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Pre-Pregnancy Health Status and Risk of Preterm Birth: A Large, Chinese, Rural, Population-Based Study

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Data Interpretation D
Manuscript Preparation E
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The aim of this study was to estimate the incidence of preterm birth (PTB) and identify maternal risk factors before pregnancy in rural China, and to determine their population-attributable fractions (PAFs).

A prospectively population-based study was conducted in the city of Fuyang, China. Surveillance locations were randomly selected by cluster sampling based on administrative areas and geographic characteristics. Data were collected through interview questionnaires and medical examination records from the participants, then follow-up until discharge, fetus death, or at a maximum of 6 weeks postpartum, whichever came first. We used logistic regression analysis to identify the associated factors. PAFs were also estimated to examine the impact of risk factors.

The incidence of PTB was 3.86% in this study. Multivariate analyses showed that risk factors for PTB were economic pressure (aOR=2.98, 95% CI, 2.40–3.71), hypertension (aOR=3.45, 95% CI, 2.23–5.36), hypoglycemia (aOR=2.07, 95% CI, 1.58, 2.72), hyperglycemia (aOR=1.69, 95% CI, 1.09, 2.62), serum creatinine (<44 μmol/L) (aOR=1.78, 95% CI, 1.13–2.40), hypothyroidism (aOR=1.37, 95% CI, 1.06–1.78), positivity for anti-CMV IgM (aOR=2.57, 95% CI, 1.21–5.45), multiple pregnancy (aOR=3.35, 95% CI, 1.87–6.00), and parity (≥3 times) (aOR=1.67, 95% CI, 1.05–2.64). Economic pressure was the most significant contributor (11.57%), while parity was the lowest (0.10%).

This study demonstrated the relatively high burden of PTBs in a rural Chinese area. A broader focus on the risk factors prior to pregnancy amenable to interventions of women may reduce the incidence of PTB.

MeSH Keywords: **Incidence • Pregnancy • Premature Birth • Risk Factors • Rural Population**

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Background

Preterm birth (PTB), defined as birth before 37 weeks of gestation, is currently a major public health concern and affects 5–18% of pregnancies [1]. It is the leading cause of neonatal death, the second leading cause of childhood death below the age of 5 years, and accounts for approximately half of long-term neurodevelopmental disabilities [2]. A recent systematic review has estimated that 12.9 million births, or 9.6% of all births worldwide, were preterm, of which approximately 11.9 million (92.3%) were in Africa, Asia, Latin America, and the Caribbean, where health systems are relatively weak and access to and utilization of health services are limited [3]. Approximately one-third of preterm survivors suffer from severe long-term neurological disabilities such as cerebral palsy or mental retardation [4], and preterm infants also carry increased risk of a range of neurodevelopmental impairments and disabilities, including behavioral problems, learning difficulties, chronic lung disease, retinopathy of prematurity, hearing impairment, and lower growth attainment [5]. Furthermore, PTB affects not only infants but also their families, who may have to spend substantial time and money to care for their preterm infants [6]. It was reported that the incidence of PTB was 7.1% in mainland China in 2011, and approximately 70 million reproductive-age women live in rural China [7]. Due to the relatively poor health services, economic, and social development, PTB is a major public health concern in rural China.

At present, most of the risk factors associated with PTB have not been identified as causal factors [8]. A history of PTB is always thought to be the strongest predictor of prematurity [9]. Risk factors for PTB include: infections during the period of pregnancy [10,11]; the uterus's structural abnormalities, such as insufficiency of the cervix [12]; some lifestyle conditions, including standing work or strenuous work, and habits such as alcohol consumption, illicit drugs consumption, and smoking [13]; advanced and young maternal age; short interval of inter-pregnancy; low body mass index (BMI) [2]; and multiple pregnancies [14]. However, the effects of maternal pre-pregnancy health status on pregnancy outcomes have not been well examined in rural China and are now receiving increased attention.

