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Analysis of maternal and fetal outcomes and establishment of prediction model of vaginal delivery in pregnant women with pre-eclampsia complicated with fetal growth restriction

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Abstract. – OBJECTIVE: This study aimed to analyze the maternal and fetal outcomes of pregnant women with pre-eclampsia (PE), complicated with fetal growth restriction (FGR), and establish a prediction model of vaginal delivery to guide the selection of the delivery mode.

PATIENTS AND METHODS: The study included 208 pregnant women with PE complicated with FGR. Of them, 49 patients were in the vaginal delivery group, and 159 patients were in the cesarean section group. The relevant maternal and fetal outcomes were analyzed. Patients were randomly divided into the training sample group and the test group with a ratio of 2:1. The three-layer neural network was used to select 24 maternal and infant outcome factors as the input nodes of the neural network to build a vaginal delivery prediction model.

RESULTS: Results showed that the gestational age, the highest systolic and diastolic blood pressure, body weight, body length, and placental weight of the newborns in the vaginal delivery group were significantly higher than those in the cesarean section group. Incidence of preterm birth, amniotic fluid grade III, oligohydramnios, and severe small-for-gestational-age (sSGA) neonates were significantly lower in the vaginal delivery group compared to the cesarean section group ($p < 0.05$). A three-layer neural network delivery prediction model was constructed, and the accuracy rate of fitting with test samples was 91.80%.

CONCLUSIONS: There is no significant difference in the incidence of maternal and fetal complications in PE complicated with FGR in different delivery methods. The three-layer neural network prediction model has good prediction ability for vaginal delivery of PE complicated with FGR and may be applied in clinical practice.

Key Words:
Pre-eclampsia, Fetal growth restriction, Vaginal delivery, Prediction model.

Introduction

Pre-eclampsia (PE) is an idiopathic disease of pregnancy, with a global incidence rate of 3%-5%. The pathophysiological changes of PE include vascular endothelial cell damage and small artery spasm. Studies showed that the expression levels of intercellular adhesion molecule-1 (ICAM1), a member of the immunoglobulin superfamily, are increased in the placental tissues of patients with pre-eclampsia[1]. Additionally, PE-induced alterations in the expression of inflammatory/signaling proteins in the decidua during singleton pregnancies were shown to play a critical role in the pathogenesis of PE[2]. All these pathophysiological changes may cause damage to multiple maternal systems and organs, often leading to accompanying fetal growth restriction (FGR). The current consensus[3,4] is that timely termination of pregnancy is the only effective treatment for PE. The American College of Obstetricians and Gynecologists (ACOG) recently discontinued the use of FGR as an indicator of severe PE presentation because of the same treatment[5]. However, China's 2020 guidelines for diagnosis and treatment of pregnancy-induced hypertension still regard FGR as one of the diagnostic indicators of severe PE[6].

At present, based on the guidelines of the American Association of Obstetricians and Gy-

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necologists Foundation (AAOGF), vaginal delivery is strongly recommended for all PE patients without other serious maternal and fetal complications[4,7,8]. However, in practice, the rate of cesarean delivery in pregnant women with PE surpasses that of vaginal delivery[9,10]. The main reasons for this discrepancy are that vaginal delivery may potentially increase maternal and fetal complications and that there is no reliable evaluation method for the feasibility of vaginal delivery in PE.

Ideally, the choice of delivery mode for pregnant women with PE complicated with FGR should comprehensively consider factors such as the health status of pregnant women, gestational weeks, fetal intrauterine conditions, cervical ripeness, etc. Therefore, in this study, a three-layer neural network model was constructed to guide the selection of delivery mode by comprehensively using the maternal and fetal outcome indicators of pregnant women's vaginal delivery with PE complicated with FGR. Our results can provide a theoretical basis and technical support for developing more comprehensive scientific and clinical guidelines for vaginal delivery in pregnant women with PE complicated with FGR.

