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Prevalence, risk factors, and adverse perinatal outcomes in Chinese women with preeclampsia: a large retrospective cohort study

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Abstract

Background Preeclampsia (PE) is the primary cause of maternal and neonatal morbidity and mortality. However, comprehensive studies on the related risk factors with PE and its effects on adverse perinatal outcomes are limited. This study aimed to evaluate the prevalence, risk factors, and adverse perinatal outcomes in Chinese women with preeclampsia.

Methods We conducted a retrospective cohort study from January 1, 2018, to December 31, 2019, which enrolled 38,496 women without preeclampsia (non-PE) and 1130 women with PE. Univariate and multivariate logistic regression models were used to determine the risk factors and adverse perinatal outcomes of PE.

Results Multivariate logistic regression models showed that maternal age > 35 years, pp-BMI overweight/obesity, excessive gestational weight gain, multiparity, twin pregnancy, IVF, cesarean section history, times of abortion history ≥ 2, GDM, and ICP were significantly associated with the risk of PE (all $P < 0.05$). Women with PE in singleton pregnancies were associated with an increased risk of maternal outcomes of cesarean section, and preterm birth, and a higher risk of neonatal outcomes of stillbirth, low birth weight, fetal distress, neonatal asphyxia, and neonatal unit admission, which were also observed in women with PE in twin pregnancies, except for stillbirth and neonatal asphyxia.

Conclusion This study identified the risk factors and associated adverse perinatal outcomes of PE, which providing comprehensive evidence for clinicians to manage women at risk of PE.

Keywords Preeclampsia, Prevalence, Risk factors, Adverse perinatal outcomes

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Background

Preeclampsia (PE), a major pregnancy-specific complication worldwide, is the primary cause of maternal and neonatal morbidity and mortality [1–3]. PE manifests as new-onset or de novo hypertension, with or without proteinuria, or end-organ injury after 20 weeks of gestation [4]. The global incidence of PE is estimated at 3–5% [5]. In China, it affects 4.02–5.22% of all pregnancies [6, 7]. PE is associated with adverse maternal and fetal outcomes, including cesarean section, preterm birth, postpartum hemorrhage, pregnancy-induced hypertension, fetal growth restriction, stillbirth, and perinatal and maternal death. Moreover, PE is related to long-term effects following delivery, specifically cardiovascular disease in mothers, thereby influencing maternal and fetal health [2, 8–11].

The etiology of PE is complex, Research on the cause of PE has recently gained much attention internationally, and the roles of maternal and fetal genetic factors, placental dysplasia, and insufficient blood supply have been reported [8, 11–13], early family-based studies suggested that genetic determinants from maternal and fetal and/or paternal may play an important role [14, 15]. However, the etiology of PE is not completely understood, although previous reports have identified some risk factors of PE, including pre-gestational hypertension and diabetes, advanced maternal age, history of PE, multiple pregnancies, pre-gestational diabetes and hypertension, obesity, use of assisted reproductive technology, and nulliparity [10, 16, 17]. Additionally, Some recent studies with small samples have shown that intrahepatic cholestasis of pregnancy (ICP) can increase the risk of preeclampsia [18, 19]. It is worth noting that most of the previous studies were small populations studies and paid few attention to Chinese population. However, the many racial and ethnic differences that were noted in reported studies [20, 21], comprehensive researches on the risk factors related to PE and its effect on adverse maternal and fetal outcomes based-on Chinese population are limited. Therefore, here, we performed a comprehensive and lager scale cross-sectional retrospective analysis to investigate the risk factors of PE and the relationship between PE and maternal and neonatal outcomes in Chinese population.

Methods

Study design and population

A large retrospective cohort study was carried out of in which women diagnosed with PE were compared with those without PE from January 1, 2018, to December 31, 2019. This study was conducted at a large tertiary obstetrics and gynecology hospital in eastern China, which has a lot of highly professional obstetricians and gynecologists and and professional pregnancy management procedures. The Ethics Committee of the hospital approved this study protocol (approval no: IRB-20230095-R), written informed consent was not required due to the study's retrospective nature, and the dataset is unavailable to protect patient privacy.

