

## Original Article

# Risk factors for preterm birth: a case-control study in rural area of western China

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**Abstract:** Preterm birth is the leading cause of perinatal morbidity and mortality in China, the study is to learn risk factors for preterm birth in rural area of western China. A 1:1 case-control study in which cases included the pregnant women of preterm birth and controls included the matched pregnant women of normal deliver was conducted in 5 counties in western China. Data about the general situation, pregnancy history, reproductive health infection (RTI) symptoms, pregnancy complications, et al were obtained by using questionnaire. The results showed that the risk factors related to preterm birth were including: family income, mother's age  $\geq 35$  years old, antenatal visiting  $\leq 4$  times, low education level, preterm birth history, abnormal vaginal discharge, pregnancy complications. The logistic regression analysis showed that only 3 factors of preterm birth were left at the last step, which of antenatal visiting  $\leq 4$  times, PROM and placenta previa had significant difference. We show that family income, age, antenatal visiting, low education level, preterm birth history, abnormal vaginal discharge, pregnancy complications are the risk factors of preterm birth.

**Keywords:** Preterm birth, western rural china, a case-control study, preterm birth history, pregnancy complications

## Introduction

Preterm birth definitions are those that child-birth occurring at less than 37 weeks' gestational age or 259 days of gestation. The preterm birth rate has risen in the world. According to the systematic review by WHO and the Institute of Medicine of National Academies USA, rate of preterm birth was 9.6% worldwide in 2005. The highest rate was 11.9% in Africa, and the lowest was 6.2% in Europe. Preterm births account for 75% of perinatal mortality and more than half the long-term morbidity. Although most preterm infants survive, they are at increased risk of developmental problems, such as birth defects, cerebral palsy, mental retardation, visual impairment, hearing loss, and other, sometimes less obvious, central nervous system disorders, including language and learning disabilities, attention-deficit hyperactivity disorder, and behavioral problems [1]. Risk factors for preterm birth are increasingly being investigated and reported, including the mother's behavior, psychological status, complications during pregnancy, environmental

exposures, genetics [2, 3], and many remain unexplained.

In recent 10 years, Rates of survival of infants have increased because of improved technical and pharmacological interventions in China. In 2010, the whole country's under-5 mortality and infant mortality rate (IMR) was 16.4% and 13.1% separately. However the preterm birth is still the main cause of infants' mortality in our country [4-7]. Several studies on preterm birth in urban areas in China are investigated and reported. In Beijing and other developed countries, reported rates are generally 6%-8%. However the study in western rural areas is still lack.

In 2010, a case-control study on preterm birth in 5 counties in western China had been carried out supported by the WHO, and the detailed risk factor information was collected. In this study, we aim to clearly identify important risk factors for preterm birth in rural area of western China. If some of these risk factors can be avoided, fewer women will experience the intense grief.

# Analysis of the risk factors of preterm birth

## Materials and methods

### *Local condition and subjects*

We carried out a 1:1 case-control study in which we tested for risk factors in “case” and “control” women in 5 counties: Fufeng, Fengxiang and Mei from Shaanxi Province; Qijiang and Tongliang from Chongqing. These 5 counties’ hospital delivery has been reached 95%, most of pregnancy women delivered in hospitals. So the investigation was in 23 health facilities that can provide delivery service in 5 counties. The rate of preterm birth from November 2010 to October 2011 was only 2.02% in five counties.

The subjects of case group were all postpartum women with preterm birth (childbirth before 37 gestation weeks or 259 days) from Nov. 1 2010 to Oct. 31 2011. The control group included 1:1 matched pregnant women of term birth (childbirth after 37 gestation weeks or 259 days). The standard criteria of cases selected into control group were including: the date of birth within  $\pm 7$  days of the date of the preterm birth, delivery in the same hospital, with the same gender infants. The research had been got the agreement of Research Ethics Committee of Peking University, the number was 2010.

Data were collected in all 5 countries using the same questionnaire. Information on general situation, gender, birth weight, family economic conditions, parents’ age, height and weight, educational level, history of pregnancy, pregnancy complications and gestational age of delivery were obtained by interview with the women after the delivery, while information on the neonatal complications, diseases and treatment situation, prenatal examinations, RTI symptoms and delivery complications were extracted directly from medical records. All the subjects will be given inform consent and if they agreed. There were 459 pairs finished the investigation, account for 96.2% of total preterm birth number in 5 counties (459/477).

