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ABOUT COVER

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The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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ORIGINAL ARTICLE

Significance of highly phosphorylated insulin-like growth factor binding protein-1 and cervical length for prediction of preterm delivery in twin pregnancies

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Abstract

BACKGROUND

A twin pregnancy can carry greater risks than singleton pregnancies. About 60 in 100 twin pregnancies result in spontaneous birth before 37 wk, which is associated with several complications in the premature babies. Clinical detection of biomarkers may help to predict the possibility of premature birth so that corresponding interventions can be given to the pregnant women in a timely manner, in order to reduce the risk of preterm birth and improve the outcomes of the newborn infants.

AIM

To explore the clinical value of transvaginal ultrasound measurement of cervical length combined with insulin-like growth factor binding protein-1 (IGFBP-1) hyperphosphorylation in cervical secretions as predictors of preterm delivery in twin pregnancies.

METHODS

A total of 254 pregnant women with twin pregnancies, who were admitted to Hainan General Hospital and underwent maternity examination, were selected as the study subjects from January 2015 to December 2018. All participants received transvaginal ultrasound measurement of cervical length and phosphorylated IGFBP-1 (phIGFBP-1) test between 24 and 34 wk gestation. The pregnancy outcomes were analyzed.

RESULTS

Of the women with a positive phIGFBP-1 test result, preterm birth rate was higher in those with a cervical length \leq 25 mm than those with a cervical length > 25 mm (all P < 0.05). Similarly, in women with a negative phIGFBP-1 test result, preterm



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birth rate was higher in those with a cervical length ≤ 25 mm than those with a cervical length > 25 mm (all P < 0.05). The sensitivity, specificity, and positive and negative predictive values of the phIGFBP-1 test combined with the cervical length test were 95.71%, 91.21%, 95.12% and 92.22%, respectively, for the prediction of preterm birth.

CONCLUSION

Cervical length combined with phIGFBP-1 tests is of value for the prediction of outcomes of preterm delivery in twin pregnancies.

Key Words: Hyperphosphorylated insulin-like growth factor binding protein-1; Cervical length; Ultrasound; Twin pregnancies; Preterm delivery

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Core Tip: This study analyzed the efficacy and feasibility of transvaginal ultrasound measurement of cervical length combined with the phosphorylated insulin-like growth factor binding protein-1 (IGFBP-1) test for the prediction of preterm birth in twin pregnancies. The accuracy of the detection was high. In pregnant women with shorter central length, those with positive phosphorylated IGFBP-1 expression had a higher preterm delivery rate than those with negative expression. In pregnant women with longer central length, the effects of phosphorylated IGFBP-1 are weak on preterm delivery.

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INTRODUCTION

The definition of preterm birth varies regionally around the world due to different degrees of treatment. In many developed countries, preterm birth takes places after week 20 or 24 and before 37 wk of pregnancy. In China, a birth that occurs after 28 wk and before 37 wk is considered preterm birth[1]. Twin delivery increases the risk of preterm birth due to the raised fetuses, amniotic fluid, and intrauterine pressure. According to the latest statistics^[2], approximately 15 million premature babies are born every year, accounting for more than 10% of newborns. Moreover, 965000 premature babies die in their neonatal period and about 12000 die within 5 years. The preterm birth rate is about 50% [3]. Over the past few years, the outcomes of preterm birth in a singleton gestation have greatly improved. However, how to decrease the preterm birth of twins is still a challenging question for obstetricians. Accurately predicting the preterm birth of twins and creating a birth plan ahead of time are important for maternal and fetal health.

This study analyzed the significance of cervical length combined with the phosphorylated insulin-like growth factor binding protein-1 (phIGFBP-1) test for the prediction of preterm delivery in twin pregnancies.

MATERIALS AND METHODS

Participants

A total of 254 women with twin pregnancies, who were admitted to the hospital and underwent maternity examination from January 2015 to December 2018, were selected as the study subjects. All participants signed the informed consent and the study design was approved by the Ethics Committee of Hainan General Hospital.

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Materials

An immunoassay-based test kit for IGFBP-1 test, produced in Finland and bought from Shanghai Boya Biotechnology Co., Ltd. (Shanghai, China) was used. Abdominal color Doppler ultrasound (LOGIQ7, United States) and transvaginal color Doppler ultrasound (SSD-1000, Japan) apparatus were used.

