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Retrospective Study

Construction and validation of a personalized prediction model for postpartum anxiety in pregnant women with preeclampsia

Le-Jing Lin, Hai-Xian Zhou, Zhi-Yun Ye, Qi Zhang, Shu Chen

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Abstract

BACKGROUND

Preeclampsia is a pregnancy-specific multi-system disease with multi-factor and multi-mechanism characteristics. The cure for preeclampsia is to terminate the pregnancy and deliver the placenta. However, it will reduce the perinatal survival rate, prolong the pregnancy cycle, and increase the incidence of maternal complications. With relaxation of the birth policy, the number of elderly pregnant women has increased significantly, and the prevalence rate of preeclampsia has increased. Inappropriate treatment can seriously affect the normal postpartum life of pregnant women. Studies have shown that postpartum anxiety in women with preeclampsia can affect physical and mental health, as well as infant growth and development.

AIM

To analyze the factors influencing preeclampsia in pregnant women complicated with postpartum anxiety, and to construct a personalized predictive model.

METHODS

We retrospectively studied 528 pregnant women with preeclampsia who delivered in Wenzhou Hospital of Integrated Traditional Chinese and Western Medicine between January 2018 and December 2021. Their basic data were collected, and various physiological and biochemical indicators were obtained by laboratory examination. The self-rating anxiety scale was used to determine whether the women had postpartum anxiety 42 d after delivery. The independent factors influencing postpartum anxiety in early pregnant women with eclampsia were analyzed with multifactor logistic regression and a predictive model was constructed. The Hosmer-Lemeshow test and receiver operating characteristic (ROC) curve

were used to evaluate the calibration and discrimination of the predictive model. Eighty pregnant women with preeclampsia admitted to our hospital from January 2022 to May 2022 were retrospectively selected to verify the prediction model.

RESULTS

We excluded 46 of the 528 pregnant women with preeclampsia because of loss to follow-up and adverse outcomes. A total of 482 cases completed the assessment of postpartum anxiety 42 d after delivery, and 126 (26.14%) had postpartum anxiety. Bad marital relationship, gender discrimination in family members, hematocrit (Hct), estradiol (E2) hormone and interleukin (IL)-6 were independent risk factors for postpartum anxiety in pregnant women with preeclampsia ($P < 0.05$). Prediction model: $\text{Logit}(P) = 0.880 \times \text{marital relationship} + 0.870 \times \text{gender discrimination of family members} + 0.130 \times \text{Hct} - 0.044 \times \text{E2} + 0.286 \times \text{IL-6} - 21.420$. The area under the ROC curve of the model was 0.943 (95% confidence interval: 0.919-0.966). The threshold of the model was -1.507 according to the maximum Youden index (0.757), the corresponding sensitivity was 84.90%, and the specificity was 90.70%. Hosmer-Lemeshow $\chi^2 = 5.900$, $P = 0.658$. The sensitivity, specificity and accuracy of the model were 81.82%, 84.48% and 83.75%, respectively.

CONCLUSION

Poor marital relationship, family gender discrimination, Hct, IL-6 and E2 are the influencing factors of postpartum anxiety in preeclampsia women. The constructed prediction model has high sensitivity and specificity.

Key Words: Preeclampsia; Postpartum anxiety; Risk factors; Predictive model

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Core Tip: Preeclampsia is a progressive multisystem disease during pregnancy, characterized by new hypertension and proteinuria after 20 wk of pregnancy, and the condition develops continuously, which has a serious effect on the health of the mother and child. We analyzed the biochemical indicators of 528 pregnant women with preeclampsia and the independent factors influencing postpartum anxiety, and constructed a predictive model, with high clinical value.

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INTRODUCTION

The incidence of preeclampsia can reach 8% [1], and studies have found that women with preeclampsia are more likely to suffer from postpartum anxiety [2-4], with an incidence of up to 20% [5]. Postpartum anxiety can aggravate maternal comorbidities, resulting in poor treatment compliance. Postpartum anxiety has short- or long-term adverse effects on maternal physical and mental health, as well as infant growth and development, and may lead to adverse events such as maternal drug abuse, suicide, and even infant injury [6,7]. Therefore, if we can predict the risk of postpartum anxiety in women with preeclampsia, targeted management and early intervention could avoid postpartum anxiety or improve postpartum psychological status. Current research focuses on the pregnancy outcome of women with preeclampsia, and few studies involve postpartum anxiety. In this study, we retrospectively studied 528 pregnant women with preeclampsia who delivered at our hospital between January 1, 2018 and December 31, 2021. The risk factors for preeclampsia in pregnant women complicated with postpartum anxiety were analyzed, and a predictive model was constructed to provide clinicians with an effective and practical risk assessment tool.

