A Bayesian Stepwise Discriminant Model for Predicting Risk Factors of Preterm Premature Rupture of Membranes: A Case-control Study

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Abstract

Background: Preterm premature rupture of membrane (PPROM) can lead to serious consequences such as intrauterine infection, prolapse of the umbilical cord, and neonatal respiratory distress syndrome. Genital infection is a very important risk which closely related with PPROM. The preliminary study only made qualitative research on genital infection, but there was no deep and clear judgment about the effects of pathogenic bacteria. This study was to analyze the association of infections with PPROM in pregnant women in Shaanxi, China, and to establish Bayesian stepwise discriminant analysis to predict the incidence of PPROM.

Methods: In training group, the 112 pregnant women with PPROM were enrolled in the case subgroup, and 108 normal pregnant women in the control subgroup using an unmatched case-control method. The sociodemographic characteristics of these participants were collected by face-to-face interviews. Vaginal excretions from each participant were sampled at 28–36[+6] weeks of pregnancy using a sterile swab. DNA corresponding to *Chlamydia trachomatis* (CT), *Ureaplasma urealyticum* (UU), *Candida albicans*, group B streptococci (GBS), herpes simplex virus-1 (HSV-1), and HSV-2 were detected in each participant by real-time polymerase chain reaction. A model of Bayesian discriminant analysis was established and then verified by a multicenter validation group that included 500 participants in the case subgroup and 500 participants in the control subgroup from five different hospitals in the Shaanxi province, respectively.

Results: The sociological characteristics were not significantly different between the case and control subgroups in both training and validation groups (all $P > 0.05$). In training group, the infection rates of UU (11.6% vs. 3.7%), CT (17.0% vs. 5.6%), and GBS (22.3% vs. 6.5%) showed statistically different between the case and control subgroups (all $P < 0.05$), log-transformed quantification of UU, CT, GBS, and HSV-2 showed statistically different between the case and control subgroups ($P < 0.05$). All etiological agents were introduced into the Bayesian stepwise discriminant model showed that UU, CT, and GBS infections were the main contributors to PPROM, with coefficients of 0.441, 3.347, and 4.126, respectively. The accuracy rates of the Bayesian stepwise discriminant analysis between the case and control subgroup were 84.1% and 86.8% in the training and validation groups, respectively.

Conclusions: This study established a Bayesian stepwise discriminant model to predict the incidence of PPROM. The UU, CT, and GBS infections were discriminant factors for PPROM according to a Bayesian stepwise discriminant analysis. This model could provide a new method for the early predicting of PPROM in pregnant women.

Key words: Bayesian Stepwise Discriminant Analysis; Etiological Factors; Infection; Preterm Premature Rupture of Membranes

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INTRODUCTION

Preterm premature rupture of membrane (PPROM) is a common perinatal complication in pregnant women.

It is responsible for one-third of all preterm births. The worldwide prevalence of PPROM ranges from 2% to 10%. PPROM might occur among women of the reproductive age group, especially during the period of pregnancy before 37 weeks of gestation. PPROM can cause maternal and fetal infection in pregnant women and their unborn children, a lower Apgar score, pulmonary hypoplasia, preterm delivery, and a low birth weight. However, the etiology of PPROM is unclear. PPROM may be caused by cervical incompetence, genital infections, and uterine abnormality. Some studies have shown that a history of PPROM, race, smoking status, poor nutrition, and genital infection are risk factors for PPROM. This study developed a model to explore genital infections that might activate inflammatory cells and then induce PPROM. The etiologies of genital infection include *Chlamydia trachomatis* (CT), *Ureaplasma urealyticum* (UU), *Candida albicans*, syphilis, *Neisseria gonorrhoea* (NG), group B streptococci (GBS), herpes simplex virus (HSV), and bacterial vaginosis (BV).[1,2]

Genital infections might cause a release of cytokines and other inflammatory mediators that may weaken the membrane and cause PPROM. Studies by Chow and Blas showed that CT infection was associated with the occurrence of PPROM.[3,4] Pregnant women with BV more readily developed PPROM than women without BV.[4-6] Candidiasis infection in pregnant women with PPROM is controversial, and a recent study showed that the treatments for candidiasis might reduce the incidence of PPROM.[7] Pregnant women who were infected with NG had a six-time higher risk of developing PPROM than women without NG infection. GBS might cause the activation of inflammatory cells in fetal membranes, which could lead to PPROM.[5,8]