Patients and Methods

General Clinical Data

From January 1, 2010, to December 31, 2019, a total of 154438 pregnant women were hospitalized and delivered in Fujian Maternal and Child Health Hospital. Of them, 150,403 were women with singleton pregnancies. Among women with singleton pregnancies, 3911 were diagnosed with PE, of which 208 singleton pregnant women had PE complicated with FGR and were selected for this retrospective cohort study.

The ethics committee of the hospital approved this study on September 24th, 2021 (number 2021KLR09006). The clinical data of women were collected and included maternal age at delivery, height, gravidity, number of deliveries gestational weeks, body mass index (BMI), BMI before delivery, liver and kidney function, blood routine, coagulation function, blood pressure, and neonatal weight, etc.

Inclusion and Exclusion Criteria

Inclusion criteria

Patients who met the following diagnostic criteria of PE and FGR were included in the study.

Diagnostic criteria for PE were patients with systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg after 20 weeks of gestation, accompanied by proteinuria ≥ 0.3 g/24 h, or random urine protein positive, or without proteinuria, but with any of the following: (1) progressive thrombocytopenia; (2) liver function damage; (3) renal function impairment; (4) pulmonary edema and heart failure; (5) new central nervous system abnormalities or visual impairment[4,11].

Diagnostic criteria for FGR were the fetal birth weight of less than 2,500 g or less than two standard deviations of the average weight of the same gestational age or less than the 10th percentile of the normal weight of the same gestational age[12,13].

Exclusion criteria

Patients with the following serious complications before delivery were excluded: uncontrolled severe hypertension, hypertensive encephalopathy, cerebrovascular accident, reversible posterior encephalopathy syndrome, eclampsia, cardiac failure, pulmonary edema, complete and partial HELLP syndrome, disseminated intravascular coagulation (DIC), placental abruption, loss or reversal of umbilical artery end-diastolic blood flow, and fetal death in utero. In addition, women with pregnancy complications other than PE and FGR, and women with incomplete medical records were excluded.

Statistical Analysis

The description of the measurement data conforming to the normal distribution was expressed by ($\bar{x} \pm s$), and the non-normal distribution data were expressed by the median and interquartile range. An independent sample *t*-test was used for the normal distribution of measurement data and consistent with homogeneity of variance, a *t*-test was used for data with uneven variance, and a nonparametric test (Mann-Whitney U test) was used for data with non-normal distribution. The counting data were expressed in percentages, and Chi-square (χ^2) test was used for comparison between groups. All analyses were performed with SPSS 26.0 software (IBM Corp., Armonk, NY, USA), and the difference was considered statistically significant when $p < 0.05$.

Using a three-layer neural network, 24 maternal and infant outcome indicators were taken as input nodes of a neural network, the delivery mode was taken as an output node, and the neural network delivery mode prediction model was established. After the training data, the weight (W1) of the input node was obtained, and the association influencing factors were determined according to the size of the weight.

Results

Comparison of General Clinical Data of Study Subjects

As shown in Table I, there was no significant difference in the maternal age, number of deliveries, pre-pregnancy BMI, pre-delivery BMI, and vaginal delivery history of pregnant women with PE and FGR in the vaginal delivery group compared to the cesarean delivery group ($p > 0.05$). However, gravidity and the history of cesarean section were significantly lower in the vaginal delivery group ($p < 0.05$).

Comparison of PE-Related Variables Between Two Groups

As shown in Table II, the highest systolic and diastolic blood pressure in the vaginal delivery group was lower ($p < 0.05$) compared to the cesarean section group (Table II). However, there was no statistical difference in the levels of alanine transaminase (ALT), platelet count (PLT), lactate dehydrogenase (LDH), and activated partial thromboplastin time (APTT) between the two groups ($p > 0.05$).

