statistics

A total of 608 pregnant women were followed from early to mid-pregnancy, resulting in 384 valid questionnaires and a follow-up loss rate of 36.8%. After excluding incomplete or erroneous data, 325 pregnant women were included in the final analysis (Fig. 1).

The median age of the participants was 28 years (interquartile range: 27–31 years). Participants were grouped based on their EPDS scores, as summarized in Table 1. Among the 325 participants, 130 (40%) were categorized as having mild depression (10 ≤ EPDS ≤ 12), while 32 (9.8%) screened positive for major depression (EPDS ≥ 13).

Analysis of body mass index (BMI) showed that 71.7% of participants had a BMI within the normal range (18.5 ≤ BMI < 24.9). Additionally, 61.8% reported regularly taking naps at noon. Significant differences ($p < .05$) were observed across 21 features between the EPDS score groups. These included BMI, sleep behavior at noon, breakfast frequency, eating habits, and RC levels.

### Analysis for PPD

#### *Univariate analysis for PPD*

Logistic regression was performed on 62 exposure characteristics (Table 2) to identify features associated with PPD. The univariate analysis identified 19 features with statistically significant associations with depression ($p < .05$). These features included nationality, breakfast frequency, and RC levels. For RC specifically, participants with major depression were found to have 4.57 times higher odds of elevated RC levels compared to those without depression (OR = 4.57, 95% CI: 2.18–9.57).

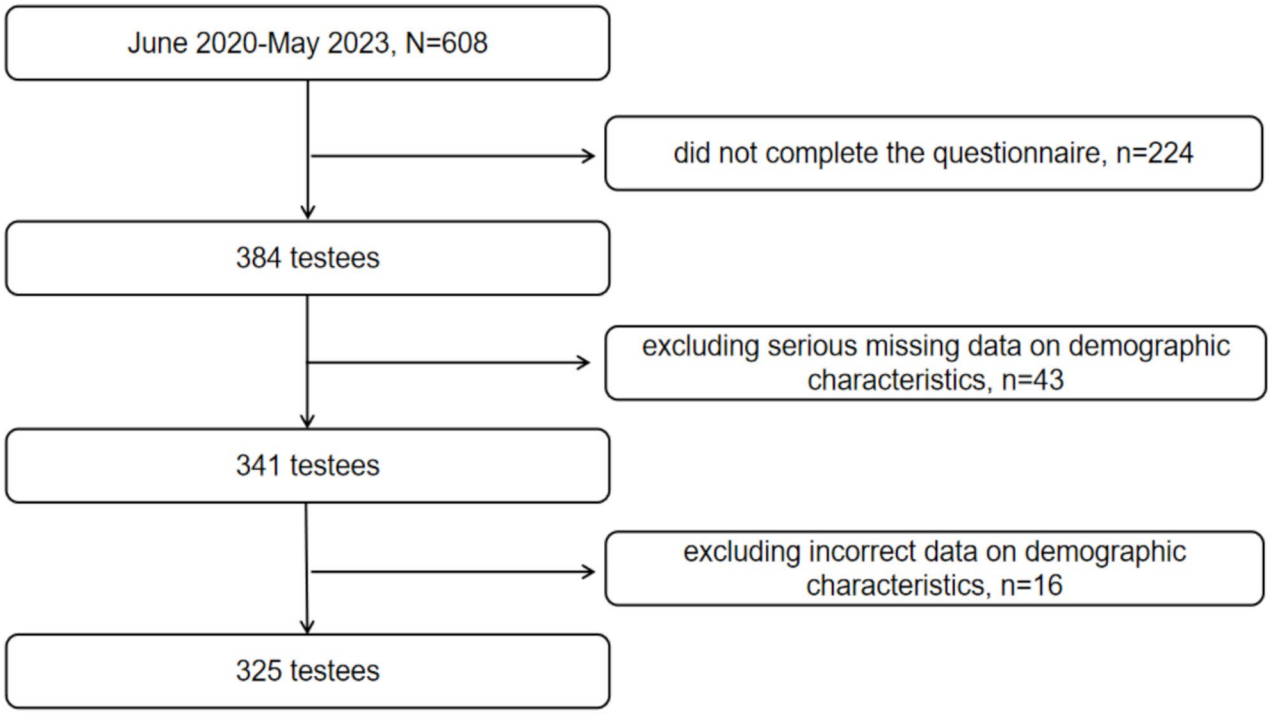


**Fig. 1** Flowchart of study participant exclusion

#### *ENR screens out important features of PPD*

The ENR model employs cross-validation to optimize parameters (α and λ) and minimize prediction error. Ten-fold cross-validation was applied as a model evaluation and selection strategy to assess the model's generalization capability and identify the best hyperparameters. The process involves:

1. Data segmentation: Dividing the dataset into training and validation subsets.
2. Model training and validation: Training the model on the training subset and validating it on the validation subset.
3. Loop iteration: Repeating the process across multiple folds.
4. Average validation error: Calculating the mean validation error across all folds.
5. Optimal parameter selection: Choosing parameters that yield the lowest average validation error.