Although some studies have reported that PPROM was related to genital infections, the proportions of women with confirmed genital infections with or without PPROM in China are unknown.[3-5,7-9] Studies of the relationship between genital infection and PPROM are still rare. This study aimed to determine the association between etiological infection and PPROM. Discriminant analysis is a multivariate statistical method that can distinguish newly acquired samples according to the quantitative characteristics of the existing observational sample. In this study, a Bayesian stepwise discriminant model was established, and a corresponding linear discriminant function was built. This model could predict and reduce the occurrence of PPROM.

METHODS

Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by Institutional Review Board of Shaanxi Provincial People's Hospital. Informed written consent was obtained from all the participants before their enrolment in this study.

Study design and participants

Abnormal vaginal discharge was examined in each of the participants. The quantitative levels of CT, UU, NG, *C. albicans*, GBS, HSV-1, and HSV-2 were detected in each of the participants. Based on the etiological detection, a type of linear discriminant analysis was used to discriminate between normal pregnant women and those with PPROM. The accuracy of the Bayesian stepwise discriminant model was validated by both a training group (including 112 cases in case subgroup and 108 cases in control subgroup) and a multicenter validation group (including 500 cases in case subgroup and 500 cases in control subgroup). An unmatched case-control design was used in this study. Inclusion criteria for normal pregnant women were as follows: women with 28–36^{+6} weeks of gestation, no use of any antibiotics within 2 months, and no history of any chronic diseases (such as diabetes, cardiovascular disease, and hypertension). Inclusion criteria for the PPROM patients were as follows: pregnant women with 28–36^{+6} weeks of gestation, membrane rupture within 12 h, no use of any antibiotics within 2 months, and no history of any basic diseases (such as diabetes, cardiovascular disease, and hypertension). The PPROM is defined as the onset of amniotic fluid leakage from the vagina before the onset of uterine contractions at less than 37 weeks' gestational age.[8] The PPROM includes having a history of drainage of clear fluid that wets the perineum and runs along the thighs and legs as well as a sterile speculum examination showing fluid pooling in the posterior vaginal fornix or fluid freely flowing from the cervix. The laboratory definition of PPROM is positivity for insulin-like growth factor-binding protein 1 in the vaginal discharge.[9]

In the preliminary study, 112 pregnant women with PPROM and 108 normal pregnant women were randomly recruited from Department of Obstetrics and Gynecology, Shaanxi Provincial People's Hospital between June 2011 and May 2012. Bayesian stepwise discriminant analysis was used to analyze the etiological infections of CT, UU, *C. albicans*, GBS, HSV-1, and HSV-2. A multicenter validation group included 500 pregnant women with PPROM (case subgroup) and 500 normal pregnant women (control subgroup) from five different hospitals in the Shaanxi province between June 2012 and January 2013, respectively. These five hospitals were Northwest Women and Children Hospital, Xi'an Fourth Hospital, Xi'an Gaoxin Hospital, Chang'an Hospital, and Xianyang 215 Hospital in Shaanxi province.

Data and specimen collection

Face-to-face questionnaires were used to collect the sociodemographic characteristics (including age, gravidity, parity, marital status, and occupation) and gynecological histories (including obstetric history, past history of PPROM, and history of trauma to the cervix). A vaginal swab and a cervical swab were collected within 12 h of membrane rupture of PPROM cases, and the control group were collected at 28–36^{+6} weeks of gestation during routine examination.

Nucleic acid extraction

Each swab was suspended in the 1.5 ml of sterile saline (0.85%). Nucleic acid was extracted from the swab specimens using QIAamp MiniStool kit (QIAGEN, Hilden, Germany) following the manufacturer's instruction, and the DNA was eluted in the 45 µl of elution buffer.

Quantitation of etiological agents by real-time polymerase chain reaction

Real-time polymerase chain reaction (PCR; Triplex International Biosciences Co., LTD., China), following the manufacturer's instructions, was used to detect NG, UU, CT, GBS, and *C. albicans* in the vaginal swabs and HSV-1 and HSV-2 in the cervical swabs. The threshold of detection of the PCR was equal to or greater than 10^3 copies/ml.