Comparison of Related Complications Between Two Groups

As summarized in Table III, compared with the cesarean section group, the gestational age of women in the vaginal delivery group was significantly increased, and the incidence of preterm birth, amniotic fluid grade III, and oligohydramnios were significantly decreased ($p < 0.05$). However, there was no significant difference in the incidence of postpartum hemorrhage, placental abruption, and HELLP syndrome between the two groups ($p > 0.05$), as shown in Table III.

Comparison of Perinatal Outcomes Between Two Groups

As shown in Table IV, there was no significant difference in neonatal asphyxia rate and Apgar score between the two groups ($p > 0.05$). However, compared with the cesarean section group, the incidence of severe small-for-gestational-age (sSGA) infants in the vaginal delivery group was significantly lower (Table IV), while the body weight, length, and placental weight of the newborns were significantly ($p < 0.05$) higher (Table V).

Table I. Comparison of general data of pregnant women in two groups ($\bar{\chi}$±s/n, %).

Group	N	Age (year)	Gravidity	Number of deliveries	Delivery history		Pre pregnancy BMI (Kg/m²)	Pre delivery BMI (Kg/m²)
					Vaginal delivery	Cesarean section		
Vaginal delivery	49	28.00 ± 4.66	1.78 ± 0.94	1.43 ± 0.65	18 (36.7%)	0 (0%)	21.70 ± 4.24	26.46 ± 4.01
Cesarean section	159	29.87 ± 5.31	2.34 ± 1.45	1.58 ± 0.70	40 (25.16%)	41 (25.79%)	20.89 ± 3.96	25.09 ± 4.11
t/t'/χ^2	-2.127	-3.185	-1.34	3.274	14.907	1.009	0.921	
p	0.053	0.002	0.182	0.07	<0.001	0.657	0.506	

BMI: body mass index.

Table II. Comparison of clinical characteristics of pregnant women in two groups ($\bar{\chi}$±s/n, %).

Group	Highest systolic blood pressure (mmHg)	Highest diastolic blood pressure (mmHg)	ALT (U/L)	PLT (10^9/L)	LDH (U/L)	APTT (Sec)
Vaginal delivery	144.88 ± 15.54	89.29 ± 17.40	30.63 ± 62.71	214.73 ± 64.32	325.03 ± 172.50	31.10 ± 5.81
Cesarean section	152.71 ± 21.31	95.36 ± 17.81	24.03 ± 22.02	209.18 ± 69.69	363.23 ± 239.64	33.23 ± 19.64
t/t'/χ^2	-2.384	-2.08	1.126	0.497	-1.035	-0.748
p	0.018	0.039	0.262	0.62	0.302	0.455

Table IV. Comparison of perinatal complications between the two groups ($\bar{\chi}$±s/n, %).

Group	N	Neonatal asphyxia		sSGA infants	Apgar score		
		Mild	Severe		1 min	5 min	10 min
Vaginal delivery	49	1 (2.04%)	0 (0%)	4 (%)	9.80 ± 0.61	9.98 ± 0.14	10.00 ± 0.00
Cesarean section	159	4 (2.52%)	2 (1.26%)	81 (%)	9.51 ± 1.297	9.91 ± 0.56	9.94 ± 0.512
t/χ^2	0.613	28.367	1.494	0.913	0.859		
p		0.736		<0.001	0.137	0.362	0.391

sSGA infants: severe small for gestational age

Table III. Comparison of complications between two groups of pregnant women ($\bar{\chi}$±s/n, %).

Group	Gestational weeks of delivery (week)	Preterm	Amniotic fluid grade III	Oligohy-dramnios	Postpartum hemorrhage	Placental abruption	HELLP syndrome
Vaginal delivery	37.81 ± 1.64	12 (24.49%)	3 (6.12%)	1 (2.04%)	1 (2.04%)	2 (4.08%)	0 (0%)
Cesarean section	35.14 ± 3.06	108 (67.9%)	13 (8.18%)	23 (14.47%)	2 (1.26%)	6 (3.77%)	4 (2.52%)
χ^2	5.801	25.73	13.256	5.665	0.162	0.027	1.191
p	<0.001	<0.001	0.01	0.017	0.688	0.868	0.275

HELLP syndrome: hemolysis, elevated liver enzymes, and low platelet count syndrome.