Using ten-fold cross-validation, the ENR model determined the optimal parameters as $\alpha = 0.18$ and $\lambda = 0.13$. The "lambda.1se" criterion was used to screen 19 features, resulting in the selection of 14 important feature variables (Fig. 2a). Receiver operating characteristic (ROC) curve analysis validated the predictive performance of the ENR model. As illustrated in Fig. 2b, the model demonstrated strong accuracy, with an AUC of 0.796 (95% CI: 0.742–0.851) in the training set and 0.742 (95% CI: 0.634–0.850) in the testing set.

The results indicated that lower levels of red blood cell count (RBC), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHc), potassium (K), magnesium (Mg), calcium (Ca), total bile acids (TBA), and superoxide dismutase (SOD), alongside higher levels of RC and triglycerides (TG), were significantly associated with an increased risk of PPD. The regression coefficients for these variables were as follows: RBC (-0.124), MCH (-0.008), MCHc (-0.007), K (-0.201), Mg (-1.370), Ca (-0.796), TBA (-0.034), SOD (-0.005), TG (0.054), and RC (0.196) (Table 3).

#### *Performance of six ML models in identifying PPD*

To analyze the 14 features identified by the ENR model, six ML models were employed: RF, DT, AdaBoost, SVM, KNN, and LD. Table 4 provides a summary of their performance metrics. Among the models, the RF approach showed the highest average precision (0.754), reflecting superior discrimination capability. Both RF and DT models demonstrated similar performance in accuracy, precision, recall, FPR, NPV, and F1 score. Additionally, the RF model achieved the highest AUC value (0.850), significantly outperforming the other models (Fig. 3). Comprehensive feature-based analysis confirmed that the RF model exhibited the best precision and robustness

**Table 1** The differences in EPDS score between groups

| Characteristics | Total (*N* = 325) | Normal (*n* = 163, 50.2%) | Mild depression (*n* = 130, 40%) | Major depression (*n* = 32, 9.8%) | F/$\chi^2$ | *P* value |
|---|---|---|---|---|---|---|
| BMI (kg/m$^2$) | | | | | 16.67 | .011[a,*] |
| < 18.5 | 23(7.1%) | 10(6.1%) | 9(6.9%) | 4(12.5%) | | |
| 18.5–24.9 | 233(71.7%) | 107(65.6%) | 107(82.3%) | 19(59.4%) | | |
| 25-29.9 | 57(17.5%) | 38(23.3%) | 11(8.5%) | 8(25%) | | |
| ≥ 30 | 12(3.7%) | 8(4.9%) | 3(2.3%) | 1(3.1%) | | |
| Sleep behavior at noon | | | | | 10.15 | .006[a,*] |
| no | 124(38.2%) | 66(40.5%) | 39(30%) | 19(59.4%) | | |
| yes | 201(61.8%) | 97(59.5%) | 91(70%) | 13(40.6%) | | |
| Frequency of eating breakfast | | | | | 15.50 | .004[a,*] |
| every day | 250(77%) | 137(84%) | 86(66.2%) | 27(84.4%) | | |
| sometimes | 58(17.8%) | 22(13.5%) | 32(24.6%) | 4(12.5%) | | |
| rare | 17(5.2%) | 4(2.5%) | 12(9.2%) | 1(3.1%) | | |
| Eating habits | | | | | 15.39 | .017[a,*] |