All pregnant women aged 18 to 55 years who delivered a singleton or twin babies at ≥ 22 weeks of gestation were enrolled. The inclusion criteria were as follows: (a) pregnant women aged ≥ 18 years and delivered singleton or twin babies at ≥ 22 weeks of gestation; (b) singleton and twin pregnancies. The exclusion criteria were as follows: (a) triplet pregnancies, (b) fetal chromosomal abnormalities, and (c) pre-gestational diabetes mellitus, chronic hypertension, heart disease, or renal disease. Overall, 1387 women (3.38%) were excluded, and 39,626 were enrolled in the final study analysis. Participants included 38,016 women with singleton pregnancies (994 women with PE) and 1,610 women with twin pregnancies (136 women with PE) (Fig. 1). Demographic information (including maternal age, pre-pregnancy body mass index (pp-BMI), education, occupational physical activity, gestational weight gain (GWG), parity, number of pregnancies, in vitro fertilization (IVF), cesarean section history, abortion history, HBsAg status, thyroid disease, gestational diabetes mellitus (GDM), and ICP, adverse perinatal outcomes (maternal and neonatal outcomes), and laboratory data for each woman were extracted from the hospital's computerized medical record system. The diagnostic information of the women in the medical record system were determined by experienced obstetricians and the general information of pregnant women was recorded in the medical system after professional inquiry.

Diagnostic criteria of PE, ICP and GDM

In the present study, PE was defined according to the American College of Obstetrics and Gynecology criteria, published in 2013 [22]. PE was defined as follows: (1) blood pressure values of ≥ 140/90 mm Hg; (2) accompanied by proteinuria (0.3 g protein in a 24-h urine specimen first diagnosed at > 20 weeks of gestation) or elevated liver enzyme or kidney dysfunction. ICP was defined as follows: (1) unexplained pruritus occurring during pregnancy and (2) unexplained abnormal liver function and/or serum total bile acid (TBA) ≥ 10 μmol/L in pregnant women. GDM was diagnosed when any blood glucose value was greater than fasting blood glucose at 5.1 mmol/L or blood glucose after 1 h at 10.0 mmol/L or after 2 h at 8.5 mmol/L based on a 75-g oral glucose tolerance test (75 g OGTT).

Definitions of demographic and clinical characteristics

Maternal education and occupational physical activity levels were categorized according to a previous report [23]. Maternal BMI (weight in kilograms divided by height in meters squared) was calculated at the first