Methods

Patients were required to empty their bladders. A probe with a frequency of 5.5 MHz was introduced into the vagina. To measure the cervical length, the probe was turned to visualize the uterus in the sagittal view and the procedure was repeated three times. The smallest length measured was recorded (unusual size was defined as cervical length \leq 25 mm). For the phIGFBP-1 test, patients were placed in the bladder lithotomy position after routine vulva skin disinfection. Swabs were inserted into the cervical tube for 15 s and removed and placed in 0.5 mL extract solution for 30 s. The test strips were dipped in the reserved extraction solution for 20 s and then taken out. The results were observed at 5 min. The appearance of two blue lines suggests positive results and one blue line suggests negative results on the test strip.

Measures

Sensitivity and specificity of phIGFBP-1 combined with cervical length tests for the prediction of preterm delivery in twin pregnancies were observed.

Statistical analyses

SPSS20.0 was used to analyze the data in the study. The χ^2 test was used. Enumeration data are expressed using "%." P < 0.05 was considered statistically significant.

RESULTS

General information for patients

The general patient information is listed in Table 1.

Analyses of preterm delivery

In pregnant women with shorter central length (≤ 25 mm), those with positive phIGFBP-1 expression had higher preterm delivery rate than those with negative phIGFBP-1 expression (P < 0.05). In pregnant women with longer central length (> 25 mm), there was no significant difference in preterm delivery rate between women with a positive or negative phIGFBP-1 test (*P* = 0.223, Table 2).

Pregnancy outcomes

The sensitivity, specificity, and positive and negative predictive values of phIGFBP-1 combined with cervical length tests were 95.71% (156/163), 91.21% (83/91), 95.12% (156/164) and 92.22% (83/90), respectively, for the prediction of preterm birth (Table 3).

DISCUSSION

Changes in the cervix in pregnant women always indicate whether the delivery begins. Effacement (shortening) and dilatation (opening up) of the cervix often occur within 2 to 3 wk before delivery. Thus, cervical length, applied as an predicator for preterm birth, is a common approach for the prediction of threatened premature delivery[3,4]. In the past, manual vaginal examination was always used to assess labor progress as well as cervical length. However, for those without enough dilatation, cervical length cannot be measured exactly by this way. Moreover, the repeated manual vaginal examination may exacerbate uterine contraction and premature rupture of membranes and even cause the occurrence of preterm birth. A study[5] showed that the incidence of preterm delivery was less than 7% in women with a cervical length beyond 35 mm. However, if the cervical length was 25 mm or less, the incidence of preterm delivery became 25%. Thus, cervical length of 25 mm was considered as the cutoff threshold value. Currently, cervical conditions can be accurately detected by transvaginal ultrasound and this examination approach is widely approved and used by doctors. Moreover, transvaginal ultrasound



Table 1 Characteristics of the twin pregnancy populations recruited in the study

Characteristic	
Maternal age (yr)	28.35 ± 4.84 (21-38)
Gravidity (times)	1.66 ± 0.35 (1-3)
Parity (times)	0.14 ± 0.03 (0-1)
Types of conception, <i>n</i> (%)	
Spontaneous conception	250 (98.43)
Medical intervention	4 (1.57)
Gestational age (wk)	26.54 ± 3.24 (24-34)
Pregnancy complications, <i>n</i> (%)	
Gestational diabetes	114 (44.88)
Gestational hypertension	36 (14.17)
Thyroid dysfunction	56 (22.05)
Other complications (e.g., placenta, amniotic fluid and baby positions in womb)	48 (18.90)

Table 2 Preterm delivery in patients with different central lengths and phosphorylated insulin-like growth factor binding protein-1 test results

Cervical length	Expression of phIGFBP-1	n	< 30 wk gestation	Between 30 and 34 wk gestation	Between 34 and 37 wk gestation	Preterm birth rate (%)
≤ 25 mm	Positive	63	20	13	12	45 (71.43)
	Negative	51	16	9	4	29 (56.86)
> 25 mm	Positive	60	0	1	3	13 (21.67)
	Negative	80	0	0	9	12 (15.00)

phIGFBP-1: Phosphorylated insulin-like growth factor binding protein-1.

