# Prediction of Subclinical Chorioamnionitis After Cervical Cerclage

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# Abstract

Objective: To explore non-invasive indices for predicting subclinical chorioamnionitis following cervical cerclage.

Methods: We performed a retrospective analysis of 80 singleton pregnant women who underwent cervical cerclage surgery in our hospital. Eighty patients were divided into either a histological chorioamnionitis group (n=57) and non-histological chorioamnionitis group (n=23). Gestational age before cervical cerclage, cervical dilation size, vaginal microbiota, cervical microbial colonization, and inflammatory indicators related to peripheral blood cells (white blood cell count, neutrophil count, lymphocyte count, platelet count, CRP, neutrophil/lymphocyte ratio, platelet/white blood cell ratio, etc.) at pre-surgery time and onset of labor post-surgery were compared, and an independent sample t-test and multivariate logistic regression analysis were performed to study the risk factors associated with histological chorioamnionitis. Histological chorioamnionitis was used as the outcome variable, and receiver operating characteristic (ROC) curve analysis was performed to determine the cut-off value and evaluate the predictive value of these indicators for chorioamnionitis.

Results: 1) Single-factor logistics analysis showed that the preoperative number of platelets, indicators related to peripheral blood cells during onset of labor post-surgery the total number of leukocytes neutrophils platelets platelet/white blood cell ratio , the area under the curve of each indice was all statistically significant. Their cut-off values were 229.5×109/L; 10.245×109/L; 9.86×109/L; 240.5×109/L; 1.022 respectively. 2) Additional multivariate logistic regression analysis was performed. Preoperative number of platelets, the number of white blood cells and platelet/white blood cell ratio during onset of labor were identified as significant variables. 3) The statistically significant variables (preoperative platelets, white blood cells and platelet/white blood cell during onset of labor) obtained from multi-factor analysis were grouped according to the cut-off value. A joint screening system was established that specified that two or more indicators are positive as joint screening, with a screening sensitivity of 87.5%, and specificity of 45.5%.

Conclusions: After cervical cerclage, the number of white blood cells and the ratio of platelet/white blood cell during onset of labor combined with preoperative number of platelets have predictive value for potential histological chorioamnionitis in pregnant women with cervical cerclage.


# Introduction

Cervical insufficiency is typically manifested clinically as painless cervical dilation with or without amnion sac. Cervical cerclage reinforces the cervix by application of special sutures at the utero-vesical pouch to achieve a supporting effect, protecting fetal membranes from pathogens, and effectively extending gestation. Existing evidence indicates that pregnant women with cervical cerclage have subclinical chorioamnionitis, and even infection in the amniotic cavity. However, such women lack the typical manifestations of clinical chorioamnionitis, such as fever (body temperature reaching or exceeding 38 °C) or accompanied by maternal tachycardia (heart rate exceeding 100 beats per minute), fetal tachycardia (more than 160 beats per minute), uterine tenderness, odor of amniotic fluid, increased maternal white blood cells, increased C-reactive protein, and increased procalcitonin. Therefore, difficulties in diagnosing subclinical chorioamnionitis increases the risk of miscarriage and causes adverse outcomes for mothers and children.

When pregnant women with cervical cerclage exhibit signs of possible premature delivery, understanding how to predict potential chorioamnionitis highly impacts the clinical anti-infection therapies, the appropriate time of termination of pregnancy and prognosis of mothers and children. At present, there is no ideal clinical method that can predict and monitor potential chorioamnionitis. The blood cell count and its derivative parameters such as platelet/white blood cell ratio have been widely recognized as markers of inflammatory diseases. This study uses retrospective analysis of cases with cervical cerclage to explore whether relevant indicators of peripheral blood cell analysis have an improved predictive role on potential chorioamnionitis during onset of labor.

## Materials And Methods

# Study population

This retrospective study included pregnant women who received transvaginal cervical cerclage in our hospital from 2018 to 2019 and gave birth between 20 weeks, 0 days and 36 weeks, 6 days of gestation. We received written informed consent from all included patients. The Ethical Review Committee of Fujian Maternity and Child Health Hospital approved the collection and use of samples and clinical information for this study (No. 2019014).