### *Indicators included in the analysis*

The dependent variable was preterm birth. Risk factors such as gestation weeks, family income, educational level and others were the explanatory factors under investigation.

The analysis included the following confounding factors:

**Gestation weeks:** the gestation weeks mainly confirmed based on the last menstrual period (LMP) and the ultrasound in the second trimester.

**Family income:** According to the report from Statistic Bureau of Chongqing and Shaanxi, the average income was 15000RMB/person and 14000RMB/person in 2009, the family income was including 2 persons’ income, so it categorized 2000RMB/month or less ( $\leq 2000$  RMB) and beyond (2000 RMB).

**Educational level:** According to the Compulsory Education Law of China, the country should provide 9 years free education (primary school and junior high school), so the education level was categorized junior high school or less ( $\leq 9$  years), and senior high school or beyond ( $> 9$  years).

**Antenatal visiting:** According to the “Routine for maternal health care”, promulgated by the Ministry of Health in 2011, antenatal visiting should be  $\geq 5$  times, so the antenatal time of was categorized junior  $\leq 4$  times, and  $> 4$  times (<http://www.nhfpc.gov.cn/>).

**BMI:** Body weight divided by the square of height in  $\text{Kg}/\text{m}^2$ . According to the Guideline on prevention and control overweight and obesity for Chinese adult (Draft) published by MOH, BMI  $< 18.5$  was low weight, BMI from 18.5 to 23.9 was normal weight, BMI from 24.0 to 27.9 was overweight, BMI  $\geq 28.0$  was obesity.

**Reproductive tract infection (RTI) symptoms:** Because of the limited condition in study areas, local health facilities cannot provide RTI diagnosis, so the survey only investigated the subjects about symptoms of RTI during pregnancy like abnormal vaginal discharge or abnormal taste of vaginal discharge according to the textbook of Obstetrics and Gynecology.

**Pregnancy complications:** The Hb  $< 110$  g/L of pregnant women was defined anemia. And other pregnancy complications were defined according to the textbook of Obstetrics and Gynecology.

### *Statistical analysis*

All data were double input into database by Epidata7.0 software, and using SPSS 13.0 to analyze. The objective’s age was described by mean  $\pm$  SD, and the difference was used by t test. For single factors analysis, like profession-

## Analysis of the risk factors of preterm birth

**Table 1.** Comparison with family income between case group and control

Average family income/month (RMB)	Case group	Control group	$\chi^2$	P
	N (%)	N (%)		
≤ 2000	210 (46.0)	167 (36.7)	8.042	0.005
> 2000	247 (54.0)	288 (63.3)		

**Table 2.** Comparison with demographic characteristics between case group and control group

Risk factors	Case group	Control group	$\chi^2$	P
	N (%)	N (%)		
Mother's age			8.120	0.004
< 35	385 (83.9)	414 (90.2)		
≥ 35	74 (16.1)	45 (9.8)		
Mother's educational level			6.152	0.013
junior high school or less	343 (74.9)	309 (67.5)		
senior high school or beyond	115 (25.1)	149 (32.5)		

**Table 3.** Comparison with gestation history between case group and control group

Risk factors	Case group	Control group	$\chi^2$	P
	N (%)	N (%)		
Previous preterm delivery history			5.528	0.019
yes	15 (4.9)	4 (1.5)		
No	289 (95.1)	268 (98.5)		
Mother was preterm birth newborn			7.457	0.011
yes	10 (2.3)	1 (0.2)		
no	429 (97.7)	438 (99.8)		

al level, educational level, family income, the high risk group of age ( $\geq 35$  years old), the gestation history, the group of antenatal visiting time > 4 times, pregnancy RTI symptoms and complications were used by  $\chi^2$  test, a two-tailed *p*-value of 0.05 was used to define statistical significant results. A logistic regression was employed to identify independent predictors of preterm birth. All the single factors were independent variables and the dependent variable was preterm birth, and Odds ratios (ORs) and 95% confidence intervals (95% CI) were reported with two-tailed probability (*p*) values. A two-tailed *p*-value of 0.05 was used to define statistical significant results.

### Results

#### Demographic characteristics

Among preterm birth cases, 68 cases' gestation age were under 34 Weeks (14.8%), the smallest case was 22 + 5 weeks. 391 cases'

gestation age were from 34 weeks to 36 + 6 weeks (85.2%). 46.0% of women's who had a preterm birth average family income were  $\leq 2000$  RMB (320USD)/month compared with 36.7% in the control group, the difference had statistic significance (**Table 1**).

