

Clinical analysis on the influencing factors related to preterm twin pregnancy

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SUMMARY

OBJECTIVE: The aim of this study was to explore the influencing factors of preterm twin pregnancy.

METHODS: In total, 602 twin-pregnant women delivered from February 2016 to February 2020 were analyzed retrospectively. According to whether the pregnant women were preterm or not, they were divided into preterm group (n=363) and term group (n=239). Baseline information, such as maternal age, address, and education level of the pregnant women, were collected. The clinical information of pregnant women, such as chorionic, preeclampsia, gestational diabetes, premature rupture of membranes, abnormal fetal position, and fetal weight, were analyzed. Logistic regression analysis was used to analyze the risk factors. p-value <0.05 was considered statistically significant.

RESULTS: In the preterm group, monochorionic diamniotic comorbidities were significantly higher compared with the control group (p<0.05). Higher risks of preterm group have lower education (p<0.05). Multiple logistic regression analysis demonstrated that education, preeclampsia, and premature rupture of membranes were risk factors for preterm twin pregnancy.

CONCLUSIONS: Preterm birth in twin pregnancy is associated with many risk factors, such as education, preeclampsia, and premature rupture of membranes. Pregnancy supervision and prenatal guidance for twin pregnancy should be strengthened. Furthermore, early detection and diagnosis of comorbidities can improve maternal and neonatal outcomes.

KEYWORDS: Twin pregnancy. Preterm birth. Incidence rate.

INTRODUCTION

Twin pregnancy is the most common form of multiple pregnancy, and it has been reported that the incidence has increased dramatically over the past few decades. Since 1987, with the rapid development of related assisted reproductive technology (ART), the incidence of twin pregnancy has been increasing year by year¹. The twin pregnancy rate in the United States has increased from 1.89–3.33% in 30 years².

The incidence of twin pregnancy is increasing year by year, followed by a variety of complications during pregnancy, child-birth, and puerperium, such as anemia, hypertensive disorders, gestational diabetes mellitus, and postpartum hemorrhage³. Preterm birth is one of the most important problems in twin pregnancy and it seriously increases the perinatal morbidity and mortality^{4,5}. A previous study demonstrated that for twin gestations, the rates of preterm birth are higher than that for singleton gestations⁶. A study reported that the rate of preterm birth in twin gestation ranges from 31–63%⁷. The incidence of preterm birth in twin gestation has also shown an increasing trend as the rate of twin pregnancy accelerates, thereby

leading to more public health challenges⁸. It is urgent to pay attention to the research and treatment of premature birth in twin pregnancy and to actively summarize the experience from clinical data.

A better understanding of patients at higher risk of preterm birth would enable optimization of the available interventions to reduce the adverse perinatal outcomes associated with preterm birth. Methods for predicting preterm birth and risk factors for preterm birth in twin pregnancy have long been studied. History of preterm birth⁹, maternal clinical characteristics (age and height)¹⁰, gestational weight gain^{11,12}, and maternal complications (preeclampsia)¹³ are all proposed to aid in identifying and optimizing the management of preterm birth in twin pregnancy. Another retrospective study showed that self-reported pain scores are a predictor of preterm birth in symptomatic twin pregnancy¹⁴.

Studies on twin pregnancy are more frequent in Western countries, while there are fewer studies analyzing the factors of preterm birth in twin pregnancy in Chinese pregnant women. The objective of this study was to investigate

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the factors influencing preterm birth in twin pregnancy in China by retrospectively analyzing the prenatal information and clinical data of pregnant women with twin pregnancy.

METHODS

Research objects

A total of 602 women with twin pregnancy who delivered in Shanxi Maternal and Child Health Hospital from February 2018 to February 2020 were selected for retrospective analysis. Initially, 630 women with twin pregnancy were selected for information and clinical data collection. A total of 28 (4.4%) cases were excluded due to incomplete data or pregnant women with complications of important organs such as the heart, brain, liver, and kidney. A total of 602 women with twin pregnancy were finally included in the study, including 363 in the preterm delivery group and 239 in the term delivery group (Figure 1). This study was approved by the Ethics Committee of our hospital. Inclusion criteria were as follows:

1. 18–55 years old;
2. gestational age <34 weeks at the time of visit;
3. without evidence of ruptured membranes; and
4. both alive fetuses.