# Inclusion criteria:

Patients were required to exhibit the following indications for cervical cerclage, including: 1) singleton pregnancy, 2) cervical length less than or equal to 25 mm during transvaginal ultrasound scan (with or without funnel-like dilatation of the internal cervix), 3) have a history of one or more incidences of miscarriage in the second trimester of pregnancy or premature delivery, 4) the cervix is dilated during physical examination, the amniotic sac protrudes into the vagina, or the fetal membrane is visible through the cervix.

# Exclusion criteria:

The following conditions were used in screening for exclusion in the study: 1) multiple pregnancy, 2) multiple cerclages in the current pregnancy, 3) full-term delivery after cervical cerclage, and 4) fetal malformations.

Cervical length and/or funnelling were examined by vaginal ultrasound. The administration of prophylactic antibiotics and spinal anesthesia were administered before cerclage. The type of cerclage performed was the McDonald method, using No. 2 Ethibond (Ethicon, UK) to suture four ports at the cervico-vaginal junction with purse-string sutures for cerclage.

Clinical indicators included: 1) General information: maternal age, number of gestations, parity, number of fetal losses in the previous second trimester, number of miscarriages, preoperative cervical dilatation, gestational week of cervical cerclage, gestational week of fetal membrane rupture after cervical cerclage, gestational week of cerclage removal, gestational week of childbirth, and peripheral blood cell analysis results including platelet/white blood cell ratio, neutral granulocyte/lymphocyte ratio, preoperative C-reactive protein (CRP) results at pre-surgery and onset of premature labor (no patients were treated with corticosteroids or antibiotics when taking a peripheral blood sample). 2) Maternal and child outcomes: delivery methods, delivery complications including premature delivery, miscarriage, premature rupture of membranes, placental abruption, sepsis, etc., use of uterine contraction inhibitors and drugs accelerating lung maturation, and placental pathology results. Newborn birth weight, Apgar score, the number of days the newborn stays in the ICU, and the complications related to premature delivery including necrotizing enterocolitis, intraventricular hemorrhage, and retinopathy were also outcomes documented.

After delivery, tissue samples were obtained from the placenta and placental membranes, and the tissue samples were embedded in paraffin and sectioned into thin slices for diagnosis of chorioamnionitis.

# Laboratory inspection index:

According to observed pathology of the placenta following delivery, 80 patients were divided into histological chorioamnionitis (n = 57) and non-histological chorioamnionitis groups (n = 23 cases). The inflammatory indicators related to peripheral blood cells (leukocytes, neutrophil counts, lymphocyte counts, platelet counts, C-reactive protein, neutrophil/lymphocyte ratio, platelet/white blood cell ratio etc.) were compared between two groups of pregnant women with cervical cerclage at pre-operation and during onset of labor post-operation. To study the risk factors related to histological chorioamnionitis, receiver operating characteristic curve analysis was performed, we calculated the area under the curve (AUC), determined the cut-off value, and evaluated its predictive value for chorioamnionitis.

# Statistical analysis:

All statistical analyses were performed using SPSS version 24.0 (IBM, Armonk, NY, United States), An independent sample t-test was used to compare differences, and logistic regression was used to evaluate risk factors related to histological chorioamnionitis. A receiver operating characteristic curve (ROC) curve was graphed to evaluate the optimal cut-off value of risk factors related to histological chorioamnionitis.