The purposes of this large, Chinese, rural, population-based study were to evaluate the incidence of PTB, and to identify the at-risk women and their risk factors associated with PTB. All these works are important for targeting of services and initiating risk-specific interventions and preventions, and study of risk factors may also provide important insights leading to new discoveries for prevention and management of PTBs.

Material and Methods

Study setting

Fuyang is the largest city in Anhui province, China, with an estimated overall population of 10.12 million residents, of which 79.5% residents hold rural household registration [15]. Health care for reproductive-age women and children is an integral part of the three-tier rural health care system, and the health care system in Fuyang city assures the performance of relevant research. Married couples who intend to conceive apply for a family planning service card at the local Family Planning Service Station (FPSS) and then are registered.

Study design and population

We conducted a population-based follow-up study from August 2010 to July 2013 in rural Fuyang city, China. Several surveillance spots were randomly selected by cluster sampling based on the administrative areas and geographic characteristics, because of their relatively complete service system for maternal and child health care. All women who applied for a family planning service card in the selected surveillance locations were invited to participate in the study if they: 1) complied with the local family planning policy and agreed to participate in the study; 2) hold rural household registration; 3) could be contacted by telephone or provided a permanent home address for follow-up. Participants who did not become pregnant after attending participating in the interviewed questionnaire within a year in the analysis were excluded from the analysis.

After obtaining informed consent, all eligible women were interviewed using a standardized questionnaire, and then underwent a set of physical and laboratory examinations. After that, all eligible women were followed up until fetus death or discharge in 2 weeks or at a maximum of 6 weeks postpartum, whichever came first. To assure the quality of data collection, teams of gynecological doctors, laboratory technicians, and health workers who participated in this study were trained together. Before the data collection, we held a meeting with all participating staff in order to standardize the procedures and processes of participant enrollment, data collection, and study management. Our research team also received electronic feedback while they are collecting the data during the study period in order to solve some specific problems. The data were double-checked after each questionnaire was finished to evaluate the consistency and completeness, and then the data were entered into the electronic database.

Variables

The following baseline information was collected using a standard questionnaire by trained staff in the first face-to-face

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interviews in the local FPSSs: socio-demographic data; lifestyle and habits (self-reported smoking, alcohol consumption); family history; clinical history; reproductive and obstetrical history, especially the history of adverse pregnancy outcomes, including PTB, spontaneous abortion, induced abortion, stillbirth, newborn with defect, and ectopic pregnancy; and economic pressure assessed by per capita net income of rural households. Ethnic minorities in China are the non-Han Chinese population in the People's Republic of China (PRC); China officially recognizes 55 ethnic minority groups within China in addition to the Han majority [16]. Cigarette smoking was defined as smoking ≥1 cigarettes/day over the past 6 months and alcohol consumption was defined as ≥1 more drinks/week (each time ≥50 g) over the past 6 months; family genetic diseases or maternal congenital defects were defined as the mother or within 3 generations suffered from thalassemia, favism, achromatopsia, hypochromatopsia, thrombocytopenia, Down syndrome, or hyperdactylia. Economic pressure was defined as per capita net income of rural households <3000 Chinese yuan (461.5 US dollars) (annual per capital income of rural Fuyang population in 2010) [17]. All of these variables were self-reported.

In the physical examination section, body weight and height were measured with participants wearing light, indoor clothing, and no shoes, according to a standardized protocol. Body mass index (BMI) was calculated and then categorized into 4 groups [18]: underweight (<18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), overweight (24.0–27.9 kg/m^2), and obese (≥28.0 kg/m^2). Blood pressure and heart rate were measured by trained gynecologists.

In the laboratory tests section, information was obtained about anemia, fasting blood-glucose (FBG), thyroid-stimulating hormone (TSH), liver function test (alanine aminotransferase), renal function examination [serum creatinine (Scr)], urinary tract infection, reproductive tract infections (RTIs) [*Candida albicans*, bacterial vaginosis (BV), *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Treponema pallidum*], cytomegalovirus (CMV), and *Toxoplasma gondii* (TOX).