Antibody against HIV and syphilis detection

All participants' serum was collected to detect antibody against HIV and syphilis using enzyme linked immunosorbent assay (ELISA) kits (Shanghai Kehua Bioengineering Co., Ltd., China).

Statistical analysis

The data were analyzed using SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA). Data were considered to have a normal distribution if the P value given by the Shapiro-Wilk test was more than 0.05. If the test data set did not show a normal distribution, the data could be normalized by logarithmic transformation. The mean levels of infectious agents were compared using the Wilcoxon two-sample test method. The Chi-square test was used to analyze the differences between categorical data. The value of $P < 0.05$ was considered to be statistically significant.

Furthermore, the original data for the etiological factors of PPROM were log-transformed and then translated as discriminant functions. The translated data were analyzed by a forward selection method (sle = 0.1, sls = 0.1). Significant variables were identified by Bayesian stepwise discriminant analysis.

The quantitative levels of the etiological agents for each of the pregnant women were skewed. Hence, these data were converted into a log-normal distribution. Linear combinations of data were used to form discriminant functions for the separation of categories by minimization of the within-class and between-class ratios of the sum of squares. Bayesian stepwise discriminant analysis was used to distinguish normal pregnant women from those with PPROM. Forward stepwise analysis was used to select significant variables for the discriminant analysis. An obvious difference in the selected variables was observed when the translated variables were used.

RESULTS

Baseline characteristics of the training group

There were no significant differences in age, gravidity, parity, marital status, and occupation between the normal pregnant women (control subgroup) and those with PPROM (case subgroup) in the training group [all $P > 0.05$, Table 1].

Univariate analysis of the etiologic agents in the training group

All participants were negative NG, HIV, and syphilis. In the training group, there were significant differences in the positive rates of abnormal vaginal discharge, UU, CT, and GBS between the normal pregnant women and those with PPROM [all $P < 0.05$; Table 2]. To study the effects of different etiological agents on PPROM, the quantitative levels of UU, CT, HSV-2, and GBS were converted into log-normal distribution data. The quantitative levels of UU, CT, GBS, and HSV-2 showed significant differences between the normal pregnant women and those with PPROM [all $P < 0.05$; Table 3]. However, the *C. albicans* and HSV-1 distributions were not significantly different between the normal pregnant women and those with PPROM [all $P > 0.05$, Table 3]. Positive rates of each etiological agent were analyzed using Chi-square test. The translated data were analyzed using Wilcoxon two-sample test method. Then, the translated data were separately analyzed by a forward selection method, and significant variables were selected for the Bayesian stepwise discriminant analysis.

Bayesian stepwise discriminant analysis

The Bayesian stepwise discriminant analysis is described in statistical language as follows: Assume g populations follow g multivariate normal distributions. Probability of misclassifying a subject in class i into class j, P(i|j); Loss due to misclassification, a(j|i). The Bayesian criterion: minimize the expected misclassification loss.

Table 1: Baseline characteristics of all participates in training group of this study

Characteristics	Case subgroup ($n = 112$)	Control subgroup ($n = 108$)	χ^2	P
Marital status, n (%)			0.303	0.860
Single	2 (1.8)	1 (0.9)		
Married/cohabiting	109 (97.3)	106 (98.2)		
Divorced/separated	1 (0.9)	1 (0.9)		
Age, n (%)			0.897	0.085
<20 years	1 (0.9)	1 (0.9)		
≥20 years and <35 years	89 (79.5)	91 (84.3)		
≥35 years	22 (19.6)	16 (14.8)		
Gravidity, n (%)			0.598	0.439
Primegravidae	85 (75.9)	77 (71.3)		
Gravida ≥2	27 (24.1)	31 (28.7)		
Parity, n (%)			0.429	0.513
Primipara	94 (83.9)	87 (80.6)		
Secondary ≥2	18 (16.1)	21 (19.4)		
Occupation, n (%)			0.001	0.984
House wife	52 (46.4)	50 (46.3)		
Employee/business	60 (53.6)	58 (53.7)		