The results are expressed in odds ratio (OR) and 95% confidence interval (CI). A *P* value < 0.05 was considered statistically significant

# Results:

1. A total of 80 women underwent cervical cerclage (including 36 rescue cervical cerclage, 31 therapeutic cerclage, and 13 prophylactic cerclage). There were 57 women with histological chorioamnionitis and 23 with non- histological chorioamnionitis. Tables 1 and 2 provide general information concerning the pregnant women and neonatal outcomes. The pregnant women in the study had an average age of 31.61 ± 4.66 years, the average gestational age at cerclage was 22.04 ± 3.79 weeks, the average gestational age at cervical cerclage removal was 28.61 ± 5.24 weeks, and the average gestational age at delivery was 28.98 ± 4.79 weeks. The average prolonged gestational age was 47.76 ± 32.56 days, and 53 pregnant women (66.25%) were treated for accelerating fetal pulmonary maturation. The average gestational age of preterm premature rupture of fetal membrane after cervical cerclage was 30.61 ± 4.22 weeks, and the average incubation period of premature rupture of fetal membrane to delivery was 5.45 days. Among these patients, 2 women (2.6%) developed sepsis, and 21 (26.3%) exhibited placental abruption.

Table 1
General study patient information

| | $\bar{\chi} \pm s/n/P_{50}(P_{25},P_{75})$ | | $\bar{\chi} \pm s/n$ |
|---|---|---|---|
| Maternal age | 31.61 ± 4.66 | Average gestational week at cerclage | 22.04 ± 3.79 |
| Proportion of women who have multipara | 32(40.0%) | The average gestational week of premature rupture of fetal membrane | 28.61 ± 5.24 |
| Number lost in the second trimester | 0(0,1) | complicated with sepsis | 2(2.6%) |
| Number of miscarriages | 0(0,1) | complicated with placental abruption | 21(26.3%) |
| History of preterm birth | 5(6.25%) | The average gestational week for removal of cervical cerclage | 28.61 ± 5.24 |
| History of hysteroscopy | 15(18.75%) | Gestational week of delivery | 28.98 ± 4.79 |
| History of cervical surgery | 4(5.00%) | Cesarean section rate | 17(21.3%) |
| | | histological chorioamnionitis | 57(71.3%) |
| | | non-histological clinical chorioamnionitis | 19(23.8%) |

Table 2
General newborn information of newborns

| | $\bar{\chi} \pm s/n/P_{50}(P_{25},P_{75})$ | | $\bar{\chi} \pm s/n/P_{50}(P_{25},P_{75})$ |
|---|---|---|---|
| Gestational week of delivery: 25-27w | 16(20.0%) | Neonatal pneumonia | 40(50.0%) |
| Gestational week of delivery: 28-31w | 20(25.0%) | Neonatal sepsis | 11(13.8%) |
| Gestational week of delivery: 32-33w | 5(6.3%) | Neonatal intraventricular hemorrhage | 15(18.8%) |
| Gestational week of delivery ≥ 34w | 21(26.3%) | Necrotizing enterocolitis of newborn | 6(7.5%) |
| Stillbirth | 22(27.5%) | Neonatal retinopathy | 4(5.0%) |
| Birth weight (g) | 1370(823.75,2235.00) | Neonatal respiratory distress syndrome | 9(11.3%) |
| Apgar score (1 min) | 10(9,10) | Neonatal Leukomalacia | 1(1.39%) |
| Apgar score (5 min) | 10(10,10) | Neonatal hyperbilirubinemia | 4(5.0%) |
| Apgar score (10 min) | 10(10,10) | Neonatal patent ductus arteriosus | 12(15.0%) |
| | | Admission time for neonatology | 16.0(7.42) |

## Neonatal outcome

In the study, there were 22 cases of stillbirth (27.5%), 3 women that quit treatment. The average birth weight was 1.37 kg. The highest incidence of complications was neonatal pneumonia (which accounted for 50%), followed by neonatal intraventricular hemorrhage (18.8%), and the average neonatal admission time was 16 days.