| drink milk or eat fruit regularly | 175(53.8%) | 99(60.7%) | 62(47.7%) | 14(43.8%) | | |
| eat green vegetables every time | 111(34.2%) | 44(27%) | 49(37.7%) | 18(56.3%) | | |
| often eat fish | 36(11.1%) | 18(11%) | 18(13.8%) | 0 | | |
| whole grains | 3(0.9%) | 2(1.2%) | 1(0.8%) | 0 | | |
| Daily meat and vegetable matching habits | | | | | 17.03 | .030[a,*] |
| more meat and less vegetables | 51(15.7%) | 28(17.2%) | 23(17.7%) | 0 | | |
| less meat and more vegetables | 154(47.4%) | 71(43.6%) | 60(46.2%) | 23(71.9%) | | |
| as much meat as vegetables | 106(32.6%) | 60(36.8%) | 38(29.2%) | 8(25%) | | |
| all meat | 7(2.2%) | 1(0.6%) | 5(3.8%) | 1(3.1%) | | |
| all vegetables | 7(2.2%) | 3(1.8%) | 4(3.1%) | 0 | | |
| What are your dietary preferences | | | | | 14.65 | .023[a,*] |
| bland taste | 191(58.8%) | 106(65%) | 63(48.5%) | 22(68.8%) | | |
| sweet | 42(12.9%) | 13(8%) | 24(18.5%) | 5(15.6%) | | |
| salty | 57(17.5%) | 2616%) | 29(22.3%) | 2(6.3%) | | |
| greasy | 35(10.8%) | 18(11%) | 14(10.8%) | 3(9.4%) | | |
| Oils commonly used at home | | | | | 24.57 | <.001[a,*] |
| salad oil or blending oil | 34(10.5%) | 6(3.7%) | 26(20%) | 2(6.3%) | | |
| not fixed | 46(14.2%) | 20(12.3%) | 22(16.9%) | 4(12.5%) | | |
| vegetable oil | 245(75.4%) | 137(84%) | 82(63.1%) | 26(81.3%) | | |
| RBC (10^9/L) | 4.21(3.93,4.52) | 4.28(4.02,4.58) | 4.15(3.82,4.46) | 4.14(3.79,4.54) | 9.20 | .010[b,*] |
| MCV (fL) | 91.30(88.03,93.90) | 91.20(88.20,93.90) | 90.50(85.50,92.90) | 92.60(89.20,97.10) | 8.66 | .013[b,*] |
| MCH (pg) | 30.40(28.90,31.25) | 30.40(29.10,31.50) | 29.90(28.33,30.69) | 31(29.40,32.30) | 18.07 | <.001[b,*] |
| MCHc (g/L) | 330(325,337) | 331(326,338) | 330(323,333) | 332(325,338) | 8.18 | .017[b,*] |
| FT4 (pmol/L) | 15.98(14.51,16.67) | 15.72(14.24,16.51) | 16.25(14.94,17.18) | 15.77(14.20,16.25) | 8.42 | .015[b,*] |
| K (mmol/L) | 3.92(3.73,4.16) | 3.95(3.78,4.36) | 3.86(3.59,4.06) | 3.94(3.74,4.13) | 14.48 | .001[b,*] |
| Mg (mg/dL) | 2.02(1.90,2.24) | 2.07(1.92,2.48) | 2.01(1.90,2.10) | 1.90(1.83,2.06) | 22.17 | <.001[b,*] |
| FPG (mmol/L) | 4.82(4.62,5.04) | 4.82(4.64,5.01) | 4.82(4.68,5.10) | 4.82(4.48,5.01) | 6.29 | .043[b,*] |
| TBA (μmol/L) | 1.80(1,3.20) | 1.90(1.15,3.25) | 1.40(0.73,2.50) | 2.30(1.40,3.25) | 12.52 | .002[b,*] |
| 5′-nucleotidase (U/L) | 2.24(1.42,3.40) | 2.40(1.50,3.50) | 1.72(1.30,2.80) | 2.89(2.20,3.90) | 13.83 | .001[b,*] |
| SOD (U/ml) | 199(179.10,202) | 202(180.75,203.50) | 191(176,202) | 202(173,206) | 13.26 | .001[b,*] |
| TC (mmol/L) | 4.13(3.72,4.51) | 4.01(3.69,4.49) | 4.21(3.76,4.45) | 4.85(3.73,5.40) | 11.95 | .003[b,*] |
| LDL-C (mmol/L) | 2.25(1.74,2.40) | 2.18(1.54,2.44) | 2.25(1.89,2.35) | 2.25(2.10,2.62) | 6.13 | .047[b,*] |
| RC (mmol/L) | 0.25(0.07,0.57) | 0.21(0.11,0.47) | 0.27(0,0.57) | 0.55(0.14,1.62) | 9.68 | .008[b,*] |