Table 2: Infectious status of training group in this study

Variables	Case subgroup (n = 112)	Control subgroup (n = 108)	χ^2	P
Abnormal vaginal discharge, n (%)			17.774	0.001
Yes	53 (47.3)	22 (20.4)		
No	59 (52.7)	86 (79.6)		
Candida albicans, n (%)			2.711	0.100
Positive	7 (6.3)	2 (1.9)		
Negative	105 (93.7)	106 (98.1)		
HSV-2, n (%)			0.376	0.617
Positive	1 (0.9)	2 (1.9)		
Negative	111 (99.1)	106 (98.1)		
UU, n (%)			4.817	0.028
Positive	13 (11.6)	4 (3.7)		
Negative	99 (88.4)	104 (96.3)		
CT, n (%)			7.105	0.008
Positive	19 (17.0)	6 (5.6)		
Negative	93 (83.0)	102 (94.4)		
GBS, n (%)			11.098	0.001
Positive	25 (22.3)	7 (6.5)		
Negative	87 (77.7)	101 (93.5)		
HSV-1, n (%)			1.218	0.270
Positive	5 (4.5)	2 (1.9)		
Negative	107 (95.5)	106 (98.1)		

UU: *Ureaplasma urealyticum*; CT: *Chlamydia trachomatis*; GBS: Group B Streptococci; HSV-1: Herpes simplex virus type 1; HSV-2: Herpes simplex virus type 2.

Table 3: Distribution of etiological agents in training group of this study

Etiological agents	Case subgroup* (n = 112)	Control subgroup* (n = 108)	Z	P
UU	6.16	5.03	3.534	0.002
CT	5.75	3.72	11.521	0.001
GBS	7.93	6.51	3.249	0.004
Candida albicans	4.66	4.66	0.168	0.569
HSV-1	3.59	3.61	−0.264	0.795
HSV-2	4.12	3.72	3.586	0.002

*The quantitative levels of UU, CT, HSV-2, and GBS were converted into log-normal distribution data. UU: *Ureaplasma urealyticum*; CT: *Chlamydia trachomatis*; GBS: Group B streptococci; HSV-1: Herpes simplex virus type 1; HSV-2: Herpes simplex virus type 2.

Classification function:

$$f_1 = a_{10} + a_{11}x_1 + \ldots + a_{1p}x_p$$

$$f_2 = a_{20} + a_{21}x_1 + \ldots + a_{2p}x_p$$

$$f_g = a_{g0} + a_{g1}x_1 + \ldots + a_{gp}x_p$$

a_{j0}, a_{j1}, a_{jp} (j = 1,2.... g): the parameters to be estimated; f_{ji} represents positively related to the probability of being in the jth population.

Bayesian stepwise discriminant analysis was used to establish a function using retrospective data, and then the individual observation indices were introduced into the equation, according to the results of the individual, to infer the type of a statistical method.

Two Bayesian function equations were established based on the discriminant coefficients. To investigate the contribution of the etiological factors, the tests of equality of three groups (UU, CT, and GBS) were statistically different ($P < 0.05$), then Bayesian discriminant method could be carried out. The significance test of the discriminant function are shown in Table 4, Wilks' λ value was 0.530, Chi-square value was 137.535, so the discriminant result was proved to be effective. The classification function of Bayesian model was established as follows:

$$f_1 = -95.383 + 0.441x_1 + 3.347x_2 + 4.126x_3$$

$$f_2 = -71.580 + 0.381x_1 + 3.263x_2 + 2.642x_3$$

X_1 is the distribution of UU, X_2 is the distribution of CT, and X_3 is the distribution of GBS. f_1 is the function for the PPROM group, and f_2 is the function for the non-PPROM group.

The results of the Bayesian stepwise discriminant analysis showed that UU, CT, and GBS infections were key factors that could affect the occurrence of PPROM, with coefficients of 0.441, 3.347, and 4.126, respectively [Table 4]. According to the Bayesian stepwise discriminant model, associations were observed among UU, CT, and GBS infections, and PPROM. No associations were found among HSV-1, HSV-2, *C. albicans*, and PPROM. The Bayesian stepwise discriminant analysis was used to differentiate normal pregnant women from those with PPROM. The results showed that the accuracy of this method was 84.1%.