Table V. Comparison of body mass and body length between the two groups ($\bar{\chi} \pm s$).

Group	N	Birth weight of newborn (g)	Length of newborn (cm)	Placental weight (g)
Vaginal delivery	49	2,197.73 ± 340.56	45.41 ± 2.45	469.55 ± 164.99
Cesarean section	159	1,709.36 ± 482.84	41.58 ± 4.60	410.30 ± 110.11
t		7.888	7.579	2.900
p		<0.001	<0.001	0.004

Establishment of Prediction Model of Vaginal Delivery of PE Complicated with FGR

The construction of a three-layer neural network labor prediction model includes input nodes, output nodes, and hidden nodes. In this study, 24 maternal and fetal outcome variables were used as input nodes of the neural network, and vaginal delivery and cesarean section were used as output nodes. Hidden nodes were calculated according to the formula ($m = \sqrt{n + l} + \alpha$, where m: number of hidden layer nodes; n: number of input layer nodes; l: output layer nodes; α: a constant between 1 and 10). According to the test, the optimal number of hidden layer nodes in this study was 10. Figure 1 shows the final neural network structure.

W1 represented a hidden layer weight matrix of 24 rows and 10 columns, and B1 was its offset vector. For W1 obtained through training, the sum of the absolute values of the weights of each row was regarded as the weights of the factors corresponding to the row. Table VI was obtained by arranging the weights in descending order; W2 was an output layer weight matrix of 10 rows and 2 columns, and B2 was its offset vector. The input was a vector of 24 rows and 1 column. After matrix multiplication with W1 and W2, an output of 1 row and 2 columns was obtained. The 2 columns represent two output nodes, respectively. The node corresponding to the larger value of the two was taken as the final prediction result of the input.

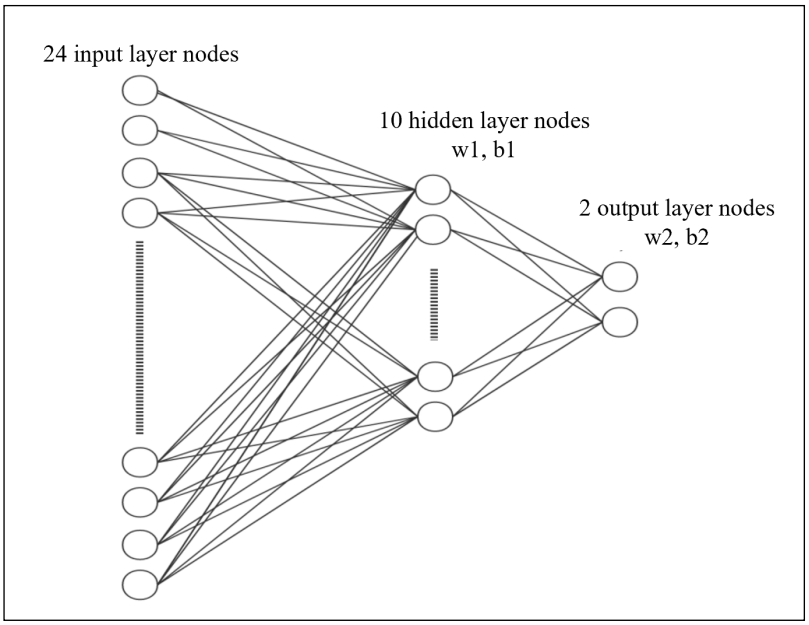

Figure 1. Construction of three-layer neural network model: W1 is a hidden layer weight matrix of 24 rows and 10 columns, B1 is a hidden layer offset vector of 10 rows and 1 column, W2 is an output layer weight matrix of 10 rows and 2 columns, and B2 is an output layer offset vector of 2 rows and 1 column.