Note:The annotations for all abbreviated variables in Table 1 can be found in the supplementary section. The table only shows the features with statistically significant differences. [a] Comparison was tested by Chi-square test (n, %); [b] Comparison was tested by Kruskal-Wallis H test (Median, Q1, Q3); * $p < .05$

**Table 2** Univariate logistic regression analysis of risk factors for PDD

| Characteristics | Mild depression (10 ≤ EPDS ≤ 12, *n* = 130) | | | Major depression (EPDS ≥ 13, *n* = 32) | | |
|---|---|---|---|---|---|---|
| | β | OR(95%CI) | *P* value | β | OR(95%CI) | *P* value |
| Nationality | | | | | | |
| The Han nationality | -1.71 | 0.18(0.04,0.87) | **0.033*** | 16.39 | -- | 0.998 |
| The Manchu | -19.81 | -- | 0.998 | -1.77 | -- | -- |
| The Hui nationality | -1.05 | 0.35(0.05,2.41) | 0.286 | 17.55 | -- | 0.997 |
| The Uighurs | -1.05 | 0.35(0.05,2.41) | 0.286 | 16.45 | -- | 0.998 |
| Other | Ref | Ref | Ref | Ref | Ref | Ref |
| Frequency of eating breakfast | | | | | | |
| every day | -1.56 | 0.21(0.07,0.67) | **0.008*** | -0.24 | 0.79(0.09,7.33) | 0.834 |
| sometimes | -0.72 | 0.49(0.14,1.70) | 0.258 | -0.32 | 0.73(0.06,8.32) | 0.798 |
| rare | Ref | Ref | Ref | Ref | Ref | Ref |
| Picky eating behavior | | | | | | |
| yes | 0.41 | 1.5(0.64,3.51) | 0.349 | -0.46 | 0.63(0.13,3.02) | 0.564 |
| occasionally | 0.63 | 1.89(1.16,3.08) | **0.011*** | -0.29 | 0.75(0.33,1.68) | 0.483 |
| no | Ref | Ref | Ref | Ref | Ref | Ref |
| Oils commonly used at home | | | | | | |
| salad oil or blending oil | 1.98 | 7.24(2.86,18.33) | **< 0.001*** | 0.56 | 1.76(0.34,9.19) | 0.505 |
| not fixed | 0.61 | 1.84(0.95,3.57) | 0.073 | 0.05 | 1.05(0.34,3.34) | 0.929 |
| vegetable oil | Ref | Ref | Ref | Ref | Ref | Ref |
| RBC (10^9/L) | -0.77 | 0.46(0.30,0.74) | **0.001*** | -0.72 | 0.49(0.23,1.02) | 0.058 |
| MCV (fL) | -0.04 | 0.96(0.92,0.99) | **0.031*** | 0.06 | 1.06(0.98,1.14) | 0.150 |
| MCH (pg) | -0.14 | 0.87(0.79,0.97) | **0.008*** | 0.16 | 1.17(0.94,1.46) | 0.168 |
| MCHc (g/L) | -0.03 | 0.97(0.95,0.99) | **0.022*** | -0.01 | 1(1,1.04) | 0.847 |
| K (mmol/L) | -1.43 | 0.24(0.12,0.46) | **< 0.001*** | -1.09 | 0.34(0.12,0.96) | **0.042*** |
| Ca (mmol/L) | -2.68 | 0.07(0.01,0.38) | **0.002*** | -2.86 | 0.06(0.04,0.81) | **0.034*** |
| Mg (mg/dL) | -2.67 | 0.07(0.03,0.19) | **< 0.001*** | -3.58 | 0.03(0,0.19) | **< 0.001*** |
| FPG (mmol/L) | 0.84 | 2.32(1.10,4.91) | **0.027*** | -0.4 | 0.67(0.20,2.26) | 0.520 |
| TBA (μmol/L) | -0.21 | 0.81(0.69,0.96) | **0.012*** | 0.04 | 1.04(0.91,1.19) | 0.530 |
| 5′-nucleotidase (U/L) | -0.19 | 0.83(0.69,0.99) | **0.035*** | 0.10 | 1.11(0.89,1.38) | 0.363 |
| SOD (U/ml) | -0.03 | 0.98(0.96,0.99) | **< 0.001*** | -0.01 | 0.99(0.97,1.01) | 0.280 |
| TG (mmol/L) | 0.11 | 1.12(0.72,1.74) | 0.630 | 0.76 | 2.15(1.27,3.64) | **0.005*** |
| TC (mmol/L) | 0.12 | 1.13(0.80,1.59) | 0.478 | 1.05 | 2.84(1.64,4.92) | **< 0.001*** |
| LDL-C (mmol/L) | 0.27 | 1.31(0.85,2.02) | 0.217 | 0.76 | 2.14(1.09,4.17) | **0.026*** |
| RC (mmol/L) | -0.05 | 0.95(0.52,1.72) | 0.863 | 1.52 | 4.57(2.18,9.57) | **< 0.001*** |

Note: The annotations for all abbreviated variables in Table 2 can be found in the supplementary section. The table only shows the characteristics that affect the outcome variables. In the multiple logistic regression analysis, Normal (0 < EPDS ≤ 9, *n* = 163) was set as the control group. Ref, means reference. "--" Indicates an invalid value, which is caused by the number of observation units in the reference category being 0 and the sample size being too small. However, based on the authenticity of the data, this cannot be changed. * $p < .05$

for identifying PPD, making it the most effective method among the six evaluated approaches.

#### *Visualization of feature importance*

The RF model was trained using optimized hyperparameters to ensure maximum performance. Feature importance was evaluated and visualized, highlighting the model's efficiency and stability. The performance metrics, illustrated by the ROC curve and out-of-bag error, indicated robust predictive capabilities. The training set achieved an AUC of 0.934 (95% CI: 0.905–0.963), while the testing set yielded an AUC of 0.824 (95% CI: 0.742–0.907).

To further explore the model's predictive insights, SHAP values were employed to graphically represent the impact of individual features on depression prediction (Fig. 4). The analysis identified Mg, RC, Ca, MCHc, and K as the top five most influential features. Notably, Mg, Ca, MCHc, and K demonstrated negative contributions, indicating their association with a reduced risk of PPD. In contrast, RC exhibited a positive contribution, linking it to an increased risk of PPD. The SHAP plot also revealed additional behavioral and dietary factors associated with a higher risk of PPD, including picky eating habits, infrequent breakfast consumption, and frequent use of salad dressing or blended oil in cooking.