Validation of Bayesian stepwise discriminant analysis

All classification rules developed through Bayesian stepwise discriminant analysis should be prospectively validated before their use in clinical practice; therefore, we designed a prospective validation group. There were no significant differences in age, gravidity, parity, marital status, and occupation between the normal pregnant women (control subgroup, 500 cases) and those with PPROM (case subgroup, 500 cases) in the validation group [all $P > 0.05$, Table 5]. The distributions of abnormal vaginal discharge, UU, CT, GBS, and *C. albicans* showed significant differences between two subgroups [all $P < 0.05$, Table 6]. However, the distributions of HSV-2 and HSV-1 were not significantly different [all $P > 0.05$, Table 6]. The log-transformed quantification of quantitative levels of UU, CT, HSV-2, and GBS showed statistical differences between the case and control groups but *C. albicans* did not show statistical difference [Table 7]. After the bias discriminant function cross-validation, the accuracy of this method was 86.8% to separate normal pregnant women and PPROM women in validation group [Table 8].

Discussion

The mechanisms of PPROM are unclear. The presence of infections may cause PPROM through the release of

Table 4: Results of Bayesian stepwise discriminant function

Variables	F	P	Coefficients		Wilks' λ	χ^2	P
			PPROM	Non-PPROM			
UU	52.999	<0.001	0.441	0.381	0.530	137.535	<0.001
CT	31.247	<0.001	3.347	3.263			
GBS	125.065	<0.001	4.126	2.642			

UU: *Ureaplasma urealyticum*; CT: *Chlamydia trachomatis*; GBS: Group B streptococci; PPROM: Preterm premature rupture of membranes.

Table 5: Baseline characteristics of all participants in validation group of this study

Characteristics	Case subgroup (n = 500)	Control subgroup (n = 500)	χ^2	P
Marital status, n (%)			1.001	0.606
Single	4 (0.8)	2 (0.4)		
Married/cohabiting	495 (99.0)	496 (99.2)		
Divorce/separated	1 (0.2)	2 (0.4)		
Age, n (%)			1.450	0.484
<20 years	6 (1.2)	6 (1.2)		
≥20 years and <35 years	432 (86.4)	444 (88.8)		
≥35 years	62 (12.4)	50 (10.0)		
Gravidity, n (%)			2.067	0.150
Primegravidae	324 (64.8)	302 (60.4)		
Gravida ≥2	176 (35.2)	198 (39.6)		
Parity, n (%)			2.569	0.109
Primipara	417 (83.4)	435 (87.0)		
Secondary ≥2	83 (16.6)	65 (13.0)		
Occupation, n (%)			0.065	0.799
Home maker	219 (43.8)	215 (43.0)		
Employed/business	281 (56.2)	285 (57.0)		

Table 6: Infectious status of validation group in this study

Variables	Case subgroup (n = 500)	Control subgroup (n = 500)	χ^2	P
Abnormal vaginal discharge, n (%)			9.019	0.003
Yes	178 (35.6)	134 (26.8)		
No	322 (64.4)	366 (73.2)		
Candida albicans, n (%)			4.384	0.036
Positive	23 (4.6)	11 (2.2)		
Negative	477 (95.4)	489 (97.8)		
HSV-2, n (%)			2.016	0.156
Positive	6 (1.2)	2 (0.4)		
Negative	494 (98.8)	498 (99.6)		
UU, n (%)			22.353	0.001
Positive	67 (13.4)	24 (4.8)		
Negative	433 (86.6)	476 (95.2)		
CT, n (%)			23.349	0.001
Positive	57 (11.4)	17 (3.4)		
Negative	443 (88.6)	483 (96.6)		
GBS, n (%)			36.424	0.001
Positive	78 (15.6)	21 (4.2)		
Negative	422 (84.4)	479 (95.8)		
HSV-1, n (%)			0.504	0.478
Positive	5 (1.0)	3 (0.6)		
Negative	495 (99.0)	497 (99.4)		

UU: *Ureaplasma urealyticum*; CT: *Chlamydia trachomatis*; GBS: Group B streptococci; HSV-2: Herpes simplex virus type 2; HSV-1: Herpes simplex virus type 1.

inflammatory cytokines and proteases.[6,9] Indeed, genital infection has been identified as a risk factor for PPROM.