The second interview was conducted to collect information about folic acid intake and gestational week (as estimated based on early pregnancy symptoms, pregnancy tests, and B-mode ultrasound tests when they came to the local FPSSs or maternal and child care service centers) to confirm the pregnancy status or when attending their first antenatal care visit.

All the information in the section on pregnancy outcomes in the questionnaire was abstracted from the hospital information system. The main dependent variable of interest was PTB (either therapeutic or spontaneous), and other pregnancy outcomes, maternal age at delivery, the number of birth (if multiple births, each baby's information was recorded), gestational weeks were also collected. Delivery at ≥37 weeks was classified as term birth, and preterm birth was defined as babies born alive before 37 weeks of pregnancy, and was sub-categorized as: 1) extremely preterm (<28 weeks), 2) very preterm (28 to <32 weeks), 3) moderately preterm (32 to <34 weeks), and 4) late preterm (34 to <37 weeks) [7,19].

Laboratory methods

Vaginal wet mounts were examined for evidence of candidiasis [20]. BV was diagnosed using the Amsel test [21]. Trichomoniasis was considered to be present if microscopic examination revealed trichomonas [20]. The diagnosis of syphilis was made first by the rapid plasma reagin test, and if the results were positive, then Treponema pallidum particle agglutination (TPPA) was specifically used to detect the patient's immune response to syphilis to make the results more accurate and credible [22]. The diagnosis of *Chlamydia trachomatis* and *gonorrhoeae* infection was determined by latex immune chromatography.

All the serum samples were tested by a quantitative enzyme-linked immunosorbent assay kit for anti-CMV IgM and anti-TOX IgM. Bioelectrical impedance analysis was performed for hemoglobin. The FBG was determined by hexokinase method, glutamic-pyruvic transaminase by rate method, Scr by picric acid method, and urinary tract infection by dry chemical test method. The level of TSH was detected with electrochemiluminescence immunoassay.

The WHO defines anemia for non-pregnant women (15 years of age and above) as hemoglobin (Hb) concentrations <120 g/L [23]. Hypertension was defined as systolic blood pressure ≥140 mmHg, and/or diastolic blood pressure ≥90 mmHg; hypotension was systolic blood pressure ≤90 mm Hg, and/or diastolic blood pressure ≤60 mm Hg; hyperglycemia was defined as a FBG level of >6.1 mmol/L; hypoglycemia was defined as a FBG level of <3.9 mmol/L; hyperthyroidism was defined as a current serum TSH level of ≤0.27 μIU/ml; and hypothyroidism was defined as a current serum TSH level of >4.2 μIU/ml. The normal range of Scr was 44–80 μmol/L and all other results of laboratory tests were defined according to the manufacturer's instructions.

Ethics approval

All procedures performed in this study involving human participants were in accordance with the ethics standards of the Research Ethics Committee of Anhui Medical University (#060230060).

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Statistical analysis

A quantitative database was set up using EpiData 3.1 software (EpiData Foreningen [EpiData Association], Odense, Denmark), and data were entered by 2 trained staff members separately and were cross-checked again to assure data accuracy. All statistical analyses were performed with SPSS version 10.01 (Statistical Product and Service Solutions, Chicago, IL). We estimated the incidence of PTB by dividing all live preterm births – whether singleton, twins, or higher-order multiples – by all live births in the population. The risk factors for PTB were identified using univariate and multivariate logistic regression models, and univariate analysis was applied to evaluate associations between independent variables and PTB. To highlight the important risk factors for PTB, multivariate regression analysis was conducted and all the variables displaying significant relationships with PTB in the univariate analysis were entered into the model (forward Wald model). For the logistic regression, results are reported as odds ratios (ORs) and 95% confidence intervals (CIs) along with P values. In all tests, $P<0.05$ was considered to be statistically significant.