Exclusion criteria were as follows:

1. women without data on the exact age and gestational age at delivery and
2. incomplete medical records.

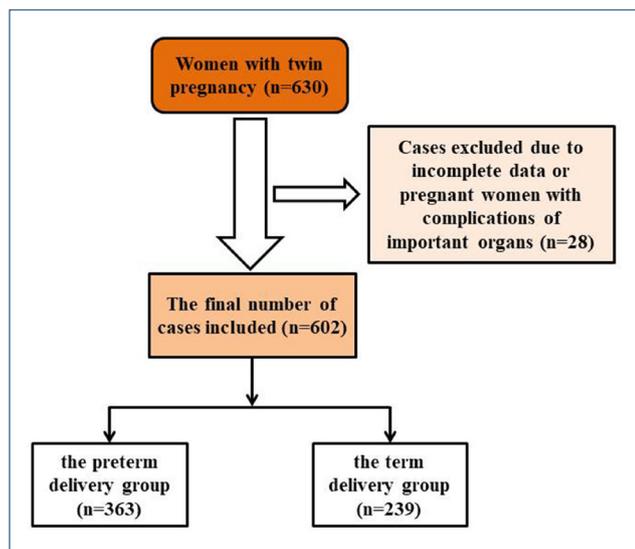


Figure 1. Flowchart for subject selection.

General information

Retrospective analysis of the general conditions of the patients in the preterm group and the term group, including age, education, place of residence, way of conception including natural conception and assisted reproductive assisted pregnancy, chorionic including monochorionic diamniotic (MCDA) and dichorionic diamniotic (DCDA), preeclampsia, gestational diabetes, premature rupture of membranes, abnormal fetal position, and fetal weight. The diagnostic criteria for preterm labor, chorionicity, preeclampsia, and other symptoms refer to the 9th edition of Obstetrics and Gynecology published by the People's Health Publishing House¹⁵.

Statistical analysis

The SPSS 22.0 statistical software was used to process the data. Continuous variables were described by means±standard deviation (range) if they were normally distributed. Categorical variables were expressed as counts (percentage). Variables were compared between the two outcomes (preterm birth or full-term birth) using univariate analysis. Continuous variables were compared using the Student's t-test or the Mann-Whitney U-test, depending on their distribution. Categorical variables were compared using the chi-squared test or Fisher's exact test. Variables in the univariate analysis with p-values <0.5 were selected for potential inclusion in the multivariate logistic regression. Then, stepwise logistic regression was performed to determine potential risk factors for preterm birth. Odds ratios (ORs) with 95% confidence intervals (CIs) and p-values were calculated. A two-tailed p-value <0.05 was considered significant.

RESULTS

Univariate analysis of two groups

Univariate analysis showed that there was no significant difference between the preterm group and the control group in terms of age, place of residence, and method of conception among pregnant women with twin pregnancy ($p>0.05$). However, educational background, chorionicity, and comorbidities significantly affected the incidence of preterm birth in twin pregnancy ($p<0.05$), and the difference was statistically significant ($p<0.05$), as shown in Table 1. The preterm birth rate of people with an associate degree and below was 73.1%, which was significantly higher than that of people with a university degree and

above (53.8%) ($p < 0.05$), which implied that the higher the preterm birth rate was at the end of the education background. In addition, the preterm birth rate of MCDA pregnant women (76.5%) was significantly higher than that of DCDA pregnant women (59.3%) ($p < 0.05$). It can be seen that the preterm birth rate of pregnant women with MCDA is higher. As for the impact of comorbidities on preterm birth, preeclampsia (75.7%) is more likely to cause preterm birth than gestational diabetes (56.4%) and premature rupture of membranes (69.9%).