The **Table 2** describes the relation between the average age of neonatal mother, profession distribution, education level and preterm birth. The average age of neonatal mother was  $27.2 \pm 6.0$  years old (16-45 years old) in case group, and the control group was  $26.4 \pm 5.1$  years old (17-44 years old). There was no significant difference between case and control group ( $t = 1.930$ ,  $P = 0.054$ ). The percent of neonatal mother with  $\geq 35$  years old in case group was

higher than that in control group, it had highly statistically significant difference (**Table 2**).

In case group of neonatal mother, 43.3% were unemployment or housewife, 30.8% were peasant, 11.4% were commercial service staffs, 7.7% were workers, professional staffs occupied 5.2%, government staffs were 1.0% and others (soldier, baker, et al ) were 1.6%. In control group, 43.5% were unemployment or housewife, 29.6% were peasant, 9.8% were workers, 6.9% were commercial, service, professional, staffs occupied 6.5%, government staffs were 2.3% and others (soldier, baker, et al ) were 3.9%. There had no statistic significance between case and control group ( $\chi^2 = 9.615$ ,  $P = 0.142$ ).

The percent of junior high school or less in case group was higher than that in control group, the difference had statistic significance (19.4% versus 12.0%) (**Table 2**).

## Analysis of the risk factors of preterm birth

**Table 4.** Comparison with antenatal visiting between case group and control group

Antenatal visiting	Case group	Control group	$\chi^2$	P
	N (%)	N (%)		
≤ 4 times	189 (41.6)	103 (22.6)	37.855	0.000
≥ 5 times	265 (58.4)	353 (77.4)		

**Table 5.** Comparison with RTI symptoms during pregnancy between case group and control group

RTI symptoms	Case group	Control group	$\chi^2$	P
	N (%)	N (%)		
yes	96 (20.9)	63 (13.7)	8.284	0.004
No	363 (79.1)	396 (86.3)		

**Table 3** shows that percent in case group with previous preterm delivery history, and mother was preterm birth newborn was higher than that in control group, there were statistically significant difference (Fisher exact test showed that  $P < 0.05$ ).

### *Situation of antenatal care and pregnancy complications*

In case group, the percent of antenatal visiting ≥ 5 times was 58.4%, 41.6% were a ≤ 4 times. But in control group, the percent of ≥ 5 times and ≤ 4 times were 77.4% and 22.6% separately. And the percent of antenatal visiting ≥ 5 times in case group was obviously lower than that in control group, and the difference is significant (**Table 4**).

20.9% cases in case group had RTI symptoms during pregnancy including excessive vaginal discharge, abnormal smell of vaginal discharge, vaginal bleeding, et al. And 13.7% had RTI symptoms during pregnancy in control group. It had statistically significant difference (**Table 5**).

There were total 159 subjects in two groups had RTI symptoms during pregnancy, only 26 patients got diagnosis (16.4%), which of 3 trichomoniasis, 11 bacteria vaginosis, 8 candidiasis and 3 had cervicitis, and other cases did not get diagnosis.

### *Pregnancy complications*

**Table 6** shows that the proportion of anemia in the third trimester. Pre-rupture of membranes (PROM), pre-eclampsia, placenta previa and oligohydramnios were higher than that in control group, with significant difference (**Table 6**).

### *Logistic regression*

The regression analysis shows that antenatal visiting ≤ times (OR = 4.072, 95% CI = 0.087-0.692,  $P = 0.008$ ), PROM (OR = 4.031, 95% CI = 1.080-170129,  $P = 0.039$ ) and placenta previa (OR = 15.304, 95% CI = 1.671-140.089,  $P = 0.016$ ) had significant difference (**Table 7**).

### **Discussion**

Our study shows that several risk factors such as lower family income (≤ 2000 RMB/month), mother's age ≥ 35 years old, and lower education level are

attributable to the preterm birth in western rural China. Several reports have showed that maternal age over 35 years was the important factor contributing to preterm birth worldwide [8, 9]. The risk of preterm birth increases in all women older than 35 years. Advanced maternal age is associated with increased risk of obesity, diabetes and so on. It is an important risk factor for preterm birth. Improved community awareness of the associated risks might lower the proportion of women becoming pregnant at older ages, and early detection of other risk factors could reduce the risk of preterm birth.

The study also shows the risk of recurrence of preterm birth accounted for 10% of preterm births (OR5.6). Although these factors were not enter logistic equation in the last step, but the percent of preterm birth was also higher in case group than that in control group. The women with these risk factors were also high risk group who should be paid more attention by health workers during antenatal care [8, 9].