Infection may impair the antimicrobial effect of the pregnant cervix, making it more susceptible to other microbes.[10,11] This

Table 7: Distribution of etiological agents in validation group in this study

Etiological agents	Case subgroup* (n = 500)	Control subgroup* (n = 500)	Z	P
UU	7.70	5.55	7.280	0.001
CT	6.12	3.95	11.183	0.001
GBS	8.44	7.55	4.453	0.001
Candida albicans	4.50	4.70	−2.291	0.091
HSV-1	3.17	3.22	−0.626	0.539
HSV-2	3.78	3.37	4.684	0.001

*The quantitative levels of UU, CT, HSV-2, and GBS were converted into log-normal distribution data. UU: *Ureaplasma urealyticum*; CT: *Chlamydia trachomatis*; GBS: Group B streptococci; HSV-1: Herpes simplex virus type 1; HSV-2: Herpes simplex virus type 2.

Table 8: Cross validation of training and validation groups in this study

Groups	PPROM	Non-PPROM	Total
Training group*, n (%)			
Case subgroup	97 (81.5)	15 (18.5)	112 (100.0)
Control subgroup	20 (18.4)	88 (86.6)	108 (100.0)
Validation group†, n (%)			
Case subgroup	426 (85.2)	74 (14.8)	500 (100.0)
Control subgroup	66 (13.2)	434 (86.8)	500 (100.0)

*The accuracy was 84.1% to separate normal pregnant women and PPROM women in training group; †The accuracy was 86.8% to separate normal pregnant women and PPROM women in validation group. PPROM: Preterm premature rupture of membranes.

study investigated the associations between the selected genital infections (abnormal vaginal discharge, UU, CT, GBS, NG, *C. albicans*, HSV-1, HSV-2, HIV, and syphilis) and PPROM in Shaanxi province, China. The distributions of abnormal vaginal discharge, UU, CT and GBS were significantly different between normal pregnant women and those with PPROM. However, the distributions of *C. albicans*, HSV-1, HSV-2, were not significantly different between normal pregnant women and those with PPROM. The relationship between abnormal vaginal discharge and PPROM has been reported in other studies.[12-14] some studies have shown that *C. albicans* was protective against PPROM.[11,15] Pregnant women with *C. albicans* were 73% less likely to develop PPROM than pregnant women without *C. albicans*. The possible reason for this finding might be that the amniotic fluid washes out the yeast cells, which could lead to negative results.[16-18] We found that the positive rate of *C. albicans* had no statistical difference between two subgroups in the training group, but had significant different between two subgroups in the validation group, and bias might be caused by the sample scale. Different outcomes were reported about the relationship between HSV-1 and HSV-2 with PPROM.[19] In the training group, the positive rate of HSV-2 showed no statistical difference, but the quantitative level of HSV-2 was significantly different between normal pregnant women and those with PPROM. This result might be caused by the use of different detection methods for HSV-1 and HSV-2 in pregnant women.[20-22]

Some studies have shown that infections with HIV, syphilis, and NG might be risk factors for PPROM in pregnant women.[8,22] In this study, all participants were HIV, syphilis and NG negative, so these three pathogens were not included in the analysis of this study.

This study showed that CT infection was associated with PPROM. Some studies have shown that CT infection of pregnant women could cause release of inflammatory mediators that could be implicated in membrane rupture.[15,23,24] Some studies have shown that infection with GBS might release cytokines and other inflammatory modulators which could cause membrane rupture.[23,25] This study found an association between PPROM and GBS. In this study, the prevalence rates of GBS in the women with PPROM ranged from 4.2% to 22.3%, similar with the results of other studies.[14,26,27]

The associations between etiological factors and PPROM are still unclear, and no tool is available to evaluate the association between quantitative levels of etiological agents and PPROM.[24,28] In this study, we established a Bayesian stepwise discriminant model to identify normal pregnant women and those with PPROM. We found that CT, UU and GBS infections were associated with PPROM. Using this method, 84.1% and 86.8% of the pregnant women with PPROM could be distinguished from the normal pregnant women in the training and validation groups, respectively. However, the cause of PPROM is complicated, only main etiological agents were involved in this study, but noninfectious factors were not included, so some pregnant women with PPROM could not be distinguished from normal pregnant women using this Bayesian stepwise discriminant analysis.

In this study, a Bayesian stepwise discriminant model was established to predict the incidence of PPROM. The UU, CT, and GBS infections were discriminant factors for PPROM according to a Bayesian stepwise discriminant analysis. This model could provide a new method for the early predicting of PPROM in pregnant women to hopefully reduce the incidence of PPROM.

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Conflicts of interest

There are no conflicts of interest.

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