Logistic regression analysis of the influencing factors of preterm birth

Logistic regression analysis showed that education (OR 0.651; 95%CI 0.525–0.807; $p < 0.001$), preeclampsia (OR 2.456; 95%CI 1.391–4.336; $p = 0.002$), and premature rupture of membranes (OR 1.770; 95%CI 1.057–2.964; $p = 0.030$) were high risk factors for premature twin birth, and the difference was statistically significant ($p < 0.05$), as shown in Table 2. In addition, preeclampsia has the greatest impact on preterm birth (OR 2.456; 95%CI 1.391–4.336; $p = 0.002$).

Table 1. Univariate analysis of twin pregnancy in preterm group and term group.

	Preterm group (n=363)			Term group (n=239)		χ^2	p-value
	Case	Proportion (%)	Preterm birth rate	Case	Proportion (%)		
Age							
<35 years	319	87.9	60.9	205	85.8	0.56617.6	0.452
≥ 35 years	44	12.1	56.4	34	14.2		
Education							
University and above	214	58.9	53.8	184	76.9	21.741	<0.001
Associate degree and below	149	41.1	73.1	55	23.1		
Place of residence							
City	278	76.6	58.5	197	82.4	2.956	0.086
Rural	85	23.4	66.9	42	17.6		
Way of conception							
Natural conception	97	26.7	62.6	58	24.3	0.454	0.500
Embryo transfer	266	73.3	59.5	181	75.7		
Chorionic							
DCDA	337	92.8	59.3	231	97.1	3.937	0.047
MCDA	26	7.2	76.5	8	2.9		
Comorbidities							
Preeclampsia	56	15.4	75.7	18	7.5	6.805	0.033
Gestational diabetes	44	12.1	56.4	34	14.2		
Premature rupture of membranes	58	16	69.9	25	10.5		

Table 2. A logistic regression analysis to identify independent factors associated with preterm birth in twin pregnancy in China from February 2018 to February 2020.

Risk factors	OR	95%CI	p-value
Education	0.651	(0.525–0.807)	<0.001
Monochorionic	0.167	(0.813–3.416)	0.163
Comorbidities			
Preeclampsia	2.456	(1.391–4.336)	0.002
Gestational diabetes	0.972	(0.617–1.531)	0.903
Premature rupture of membranes	1.770	(1.057–2.964)	0.030

DISCUSSION

With the promotion of ART, the incidence of twin pregnancy is on the rise [1], and subsequently, the risk of pregnancy complications in women with twin pregnancy is significantly higher than that in women with single pregnancy, such as preterm birth, high gestation period blood pressure disease, gestational diabetes, and premature rupture of membranes.

This study retrospectively analyzed the clinical data of 363 pregnant women with preterm twin pregnancy and 239 pregnant women with full-term twin pregnancy in our hospital. The incidence of preterm birth in twin pregnancy was 60.29%. Preterm birth is a common complication of twin pregnancy and the leading cause of perinatal morbidity and mortality. Preterm births account for 5–15% of all deliveries, and the incidence of preterm birth in twin pregnancy is approximately nine times higher than in singleton pregnancy⁶. The causes of premature twin birth are premature rupture of membranes, chorionicity, and iatrogenic premature birth caused by other complications of twins¹⁶. This analysis showed that education, chorionicity, and comorbidities were high-risk factors for twin preterm birth.

The results showed that the incidence of premature rupture of membranes in the preterm group was significantly higher than that in the term group, which was one of the risk factors for preterm birth in twin pregnancy. Studies have shown that the risk of preterm birth within 72 h after premature rupture of membranes in twin pregnancy is greater than that in singleton pregnancy¹⁷, which is related to factors such as reproductive tract infection, increased amniotic pressure, and uneven force on fetal membranes¹⁸. Therefore, for the prevention of premature rupture of membranes and active treatment of premature rupture of membranes, delaying the gestational age as much as possible is suggested in order to reduce the occurrence of premature birth in twin pregnancy, strict monitoring of reproductive tract infection during pregnancy, avoid strenuous activities in the late stage¹⁹, prohibit sexual life²⁰, and develop a healthy lifestyle habits²¹.