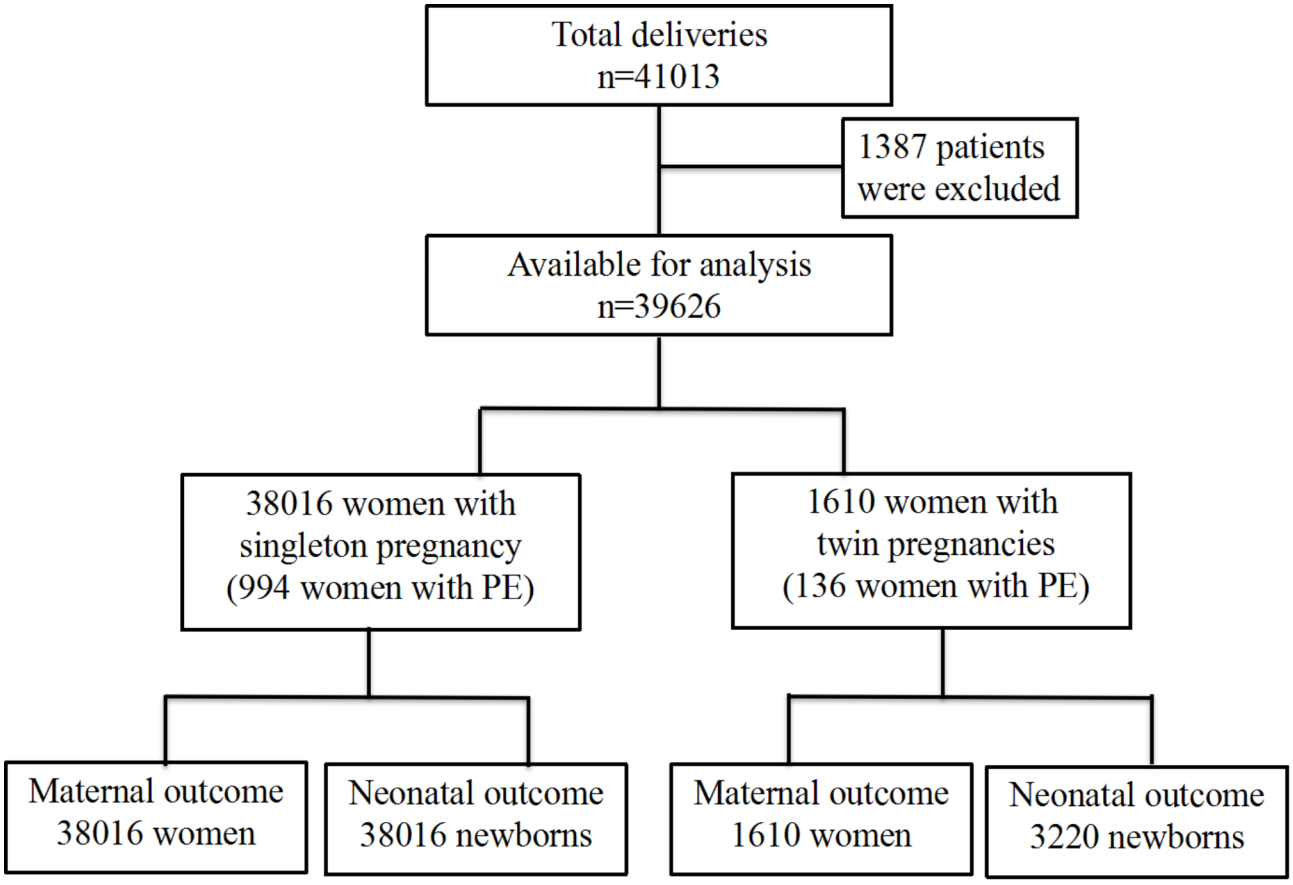

Fig. 1 Flowchart of the study population

prenatal care visit and classified using the World Health Organization (WHO) definition. The classification criteria of pp-BMI were based on the following WHO recommendations: underweight, < 18.5 kg/m^2; normal weight, 18.5–24.9 kg/m^2; overweight, 25.0–29.9 kg/m^2; obese, > 30.0 kg/m^2) [24]. According to the Institute of Medicine guidelines, GWG is divided into three categories: inadequate, adequate, and excessive. The Institute of Medicine recommends adequate GWG as follows: 12.5–18 kg/m^2 for pp-BMI < 18.5, 11.5–16 kg/m^2 for ppBMI 18.5–24.9, 7–11.5 kg/m^2 for ppBMI 25–29.9 kg/m^2.

Adverse perinatal outcomes

The perinatal outcomes investigated included maternal and neonatal outcomes. Maternal outcomes included cesarean section, pre-labor rupture of membranes, preterm birth, abruptio placentae, meconium amniotic fluid, and postpartum hemorrhage. Neonatal outcomes included stillbirth, macrosomia, low birth weight (LBW), fetal distress, neonatal asphyxia, and neonatal unit admission. Preterm birth was defined as delivery after 24 weeks and before 37 weeks of gestation. Postpartum hemorrhage was defined as blood loss ≥ 500 mL within 24 h after vaginal delivery or ≥ 1,000 mL after cesarean delivery. Macrosomia was defined as birth weight ≥ 4000 ×*g*, and LBW was defined as birth weight < 2500 g.

Statistical analysis

Descriptive comparisons were reported for demographic and clinical characteristics, in which $\chi 2$ and student t-tests were used for categorical and continuous variables, respectively. Univariate and multivariate logistic regression analyses were used to calculate crude and adjusted odds risks with 95% confidence intervals (CI) for PE, and possible confounding factors were considered, including the independent risk factors of PE and the association of PE with adverse perinatal outcomes. Maternal age, pre-pregnancy BMI, GWG, parity, number of pregnancies, IVF, cesarean section history, GDM, and ICP, were adjusted for in the multivariate regression models to determine the association between PE and perinatal outcomes. SPSS 23.0 (Armonk, NY, IBM Corp.) was used to analyze the data and statistical significance was accepted at a two-tailed P-value of < 0.05.