MATERIALS AND METHODS

General data

A total of 528 pregnant women with preeclampsia who delivered at Wenzhou Hospital of Integrated Traditional Chinese and Western Medicine Jianka between January 2018 and December 2021 were retrospectively selected. Inclusion criteria were: (1) Pre-eclampsia was diagnosed according to the relevant standards of obstetrics and gynecology [8]; (2) Conception occurred naturally, the fetus was normal, and the pregnancy was singleton; (3) No cognitive impairment or history of mental illness, and normal communication; and (4) Age > 18 years and living in the local area. Exclusion criteria were: (1) Prenatal anxiety; (2) Medical history of encephalopathy; (3) Severe heart, liver, kidney and other organ diseases; (4) Concurrent diseases of the immune system, nervous system, severe cardiovascular disease and malignant

tumors; (5) Adverse pregnancy outcomes (including arrhythmia, fetal growth restriction, intrauterine fetal death, neonatal death, severe neonatal asphyxia, neonatal defects and serious postpartum complications); and (6) Patients who had to withdraw from the study due to an emergency.

The predictive model was clinically verified by retrospectively selecting 80 pregnant women with preeclampsia who met the above criteria in Wenzhou Hospital of Integrated Traditional Chinese and Western Medicine between January and May 2022. Sample size calculation: (1) According to references, preeclampsia and the incidence of postpartum anxiety at about 20%, this study is expected to end in the multi-factor regression model analysis of 10 variables, according to the average number of events per predictor variable (EPV) sample size calculation, take $EPV = 10$, sample size = into variables $\times EPV / \text{incidence rate} = 10 \times 10 / 20\% = 500$ cases, according to the inclusion and exclusion criteria and considering adverse outcomes, the sample size was 528; and (2) The sample size of the external validation was generally 1/4 to 1/2 of the modeling set, and the sample size = 1/4 of the modeling set, 120 cases (482/4) should be included. However, due to the influence of the external environment such as the epidemic situation and the actual situation of our hospital, 80 cases of preeclampsia pregnant women were finally included.

Data collection

General information: Age, educational level and occupation of pregnant women; occupation and educational level of spouse; family economic status; emotional status of husband and wife (self-rated as good or bad); whether pregnancy was planned; whether there was experience of raising children; whether there was gender discrimination on the part of oneself or family members (expecting to have male or female baby); whether there was regular maternity examination; and history of adverse pregnancy outcomes. Laboratory indicators included: Routine blood tests [including hematocrit (Hct), hemoglobin, and platelet count]; estrogen [including estradiol (E2)]; liver function (including alanine aminotransferase and aspartate aminotransferase); renal function (including creatinine and urea nitrogen); coagulation indicators (including fibrinogen and prothrombin time); and other biochemical indicators [including triglycerides and interleukin (IL)-6].

Postpartum anxiety criteria

The self-rating anxiety scale (SAS) was used to determine whether the parturients who completed the study had postpartum anxiety at 42 d postpartum. The SAS consisted of 20 items, with each item scoring 1 (none or few), 2 (sometimes yes), 3 (most of the time yes), and 4 (most of the time yes). In accordance with the Chinese standard, SAS score ≥ 50 indicated the presence of postpartum anxiety; a score of 50-59 indicated mild anxiety, 60-69 moderate anxiety, and ≥ 70 severe anxiety.

Statistical analysis

The data obtained were processed by SPSS 27.0. Measurement data and numerical data were expressed as mean \pm SD and percentage, respectively, using t and χ^2 tests, respectively. The independent factors influencing postpartum anxiety in pregnant women with preeclampsia were analyzed using multifactor logistic regression and a predictive model was constructed. The Hosmer-Lemeshow test and receiver operating characteristic (ROC) curve were used to evaluate the calibration and discrimination of the predictive model. $P < 0.05$ indicated a significant difference.