The proportion of premature birth among women with a college education and above is 53.8%, and the proportion of premature birth among women with an associate degree and below is 73.1%, indicating that the risk of premature birth is higher with low education level ($p < 0.05$). Most pregnant women generally live in rural areas, where health awareness and living standards are poor and the local medical level is limited²². We should popularize reproductive health knowledge during pregnancy, vigorously publicize and advocate regular prenatal examinations for pregnant and lying-in women, and strengthen supervision during pregnancy.

The incidence of MCDA in the preterm group was significantly higher than that in the control group. Due to the extensive vascular communication on the surface of the placenta in twin pregnancy, complications such as twin-to-twin transfusion syndrome and selective fetal growth restriction were prone to occur clinically. The gestational age of termination of pregnancy in the preterm group was also relatively earlier than that of double chorionic twins, and preterm birth was more likely to occur. Furthermore, in monochorionic twin pregnancy, the generally accepted approach is to terminate the pregnancy before term²³, which apparently contributes to a higher incidence of preterm birth in this group of pregnant women.

In a retrospective study involving 193 pairs of monoamniotic twins, it was found that the mortality rate of the fetus and neonate was lower when the pregnancy was closely monitored at 26–28 weeks of gestation and terminated at 33 weeks of gestation²⁴. Liu et al.²⁵ reported that the incidence of monochorionic twins in the preterm group was 32.94%, which was significantly higher than the 10.98% in the full-term group, which was consistent with the results of this study. Interestingly, although univariate analysis suggested that chorionicity was associated with preterm birth in twin pregnancy, a logistic regression analysis showed that chorionicity was not a risk factor for preterm birth in twin pregnancy ($p = 0.163$). We speculate that preterm birth in twin pregnancy may be caused by a combination of factors. In this study, univariate analysis was used to explore the association between chorionicity and preterm birth in twin pregnancy. In the next step, we will analyze the relationship between these risk factors and preterm delivery in twin pregnancy through correlation analysis and will also conduct a large sample multicenter prospective study to further confirm the impact of chorionicity on preterm birth in twin pregnancy.

Preeclampsia is a pregnancy-specific disease and one of the important causes of maternal and perinatal death, with an incidence of about 9.4% in China²⁶. Twin pregnancy is more likely to cause preeclampsia than singleton pregnancy^{27,28}. In this study, the incidence of preeclampsia in the preterm group was 75.7%, which was significantly higher than that in the full-term group, which was consistent with the findings of Butali et al.²⁹.

Studies have shown that the rate of preterm birth in the twin pregnancy group is higher than that in the singleton pregnancy group in ART patients ($p < 0.05$).

However, the results of this study showed that different methods of conception had no effect on the occurrence of preterm birth in twin pregnancy, which may have been inconsistent due to differences in the selected samples. Chambers et al.³⁰ suggested that blastocyst-stage transfer may be associated

with preterm birth in twin pregnancy compared with cleavage-stage embryo transfer (ET) in pregnant women undergoing ART. Therefore, potential confounding factors such as the ET method were not considered in the sample selection in this study, resulting in differences between samples. In the future, ET methods will be included in the evaluation for more in-depth exploration.

This study also has some limitations. First, this study is a single-center study, and the conclusions are not generalized. The next step will be a multicenter in-depth study. Second, there is a lack of consideration of potential variables. For example, the income of the families of the women studied was not included in the assessment, which in fact must be the main factor to explain the higher incidence of prematurity in pregnant women with lower levels of education.

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CONCLUSIONS

Twin pregnancy has a high rate of premature birth with many complications. Educational background, preeclampsia, and premature rupture of membranes are high risk factors for twin pregnancy. Pregnancy supervision and prenatal guidance for twin pregnancy should be strengthened to detect early. It is of great significance to reduce the incidence of preterm birth in twin pregnancy.

AUTHORS' CONTRIBUTIONS

LJD: Conceptualization, Formal Analysis, Supervision, Writing – original draft. **XPD:** Data curation, Formal Analysis. **WJW:** Data curation, Formal Analysis. **LYH:** Data curation. **CFQ:** Formal Analysis. **RS:** Formal Analysis.

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