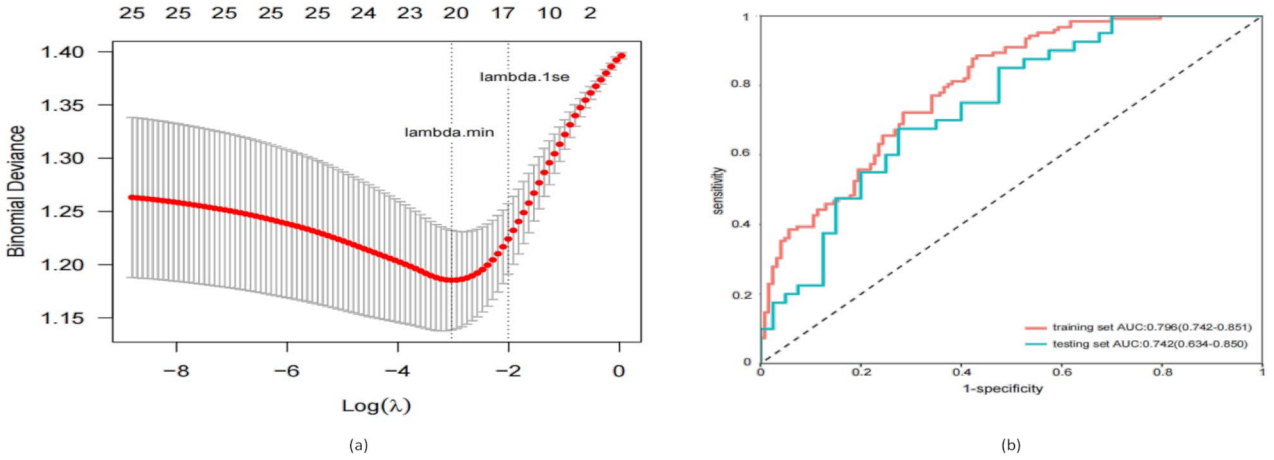


**Fig. 2** Elastic net regression completes the prognostic model variable screening. (**a**) Quantitative display of important features filtered out by elastic net regression. (**b**) Superposition of ROC curves of training set and test set in elastic net regression model
Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve
Note: All categorical variables in the model have been one-hot encoded

**Table 3** Elastic net regularized regression screens the predictive features of PPD

| Characteristics | Non-zero coefficient (β) | Characteristics | Non-zero coefficient (β) |
|---|---|---|---|
| Nationality(years) | | RBC (10^9/L) | -0.124 |
| The Han nationality | Ref | MCV (fL) | NA |
| The Manchu | -0.407 | MCH (pg) | -0.008 |
| The Hui nationality | 0.259 | MCHc (g/L) | -0.007 |
| The Uighurs | 0 | K (mmol/L) | -0.201 |
| Other | 0.869 | Mg(mg/dL) | -1.370 |
| Frequency of eating breakfast | | Ca (mmol/L) | -0.796 |
| every day | Ref | FPG (mmol/L) | NA |
| sometimes | 0.166 | TBA (μmol/L) | -0.034 |
| rare | 0.412 | 5′-nucleotidase (U/L) | 0 |
| Are you picky eaters | | SOD (U/ml) | -0.005 |
| yes | Ref | TG (mmol/L) | 0.054 |
| occasionally | 0 | TC (mmol/L) | 0 |
| no | -0.176 | LDL-C (mmol/L) | 0 |
| Oils commonly used at home | | RC (mmol/L) | 0.196 |
| salad oil or blending oil | Ref | | |
| not fixed | 0 | | |
| vegetable oil | -0.427 | | |

Abbreviations: RBC, red blood cell count; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHc, mean corpuscular hemoglobin concentration; K, serum potassium; Mg, serum magnesium; Ca, serum calcium; FPG, fasting plasma glucose; TBA, total bile acids; SOD, superoxide dismutase; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol

Note: Ref, means reference

## Discussion

This study represents a pioneering approach by combining ENR with six interpretable ML algorithms to explore exposure factors associated with PPD. After comprehensive performance evaluations, the RF model emerged as the most effective for identifying PPD. SHAP analysis further highlighted the five most influential features, with Mg, Ca, MCHc, and K showing protective effects against PPD. In contrast, RC, the second most influential feature, was positively associated with PPD, suggesting it as a potential risk factor.

In recent years, ML has become a prominent tool in disease prediction, offering unique advantages in PPD risk assessment. Its effectiveness depends on factors such as data quality, feature selection, and sample size. A review of ML applications in predicting postpartum depression found these methods to be effective tools for identifying individuals at risk, especially given the expanding computational data in psychiatric research

**Table 4** Comparison of discrimination characteristics among six machine learning models

| Characteristics | RF | AdaBoost | SVM | DT | KNN | LD |
|---|---|---|---|---|---|---|
| Accuracy | 0.738 | 0.569 | 0.677 | 0.708 | 0.677 | 0.646 |
| Precision /Positive Predictive Value | 0.754 | 0.611 | 0.683 | 0.720 | 0.683 | 0.653 |
| Recall /True Positive Rate | 0.738 | 0.569 | 0.677 | 0.708 | 0.677 | 0.646 |
| FPR | 0.255 | 0.409 | 0.323 | 0.288 | 0.323 | 0.354 |
| $F_1$ Score | 0.738 | 0.562 | 0.678 | 0.710 | 0.678 | 0.648 |
| AUC* | 0.850 | 0.655 | 0.677 | 0.712 | 0.677 | 0.777 |
| NPV | 0.749 | 0.598 | 0.674 | 0.706 | 0.674 | 0.643 |
| True Negative Rate | 0.745 | 0.591 | 0.677 | 0.712 | 0.677 | 0.646 |
| False Negative Rate | 0.255 | 0.409 | 0.323 | 0.288 | 0.323 | 0.354 |

Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; RF, random forest; AdaBoost, adaptive boosting; SVM, support vector machine; DT, decision tree; KNN, k-nearest neighbors; LD, linear discriminant; FPR, false positive rate; AUC, area under curve; NPV, negative predictive value

Note: *The corresponding *p*-values and confidence intervals for the above values are not displayed in the JASP platform

