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The Significance of the Expression Level of Carbohydrate Antigen 125 (CA125) in Threatened Miscarriage

Linying Shi[1]* , Feng Chen[1] , Qin Wang[1] , Lingjie Shi[2]

[1]Department of Laboratory Medicine, Haimen District Traditional Chinese Medicine Hospital, Nantong 226100, Jiangsu, China
[2]Department of General Surgery, Haimen District Traditional Chinese Medicine Hospital, Nantong 226100, Jiangsu, China

**Corresponding author: Linying Shi, sly9018@163.com*

Abstract: *Objective*: To investigate the expression level of carbohydrate antigen 125 (CA125) in threatened miscarriage and explore its significance in the auxiliary diagnosis of threatened miscarriage. *Method*: Pregnant women who underwent prenatal examinations in the hospital from June 2023 to June 2024 were collected. Among them, 66 cases were clinically diagnosed with threatened miscarriage and 74 cases had early normal pregnancies. The expression levels of CA125 in the serum of the above research subjects and the HCG levels of pregnant women with different pregnancy conditions were compared. *Result*: The expression level of CA125 in the threatened abortion group (119.0 ± 23.37) was significantly higher than that in the normal pregnancy group (57.15 ± 5.554), and the difference was significant ($p < 0.05$). Clinical data analysis showed that the expression level of human chorionic gonadotropin (HCG) in the threatened abortion group (11690 ± 2337) was significantly lower than that in the normal pregnancy group (36130 ± 6855), and there was a significant difference between the two ($p < 0.05$); The expression level of progesterone (P) in the threatened abortion group was also significantly lower than that in the normal pregnancy group ($P < 0.05$). *Conclusion*: CA125 is abnormally expressed in the serum of pregnant women with threatened miscarriage and can be used as a molecular marker for the auxiliary diagnosis of threatened miscarriage. Regular detection of the concentration of CA125 in the serum of pregnant women can provide a reference for clinical assessment of decidual damage and can be used as an auxiliary basis for predicting the risk of threatened miscarriage.

Keywords: Threatened miscarriage; Carbohydrate antigen 125; Molecular markers

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1. Introduction

Threatened abortion refers to the condition where there is a small amount of vaginal bleeding, often dark red or bloody leucorrhea, before 28 weeks of gestation, without the expulsion of pregnancy tissue, followed by paroxysmal lower abdominal pain or back pain. Gynecological examination shows that the cervix is not open, the membranes are not ruptured, and the uterus size corresponds to the gestational week. The incidence rate is 20–25% [1]. Depending on the time of occurrence, it can be divided into two types: early threatened abortion, which occurs before 12 weeks of gestation, and late threatened abortion, which occurs at or after 12 weeks. Nearly 50% of pregnant women are forced to terminate their pregnancies, severely affecting their physical and mental health as well as their family's quality of life [2].

Currently, the clinical diagnosis of threatened abortion mainly relies on the clinical manifestations of pregnant women, such as irregular vaginal bleeding, abdominal pain, sound monitoring, and detection of human chorionic gonadotropin (HCG) in peripheral blood [3]. However, this method often considers ultrasound and peripheral blood testing only after pregnant women consciously experience corresponding clinical manifestations, and thus cannot play an early "warning" role. Therefore, finding markers for the auxiliary diagnosis of threatened abortion has become a top priority. According to literature studies, carbohydrate antigen 125 (cancer antigen 125, CA125), as an emerging biomarker, has received increasing attention in the field of early threatened abortion. This indicator may have potential value in predicting and diagnosing early threatened abortion.

CA125 is a glycoprotein derived from the coelomic epithelium during embryonic development. It is low or even not expressed in normal ovarian tissue but is highly expressed in the peripheral blood of patients with ovarian tumors. Currently, CA125 has been widely used as a molecular marker for ovarian tumors in clinical practice for many years. In recent years, studies have found abnormal expression of CA125 in tumor diseases such as rectal cancer and breast cancer [4, 5]. However, its role in threatened abortion is less understood.