Table 3 Predictive performance of phosphorylated insulin-like growth factor binding protein-1 expression combined with cervical length test for preterm delivery in twin pregnancies

Brognonov outcomes	phIGFBP-1 expression combi	Total		
Freghancy outcomes	+	•	Total	
+	156	8	164	
-	7	83	90	
Total	163	91	254	

"+": Preterm delivery; "-": Non-preterm delivery; phIGFBP-1: Phosphorylated insulin-like growth factor binding protein-1.

examination of changes in the cervix have become key in predicting the risk of preterm delivery. According to Ma et al[6], an analysis of cervical lengths in 60 women who presented with threatened preterm labor showed that women with a cervical length beyond 30 mm experienced delivery before 36 wk of gestation and the sensitivity was as high as 100%. However, another study conducted by Sun *et al*[7] showed that cervical length of about 25 mm was the cutoff threshold value for the risk of preterm birth. Accordingly, Nikolova et al[8] suggested it is necessary to track changes to the cervix between 24 and 28 wk of pregnancy to detect abnormal status in women.

IGF, which is mainly secreted by the liver, can effectively regulate proteins, fats, and carbohydrates. IGFBP-1, a major regulator, plays a critical role in fetal growth[9,10]. IGFBP-1, which is present in the cervical secretion of women, is insulin combined with a progesterone-dependent protein. The degree of IGFBP-1 phosphorylation may vary



in different combinations and in different stages of pregnancy. The mid-trimester and third trimester amniotic fluid of pregnant women mainly contains more hypophosphorylated and dephosphorylated IGFBP-1. Comparatively, more hyperphosphorylated IGFBP-1 exist in the mother's serum tissues. IGFBP-1 binds IGF when the former is unsaturated, and modulates the activities of IGF, which promote fetal growth and development[11-13]. In a study[14], the incidence of preterm delivery was as high as 54.2% predicted by the phIGFBP-1 test combined with cervical length in 106 women pregnant with twins. However, some investigators believe that IGFBP-1 hyperphosphorylation is not significantly associated with the occurrence of preterm birth. During preterm delivery, the decidua and chorion detach causing hyperphosphorylated IGFBP-1 to leak in the cervical canal, which account for hyperphosphorylated IGFBP-1 as a subject predictor for preterm delivery.

CONCLUSION

This study analyzed the performance of the phIGFBP-1 test combined with cervical length for preterm delivery in twin pregnancies. Comparing the actual pregnant outcomes with the prediction results made by phIGFBP-1 combined with cervical length tests showed that in women with cervical length ≤ 25 mm, the incidence of preterm delivery was higher in those with positive expression of phIGFBP-1 than those with negative expression of phIGFBP-1. The sensitivity and specificity of phIGFBP-1 combined with cervical length tests was 95.71% and 91.21%, respectively, for preterm delivery. In conclusion, the phIGFBP-1 test combined with cervical length can effectively predict preterm delivery in twin pregnancies and can be applied to clinical practice.

ARTICLE HIGHLIGHTS

Research background

Twins are at higher risk of preterm labor and delivery. As a result of being born too early, twins may be born with a higher risk of complications. Detection should be performed in pregnant women to reduce the risk of preterm birth.

Research motivation

Transvaginal ultrasound measurement of cervical length phosphorylated insulin-like growth factor binding protein-1 (phIGFBP-1) test were two approaches used for the prediction of preterm birth. This study researched the accuracy of these two tests in determining the chances of preterm birth occurrence.

Research objectives

This study studied the feasibility of cervical length and phIGFBP-1 test for the prediction of preterm birth in twin pregnancy.

Research methods

A total of 254 pregnant women with twin pregnancies were included in the study. Transvaginal ultrasound measurement of cervical length and the phIGFBP-1 test were performed on all of the participants. The test results were compared with the actual pregnancy outcomes of these women and the relevant data were analyzed.

Research results

In women with a positive phIGFBP-1 test result, preterm birth rate was higher in those with cervical length ≤ 25 mm than those with cervical length > 25 mm (all P < 0.05). Moreover, in women with a negative phIGFBP-1 test result, preterm birth rate was higher in women with cervical length ≤ 25 mm than those whose cervical length > 25 mm (all P < 0.05). The sensitivity, specificity, positive predict value and negative predictive values of phIGFBP-1 test combined with cervical length were 95.71%, 91.21%, 95.12% and 92.22%, respectively, for the prediction of preterm birth.

Research conclusions

Transvaginal ultrasound measurement of cervical length combined with the phIGFBP-1 test may effectively predict the possibility of preterm birth in twin pregnancy.



Research perspectives

Detection of multiple biochemical indices may help to predict preterm birth and reduce the risk in twin pregnancies. Larger studies are warranted to further discuss the accuracy of these biochemical indices and to reduce the screening test-associated harms to mothers and their babies.

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