RESULTS

Comparison of baseline data of pregnant women with preeclampsia

We excluded 46 of 528 pregnant women with preeclampsia because of loss to follow-up and adverse outcomes, and 482 women completed the anxiety assessment 42 d after delivery. Among them, 126 women (26.14%) experienced postpartum anxiety. The analysis of baseline data of 482 pregnant women with preeclampsia showed that marital relationship, gender discrimination of family members, Hct, E2 and serum IL-6 levels were factors potentially influencing postpartum anxiety in pregnant women with preeclampsia ($P < 0.05$) (Table 1).

Multifactor logistics regression analysis of pregnant women with preeclampsia complicated with postpartum anxiety

The significant factors above were used as covariates marital relationship (0 = good, 1 = bad), gender discrimination among family members (0 = none, 1 = yes). Concurrent postpartum anxiety was used as the dependent variable (0 = none, 1 = yes), and multifactor logistic regression analysis was performed. Bad marital relationship, gender discrimination among family members, Hct, E2 and IL-6 were independent risk factors for postpartum anxiety in pregnant women with preeclampsia ($P < 0.05$) (Table 2).

Construction and validation of predictive model for pregnant women with preeclampsia complicated with postpartum anxiety

According to the multivariate logistic regression model, a predictive model of postpartum anxiety in pregnant women with preeclampsia was constructed: $\text{Logit}(P) = 0.880 \times \text{conjugal affection} + 0.871 \times \text{gender discrimination in family members} + 0.130 \times \text{Hct} - 0.044 \times \text{E2} + 0.286 \times \text{IL-6} - 21.420$. The ROC curve was drawn to evaluate the discrimination of the predictive model. The area under the ROC curve was 0.943 (95% confidence interval: 0.919-0.966). The threshold of the model was -1.507 according to the most approximate maximum Youden index (0.757), and the corresponding sensitivity and specificity were 0.849 and 0.907, respectively (Figure 1). The goodness-of-fit test was used to evaluate the

Table 1 Comparison of baseline data of pregnant women with preeclampsia, *n* (%)

Variable	Postpartum anxiety (<i>n</i> = 126)	No postpartum anxiety (<i>n</i> = 356)	<i>t/χ²</i>	<i>P</i> value
Age (mean ± SD)	31.80 ± 3.99	32.04 ± 4.09	0.491	0.624
Degree of education			1.853	0.396
Junior high school and below	31 (24.60)	70 (19.66)		
Senior high school (technical secondary school)	61 (48.41)	172 (48.31)		
College (higher vocational) or above	34 (26.98)	114 (32.02)		
Occupation			5.433	0.143
Unemployed	25 (19.84)	50 (14.04)		
Workers and peasants	43 (34.13)	150 (42.13)		
Public official	19 (15.08)	37 (10.39)		
Other	39 (30.95)	119 (33.43)		
Per capita monthly household income			4.491	0.106
< 2500 RMB yuan	22 (17.46)	68 (19.10)		
2500-5000 RMB yuan	65 (51.59)	146 (41.01)		
> 5000 RMB yuan	39 (30.95)	142 (39.89)		
Spousal occupation			3.390	0.335
Unemployed	13 (10.32)	20 (5.62)		
Workers and peasants	59 (46.83)	181 (50.83)		
Public official	21 (16.67)	57 (16.01)		
Other	33 (26.19)	98 (27.53)		
Education level of spouse			3.994	0.136
Junior high school and below	19 (15.08)	40 (11.24)		
Senior high school (technical secondary school)	58 (46.03)	200 (56.18)		
College (higher vocational) or above	49 (38.89)	116 (32.58)		
Marital relationship			37.665	< 0.001
Good	39 (30.95)	223 (62.64)		
Bad	87 (69.05)	133 (37.36)		
Whether it was a planned pregnancy			1.338	0.247
Yes	80 (63.49)	246 (69.10)		
No	46 (36.51)	110 (30.90)		
Have any experience raising children			0.253	0.615
Yes	38 (30.16)	99 (27.81)		
No	88 (69.84)	257 (72.19)		
Whether the pregnant woman herself has gender discrimination			0.471	0.493
Yes	28 (22.22)	90 (25.28)		
No	98 (77.78)	266 (74.72)		
Gender discrimination among family members			24.318	< 0.001
Yes	86 (68.25)	152 (42.70)		
No	40 (31.75)	204 (57.30)		
Whether regular birth inspection			1.846	0.174