1. 2. Regardless of whether the women were diagnosed with histological chorioamnionitis, the cases were grouped. The routine blood analysis distribution between the two groups was analyzed and the results are shown in Table 3. The platelet counts pre-surgery in patents with histological chorioamnionitis, total number of white blood cells and the total number of neutrophils and platelets during onset of labor were higher than those with non-histological chorioamnionitis patients, and the ratio of platelet/white blood cell during onset of labor was lower than those with non-histological chorioamnionitis. The difference was statistically significant.
2. 3. In groups based on diagnosis with histological chorioamnionitis, univariate analysis of meaningful variables with single factor, receiver operating characteristic curve (ROC) analysis, and cutoff value with the maximum value of Youden index determination results are shown in Table 4

and Fig. 1. The area under the curve of the number of platelets before the operation, the total number of white blood cells, neutrophils, platelets, and platelet/white blood cell ratio during onset of labor were statistically significantly increased in women with histologic chorioamnionitis. The cut-off values were 229.5 × 109/L; 10.245 × 109/L; 9.86 × 109/L; 240.5 × 109/L; 1.022 respectively.

Table 3
Univariate analysis of histological chorioamnionitis

| | | Non-histological | Histological | t | *P* |
|---|---|---|---|---|---|
| Pre-surgery | Total number of white blood cells | 10.024 ± 2.434 | 10.997 ± 2.521 | 1.575 | 0.119 |
| | Total number of neutrophils | 7.643 ± 2.302 | 8.483 ± 2.375 | 1.439 | 0.154 |
| | Lymphocyte count | 1.65 ± 0.486 | 1.754 ± 0.511 | 0.837 | 0.405 |
| | Platelet count | 208.43 ± 43.8 | 231.05 ± 44.532 | 2.061 | 0.043 |
| | Platelet distribution width | 11.439 ± 1.739 | 11.582 ± 2.163 | 0.281 | 0.779 |
| | Average platelet volume | 10.17 ± 0.866 | 10.209 ± 0.906 | 0.179 | 0.859 |
| | Hemoglobin | 112.7 ± 8.38 | 117.3 ± 11.163 | 1.782 | 0.079 |
| | C-reactive protein | 5.162 ± 6.877 | 2.523 ± 2.379 | 1.211 | 0.245 |
| | Neutrophil/lymphocyte ratio | 5.061 ± 2.157 | 5.249 ± 2.010 | 0.141 | 0.889 |
| | Platelet/white blood cell ratio | 21.635 ± 5.688 | 21.834 ± 5.772 | 0.370 | 0.712 |
| During onset of labor | Total number of white blood cells | 10.611 ± 2.705 | 13.24 ± 3.499 | 3.040 | 0.003 |
| | Total number of neutrophils | 8.329 ± 2.779 | 10.645 ± 3.474 | 2.682 | 0.009 |
| | Lymphocyte count | 1.521 ± 0.516 | 1.62 ± 0.556 | 0.694 | 0.490 |
| | Platelet count | 205.1 ± 49.949 | 234.346 ± 46.804 | 2.351 | 0.021 |
| | Platelet distribution width | 11.795 ± 1.902 | 11.093 ± 1.763 | 1.490 | 0.141 |
| | Average platelet volume | 10.355 ± 0.888 | 10.033 ± 0.872 | 1.403 | 0.165 |
| | Hemoglobin | 111.55 ± 12.237 | 115.278 ± 11.939 | 1.185 | 0.240 |
| | C-reactive protein | 6.153 ± 9.502 | 20.678 ± 22.898 | 1.638 | 0.109 |
| | Neutrophil/lymphocyte ratio | 6.46 ± 4.242 | 7.543 ± 4.14 | 0.992 | 0.324 |

| | Non-histological | Histological | t | *P* |
|---|---|---|---|---|
| Platelet/white blood cell ratio | 1.177 ± 0.324 | 0.893 ± 0.267 | 3.837 | 0.000 |