In this study, the population-attributable fraction (PAF) was interpretable as the proportion of PTB that would be prevented following elimination of one or more specified antecedents, assuming the exposures are causal. PAF was estimated based on the formula: $PAF=p(OR-1)/(1+p(OR-1))$ [24]. The formula requires that we know the proportion (p) of the at-risk population exposed to the factor of interest and also the OR of disease in the exposed fraction of the population over the period of interest.

Results

Over the course of 35 months, the study population consisted of 16 983 pregnant women, including 656 cases the resulted in PTB (Figure 1). The incidence of PTB was 3.86%, and 20.58% of preterm births were very preterm.

Compared to term births, maternal age 30–34 years, ethnic minority, alcohol consumption, and economic pressure were significantly associated with PTB (Table 1). No associations were found between PTB and other factors, including occupation, education level, and folic acid intake. Since there were only women actively smoking, we excluded this variables from the study population (not listed in Table 1).

Table 2 shows that parity and multiple pregnancies were significantly associated with PTB. Of the 16 983 women available for analysis, 8317 women (48.97%) had a history of pregnancy and included 7910 term births and 406 PTBs. History of adverse pregnancy outcomes, especially PTB history, was not

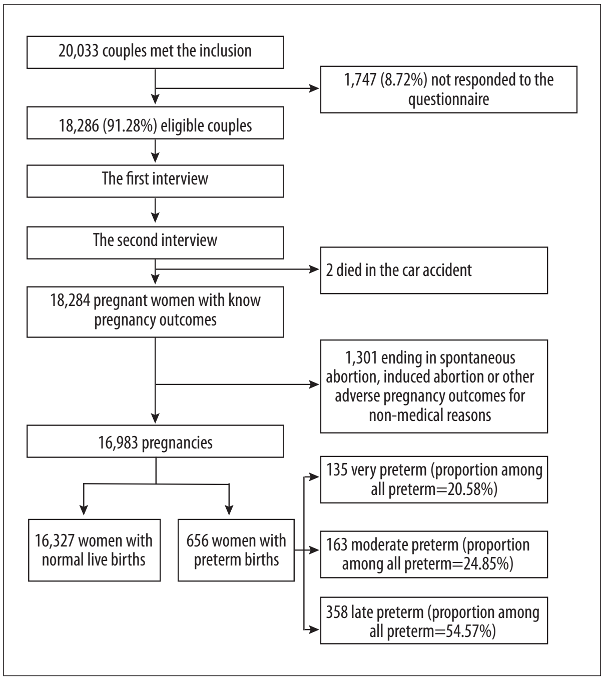

Figure 1. Study profile.

significantly associated with PTB among multiparas. Table 2 also shows that in physical examinations, hypertension and heart rate >100 were all associated with an increased risk of PTB. In addition, the analysis of pre-pregnancy BMI shows that, compared with normal weight, both overweight and obesity were associated with PTB. On the other hand, maternal congenital defects or family genetic diseases were not significantly associated with PTB.

The assessments of maternal laboratory examination and virus screening are shown in Table 3. Anemia, hypothyroidism, and positive anti-CMV IgM before pregnancy were associated with an increased risk of PTB. Fasting blood glucose and Scr below or above the normal range were both associated an increased risk of PTB. Urinary tract infection, alanine aminotransferase, reproductive tract infections, and positive anti-TOX IgM were not significantly associated with PTB.

Table 4 presents the results of multiple logistic regression analysis with 16 983 women: multiple pregnancy, hypertension, economic pressure, positive anti-CMV IgM, Scr <44 μmol/L, parity ≥3, and hypothyroidism were identified as independent risk factors for PTB. Both hyperglycemia and hypoglycemia were also described as risk factors associated with a higher proportion of PTBs. Maternal age, pre-pregnancy BMI, anemia, heart rate, and positive anti-CMV IgM became non-significant after being entered into the multiple logistic regression model.

The PAFs identified economic pressure as the most important significant contributor to PTB (11.57%), followed by

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Table 1. Risk estimates for preterm birth according to some maternal socio-demographic, dietary habit, behavioural characteristics, and social psychological factors, comparing women who delivered prematurely and women who delivered at term.