The neural network prediction model constructed according to the training data was then fitted with the test data, and the accuracy rate of the neural network was 91.80%. Among the 24 factors studied, the five factors that have the greatest impact on the prediction of delivery mode were scarred uterus, birth weight, gestational age, oligohydramnios, and age.

Discussion

Pre-eclampsia (PE) is a common idiopathic disease in obstetrics[15]. Studies[16,17] have found that pregnant women with PE have a higher cesarean section rate compared to healthy pregnant women. A study by Chibber[16] showed that while the incidence of neonatal Apgar score ≤ 3 in 5 min

Table VI. Weights of relevant maternal and infant outcome variables in the prediction model of delivery mode constructed by three-layer neural network.

Maternal and fetal pregnancy outcomes	Weight	Maternal and fetal pregnancy outcomes	Weight
Scar uterus	6.365872	ALT	2.014578
Newborn weight	4.215487	AST	1.978455
Gestational age	4.022587	LDH	1.788887
Oligohydramnios	3.79854	Pre delivery BMI	1.678977
Age	3.578965	Uric acid	1.665487
High systolic blood pressure	3.005887	Adverse reproductive history	1.521278
High diastolic pressure	2.958411	Gravida times	1.456487
Low diastolic pressure	2.455478	Parity	1.324578
APTT	2.354789	Fetal sex	1.204547
Low systolic pressure	2.245678	Infantile deformity	1.212457
Pre pregnancy BMI	2.234788	Neonatal diagnosis	1.145787
PLT	2.024788	Height	0.256789

ALT: alanine transaminase, AST: aspartate transaminase, LDH: lactate dehydrogenase, PLT: platelet count, APTT: activated partial thromboplastin time, BMI: body mass index.

in the severe PE vaginal delivery group is higher than that in the cesarean section group, there is no significant difference in respiratory distress syndrome, intraventricular hemorrhage, sepsis, convulsion, and neonatal death between the two groups. Vaginal delivery is considered relatively safe for severe PE patients. FGR mainly refers to the fact that the fetal growth does not reach its genetic potential due to the influence of maternal, fetal, placental, and other factors. Compared with normal-weight infants, SGA infants are more prone to mutation deceleration. Studies[18-20] show that although the probability of cesarean section due to fetal distress was increased, the outcome difference between the two groups of newborns was not significant. At present, many medical guidelines[12,21] point out that FGR is not an indication for cesarean section. However, PE complicated with FGR may further increase maternal and neonatal risk. Therefore, choosing the appropriate delivery mode can effectively improve the outcome for both mother and offspring. Current guidelines[4,5] classify PE complicated with FGR as "severe PE", but state that vaginal delivery is feasible when there are no serious complications and other indications of obstetric cesarean section.

In this study, the cesarean section rate of pregnant women with PE+FGR, without additional serious complications before the delivery, reached 76.4%, which is consistent with the cesarean section rate of severe PE reported by Zhang et al[14] and Sukmawati et al[10]. These high rates of cesarean sections may be due to the fear of adverse effects of vaginal delivery on mother and child. Our study found no statistically significant differences in the maternal and fetal outcomes, such as the age, number of deliveries, pre-pregnancy BMI, pre-delivery BMI, ALT, PLT, LDH, APTT, Apgar score at 1 min, 5 min, and 10 min after birth, in PE+FGR pregnant women who underwent vaginal or cesarean delivery. We showed that the incidences of postpartum hemorrhage, placental abruption, HELLP syndrome, and neonatal asphyxia in the vaginal delivery group were significantly lower than those of the cesarean section group. We may speculate that women with PE complicated with FGR may receive more attention and more monitoring during the vaginal delivery, which allows for better prevention and treat the occurrence of mother- and child-related complications[22,23].