Results

The characteristics of the study population

The demographic and clinical characteristics of the women with ($n = 1130$) and without ($n = 38496$) PE are presented in Table 1. The overall prevalence of PE was 2.85%. Women with PE were significantly older than those without PE (31.96 ± 4.98 vs. 31.11 ± 4.39, $P < 0.001$), and the percentage of advanced maternal age (age > 35 years) in women with PE was significantly higher than in those without PE. The pp-BMI was higher in the PE group than in the non-PE group (22.81 ± 3.55 vs. 20.80 ± 2.70, $P < 0.05$), and the proportion of overweight and obese women in the PE group was higher than those in the non-PE group. In addition, we observed higher rates of excessive GWG, multiparity, twin pregnancy, IVF, and cesarean section history in women with PE than in those without PE. ($P < 0.05$). Furthermore, the rates of GDM and ICP were significantly higher in women with PE than in those without PE (GDM: 298 [26.37%] vs. 7164 [18.61%], $P < 0$ 0.001; ICP: 114 [10.09%] vs. 1386 [3.60%], $P < 0.001$).

Prevalence of PE stratified by age/pp-BMI, IVF, twin pregnancy, ICP, and GDM

The prevalence of PE according to age and pp-BMI is illustrated in Fig. 2. The prevalence of PE stratified by ppBMI (underweight, normal weight, overweight, or obese) was 1.3, 2.0, 6.3, and 12.7% among women aged < 25 years; 1.0, 2.2, 6.6, and 13.5% among women aged 25–34 years; and 1.0, 3.8, 9.3, and 16.5% among women aged ≥ 35 years, respectively. The prevalence of PE in women of different age groups increased significantly with an increase in BMI, especially in women aged > 35 years who were overweight or obese before pregnancy, and the prevalence of PE was significantly higher than that in the other two age groups. In addition, the prevalence of PE was significantly higher in women who underwent IVF and those who had twin pregnancies than in those who did not undergo IVF. Moreover, the prevalence of PE was significantly higher in women with GDM and ICP complications during pregnancy than in those without GDM and ICP. (Fig. 3, $P < 0.01$).

Risk factors for PE

Table 2 presented the crude and adjusted ORs of the association between the characteristics and PE risk are presented. Maternal age > 35 years was associated with a higher risk of PE than maternal age within 25–34 years (aOR = 1.44, 95% CI: 1.18–1.75). Regarding pp-BMI, women with overweight/obesity had more than two-fold (aOR = 2.34, 95% CI: 1.26–2.79)/five-fold (aOR = 5.67, 95% CI: 3.23–8.00) increased risk of PE compared with normal weight women; however, underweight was associated with a lower risk of PE (aOR = 0.65, 95% CI: 0.41–0.72). In addition, excessive GWG, multiparity, twin pregnancy, IVF, cesarean history, and times of abortion history ≥ 2 were significantly associated with increased risk of PE (all $P < 0.05$). Furthermore, women with GDM or ICP showed an increased risk of PE.

Association between singleton pregnancy and adverse perinatal outcomes of PE

The perinatal outcomes of singleton pregnancies were significantly associated with PE (Table 3). In the multivariate analyses, singleton pregnancy with PE was associated with a higher risk of maternal outcomes of cesarean section (aOR = 3.89, 95% CI: 3.16–4.33) and preterm birth (aOR = 4.98, 95% CI: 4.18–5.92), and neonatal outcomes of stillbirth (aOR = 4.32, 95% CI: 2.44–7.63), low birth weight (aOR = 7.40, 95% CI: 5.28–10.38), fetal distress (aOR = 1.20, 95% CI: 1.06–1.48), neonatal asphyxia (aOR = 2.11, 95% CI: 1.22–3.62), and neonatal unit admission (aOR = 5.21, 95% CI: 3.15–6.87). In addition, we observed that singleton pregnancy with PE had a significant reduction in the risk of PROM (aOR = 0.64, 95% CI: 0.51–0.80). Furthermore, there were no significant differences in placental abruption, meconium amniotic fluid, postpartum hemorrhage, and neonatal outcomes of macrosomia between singleton pregnancies with and without PE.

Associations between the perinatal outcomes of twin pregnancy and adverse perinatal outcomes of PE

The prevalence of PE is significantly higher in twin pregnancies than in singleton pregnancies. Therefore, we evaluated the impact of PE on perinatal outcomes in twin pregnancies. Twin pregnancy with PE had more than a four-fold and two-fold increased risk of maternal outcomes of cesarean section (aOR = 4.30, 95% CI: 1.84–10.28) and preterm birth (aOR = 2.90, 95% CI: 1.74–4.82), respectively, after multivariate analysis. Furthermore, twin pregnancies with PE are associated with an increased risk of neonatal outcomes such as low birth weight (aOR = 2.23, 95% CI: 1.50–2.71), fetal distress (aOR = 1.33, 95% CI: 1.13–1.99), and neonatal unit admission (aOR = 2.13, 95% CI: 1.67–3.03) than those without PE. In addition, we observed that twin pregnancies with PE had a significantly reduced risk of PROM (aOR = 0.26, 95% CI: 0.09–0.71). Furthermore, twin pregnancies with and without PE did not differ significantly in maternal outcomes (placental abruption, meconium amniotic fluid, and postpartum hemorrhage) or in neonatal outcomes (stillbirth, macrosomia, and neonatal asphyxia). (Table 4).

