



## Vaginal microecological imbalance and expression of serum inflammatory factors in pregnant women with group B streptococcus infection and pregnancy outcome

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### ABSTRACT

The objective of this study was to explore the correlation between vaginal microecological imbalance and the expression of related inflammatory factors in pregnant women with group B streptococcus (GBS) infection and pregnancy outcomes. For this purpose, 100 GBS-positive pregnant women were recruited as the experimental group, and 100 GBS-negative pregnant women were recruited as the controls. The balance of vaginal microecology of pregnant women in different groups was compared. Results showed that the probability of vaginal microecological imbalance in the experimental group was much higher than against the controls. Fasting venous blood was drawn from the pregnant women in two groups. After centrifugation, the expression levels of interleukin-6 (IL-6), tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), and interleukin-1 $\beta$  (IL-1 $\beta$ ) in serum were detected. It was found that the expression levels of IL-6, IL-1 $\beta$ , and TNF- $\alpha$  in the experimental group were higher than against the controls. After delivery, it suggested that the incidence of premature delivery, neonatal infection, premature rupture of membranes, and other adverse childbirth in the experimental group was much higher in contrast to the controls, up to 87%. In conclusion, GBS infection can increase the incidence of vaginal microecological imbalance and the expression of serum inflammatory factors in pregnant women, and it can greatly raise the incidence of adverse pregnancy outcomes.

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### Introduction

GBS is an anaerobic gram-positive, hemolytic coccus, which is mainly present in the lower part of the reproductive tract and digestive tract of women, threatening the life and health of pregnant women and newborns (1). Most women have GBS in the vagina, but GBS is not pathogenic to healthy women. However, if a pregnant woman is infected with GBS and does not receive timely treatment, GBS may infect the fetus through amniotic fluid and vaginal secretions during childbirth, causing pneumonia, meningitis, and other diseases (2). According to statistics, GBS infection causes more than 300,000 newborn infections worldwide every year, of which more than 90,000 infants die and about 60,000 dead babies are born. According to relevant studies (3), the mortality rate of newborns after GBS infection is between 20% and 50%, which is the main factor leading to neonatal disease and death (4). At present, many obstetrics and gynecology hospitals in China have carried out GBS screening programs during pregnancy. According to studies, 35 to 37 weeks of pregnancy is the best period for GBS screening (5). Many different types of GBS vaccines have been developed and widely used in clinical practice. However, due to the use of antibiotics, more and more drug-resistant strains of GBS appear, so relevant researchers are looking for new treatment methods for GBS infection (6).

There are a variety of microorganisms in the vagina of healthy women, a dynamic balance environment between a variety of microorganisms and the vaginal ecological environment as well as the human body is formed, namely

the vaginal microecology (7). Under normal circumstances, there is no GBS in female vaginal flora. Due to the pregnancy, hormone imbalance and the increase of estrogen in the body lead to the increase of the proportion of Candida, and the change of the vaginal environment, which destroys the dynamic balance of vaginal microorganisms and the body, easily leading to GBS invasion (8). However, GBS can encode a variety of pathogenic factors such as capsular polysaccharides, which can hinder the immune system from discovering GBS and enable GBS to successfully enter the host cells for growth and proliferation (9). Because the resistance of pregnant women is low, the large number of Candida increases will destroy the vaginal mucosa, so that the proportion of vaginal flora changes, leading to vaginitis. If the correct treatment is not taken, the inflammation will continue to ferment, spread to the cervical canal, enter the uterus, cause intrauterine infection, and cause fetal infection; In the third trimester of pregnancy, pregnant women with decreased resistance may have GBS reverse infection, invading the uterus and causing fetal membrane rupture, resulting in adverse pregnancy outcomes such as premature rupture of membranes, abortion, or threatened premature delivery (10). Relevant studies have shown that the vaginal microecological imbalance of pregnant women is closely related to the occurrence of GBS infection (11). Factors such as the decrease in the number of Lactobacillus in the vagina, the increase in the number of Gram-negative bacteria, and the increase in vaginal pH value will lead to the destruction of vaginal microecology and promote GBS infection.