2. Materials and methods

2.1. Materials

A total of 140 pregnant women undergoing prenatal examination in our hospital from June 2023 to June 2024 are collected, including 66 cases clinically diagnosed with threatened abortion with an average age of 33.5 years (range: 20–46 years), and 74 cases of early normal pregnancy with an average age of 31.5 years (range: 20–43 years). All pregnant women and their families are informed of the purpose and significance of this study and volunteer to participate.

The inclusion criteria are:

(1) The diagnosis of threatened abortion meets the relevant standards, that is, a small amount of vaginal bleeding occurs before 28 weeks of gestation, often dark red or bloody leucorrhea, without the expulsion of pregnancy tissue, followed by paroxysmal lower abdominal pain or back pain. Gynecological examination shows that the cervix is not open, the membranes are not ruptured, and the uterus size corresponds to the gestational week.

(2) Natural pregnancy

(3) Human chorionic gonadotropin in the serum and urine of all pregnant women is positive

(4) Ultrasound shows intrauterine singleton pregnancy

(5) No drug or surgical embryo killing was performed before detection.

The exclusion criteria include:

(1) Ectopic pregnancy

(2) Clinically diagnosed with tumors or severe liver, kidney, and other organ diseases.

2.2. Methods

On the day of testing, 5 mL of blood is collected from the elbow vein on an empty stomach in the morning and placed in a biochemical tube. After standing, the supernatant serum is collected by centrifugation at 4000r for 20 minutes. The expression level of CA125 is examined using a chemiluminescence method. The CA125 reagent is an Abbott CA125 chemiluminescent microparticle immunoassay kit, and the instrument is Abbott I2000.

2.3. Statistical analysis

Data analysis is performed using GraphPad Prism 5.0 software. The expression levels of CA125 in the threatened abortion group and the normal pregnancy control group are analyzed using a non-parametric test for two independent samples. A *P*-value less than 0.05 is considered statistically significant.

3. Results

3.1. Comparison of CA125 between the two groups (±S)

The expression level of CA125 in the threatened abortion group was 119.0 ± 23.37, while the expression level of CA125 in the normal pregnancy group was 57.19 ± 5.554. The level of CA125 in the threatened abortion group was significantly higher than that in the normal pregnancy group ($P < 0.05$), as shown in **Figure 1** (unit: U/ml).

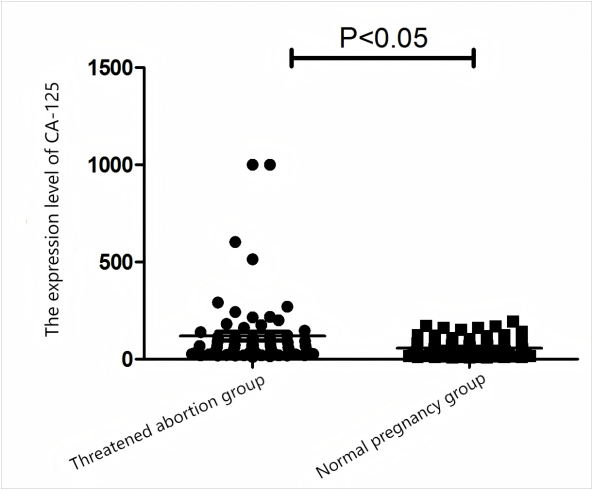

Figure 1. Expression levels of CA125 in maternal serum between threatened abortion and normal pregnancy groups

3.2. Comparison of HCG and P between the two groups (±S)

Based on the analysis of clinical case data, the expression level of HCG in the threatened abortion group was 11690 ± 2337, while that in the normal pregnancy group was 36130 ± 6855. The HCG level in the threatened abortion group was significantly lower than that in the normal pregnancy group ($P < 0.05$), as shown in **Figure 2** (unit: U/L). The expression level of P in the threatened abortion group was 42.82 ± 4.383, while that in the normal

pregnancy group was 63.81 ± 4.151. The P level in the threatened abortion group was significantly lower than that in the normal pregnancy group ($P < 0.05$), as shown in **Figure 3** (unit: nmol/L).