Variables	Total sample	Preterm birth	
	n (%)	n (%)	OR (95% CI)
Maternal age (years)			
<20	1504 (8.85)	64 (9.76)	1.18 (0.88–1.57)
20–24	8839 (52.05)	327 (49.85)	1.02 (0.85–1.22)
25–29	5405 (31.82)	197 (30.03)	Ref.
≥30	1235 (7.28)	68 (10.36)	**1.54 (1.16–2.04)**
Ethnic group			
The Han	16940 (99.75)	650 (99.09)	Ref.
The ethnic minorities[a]	43 (0.25)	6 (0.91)	**4.06 (1.71–9.66)**
Occupation			
Farmer	16841 (99.16)	652 (99.39)	Ref.
Others[b]	142 (0.84)	4 (0.61)	0.72 (0.27–1.95)
Education level			
≤6 years	91 (0.54)	7 (1.07)	Ref.
6–9 years	16743 (98.5)	644 (98.17)	0.48 (0.22–1.04)
>9 years	149 (0.88)	5 (0.76)	0.42 (0.13–1.35)
Alcohol consumption			
No	16783 (98.82)	642 (97.87)	Ref.
Yes	200 (1.18)	14 (2.13)	**1.89 (1.09–3.28)**
Economic pressure			
No	15860 (93.39)	536 (81.71)	Ref.
Yes	1123 (6.61)	120 (18.29)	**3.42 (2.78–4.21)**
Folic acid consumption[c]			
No consumption	8920 (53.50)	344 (52.76)	Ref.
≥3 months before the cessation of menstruation	3498 (20.98)	125 (19.17)	0.92 (0.75–1.14)
1–2 months before the cessation of menstruation	1458 (8.75)	52 (7.98)	0.92 (0.69–1.24)
After the cessation of menstruation	2796 (16.77)	131 (20.09)	1.23 (0.10–1.51)

Values in bold mean they are statistically significant. OR – odds ratio; CI – confidence interval. [a] The ethnic minorities included all the other ethnic groups except Han; [b] included worker, businessman, etc.; [c] 311 missing.

FBG (6.83%). On the other hand, the PAFs of parity (≥3 times) was lowest, at just 0.10%. The sum of PAFs of FBG, blood pressure, Scr, and TSH was 16.08%.

Discussion

We have presented the incidence of PTB and its risk factors using prospectively collected data from a population-based follow-up study. The incidence of PTB was 3.86%, which is similar to the result in another rural population of Liuyang city, China (4.13%) [25]. However, the true incidence of PTB might

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Table 2. Risk estimates for preterm birth according to some maternal obstetric history and physical examination, comparing women who delivered prematurely and women who delivered at term.