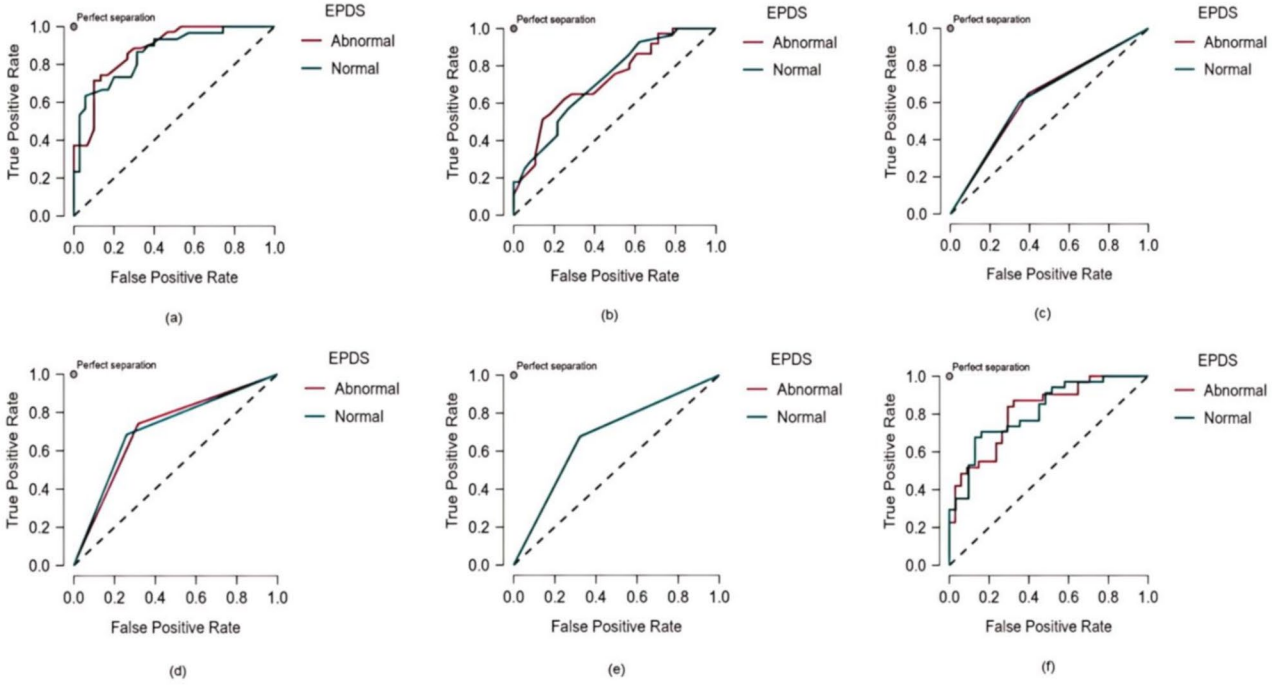


**Fig. 3** The AUC comparison of six machine learning models. (**a**) RF model, AUC = 0.850; (**b**) AdaBoost model, AUC = 0.655; (**c**) SVM model, AUC = 0.677; (**d**) DT model, AUC = 0.712; (**e**) KNN model, AUC = 0.677; (f) LD, AUC = 0.777

Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; AUC, area under the curve; RF, random forest; AdaBoost, adaptive boosting; SVM, support vector machine; DT, decision tree; KNN, k-nearest neighbors; LD, linear discriminant

Note: Normal (0 < EPDS ≤ 9), Abnormal (EPDS ≥ 10)

[19]. In this study, all six ML models demonstrated good predictive reliability, with AUC values exceeding 0.7.

Among the models, the RF algorithm consistently outperformed others. By constructing multiple decision trees and combining their outputs through majority voting, RF minimizes the risk of overfitting seen in single models, enhancing generalization. Additionally, its robustness to outliers and noisy data makes RF particularly suitable for the heterogeneous datasets typical in PPD research, encompassing demographic, psychological, and biological variables. In comparison, other ML models, such as the SVM, require meticulous hyperparameter tuning and are computationally intensive, limiting their practicality in complex datasets. These advantages establish RF as a reliable and efficient tool for predicting PPD risk.

The link between RC and depression is not yet fully understood, but several plausible biological mechanisms have been proposed. Elevated RC levels have been associated with low-grade inflammation and endothelial dysfunction, which may impair brain microvascular function and contribute to depression [20–22]. Specifically, RC-induced inflammation promotes the production of mediators like interleukin-6 (IL-6) and tumor necrosis factor-alpha, leading to neuronal damage and