According to the "Routine for maternal health care", promulgated by the Chinese Ministry of Health in 2011, antenatal visiting should be ≥ 5 times (<http://www.nhfpc.gov.cn/>). In our study, the proportion of patients with antenatal visiting ≥ 5 times in case group was only 58.2%. The risk of preterm birth increased 4.2-fold among those who attended ≤ 4 times antenatal visiting than those who attended ≥ 5 times during the entire pregnancy period. The literature shows that that attending < 6 prenatal care visits was significantly associated with preterm labor [8]. It is worth noting that sufficient timely antenatal health care can be favorable in

## Analysis of the risk factors of preterm birth

**Table 6.** Comparison with complications during pregnancy between case group and control group

Items	Case group	Control group	$\chi^2$	P
	N (%)	N (%)		
PROM			73.486	0.000
yes	161 (26.1)	51 (10.1)		
no	289 (73.9)	395 (89.9)		
Anemia in the third trimester			22.783	0.001
yes	229 (57.8)	165 (40.9)		
No	167 (42.2)	238 (59.1)		
Pre-eclampsia			238 (59.1)	0.001
yes	26 (20.2)	4 (7.2)		
no	103 (79.8)	63 (92.8)		
Placenta previa			4.257	0.039
yes	18 (14.0)	3 (4.4)		
no	118 (86.0)	65 (95.6)		
Birth outcome			60.204	0.000
Singleton	397 (86.5)	457 (99.6)		
polyembryony	62 (13.5)	2 (0.4)		

**Table 7.** Regression for risk factor of preterm birth

Risk factors	P	OR	95% C.I.	
			upper	lower
Antenatal visiting times $\leq 4$	0.008	4.072	1.445	11.473
PROM	0.039	4.031	1.080	17.129
Placental previa	0.016	15.304	1.671	140.189

detecting and treatment of pregnant complications, especially for high risk group.

In this study, we show that the risk of preterm birth in 5 counties remains associated with treatable or preventable pregnancy complications. Studies have indicated that PROM occurred in 40% of preterm birth, while in this study the proportion was 35.9%, similar to other researches. PROM is mainly caused by infections and other harmful life habits, such as smoking or drinking. Many studies indicated that infections were the main factor leading to preterm birth [10, 11], about 40% preterm birth was related to infections. Intrauterine infection was the main infection and it was caused by lower genital tract infection commonly, such as bacterial vaginosis, chlamydia trachomatis infection, etc. Because of the limited condition in study areas, the survey only investigated symptoms of RTI like abnormal vaginal discharge. The results showed that 20.7% preterm birth cases are positive, it was higher than 13.3% in control group obviously. According to

the -Routine for maternal health care, vaginal discharge should be test if the pregnancy women were high risk group or having RTI symptoms. But in study spots, only 16.4% subjects who had RTI symptoms got diagnosis and treatment. So it needs to treat local health workers to improve the awareness and skills about RTI routine service. Logistic regression indicated that the risk of preterm birth increased 15.304-fold among those who with placenta previa than those who without placenta previa. Placenta previa was one of the serious complications which should timely termination of pregnancy, so it can be lead to iatrogenic preterm delivery.

Some reports have showed that the risk of preterm birth in gestational anemia women is 2-3 times than that of normal women.

According to the WHO diagnostic criteria, hemoglobin value  $\leq 110$  g/L makes the diagnosis of gestational anemia. In this study, the percent of anemia in the third trimester in case group was higher than that in control group; the difference was statistically significant (57.8% VS 40.9%). Although anemia during pregnancy was not in the logistic regression, but the rates of anemia during pregnancy in two groups were both very high. It is the similar rate with whole country's investigation in 1998 in rural areas (43.5%) and also higher than that in urban area (35.5%). So it was necessary to screening HB and treat in time at antenatal care.

The increasing rates of some important risk factors (e.g., low family income, advanced maternal age, education level, etc), and the interdependent effects (such as pregnancy complications, gestational anemia) of these constitute a major challenge in ensuring optimum pregnancy outcomes for women in 5 counties in western rural China. These factors also influence adverse maternal and infant

## Analysis of the risk factors of preterm birth

health outcomes. Thus, increased prevention strategies are likely to made far reaching effects on the health and wellbeing of the wider population in the western rural China.

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### Disclosure of conflict of interest

None.

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