Serum inflammatory factors are biomarkers reflecting

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the inflammatory state of the body, which can cause inflammatory responses, including IL-6, TNF- $\alpha$ , IL-1 $\beta$ , etc. (12). During pregnancy, the level of inflammatory factors may increase, which may have an impact on the outcome of pregnancy (13). Increased levels of inflammatory factors may lead to the occurrence of complications such as premature delivery, premature rupture of membranes, intrauterine growth restriction, and placental abruption (14). In addition, inflammatory factors may also affect the development of fetal neurodevelopment and immune system, and increase the risk of certain diseases after birth (15). Therefore, it is important for pregnant women to maintain a healthy lifestyle and have regular prenatal visits to ensure that the levels of inflammatory factors are within the normal range, thereby reducing the risk of adverse pregnancy outcomes. If the levels of inflammatory factors are elevated, the doctor may recommend further tests and treatment to protect the health of the mother and child. Studies have shown that inflammation during pregnancy is closely correlated with preterm birth, but the relationship between GBS infection and preterm birth has not been clear (16). GBS infection can cause inflammation in preterm neonates and increase the expression levels of serum inflammatory factors in pregnant women, such as IL-6, TNF- $\alpha$ , and IL-1 $\beta$ . The increase of these inflammatory factors may lead to the activation of the maternal immune system and the enhancement of inflammatory response, thus having adverse effects on pregnancy outcomes (17).

## Materials and Methods

### Study subjects

100 GBS-positive pregnant women and 100 GBS-ne-

gative pregnant women were recruited from Chongqing General Hospital Obstetrics and Gynecology Hospital, with 100 GBS-positive pregnant women as the experimental group, and 100 GBS-negative pregnant women as the controls. The inclusion criteria are given in Table 1, and the exclusion criteria are presented in Table 2. This article was approved by the Ethics Committee of Chongqing General Hospital, and informed consent was obtained from patients and their families.

## Research Methods

### GBS detection method

Following cleaning, vaginal swabs can be adopted to collect vaginal secretions. Sterile gloves should be adopted to prevent cross-infection. After collection, the swab was placed in a sampling tube to avoid contamination. GBS identification cards (immunochromatography) can be applied to identify pregnant women with GBS infection.

Operation steps: Vaginal sampling: a sterile vaginal swab was adopted to slide back and forth on the vaginal wall several times to collect vaginal secretions. Sample processing: the collected vaginal swab was placed in the sampling tube and the sample was processed according to the instructions. Sample addition: the sample was dripped into the sample well in the kit and the sample was added according to the instructions. Waiting: the kit was placed on the platform or prepared work table for reaction time.

Result determination: The results were determined according to the instructions, and whether the sample was positive or negative was judged according to the color and stripe number of the control line and the test line. In

**Table 1.** Inclusion criteria.

| No. | Inclusion criteria   |
|-----|--|
| 1   | Conceived naturally, the pregnancy was more than 7 months old                            |
| 2   | Age between twenty and thirty-five   |
| 3   | No sexual life for a month   |
| 4   | Pregnant women and their families were informed and signed the relevant informed consent |

**Table 2.** Exclusion criteria.

| No. | Exclusion criteria   |
|-----|--|
| 1   | Have a serious immune system disorder or have a serious blood disorder   |
| 2   | Have taken antibacterial drugs or antibiotics within one month, used antibacterial lotion within one week, etc |
| 3   | Carrying a twin or multiple births   |
| 4   | Fetal malformation, polyhydramnios, and other situations that are not conducive to production                  |
| 5   | Suffering from an acute infectious disease   |
| 6   | The internal organs are damaged and dysfunctional  |
| 7   | Genital malformations  |

**Table 3.** Criteria for vaginal microecological balance.

| No. | Vaginal microecological balance                                 |
|-----|---|
| 1   | The number of bacterial colonies ranged from 10 to 1,000/ field |
| 2   | Variety 4 to 9  |
| 3   | Lactobacillus ratio > 85%                                       |
| 4   | The number of white blood cells was $\leq 5$                    |
| 5   | Absence of pus cells  |
| 6   | No specific pathogen  |

the identification of GBS infection, if the test line and the control line appeared and the color was the same, the sample was positive. If only the control line appeared and the test line did not appear, the sample was negative. GBS identification card was purchased from Zhuhai Hua'ao Biotechnology Co., LTD. The operation steps were carried out in strict accordance with the instructions, and the test results were recorded.

### Vaginal microecology detection

Vaginal secretions were collected with vaginal swabs and made into glass slides. The prepared glass slides were observed with an electron microscope to detect and observe the status, number, and type of colonies on the glass slides. The criteria for vaginal microecological balance are illustrated in Table 3, and the vaginal microecological imbalance, that is, the situation opposite to Table 3. The diseases caused by vaginal imbalance in pregnant women were counted.