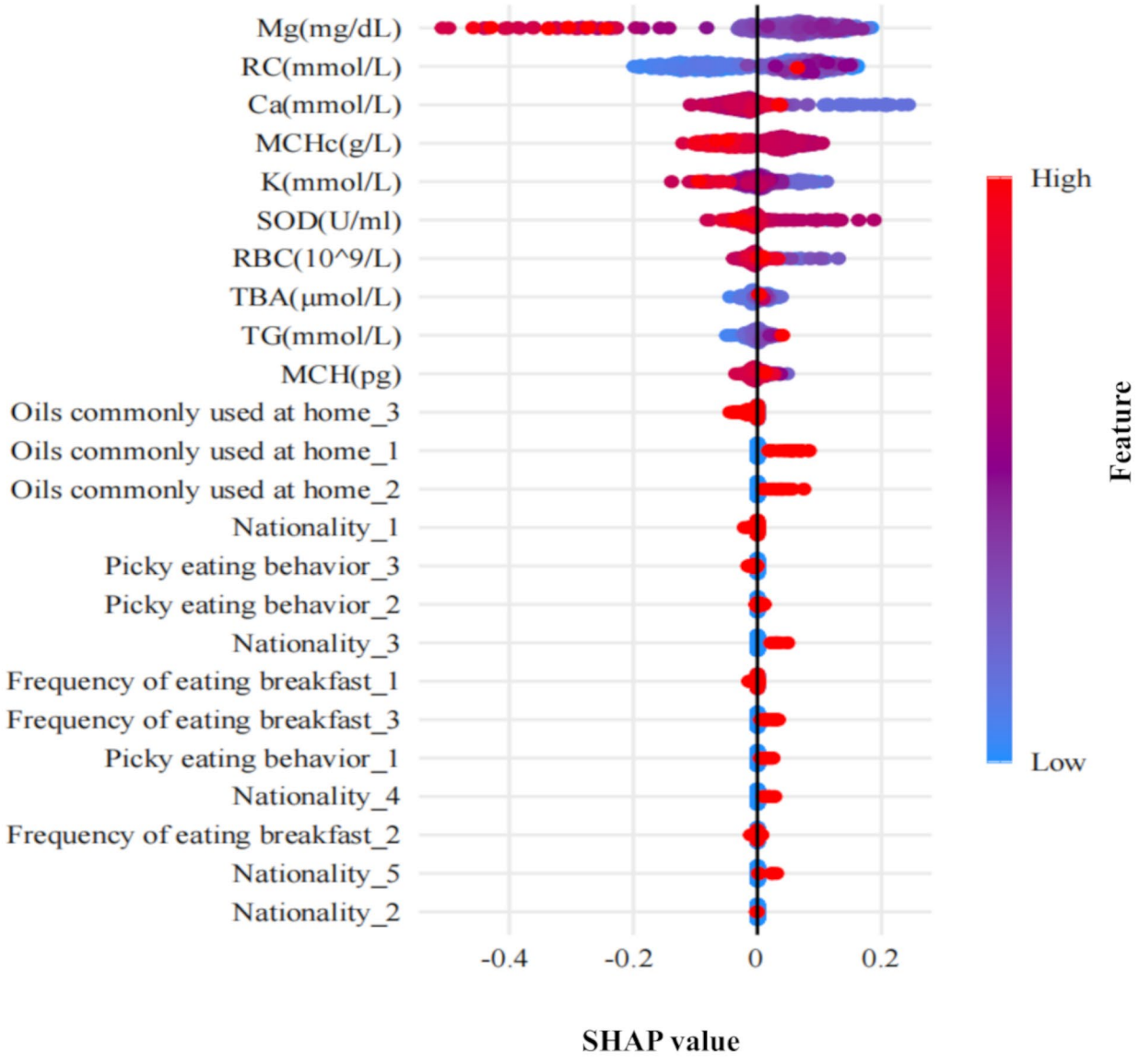


**Fig. 4** SHAP feature importance summary plot. Each feature corresponds to a specific shapley value and is sorted according to importance from large to small

Abbreviations: SHAP, SHapley Additive exPlanations. Mg, magnesium; RC, remnant cholesterol; Ca, calcium; MCHc, mean corpuscular hemoglobin concentration; K, potassium; SOD, superoxide dismutase; RBC, red blood cell count; TBA, total bile acids; TG, triglycerides; MCH, mean corpuscular hemoglobin; Nationality_1, The Han nationality; Nationality_2, The Manchu; Nationality_3, The Hui nationality; Nationality_4, The Uighurs; Nationality_5, Other; Oils commonly used at home_1, salad oil or blending oil; Oils commonly used at home_2, not fixed; Oils commonly used at home_3, vegetable oil; Picky eating behavior_1, yes; Picky eating behavior_2, occasionally; Picky eating behavior_3, no; Frequency of eating breakfast_1, every day; Frequency of eating breakfast_2,sometimes; Frequency of eating breakfast_3, rare

Note: All categorical variables in the RF model have been one-hot encoded

neurotransmitter dysregulation, which disrupts emotional regulation [23]. Moreover, RC may compromise endothelial integrity, increasing vascular permeability and promoting leukocyte infiltration and platelet aggregation. These changes are hypothesized to result in microvascular dysfunction, reducing cerebral perfusion and impairing the delivery of essential nutrients and oxygen to neurons, thereby exacerbating depression's neurobiological underpinnings [24].

Our findings linking RC to PPD are supported by recent studies [25]. One proposed mechanism involves RC's role in activating the hypothalamic-pituitary-adrenal (HPA) axis, a pathway closely associated with depression. Elevated RC levels may enhance arterial wall penetration, where RC particles are more readily

absorbed by macrophages than LDL-C, accelerating foam cell formation. Macrophage foam cells express IL-6 and circulating IL-6 stimulates the HPA axis [26]. Dysregulation of the HPA axis is extensively implicated in depression's pathophysiology [27, 28].