Variables	Total sample		Preterm birth			
	n (%)		n (%)		OR (95% CI)	
Menarche age (years)						
<13	774	(4.56)	37	(5.64)	1.27	(0.90–1.78)
13–18	16167	(95.20)	616	(93.90)	Ref.	
>18	42	(0.24)	3	(0.46)	1.94	(0.60–6.30)
Parity (times)						
0	8666	(51.02)	250	(38.11)	0.59	(0.51–0.70)
1–2	8063	(47.48)	384	(58.54)	Ref.	
≥3	254	(1.50)	22	(3.35)	**1.90**	**(1.21–2.97)**
History of preterm birth*						
No	8284	(99.60)	402	(99.01)	Ref.	
Yes	33	(0.40)	4	(0.99)	2.70	(0.95–7.73)
History of stillbirth or abortion*						
No	6569	(78.99)	324	(79.80)	Ref.	
Yes	1747	(21.01)	82	(20.20)	0.95	(0.74–1.22)
Newborn with defect*						
No	8260	(99.31)	403	(99.26)	Ref.	
Yes	57	(0.69)	3	(0.74)	1.08	(0.34–3.48)
Multiple pregnancy						
No	16872	(99.35)	642	(97.87)	Ref.	
Yes	111	(0.65)	14	(2.13)	**3.65**	**(2.07–6.43)**
BMI (kg/m²)						
Underweight	1947	(11.46)	78	(11.89)	1.10	(0.86–1.40)
Normal weight	13050	(76.84)	479	(73.02)	Ref.	
Overweight	1649	(9.71)	79	(12.04)	**1.32**	**(1.04–1.69)**
Obesity	337	(1.98)	20	(3.05)	**1.66**	**(1.04–2.63)**
Blood pressure						
Hypotension	393	(2.31)	21	(3.20)	1.47	(0.94–2.29)
Normotension	16418	(96.67)	609	(92.84)	Ref.	
Hypertension	172	(1.01)	26	(3.96)	**4.62**	**(3.02–7.07)**
Heart rate (times/minute)						
<60	16	(0.09)	1	(0.15)	1.69	(0.22–12.79)
60–100	16755	(98.66)	637	(97.10)	Ref.	
>100	212	(1.25)	18	(2.74)	**2.35**	**(1.44–3.83)**
Family genetic diseases or maternal congenital defects						
No	16908	(99.56)	650	(99.01)	Ref.	
Yes	75	(0.44)	6	(0.91)	2.18	(0.94–5.03)

Values in bold mean they are statistically significant. BMI – body mass index; OR – odds ratio; CI – confidence interval. * Excluded primigravida from the analysis.

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Table 3. Risk estimates for preterm birth according to some maternal laboratory examination and virus screening, comparing women who delivered prematurely and women who delivered at term.

Variables	Total sample	Preterm birth	
	n (%)	n (%)	OR (95% CI)
Pregestational anemia (g/L)			
No	14472 (85.21)	535 (81.55)	Ref.
Yes	2511 (14.79)	121 (18.45)	**1.32 (1.08–1.61)**
FBG			
Normal	15722 (92.57)	568 (86.59)	Ref.
Hypoglycemia	893 (5.26)	65 (9.91)	**2.10 (1.61–2.73)**
Hyperglycemia	368 (2.20)	23 (3.50)	**1.78 (1.16–2.74)**
Urinary tract infection			
No	14668 (86.37)	565 (86.13)	Ref.
Yes	2315 (13.63)	91 (13.07)	1.02 (0.82–1.28)
TSH			
Normal	15544 (91.53)	579 (88.26)	Ref.
Hyperthyroidism	198 (1.17)	6 (0.91)	0.81 (0.36–1.83)
Hypothyroidism	1241 (7.31)	71 (10.83)	**1.57 (1.22–2.02)**
ALT (U/L)			
0–35	15757 (92.78)	613 (93.45)	Ref.
>35	1226 (7.22)	43 (6.55)	0.90 (0.66–1.23)
Scr (μmol/L)			
<44	957 (5.64)	54 (8.23)	**1.68 (1.25–2.25)**
44–80	12264 (72.21)	422 (64.33)	Ref.
>80	3762 (22.15)	180 (27.44)	**1.41 (1.18–1.69)**
RTIs			
No	15840 (93.27)	600 (91.46)	Ref.
Yes	1143 (6.73)	56 (8.54)	1.31 (0.99–1.73)
Anti-CMV IgM			
No	16906 (99.55)	648 (98.78)	Ref.
Yes	77 (0.45)	8 (1.22)	**2.11 (1.11–4.00)**
Anti-TOX IgM			
No	16954 (99.83)	655 (99.85)	Ref.
Yes	29 (0.17)	1 (0.15)	0.75 (0.14–3.92)

OR – odds ratio; CI – confidence interval; FBG – fasting blood-glucose; TSH – thyroid stimulating hormone; ALT – alanine aminotransferase; Scr – serum creatinine; RITs – reproductive tract infections; CMV – cytomegalovirus; TOX – toxoplasma gondii.