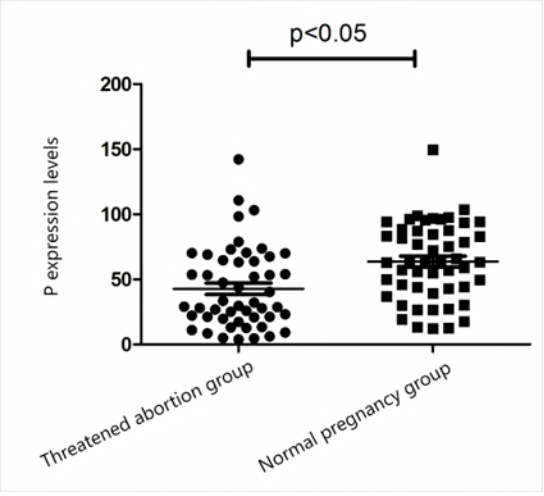

Figure 2. Expression levels of CA125 in the serum of pregnant women in the threatened abortion group and the normal pregnancy group

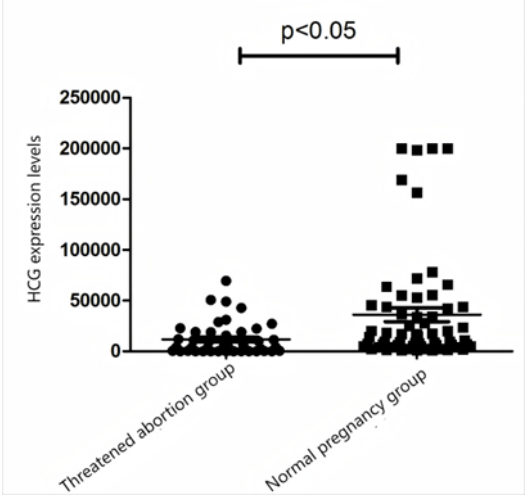

Figure 3. Expression levels of progesterone in maternal serum between threatened abortion and normal pregnancy groups

3.3. Analysis of the effectiveness of CA125 as a molecular marker for auxiliary diagnosis of threatened abortion

Using GraphPad Prism 5.0 software, a ROC curve was plotted to analyze the expression level of CA125 in 66 pregnant women with threatened abortion and 74 pregnant women with normal pregnancies (**Figure 4**). The area under the curve was 0.6144 (95% CI: 0.52–0.70).

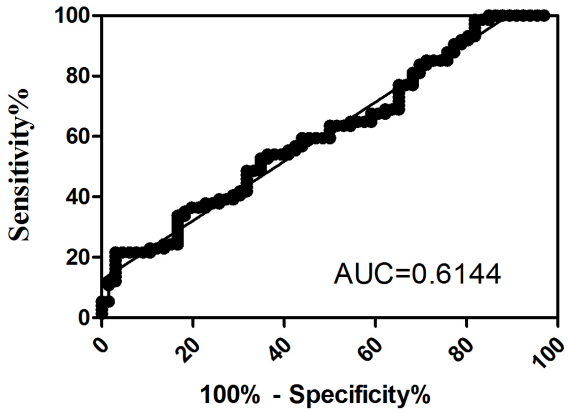

Figure 4. CA125 ROC curve

4. Discussion

Research indicates that the pathogenesis of threatened abortion involves multiple factors, which can be primarily attributed to embryonic chromosomal abnormalities, maternal health issues, infectious etiologies, and immune dysfunction. From the chromosomal perspective, common types of abnormalities include trisomy syndromes, polyploidy variations, X chromosome monosomy, and specific chromosomal structural aberrations. Maternal influencing factors can be divided into two categories: one is organic lesions of the reproductive system, such as congenital uterine malformations, cervical or uterine cavity adhesions, and uterine fibroids; the other is pregnancy comorbidities, including gestational diabetes, gestational hypertension syndrome, pelvic inflammation, and thyroid dysfunction. Infectious factors include bacterial vaginosis, toxoplasmosis, listeriosis, and other pathogenic microorganisms. Complex factors such as antiphospholipid antibody syndrome, autoimmune system diseases, and allogeneic immune abnormalities in immune mechanisms may also trigger the risk of abortion. Additionally, the physical condition and psychological trauma of pregnant women significantly affect the development process of threatened abortion, and the high incidence of this disease severely impacts the physical and mental health of pregnant women.