Table 1 Demographic description of the pregnant women according to PE

	Preeclampsia (*n* = 1130)	Non-preeclampsia (*n* = 38496)	*P* value
Maternal Age, mean (SD), years	31.96 ± 4.98	31.11 ± 4.39	< 0.001
Maternal Age category [n (%)] years			< 0.001
< 25	381(33.72)	15,291(39.72)	
25–34	405(35.84)	14,644(38.04)	
≥ 35	344(30.44)	8561(22.24)	
Pre-pregnancy BMI, mean (SD), (kg/m^2)	22.81 ± 3.55	20.80 ± 2.70	< 0.001
Pre-pregnancy BMI [n (%)] (kg/m^2)			< 0.001
Underweight (< 18.5)	99(8.76)	6767(17.58)	
Normal weight (18.5–24.9)	715(63.27)	26,416(68.62)	
Overweight (25.0-29.9)	207(18.32)	2378(6.18)	
Obesity(≥ 30)	39(3.45)	221(0.57)	
Data missing	70(6.20)	2714(7.05)	
Maternal education [n (%)]			< 0.001
Low	17(1.50)	219(0.57)	
Medium	301(26.64)	6106(15.86)	
High	781(69.12)	31,374(81.50)	
Data missing	31(2.74)	797(2.07)	
Occupational physical activity [n (%)]			< 0.001
Light	598(52.92)	24,445(63.50)	
Moderate	313(27.70)	7264(18.87)	
Active	188(16.64)	5990(15.56)	
Data missing	31(2.74)	797(2.07)	
Gestational weight gain [n (%)]			< 0.001
Inadequate	268(23.72)	9574(24.87)	
Adequate	245(21.68)	15,587(40.49)	
Excessive	446(39.47)	9994(25.96)	
Data missing	111(9.82)	3341(8.68)	
Parity [n (%)]			< 0.001
Primiparous	528 (34.83)	15,687(40.75)	
Multiparous	988 (65.17)	22,809(59.25)	
Number of pregnancy [n (%)]			< 0.001
Singleton pregnancy	994(87.97)	36,979(96.06)	
Twin pregnancy	136(12.04)	1517(3.94)	
IVF [n (%)]			< 0.001
No	933(82.57)	35,486(92.18)	
Yes	197(17.43)	3010(7.82)	
Caesarean history [n (%)]			< 0.001
No	260(23.01)	22,351(58.06)	
Yes	870(76.99)	16,145(41.94)	
Abortion history [n (%)]			0.002
0	582(51.50)	21,007(54.57)	
1	287(25.40)	10,386(26.98)	
≥2	261(23.10)	7103(18.45)	
HBsAg [n (%)]			0.860
Negative	1066(94.34)	36,363(94.46)	
Positive	64(5.66)	2133(5.54)	
TD [n (%)]			0.18
No	1017(90.00)	35,312(91.73)	
Hypothyroidism in pregnancy	92(8.14)	2672(6.94)	
Hyperthyroidism in pregnancy	21(1.86)	512(1.33)	
GDM [n (%)]			< 0.001
No	832(73.63)	31,332(81.39)	
Yes	298(26.37)	7164(18.61)	

Table 1 (continued)

	Preeclampsia ($n=1130$)	Non-preeclampsia ($n=38496$)	*P* value
ICP [n (%)]			< 0.001
No	1016(89.91)	37,110(96.40)	
Yes	114(10.09)	1386(3.60)	

Two independent sample *t* tests were used for normally distributed variables; Pearson's Chi-square test or Fisher's exact test were used for categorical variables; The differences of non-normally distributed parameters were analyzed using Mann–Whitney U test