Yes	84 (66.67)	260 (73.03)		
No	42 (33.33)	96 (26.97)		
History of adverse pregnancy outcomes			0.256	0.613
Yes	30 (23.81)	77 (21.63)		
No	96 (76.19)	279 (78.37)		
Systolic blood pressure (mean ± SD, mmHg)	149.57 ± 7.3	149.50 ± 8.08	-0.087	0.930
Diastolic blood pressure (mean ± SD, mmHg)	100.37 ± 5.97	99.62 ± 6.70	-1.113	0.266
Hemoglobin (mean ± SD, g/L)	108.47 ± 25.25	112.90 ± 30.02	1.700	0.090
Hct (mean ± SD, %)	63.16 ± 8.49	47.23 ± 6.18	-22.421	< 0.001
Platelets (mean ± SD, × 10 ⁹ /L)	137.72 ± 33.06	141.53 ± 32.63	1.121	0.263
Fibrinogen (mean ± SD, g/L)	4.38 ± 1.03	4.59 ± 1.11	1.749	0.081
Prothrombin time (mean ± SD, s)	10.96 ± 3.04	11.27 ± 3.01	0.991	0.322
Creatinine (mean ± SD, mmol/L)	60.64 ± 18.51	58.91 ± 16.86	-0.963	0.336
Urea nitrogen (mean ± SD, mmol/L)	4.16 ± 1.09	3.99 ± 0.97	-1.597	0.111
Alanine transaminase (mean ± SD, U/L)	27.21 ± 7.12	26.70 ± 7.23	-0.685	0.494
Aspartate aminotransferase (mean ± SD, U/L)	29.85 ± 9.05	28.82 ± 9.31	-1.071	0.285
Triglyceride (mean ± SD, mmol/L)	4.67 ± 1.08	4.18 ± 1.09	-1.657	0.098
Estradiol (mean ± SD, pg/mL)	50.23 ± 15.00	57.97 ± 11.95	5.845	< 0.001
Interleukin-6 (mean ± SD, pg/mL)	56.39 ± 12.22	40.24 ± 10.12	-14.554	< 0.001

Hct: Hematocrit.

Table 2 Multifactor logistic regression analysis of postpartum anxiety in pregnant women with preeclampsia

Factor	β	Wald χ^2	P value	OR (95%CI)
bad marital relationship	0.880	4.594	0.032	2.412 (1.078-5.394)
Gender discrimination among family members	0.871	4.339	0.037	2.390 (1.053-5.425)
Hematocrit	0.130	35.391	< 0.001	1.139 (1.091-1.189)
Eastradiol	-0.044	8.039	0.005	0.957 (0.928-0.986)
Interleukin-6	0.286	64.504	< 0.001	1.331 (1.242-1.428)
Constant	-21.420	72.926	< 0.001	

OR: Odds ratio; CI: Confidence interval.

calibration of the predictive model, which showed Hosmer-Lemeshow $\chi^2 = 5.900$, and $P = 0.658$ (Figure 2).

Clinical verification of predictive model for pregnant women with preeclampsia complicated with postpartum anxiety

We retrospectively selected 80 pregnant women with preeclampsia in our hospital between January and May 2022 to clinically verify the predictive model. The sensitivity was 81.82%, specificity 84.48%, and accuracy 83.75% (Table 3).

DISCUSSION

The results of this study showed that serum transaminase levels, blood pressure, platelet levels, and coagulation indicators in pregnant women with preeclampsia with postpartum anxiety did not differ significantly from those in women without postpartum, which was consistent with previous studies[4]. We found that bad marital relationship, gender discrimination among family members, Hct, IL-6 and E2 were all independent factors influencing postpartum anxiety in pregnant women with preeclampsia. The care and support of husbands play a key role in improving the psychological status of pregnant women[9,10]. Therefore, strengthening the health education of the spouses of pregnant and lying-in

Table 3 Clinical validation of the predictive model

Postpartum anxiety	Models predict postpartum anxiety		Total
	Yes	No	
Yes	18	4	22
No	9	49	58
Total	27	53	80