Currently, clinical diagnostic criteria often rely on blood and imaging tests after pregnant women experience abnormal symptoms, which often misses the optimal time for preserving the pregnancy [6]. Investigations have shown that patients with threatened abortion presenting with irregular vaginal bleeding during early pregnancy often exhibit subchorionic hematoma characteristics on ultrasonography. Studies have pointed out that there is a positive correlation between serum CA125 concentration and the amount of vaginal bleeding, suggesting that the degree of elevation of this marker can serve as an important reference for evaluating the risk of abortion. CA125, as a tumor-associated glycoprotein antigen, is mainly produced in epithelial tissues of body cavities, mucosal tissues of the genital tract, and epithelial cells of the ovary. Although traditionally used as a marker for ovarian cancer diagnosis, research has revealed its specificity in biological behavior during pregnancy, with significant concentrations present in amniotic fluid, decidual tissue, and chorion. Increasing studies have demonstrated its abnormal expression in other tumors or tumor-related diseases, but there are limited reports on its role in threatened abortion [7]. Regarding the mechanism of elevated maternal blood CA125 during early pregnancy, existing research focuses on two directions: first, it is believed that decidua-derived CA125 enters the maternal circulatory system

through the fallopian tubes in a reverse direction, leading to increased serum levels via peritoneal lymphatic absorption. As the pregnancy progresses, the fallopian tube endometrium merges to form a physiological barrier, resulting in a decrease in CA125 concentration. Second, it is advocated that early pregnancy villus invasion, i.e., damage to decidual cells during placental formation, allows CA125 to enter the maternal bloodstream. In cases of threatened abortion, destruction of decidual tissue or separation of the trophoblast-decidua interface triggers the massive release of CA125. Therefore, dynamic monitoring of CA125 level changes can effectively evaluate the degree of damage to decidual and chorionic cells and disease progression.

HCG is an important glycoprotein hormone secreted by placental syncytiotrophoblast cells. In normal healthy pregnancies, HCG starts to double from 40 days after the last menstrual period, peaks between the 8th and 10th weeks, and then begins to decline after 12 weeks. When placental dysfunction or ectopic pregnancy occurs, the rate of HCG increase is far less than that in normal pregnancies. Therefore, clinically, HCG levels are often measured to confirm pregnancy, understand placental function, and detect ectopic pregnancies [8]. Meanwhile, P is a crucial steroid hormone produced by the placenta and corpus luteum. In pregnant women, serum P levels continuously increase from the 5th week until slightly decreasing before delivery and rapidly decreasing after placental expulsion. It plays a significant role in maintaining pregnancy, influencing menstruation, and promoting breast development. Clinically, it is commonly used to assess placental and corpus luteum function [9, 10]. In this study, serum samples from women with threatened abortion and normal pregnancies were collected to detect CA125 expression levels. Statistical analysis revealed that CA125 was highly expressed in the serum of women with threatened abortion, with statistical significance, and the area under the ROC curve was 0.6144. Clinical case data analysis showed that HCG and P were low in the serum of women with threatened abortion, consistent with their physiological roles during human pregnancy. These data confirm that abnormally elevated serum CA125 levels in early threatened abortion patients are significantly associated with poor pregnancy outcomes. For pregnant women with symptoms of threatened abortion, CA125 level determination has significant clinical predictive efficacy in judging the possibility of pregnancy continuation. However, due to limited time and insufficient sample size, this study did not include detection and correlation analysis of more indicators, and further research will be conducted with an expanded sample size.

5. Conclusion

In conclusion, CA125 can serve as a molecular marker for the auxiliary diagnosis of threatened abortion, providing value for clinical diagnosis and further demonstrating the predictive value of this indicator.

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Disclosure statement

The authors declare no conflict of interest.

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