PE, preeclampsia; ICP, intrahepatic cholestasis pregnancy; SD, standard deviation; BMI, body mass index; IVF, in vitro fertilization; TD, thyroid disease; GDM, Gestational Diabetes Mellitus

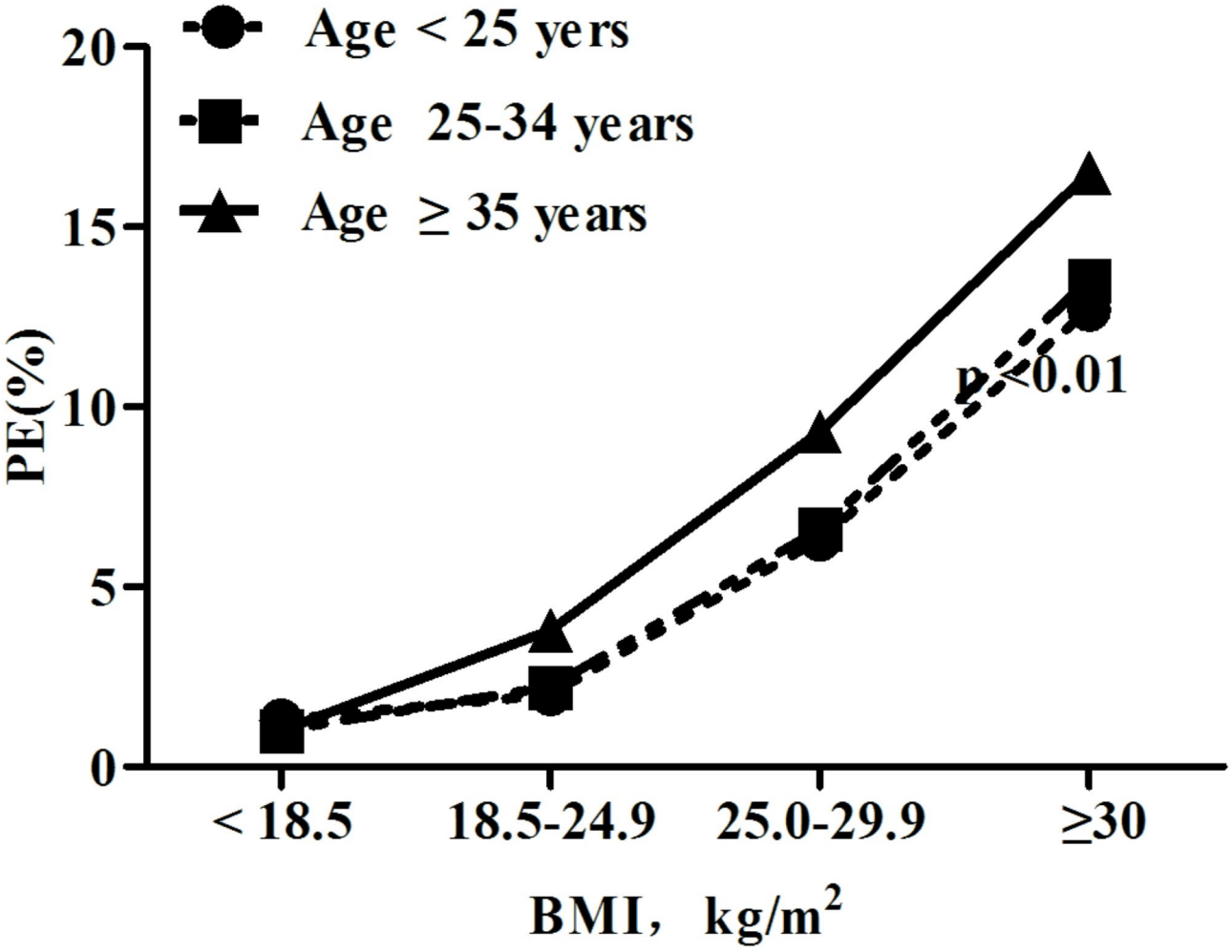

Fig. 2 Prevalence of PE stratified by age or pp-BMI. PE, pre-eclampsia; pp-BMI, pre-pregnancy body mass index

Discussion

The present study is a large epidemiological survey of PE in China and is very helpful for better understanding the prevalence rate and risk factors of PE and its relationship with maternal and fetal outcomes. We observed that the overall prevalence of PE was 2.85%, stratified by age, pp-BMI, IVF, twin pregnancy, ICP, and GDM. We further found maternal age > 35 years, pre-pregnancy overweight/obesity, excessive GWG, multiparity, twin pregnancy, IVF, cesarean section history, times of abortion history ≥ 2, and pregnancy with GDM or ICP were significant risk factors for PE after adjusting for various confounders. Moreover, our study showed that singleton as well as twin pregnancies with PE were at higher risk of adverse perinatal, maternal, and neonatal outcomes.