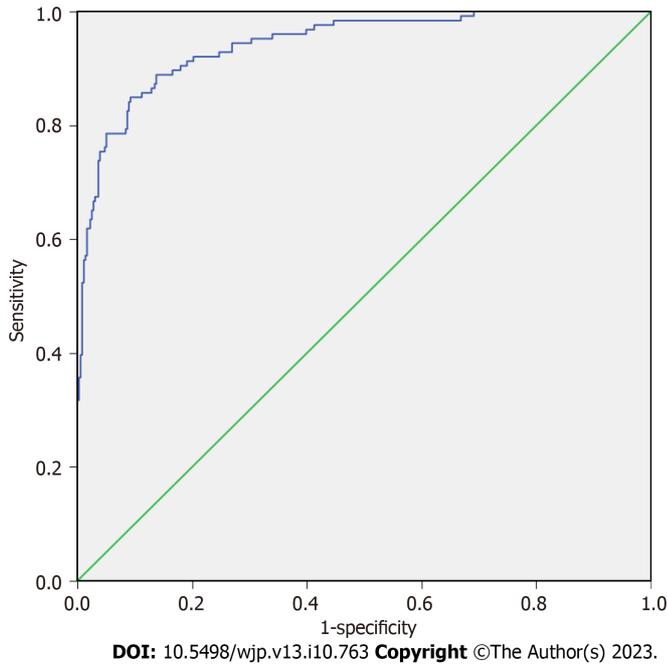


Figure 1 Receiver operating characteristic curve analysis of the predictive model for postpartum anxiety in preeclampsia.

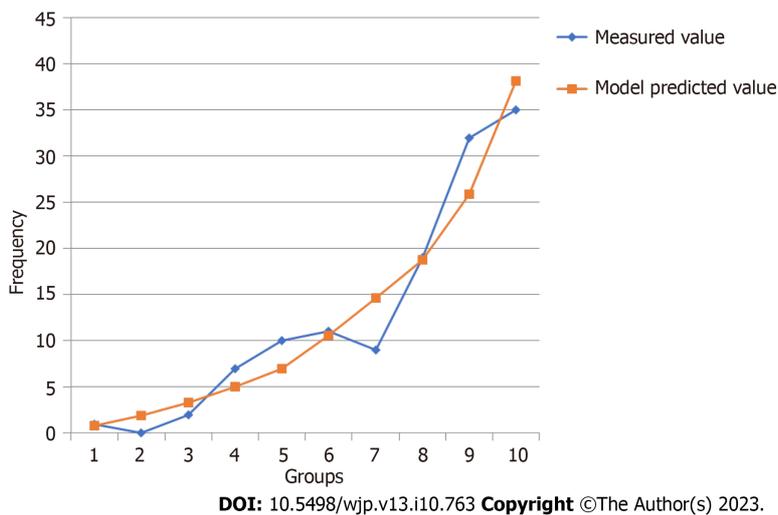


Figure 2 Goodness of fit test of a predictive model for postpartum anxiety in women with preeclampsia.

women and guiding them to attach importance to psychological care and support are important to reduce the risk of postpartum anxiety. The feudal thought of “son preference” is deeply rooted in China. Family members and even the pregnant women themselves care about the gender of the newborn[11]. When pregnant women with preeclampsia excessively consider the views of family members on the gender of their newborn, it can easily exert psychological pressure, leading to postpartum anxiety. Therefore, for pregnant women with preeclampsia, health education should be strengthened during prenatal examination, the idea of gender equality should be advocated, and possible gender discrim-

ination should be corrected in time to reduce the risk of postpartum anxiety of pregnant women.