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Table 4. Multivariate analyses of factors and its partial population attributable independently risk associated with preterm birth.

Variables	P-value	aOR (95% CI)	PAF (%)
Economic pressure (Ref.: "No")	<0.001	**2.98 (2.40–3.71)**	11.57
Blood pressure			
Hypotension	0.466	1.18 (0.75–1.87)	
Normal		Ref.	
Hypertension	<0.001	**3.45 (2.23–5.36)**	2.41
FBG			
Hypoglycemia	<0.001	**2.07 (1.58–2.72)**	5.33
Normal		Ref.	
Hyperglycemia	0.020	**1.69 (1.09–2.62)**	1.50
Scr (μmol/L)			
<44	<0.001	**1.78 (1.33–2.40)**	4.21
44–80		Ref.	
>80	0.123	1.16 (0.96–1.39)	
TSH			
Hyperthyroidism	0.424	0.71 (0.31–1.63)	
		Ref.	
Hypothyroidism	0.018	**1.37 (1.06–1.78)**	2.63
Anti-CMV IgM	0.014	**2.57 (1.21–5.45)**	0.70
Parity (times)			
Nulliparous	<0.001	0.61 (0.51–0.71)	
1–2		Ref.	
≥3	0.031	**1.67 (1.05–2.64)**	0.10
Multiple pregnancy (Ref.: "singleton")	<0.001	**3.35 (1.87–6.00)**	1.51

Bold type indicates a statistically significant result. aOR – adjusted odds ratio; CI – confidence interval; FBG – fasting blood-glucose; Scr – serum creatinine; TSH – thyroid stimulating hormone; CMV – cytomegalovirus; PAF – population attributable risk.

be higher than reported here, because records are poor in rural hospitals and some preterm births between 20 and 28 weeks are not consistently recorded, even though these preterm newborns survive [7]. On the other hand, the accuracy of the obtained data in the rural hospitals may influence the PTB rate, and another potential selection bias is that women included in this study are women seeking family planning, which may show a differentiated, more health-conscious population, possibly with lower risk factors for PTB. Previous studies conducted in Anhui province, China reported the incidence of PTB was closed to 5.50% [26,27]. In this study, the proportion of very preterm birth was 20.58% in the total preterm births and no extremely preterm birth was reported. As we all know, very preterm birth has been reported to be the most frequent cause of neonatal mortality and a primary contributor to long-term neurological and pulmonary disorders in children [19], contributing 57.9% of preterm neonatal deaths in China [7]. To improve the outcomes of neonates born preterm, it is important to focus on the incidence of very preterm birth. More interesting, the smoking rate in this study was low (0.10%), and can be explained by the following ways. Firstly, the Chinese government has recently implemented a strict ban on smoking in public places, and with the help of public education, more and more populations chose to stop smoking as they realized the detrimental effect of smoking. Secondly, the female smoking rate is only 2.60% in the Chinese mainland and a 2013 study conducted in Jiangxi province, which borders Anhui province, revealed that the smoking rate of women was 1.46% [28]. Our study was

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conducted in rural areas of Anhui, and we speculate that the rate was lower because of the influence of Chinese conservative traditional culture, in which few women choose to smoke, as almost all of them think that smoking is a bad behavior.

In this study, we focused on many predictors, and the results showed that the identified factors associated with PTB were also in accordance with most similar studies. PAFs identified economic pressure as the most important significant contributor. Household income was intimately linked to the times of prenatal care visits, which was associated with PTB [29]. Combined with the current situation of China, we advise having a policy that prenatal care can be considered in the free medical service list, just as free premarital medical examinations are.

Blood pressure, FBG, TSH, and renal function examinations are important indexes in the evaluation of maternal pre-pregnancy health status. In accordance with previous studies [30–32], the present study demonstrated that hypoglycemia/hyperglycemia, hypertension, hypothyroidism, and renal function (Scr <44 μmol/L) significantly increased the risk of PTB. Regarding occupation, 98.58% of the eligible women were farmers, and long-term performance of field work affects maternal health status. Given that these variables accounted for half of the predictors, and the total PAFs was 16.08%, it is necessary to introduce a policy that requires healthy women to have a pre-pregnancy physical examination when applying for a family planning service card.