Further analysis showed that the incidence of amniotic fluid grade III, the highest systolic blood pressure, and the highest diastolic blood pressure in the vaginal delivery group was lower than those in the cesarean section group, while the incidence of sSGA infants in the vaginal delivery group was lower than that in the cesarean section group. Gestational age, birth weight, length, and placental weight of the newborn were all higher in the vaginal delivery group. These differences may be due to a more comprehensive evaluation of the maternal and fetal condition in women with PE complicated with FGR before allowing a vaginal delivery mode. Our study showed that the overall incidence of maternal and fetal complications of vaginal delivery was low. Therefore, vaginal delivery is still a safe delivery method for PE complicated with FGR after evaluation.

There is still no consensus on whether the maternal and fetal outcome factors included in the evaluation can be used to predict the delivery mode of PE complicated with FGR. In our study, 24 factors, such as the general condition of pregnant women and the fetus, and the indicators related to the severity of PE were used as the input nodes of the neural network to establish a three-layer neural network model for predicting the mode of delivery. Our results showed that the most influential factor in predicting the mode of delivery was the scarred uterus. The scarred uterus is a relative contraindication to the induction of labor, and in pregnant women with FGR will undoubtedly increase the risk of maternal and neonatal complications. Therefore, in pregnant women with PE and FGR combined with the scarred uterus, the preferred mode of delivery should be inclined toward the cesarean section. Neonatal birth weight and gestational age are two other important factors in predicting the mode of delivery.

In this study, the average gestational age of pregnant women in the vaginal delivery group was about 37 weeks, and the premature birth rate was only 24.49%. The average gestational age of pregnant women in cesarean delivery was about 35 weeks, and the premature birth rate was 70%. Studies[24-26] have shown that the incidence of severe pulmonary hyaline membrane disease and sepsis in neonates with early-onset severe PE is significantly lower after vaginal delivery than after the cesarean section. Vaginal delivery does not cause adverse effects on the fetus. Therefore, it is suggested that women with severe PE with gestational age < 34 weeks may consider vaginal delivery. Insufficient placental blood perfusion is the most common cause of FGR. The process of induced labor and vaginal delivery aggravates the lack of fetal blood supply, which can increase the

risk of maternal and fetal complications. Therefore, fetal weight and gestational age are important factors for selecting the delivery mode.

The prediction accuracy of the three-layer neural network model in our study was 91.80%. This model calculates the success rate of vaginal delivery according to the conditions of pregnant women before the delivery. It provides a certain basis for obstetricians to guide pregnant women with PE complicated with FGR to choose the appropriate delivery mode and offers pregnant women and their families relatively clear information for decision-making. Pregnant women with high predictive success rates can be encouraged to attempt a vaginal delivery. In contrast, pregnant women with low predictive success rates can be guided to choose a cesarean section to reduce the risk of more serious complications such as emergency cesarean section and severe asphyxia of the newborn.

Limitations

Our article has some limitations. The major limitation of the present study is that it was a single-center retrospective study with a small sample size. Further multi-center prospective studies with a large number of participants are needed to confirm our data.

Conclusions

In conclusion, our study showed that in pregnant women with PE+FGR who do not have additional serious complications, vaginal delivery after comprehensive evaluation is not associated with the increased risk of adverse maternal and neonatal outcomes. We used a three-layer neural network model to establish the prediction model of delivery mode for PE+FGR pregnancies and showed that it has a relatively accurate prediction ability for the delivery mode. This model may assist obstetricians and pregnant women in deciding whether to attempt vaginal delivery. Further multicenter studies with larger sample sizes are needed to confirm our results.

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Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' Contributions

LL and YG conceived and designed the study. XX, LH and QY collected the data and performed the analysis. LL and YG were involved in the writing of the manuscript. JY edited the manuscript. All authors have read and approved the final manuscript.

Ethics Approval

The ethics committee of the Fujian Maternal and Child Health Hospital approved this study on September 24th, 2021, number 2021KLR09006.

Informed consent

Not applicable.

Conflict of Interest

The authors declare that they have no competing interests.

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