### Detection methods of serum inflammatory factors

Fasting venous blood was collected from the pregnant women. The venous blood was put into a sterile centrifuge tube, and the upper layer of serum was taken after centrifugation. The serum samples were taken into different centrifuge tubes and stored, and the sample number was marked. The collected serum was stored in the refrigerator until all the samples were collected and tested together. The expression levels of IL-6, TNF- $\alpha$ , and IL-1 $\beta$  were detected by enzyme-linked immunosorbent assay (ELISA) kit from Shanghai Mlbio Co., LTD, and the operation steps on the kit were strictly followed. The various reagents in the ELISA kit were added to the corresponding wells, respectively, and operations such as washing, incubation, and color development were performed. The relevant absorbance values of each sample well were read by an ELISA reader, and the data were analyzed and counted by SPSS and other software.

### Statistics of pregnancy outcomes

After the delivery of the pregnant women, the problems of the pregnant women during the delivery process were counted, whether the newborn had inflammatory diseases and whether the mother had adverse pregnancy were counted, and the statistics were filled in according to the real situation.

### Statistical methods

Excel database was established and imported into IBM SPSS Statistics 20 software for data analysis. The imbalance of vaginal microenvironment, the expression level of serum inflammatory factors, and pregnancy outcome of the experimental group and the controls were analyzed by statistical analysis method and  $X^2$  test. The relationship between GBS infection and vaginal microecological imbalance, the expression of serum inflammatory factors, and pregnancy outcome was analyzed by two-way analysis of variance. Infection status and vaginal microecological imbalance status as two independent variables, pregnancy outcome as the dependent variable, and serum inflammatory factor expression was adopted as a mediator variable.  $P < 0.05$  was considered statistically meaningful.

## Results

### Maternal data

The  $P$  values of maternal age, month of pregnancy, number of pregnancies, number of deliveries, and pregnancy complications (gestational hypertension, diabetes, hypothyroidism) in the controls and the experimental group were all greater than 0.05. It indicated that the maternal age, month of pregnancy, number of pregnancies, number of deliveries, and pregnancy complications were not related to this experiment. The experiments were comparable (Figure 1).

### Vaginal imbalance

Figure 2 shows that the proportion of vaginal microecological imbalance in the experimental group was 40% and that in the controls was 25%, indicating that the probability of vaginal microecological imbalance became greater after GBS infection ( $P < 0.05$ ). Figure 3 suggests

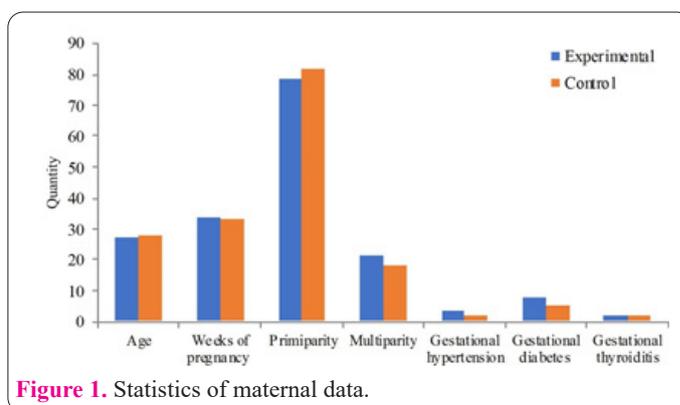


Figure 1. Statistics of maternal data.

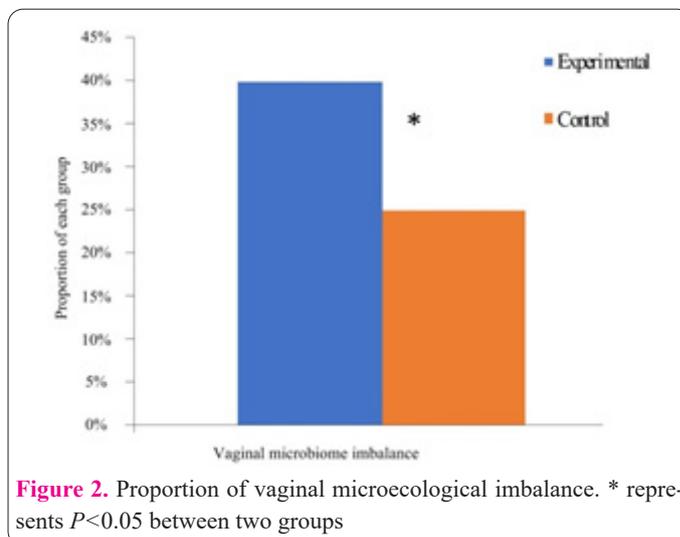


Figure 2. Proportion of vaginal microecological imbalance. \* represents  $P < 0.05$  between two groups