The findings of this study show that cytomegalovirus infection prior to conception may have effects on PTB. Combined with previous research results showing that maternal CMV infection during pregnancy might be a risk factor for adverse pregnancy/neonatal outcomes, and congenital cytomegalovirus infection may cause deafness in neonates [33], our analysis on the role of cytomegalovirus infection supports the suggestion that screening and treatment of CMV infection is accepted into the one of the pre-pregnancy health policies. A positive anti-CMV IgM result indicates a recent infection, and if reproductive-aged women are diagnosed with CMV infection in conjunction with clinical presentation, patient history, and other laboratory findings, doctors should advise some specific treatments or wait until after the anti-CMV IgM changed to negative before couples consider pregnancy. These measures may decrease the risk of PTB.

Our results confirmed previous findings that multiple pregnancies increased the risk of PTB [6,34]. In addition, our study showed that parity of 3 may increase the risk of PTB, which is consistent with a previous study [34]. Thanks to family planning practiced by the rural population, the PAFs of parity (≥3) was just 0.10%. Still, the findings suggest that it may be effective to reduce the parity to protect pregnant women from the elevated risk of PTB. Interestingly, we found that a history of PTB, a well-studied risk factor for PTB, was not associated with PTB in this study, which is inconsistent with other studies [1,35]. It can be speculated that because information about history of PTB was self-reported, we cannot avoid recall bias. On the other hand, most of the eligible pregnant women (98.5%) only had a junior high school (6–9 years) education level, and it may be hard for them to report that whether their infants were born preterm or to accurately recall weeks of gestation. We evaluated the prematurity of spontaneous and provider initiated together because we had no available data provided by the hospitals with which to differentiate the prematurity, and this could bias the estimates towards the null hypothesis.

It is also interesting that there were so few prior PTBs in this cohort population. One possible explanation is due to the regulation and restriction of family planning/One Child policy in China, the proportion of women with no or little prior birth history was most likely much larger in this setting. Another previous study demonstrated that 25% of women forget their reproductive history even if their received a good education [36].

The strengths of this study included its prospectively population-based follow-up design, the large dataset which was prospectively collected, and a relative complete battery of laboratory tests. Of note, except for 2 participants who died in a car accident, all the participants responded to the questionnaire and completed the follow-up period in this large population-based study, which ensured the quality of this study. In addition, pre-pregnancy health status was assessed by trained doctors rather than self-reported in our study. For example, weight and height were assessed using standardized measurements prior to pregnancy instead of recall after pregnancy or delivery. These health status measures have been shown to be reliable during a 1-year period [37]. However, there are some limitations in the study that we need to acknowledged. Firstly, as previously stated, 8.72% of eligible women refused to respond to the questionnaire, and the variable of folic acid intake had missing data; we believe that this may represent a selection bias. Secondly, some physical examination measures such as blood glucose, blood pressure, and heart rate were assessed just one time, and the results are not perfectly accurate. Thirdly, the study was limited to a single city and specific geographic area of China, and the findings of this study were not sufficient to generalizing to all Chinese pregnant women. Finally, as with any observational study, we cannot exclude the possibility of unmeasured confounding or residual effects. However, we are reassured by similar findings in different racial/ethnic populations in our cohort and in previous studies in other areas.

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Conclusions

This study demonstrated the relatively high burden of preterm births in a Chinese rural area. Moreover, we also found that multiple risk factors prior to pregnancy, especially economic pressure and health status, were associated with PTB and some of them may be preventable or treatable in rural China, which may be useful as guidance for future prevention strategies towards health policies. Effectively decreasing the incidence of PTB may require attention to the risk factors amenable to interventions for women before pregnancy.

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Conflict of interest

None.

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