Previous research has suggested a connection between trace element deficiencies and depression [29]. Our findings support this association, showing that individuals with PPD have lower serum levels of Mg, Ca, and K. Mg plays a vital role in the synthesis and release of neurotransmitters, and supplementation has shown potential in alleviating depressive symptoms [30]. Similarly, Ca is integral to nervous system functions such as nerve conduction and cellular signaling [31]. Ca deficiencies may lead to abnormal neuronal excitability and impaired nerve conduction, which could affect mood regulation and increase the risk of depression [32]. K is critical for maintaining ion balance within and between cells, ensuring proper neuromuscular function. Low K levels may disrupt nervous system function, adversely affecting mood and mental health [33].

Our study also revealed a negative correlation between MCHc and depression. Although the precise mechanism underlying this association remains unclear, existing research suggests that low MCHc levels may be linked to inflammation, oxidative stress, and insufficient oxygen delivery to the brain [34]. These factors can impair neurotransmitter function, thereby influencing emotional and psychological well-being [35].

This study has several limitations that should be considered. (1) PPD Identification: PPD was identified based on self-reported EPDS scores. While self-reports may be participant to information bias due to personal feelings and memory recall, the EPDS scale is a reliable and valid tool for PPD screening, as supported by numerous studies [36, 37]. Additionally, the EPDS threshold for diagnosing PPD varies from some guidelines, which could influence the study's results. However, many clinical studies still use an EPDS score of ≥ 10 as the cut-off for identifying PPD [38–40]. It is important to note that investigating the impact of different EPDS cut-off values in other populations will be a focus of our future research. (2) Fasting Data: The analysis was based solely on fasting data, excluding non-fasting samples. While previous research suggests minimal differences in most lipid parameters between fasting and non-fasting states [41], future studies incorporating non-fasting data may provide additional insights. Non-fasting lipid samples have also shown comparable prognostic value to fasting samples for general risk assessment [42]. (3) Model Complexity: The complexity of the machine learning models used in this study may present challenges for reproducibility and real-world application. Simplifying the models or exploring alternative methods could improve their practical utility.

## Conclusion

This study identified the RF model as an efficient and robust tool for analyzing the association between exposures and PPD. The findings suggest that Mg, Ca, MCHc, and K are protective factors, while RC serves as a risk factor for PPD. These results underscore the potential of RC as a biomarker for PPD screening. However, further validation through large cohort studies or clinical trials is essential to confirm these findings and clarify their causal relationships.

**Abbreviations**

| | |
|---|---|
| EPDS | Edinburgh Postnatal Depression Scale |
| PPD | Peripartum depression |
| ENR | Elastic net regression |
| M | Machine learning |
| SHAP | SHapley Additive exPlanations |
| BMI | Body mass index |
| WBC | White blood cell count |
| RBC | Red blood cell count |
| HGB | Hemoglobin |
| PLT | Platelet count |
| HCT | Hematocrit |
| MCV | Mean corpuscular volume |
| MCH | Mean corpuscular hemoglobin |
| MCHc | Mean corpuscular hemoglobin concentration |
| LYC | Lymphocyte count |
| MONO | Number of monocytes |
| NEUT | Neutrophils count |
| Fbg | Fibrinogen |
| FT4 | Free thyroid |
| TSH | Thyroid stimulating hormone |
| K | Potassium |
| Na | Sodium |
| Cl | Chloride |
| Ca | Calcium |
| Mg | Magnesium |
| P | Phosphorus |
| Fe | Iron |
| FPG | Fasting plasma glucose |
| BUN | Blood urea nitrogen |
| CR | Creatinine |
| UA | Uric acid |
| TBIL | Total bilirubin |
| DBIL | Direct bilirubin |
| IBIL | Indirect bilirubin |
| TP | Total protein |
| ALB | Albumin |
| GLO | Globulin |
| ALT | Alanine aminotransferase |
| AST | Aspartate aminotransferase |
| ALP | Alkaline phosphatase |
| GGPT | Glutamyl-transpeptidase |
| LDH | Lactate dehydrogenase |
| TBA | Total bile acids |
| SOD | Superoxide dismutase |
| TG | Triglycerides |
| TC | Total cholesterol |
| LDL-C | Low-density lipoprotein cholesterol |
| HDL-C | High-density lipoprotein cholesterol |
| RC | Remnant cholesterol |
| RF | Random forest |
| AdaBoost | Adaptive boosting |
| SVM | Support vector machine |

| | |
|---|---|
| DT | Decision tree |
| KNN | k-nearest neighbors |
| LD | Linear discriminant |
| AUC | Area under the curve |
| ROC | Receiver operating characteristic |
| IL-6 | Interleukin-6 |
| HPA | Hypothalamic-pituitary-adrenal |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-07656-3.

Supplementary Material 1

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**Author contributions**
HC and FW designed the study. FW, TK, DW secured funding for the study. JS, BG, and CS collected the data. HC, TK, YW, and DM led the drafting of the manuscript. HC, GL, GC, and YN finished the statistical analyses and drew the graph. All authors approved the final manuscript for submission.

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**Data availability**
As this study is only part of the subject matter, the datasets generated and analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**
The study protocol was approved by the Ethics Review Committee of the Second Affiliated Hospital of Xinjiang Medical University [approval number: 20200531-13, KY2023112109]. All participants were informed about the research purpose and significance of this investigation and provided written informed consent. In addition, this study strictly adhered to the Declaration of Helsinki.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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## Publisher's note