There is a biological basis for postpartum anxiety in pregnant women with preeclampsia. Postpartum estrogen deficiency is an important reason for the significantly increased incidence of mental illness at 30 d postpartum[12], and E2 level is negatively correlated with the severity of female anxiety[13], which is similar to our study. The possible causes are that E2 can play an antianxiety role by improving the binding rate of serotonin reuptake transporter and the reuptake capacity of cells for serotonin. However, postpartum estrogen secretion from the uterus is stopped, the recovery of ovarian estrogen secretion function is slow, and the level of E2 is low, thus the antianxiety effect is weakened. If the level of E2 is low in pregnant women with preeclampsia, it may further decrease the level of postpartum estrogen, so anxiety is more likely to occur[14,15]. Ramiro-Cortijo *et al*[16] confirmed that the Hct in patients with preeclampsia was significantly higher than that of healthy people, and increased with aggravation of preeclampsia. Noori *et al*[17] showed that the prenatal Hct accurately predicted severity of depression and anxiety 6 wk after delivery. The results of this study showed that Hct was an independent factor influencing postpartum anxiety in pregnant women with preeclampsia, which was consistent with the above conclusions. Pregnant women with preeclampsia usually have overactivation of inflammation and immunity, and a large number of inflammatory factors are released into the blood, resulting in increased serum IL-6 level, which is positively correlated with the severity of preeclampsia[18]. Immune activation caused by inflammatory factors can lead to dysfunction of the neuroendocrine and immune systems[19,20]. Therefore, elevated serum IL-6 levels may cause postpartum anxiety in women with preeclampsia. Therefore, clinical attention should be paid to patients with abnormal indicators, and follow-up observation should be strengthened, or appropriate treatment should be given to adjust the level of related indicators.

In this study, a risk predictive model for pregnant women with preeclampsia complicated with postpartum anxiety was constructed based on the above independent influencing factors (bad marital relationship, gender discrimination of family members, Hct, IL-6 and E2). The ROC curve analysis results showed that the predictive model had good discrimination, and the goodness-of-fit test showed that the model had good calibration. The prospective clinical validation showed that the model had high sensitivity (81.82%), specificity (84.48%) and accuracy (83.75%), indicating that the predictive model had clinical practicability. The model was simple to use and had high accuracy. However, the number of cases in the time period selected for clinical verification is small, and the results may have certain errors. In the future will be incorporated into various validation.

CONCLUSION

Bad marital relationship, gender discrimination of family members, Hct, IL-6 and E2 are independent factors influencing postpartum anxiety in pregnant women with preeclampsia. The predictive model established based on these factors has high sensitivity, specificity and accuracy, strong operability, and high clinical value. However, this study was a single-center study, the clinical validation of the model was only conducted in our hospital, and the sample size was insufficient, so the results were inevitably biased. In the future, multi-center research and multi-center clinical verification will be carried out, and multi-factor, multi-sample and multi-time span will be adopted to explore, so as to enhance the reliability of the research results.

ARTICLE HIGHLIGHTS

Research background

Relaxation of the maternity policy has resulted in an increase in the number of elderly pregnant and lying-in women, and the prevalence of preeclampsia. Preeclampsia can lead to organ damage and system dysfunction.

Research motivation

To explore the factors influencing postpartum anxiety in pregnant women with preeclampsia and construct a predictive model, to provide an effective and practical risk assessment tool for clinical practice.

Research objectives

The object of this study is to explore the factors influencing postpartum anxiety in pregnant women with preeclampsia and construct a personalized model for predicting postpartum anxiety, to provide a reference for clinical trials.

Research methods

We retrospectively analyzed 528 pregnant women with preeclampsia who delivered in our hospital between 2018 and 2021. Various physiological and biochemical indicators were obtained through laboratory tests. Multivariate logistic regression, receiver operating characteristic curve, Hosmer-Lemeshow and other methods were used to analyze the factors influencing postpartum anxiety in pregnant women with preeclampsia and to construct a predictive model.

Research results

A total of 126 pregnant women with preeclampsia experienced postpartum anxiety. Bad marital relationship, gender discrimination among family members, hematocrit, estradiol hormone and interleukin-6 were independent risk factors

for postpartum anxiety in pregnant women with preeclampsia, and the predictive model constructed based on these factors had high accuracy.

Research conclusions

We analyzed the factors influencing postpartum anxiety in pregnant women with preeclampsia and constructed a predictive model with high sensitivity and accuracy, which provided a reference value for clinical practice.

Research perspectives

Firstly, multi-sample, multi-factor, multi-center and multi-time span clinical studies will be carried out in the future to enhance the reliability of the research results. In addition, different models were constructed for clinical application in pregnant women with preeclampsia and postpartum anxiety.

FOOTNOTES

Author contributions: Lin LJ and Chen S designed the study and wrote the paper; Zhou HX participated in the analysis; Ye ZY and Zhang Q provided clinical advice.

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