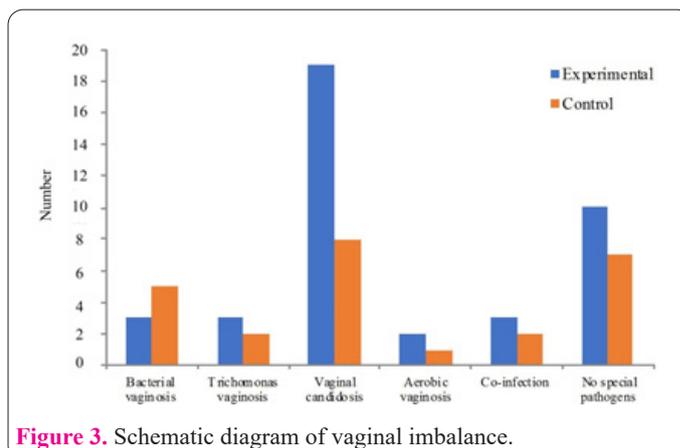


Figure 3. Schematic diagram of vaginal imbalance.

that GBS infection can increase the incidence of vaginosis, but the incidence of bacterial vaginosis decreases, and the incidence of vaginal candidiasis (candida vaginitis) was greatly increased.

### Comparison of serum inflammatory factor levels

Figure 4 shows that the expression level of serum inflammatory factors in the experimental group was greater than that in the controls, indicating that GBS infection in pregnant women can cause inflammatory responses in the body, thereby increasing the expression level of serum inflammatory factors. Therefore, GBS infection can cause inflammation.

### Pregnancy outcomes

Figure 5 reveals that the proportion of adverse pregnancy outcomes in the experimental group was 87% and that in the controls it was 18%, indicating that GBS infection had adverse effects on the pregnancy outcomes. The incidence of premature rupture of membranes in the experimental group was much higher than against the controls, indicating that GBS infection caused damage to fetal membranes, which increased the incidence of premature rupture of membranes. Neonatal infection is mainly due to the lack of timely treatment after maternal infection with GBS, which leads to neonatal infection with GBS through amniotic fluid. Chorioamnionitis and puerperal infection were also caused by GBS infection. On the one hand, GBS infection can increase the imbalance of vaginal microecology of pregnant women and lead to adverse pregnancy outcomes. On the other hand, GBS infection can increase the expression of serum inflammatory factors in pregnant women and increase the incidence of adverse pregnancy outcomes ( $P < 0.05$ ).

### Discussion

Many literatures have reported the harm of GBS infection to pregnant women and newborns (18). In the 1990s, the Centers for Disease Control and Prevention of the United States issued guidelines for the prevention of GBS (19). Due to the penetrating effect of GBS on the chorion, GBS can increase inflammatory factors in serum and reduce the elasticity of fetal membranes, leading to premature rupture of fetal membranes. It can cause GBS to invade the uterine cavity, leading to intrauterine infection, puerperal infection, or postpartum hemorrhage (20). According to the results of this experiment, the incidence of adverse pregnancy outcomes caused by GBS was greatly increased, and only 13 of 100 pregnant women with GBS infection had normal delivery. Therefore, pregnant women must be tested whether they are infected with GBS before delivery. After pregnant women are infected with GBS, timely treatment can avoid the formation of adverse pregnancy outcomes.

Prevention and treatment of the reproductive system has always been a key research topic in obstetrics (21). A variety of microorganisms, led by Lactobacillus, exist in the vagina of normal women. They balance each other and resist the invasion of foreign pathogenic bacteria together, maintain the health of vaginal microenvironment, and form a dynamic balance microecological environment with the human body (22). The establishment of a microecological environment can protect vaginal health from encroachment (23). In this experiment, 40 puerpera in the experimental group had vaginal microecological imbalance, while only 25 puerpera in the controls had vaginal microecological imbalance, indicating that GBS infection could cause vaginal microecological imbalance. In the experimental group, 40 pregnant women infected with GBS led to vaginal microecological imbalance, and these 40 pregnant women had adverse pregnancy outcomes. In the controls, 25 pregnant women had vaginal microenvironment disorder, and these pregnant women had a small probability of adverse pregnancy outcomes. It is suggested that the imbalance of vaginal microecology caused by GBS may lead to a great increase in the probability of adverse pregnancy outcomes. Therefore, timely treatment of vaginal microecological imbalance is an important protective measure to prevent adverse pregnancy outcomes for pregnant women.