Table 4
ROC curve of histological chorioamnionitis patients

| | AUC | Standard error | *P* | 95% CI | | Cutoff value |
|---|---|---|---|---|---|---|
| Number of platelets before operation | 0.663 | 0.068 | 0.023 | 0.530 | 0.797 | 229.5 |
| Total number of white blood cells during onset of labor | 0.723 | 0.066 | 0.003 | 0.593 | 0.853 | 10.245 |
| Total number of neutrophils during onset of labor | 0.698 | 0.067 | 0.009 | 0.566 | 0.829 | 9.86 |
| Number of platelets during onset of labor | 0.679 | 0.070 | 0.019 | 0.541 | 0.816 | 240.5 |
| platelet/white blood cell ratio during onset of labor | 0.254 | 0.068 | 0.001 | 0.120 | 0.387 | 1.022 |

1. 4. According to the cut-off value, the number of platelets prior to surgery, the total number of leukocytes, neutrophils, and platelet/white blood cell ratio during onset of labor, cerclage gestational age, cervical dilatation, vaginal microbiota, and cervical microbial settings are independent variables. Chorioamnionitis is the dependent variable, and a univariate logistic regression was determined. We found that preoperative platelets, the number of white blood cells, the number of neutrophils, and the number of platelets and the ratio of platelet/white blood cell during onset of labor are risk factors for histological chorioamnionitis. The risk of histological chorioamnionitis for patients with preoperative platelets ≥ 229.5 × 109/L, leukocytes ≥ 10.245 × 109/L, neutrophils ≥ 9.86 × 109/L, platelet counts ≥ 240.5 × 109/L, platelet to white blood cell ratio < 1.02 during onset of labor, is 7.692, 6.750, 4.800, 9.333, 6.529 times as high (respectively) as those with preoperative platelets < 229.5 × 109/L, leukocytes < 10.245 × 109/L, neutrophils < 9.86 × 109/L, platelet counts < 240.5 × 109/L, and the ratio of platelet/white blood cells ≥ 1.022 during onset of labor. The regression method ($P = 0.15$) for single-factor meaningful variables was used to fit the multi-factor logistic regression. Preoperative platelets, the number of white blood cells and platelet to white blood cell ratio during onset of labor were significantly elevated in individuals with histological chorioamnionitis (Table 5).
2. 5. The predicted probability was calculated by multi-factor analysis which was analyzed again by receiver operating curve (Table). The area under the curve was 0.795 ($P = 0.000$), and its predictive effect is greater than that of single routine blood analysis.
3. 6. The sensitivity and specificity of combined screening

Table 5
Univariate and multivariate logistic regression analysis of histological chorioamnionitis

| | **Univariable logistic regression** | | | **Multivariable logistic regression** | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* | OR | 95% CI | *P* |
| Number of platelets pre-surgery | | | | | | |
| ≥ 229.5 | 7.692 | 2.050-28.861 | 0.002 | 6.896 | 1.699–28.490 | 0.008 |
| < 229.5 | 1 | | | 1 | | |
| White blood cell count during onset of labor | | | | | | |
| ≥ 10.245 | 6.750 | 2.187–20.830 | 0.001 | 6.012 | 1.773–20.389 | 0.004 |
| < 10.245 | 1 | | | 1 | | |
| Number of neutrophils during onset of labor | | | | | | |
| ≥ 9.86 | 4.800 | 1.421–16.217 | 0.012 | | | |
| < 9.86 | 1 | | | | | |
| Platelet count during onset of labor | | | | | | |
| ≥ 240.5 | 9.333 | 1.974–44.131 | 0.005 | | | |
| < 240.5 | 1 | | | | | |
| Platelet/white blood cell ratio during onset of labor | | | | | | |
| < 1.022 | 6.529 | 2.039–20.905 | 0.002 | 3.888 | 1.068–14.154 | 0.039 |
| ≥ 1.022 | 1 | | | 1 | | |

Table 6
Receiver operating characteristic curve of histological chorioamnionitis prediction probability

| **AUC** | **Standard error** | ***P*** | **95% CI** | |
|---|---|---|---|---|
| 0.795 | 0.057 | 0.000 | 0.684 | 0.907 |

Following multivariate analysis, the statistically significant variables (preoperative platelets, white blood cells and platelet to white blood cell ratio during onstet of labor) were grouped according to cut-off value.

Then, a joint screening system was established to specify that 2 or more indicators were positive as a joint screening is positive, with a sensitivity of 87.5%, and a specificity of 45.5%.

# Discussion:

Chorioamnionitis is defined as inflammation or infection of the placenta and placental membranes after 20 weeks of gestation. It is one of the primary causes of perinatal morbidity and mortality, which seriously negatively affects the prognosis of the perinatal infant. According to the different stages of its clinical manifestations, it is divided into histological chorioamnionitis and clinical chorioamnionitis. Histological chorioamnionitis, also known as subclinical chorioamnionitis, has hidden clinical manifestations and requires confirmation by a thorough pathological examination of the placenta. Clinical chorioamnionitis is the final stage of histological chorioamnionitis progression. At this stage, the fetus in utero has been exposed to the inflammatory environment for an extended time period, which greatly impacts the prognosis of the newborn.

Prior studies have reported the different incidence of chorioamnionitis in pregnant women with cervical cerclage. Lee et al. reported that 81% (42/52) of patients with cervical insufficiency have evidence of intraamniotic inflammation [1, 2]. In the present study, the diagnosis rate of clinical chorioamnionitis is only 23.8% and tissue chorioamnionitis incidence is 70%. For pregnant women with cervical cerclage, it often indicates potential chorioamnionitis when signs of labor appear. The removal or retention of cervical cerclage suture and the time for expected continued treatment are clinically controversial issues. Clinical decision-making is necessary to balance the potential benefits of prolonged pregnancy with risk of intrauterine infection. Amniocentesis is an invasive test, and if maternal serum markers can be obtained non-invasively to predict tissue chorioamnionitis, management after cervical cerclage could be improved.

At present, many studies describe predictive indicators of tissue chorioamnionitis, and the results of clinical studies are also quite different. There are currently no recommended clinical or laboratory indicators. In particular, the predictive value of amniotic fluid inflammatory factors is highly debatable. Yoneda et al. reported that the IL-8 level in amniotic fluid can more accurately predict tissue chorioamnionitis [3]. Park et al. reported that maternal plasma IL-6 can independently predict intraamniotic infection in preterm women. However, its diagnostic value is inferior to assessing IL-6 levels in amniotic fluid and similar to that of serum CRP [4]. Horinouchi et al. found that the IL-6 and PCT levels in umbilical vein can predict histological chorioamnionitis [5]. Another prospective study found no connection between inflammatory markers in amniotic fluid and preterm birth [6]. Kim et al. found that for patients with preterm premature rupture of fetal membranes, non-invasive parameters (serum CRP) and invasive parameters (amniotic fluid IL-6 levels) were not significantly different in predictive ability for histological chorioamnionitis [7]. A recent systematic review and meta-analysis of diagnostic indicators for histological chorioamnionitis indicated that simply using CRP and maternal leukocytosis as predictive indicators shows low sensitivity and specificity. In a combination of 13 studies, CRP sensitivity was 68.7% (95% CI 58–77%) and specificity was 77.1% (95% CI 67–84%). A combination of 4 studies to

evaluate the quantity of maternal white blood cells revealed that the combinatorial sensitivity was 51% (95% CI 40–62%) and specificity was 65% (95% CI 50–78%) [8]. In light of these findings, current recommendations support a combination of maternal blood and amniotic fluid biomarkers for improved accuracy in predicting histological chorioamnionitis [9].

Recent data suggest complete blood count (CBC) and its derived parameters including neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and platelet to white blood cell ratio are recognized inflammatory markers for low-grade inflammation [10, 11]. These non-invasive inflammatory markers are highly correlated with neonatal outcomes, suggesting a poor neonatal prognosis [12]. Our research on the prediction of preterm birth found that the combination of three parameters of blood cell components such as NLR, PDW (platelet distribution width) and HGB (hemoglobin) can better predict preterm birth, and the predictive sensitivity of the combined diagnostic markers is 88.6% and the specificity is 40.5% [13, 14]. Another of our studies on the prediction of preterm birth found that platelets and PLT/WBC as a potential marker have certain significance in predicting the occurrence of histological chorioamnionitis [15]. Using blood cell-related parameters to predict preterm labor requires no concomitant drug therapy to promote lung maturity. However, Winkler et al. suggest that the dose of corticosteroids used to prevent respiratory distress syndrome does not affect early prediction of asymptomatic infections in preterm labor [16].