GBS infection can cause abnormal expression of serum inflammatory factors in pregnant women, thereby causing an inflammatory response and affecting the growth and development of the fetus and the pregnancy outcome of pregnant women (24). The increased expression of serum inflammatory factors may lead to the problem of premature delivery, and may also lead to hypertension, gestational diabetes, and other diseases in pregnant women (25). According to the results of this experiment, after pregnant women are infected with GBS, the expression levels of IL-6, TNF- $\alpha$ , and IL-1 $\beta$  in serum and serum inflammatory factors increase, and inflammation occurs in pregnant women, leading to problems in neonatal production and adverse pregnancy outcomes. Therefore, pregnant women should have regular prenatal examinations to ensure that the levels of inflammatory factors in the serum are normal and reduce the risk of elevated serum inflammatory factors.

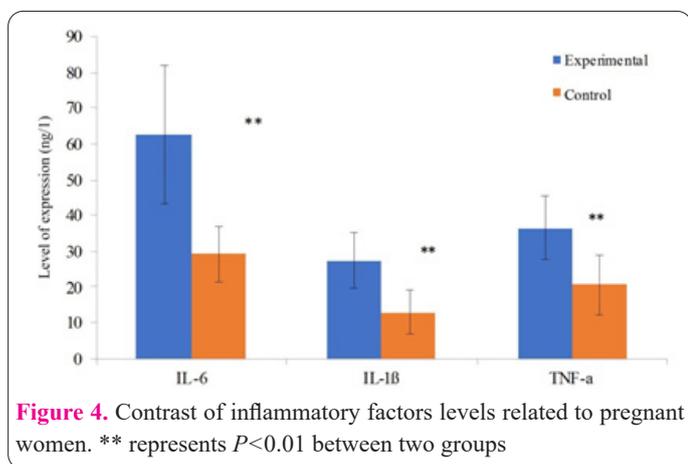


Figure 4. Contrast of inflammatory factors levels related to pregnant women. \*\* represents  $P < 0.01$  between two groups

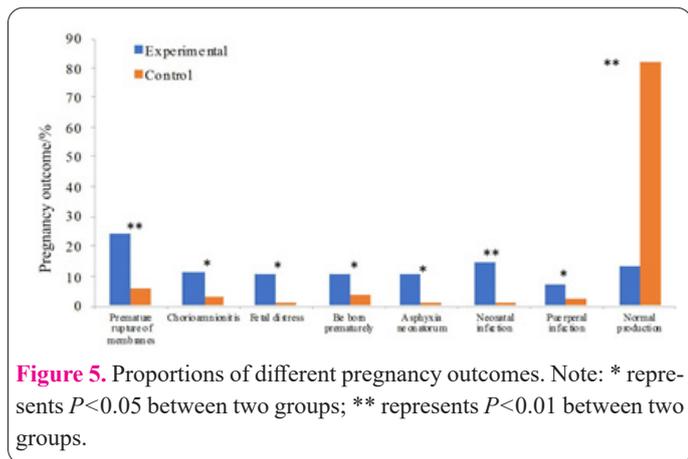


Figure 5. Proportions of different pregnancy outcomes. Note: \* represents  $P < 0.05$  between two groups; \*\* represents  $P < 0.01$  between two groups.

GBS infection is one of the common infections in pregnant women, which can lead to health problems of the fetus and mother in severe cases (26). Vaginal microecological imbalance is an important factor in GBS infection, so the study of the relationship between vaginal microecology and GBS infection is of great significance for the prevention and treatment of GBS infection (22). In addition, the expression of serum inflammatory factors is also related to GBS infection and its severity, so it also has an important impact on pregnancy outcomes. Further studies on the relationship between vaginal microecological imbalance and the expression of serum inflammatory factors and GBS infection can provide more effective prevention and treatment strategies for maternal health, and help to improve pregnancy outcomes. Compared with other experimental studies (27-31), this experiment analyzed the proportion of vaginal microecological imbalance and the expression of serum inflammatory factors in pregnant women with GBS infection and those without GBS infection. It concluded that GBS infection can increase the probability of vaginal microecological imbalance and the expression level of serum inflammatory factors in pregnant women, which will lead to an increase in adverse pregnancy outcomes.

The results show that GBS infection can lead to vaginal microecological imbalance, increase the incidence of vaginal inflammation, increase the expression level of serum inflammatory factors, and increase the possibility of inflammatory diseases in pregnant women, resulting in adverse outcomes. It is necessary to detect and treat GBS infection in time. GBS infection screening in late pregnancy is a very important way to protect maternal and child health.

Because the pregnant women in the experimental group were all in late pregnancy, it is unknown whether the effects of GBS infection in the first trimester and in the second trimester on pregnancy outcomes are consistent with this experiment. The effects of GBS infection in the first and second trimesters of pregnant women need to be further verified.

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