The findings presented here indicate that the number of platelets in patients with cervical cerclage before surgery is a risk factor for chorioamnionitis. The post-surgery risk of histological chorioamnionitis for pregnant women with cervical cerclage whose preoperative platelets $\geq 229.5 \times 109/L$ was 7.692 times greater than those with preoperative platelets $< 229.5 \times 109/L$. Multivariate regression analysis also indicated that preoperative platelet count is a potential serum marker of histological chorioamnionitis. Multiple studies have confirmed that platelet activation participates in the pre-inflammatory response and can be used as a predictor of inflammation. In the course of inflammation, platelets rapidly participate in inflammatory pathogenesis through the secretion of cytokines, chemokines and other inflammatory mediators [17]. Our team's prospective study on spontaneous preterm birth also found that the platelet count of histological chorioamnionitis (HCA) patients was significantly higher than that of the non-HCA and control groups ($P < 0.001$). In addition, the AUC of the PLT count was 0.8095, indicating that the PLT count is a sensitive predictor of HCA in preterm patients.

The platelet/white blood cell ratio (PLT/WBC) as a hematological marker of systemic inflammation has been widely used to predict postoperative infection and disease prognosis [18, 19]. We have found that PLT/WBC are sensitive biomarkers for the diagnosing HCA. Our data also attempts to verify that the PLT/WBC ratio can be used as an index to predict histological chorioamnionitis during onset of labor following cervical cerclage. The data in this study also confirms that the number of white blood cells and platelet/white blood cell ratio during onset of labor are risk factors for subclinical chorioamnionitis are also likely risk factors after multivariate logistic regression analysis. After further grouping the platelets before cervical cerclage, the number of white blood cells and the platelet/white blood cell ratio during onset of labor according to the cut-off values, a joint screening system was established. When these three

indicators have 2 or more values greater than or equal to the corresponding cut-off value, the sensitivity for predicting subclinical chorioamnionitis is 87.5%, and the specificity is 45.5%.

Park et al. reported that non-invasive parameters, including maternal white blood cell count, CRP level, parity and gestational age, can strongly predict intraamniotic infection in women with preterm premature rupture of membranes (PPROM) [20]. The present study attempted to find appropriate clinical and laboratory indicators to predict chorioamnionitis. However, no clinical indicators such as parity, cervical cerclage gestational age, and cervical dilatation were found to be risk factors for chorioamnionitis. This difference may be due to the different sample sources in different studies.

Our research has certain limitations that must be mentioned. One limitation is that this study is retrospective and was conducted in a single center. The small sample size limits the widespread application of our results. Secondly, we will further verify the effectiveness of the noninvasive prediction model through prospective studies in future clinical studies.

# Declarations

**Author contributions:**

Li Li, Mian Pan and Jianying Yan designed the study, collected the data, analyzed the data and wrote the manuscript; Xinxin Huang, Liyin Qiu, Mei Ma and Jun Zhang collected the data. All authors have read and approved the manuscript.

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**Institutional review board statement:**

This research did not increase the risk and economic burden of patients; the patients' rights were fully protected; the project design was conducted in line with scientific and ethical principles. The institutional review board of Fujian Provincial Maternity and Children's Hospital approved this project.

**Informed consent statement:**

All participants in this study have provided informed written consent prior to enrollment.

**Conflict-of-interest statement:**

The authors declare that they have no conflict of interest.

**Data sharing statement:**

All data will be available from the corresponding author upon reasonable request.

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# Figures

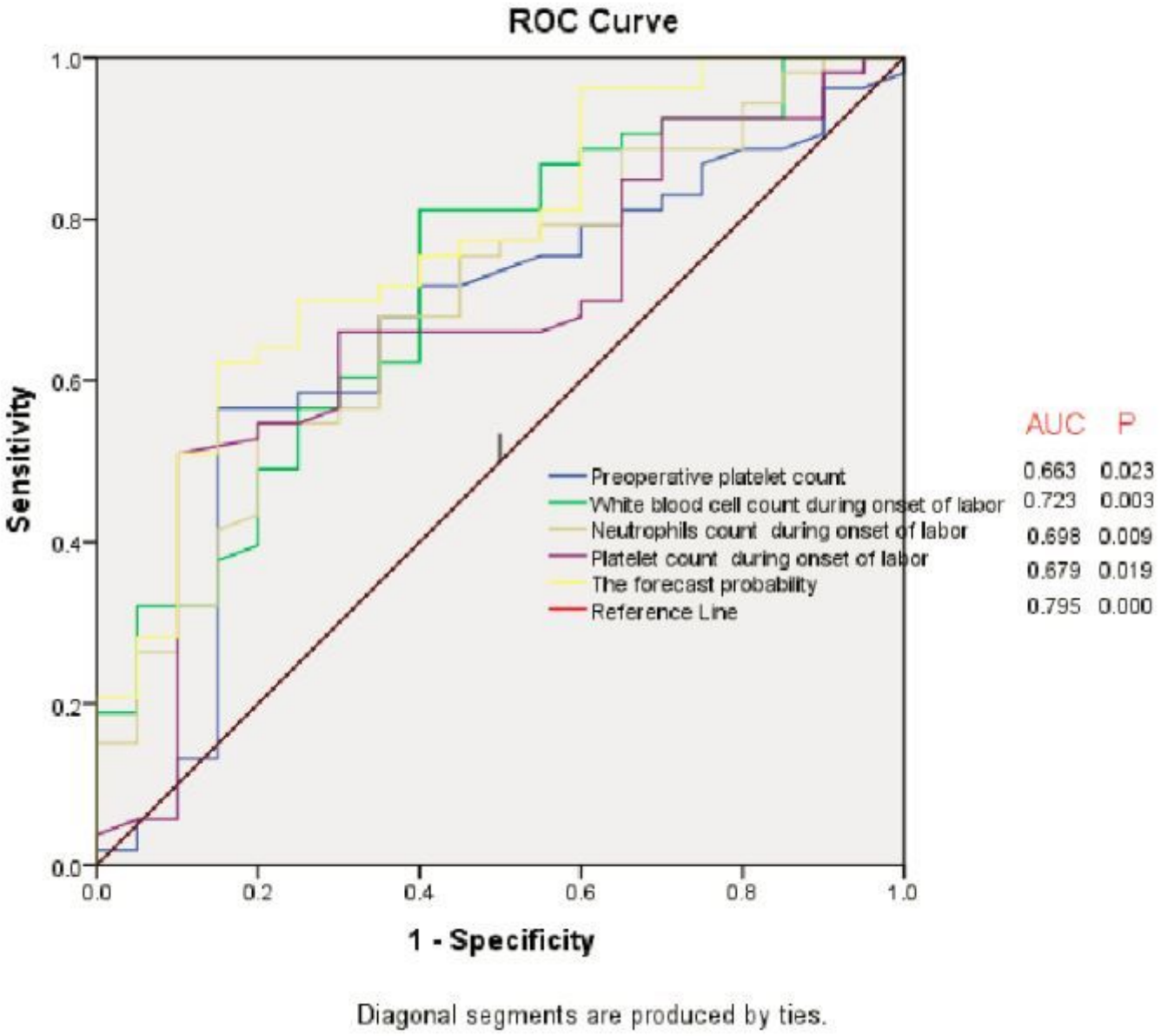


**Figure 1**

Receiver operating characteristic curve of histological chorioamnionitis prediction probability