The prevalence of PE varies globally, a review study reported the prevalence of PE of 0.2–6.7% in Asia, 0.5–2.3% in Africa, 2.8–5.2% in Europe, 2.8–9.2% in Oceania, 1.8–7.7% in South America and the Caribbean, and 2.6–4.0% in North America [25]. Two recent studies in China respectively found that the prevalence of PE was 1.92% [20] and 2.3% [6], this study firstly found that the

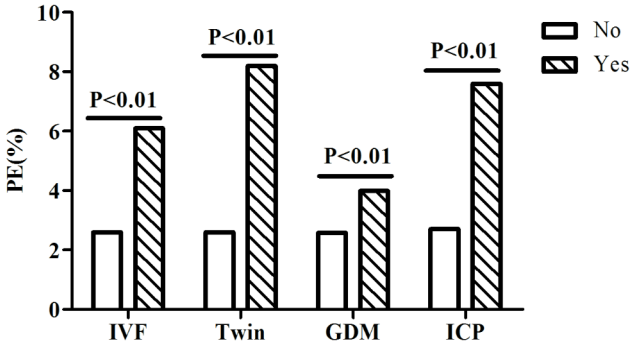

Fig. 3 Prevalence of PE stratified by IVF, twin pregnancy, ICP, and GDM. PE, pre-eclampsia; IVF, in vitro fertilization; ICP, intrahepatic cholestasis of pregnancy; GDM, gestational diabetes mellitus

prevalence of PE in eastern China was higher than previously reported, these inconsistency may be due to ethnicity, geographic location, and lifestyle [26, 27]. It is worth noting that the prevalence of PE in different regions of China needs more reporting. Moreover, this study showed the prevalence of PE in women of different age groups increased significantly with an increase in pp-BMI, especially in women aged ≥ 35 years who were overweight or obese before pregnancy. In addition, we showed that women undergoing IVF and those with twin pregnancies, ICP, or GDM had a higher prevalence of PE. These suggests that population differences in different studies were possible reasons for the global differences in the prevalence of PE. A large proportion of pregnant women with advanced age, abnormal BMI and other pregnancy complications maybe the possible underlying factors of higher prevalence of preeclampsia in our study.

Previous studies showed that advanced maternal age [20, 28] and overweight/obese had an increased risk of PE [29], and we observed that maternal age > 35 years and pre-pregnancy overweight or obesity also were independent risk factors of PE in this study. A study found white or black women with obesity in Non-Hispanic have a 2 ~ 3 fold increased risk of PE [30], which is more lower than the 5.67 fold increased risk of PE in our study and the 4 ~ 5 fold increased risk of PE associated with obesity in a recent cross-sectional Chinese study [6]. Studies have suggested an association between pre-pregnancy obesity and PE due to metabolic disorders, such as pro-inflammatory status and elevated leptin levels [31]. However, the mechanism underlying the correlation between PE and BMI remains unclear and requires further investigation. Moreover, our results showed that excessive GWG is associated with an increased risk of PE, which is consistent with some previous studies [32–34], but also contrary to other studies [35–37]. The differences in results could be due to the GWG categorization (2009 and 1990 Institute of Medicine GWG Guidelines Guidelines), heterogeneity of population (different ethnic/race distribution) and sources of GWG data (self-reported vs. medical record). Our findings suggest that age < 35 years, pre-pregnancy maintenance of an optimal BMI and adequate GWG may decrease the risk of PE,.

IVF has been reported to be a risk factor for PE [16]. Here, we found a higher rate of PE in women who underwent IVF than in those who did not undergo IVF, and IVF was associated with an increased risk of PE, consistent with the findings of previous studies [11]. The pathogenesis of PE involves placental dysplasia, and IVF is significantly associated with ischemic placental disease, which might explain the association between IVF and PE [38, 39]. However, the underlying mechanisms need more exploration. Moreover, we observed that twin pregnancies were significantly associated with an increased risk of PE, consistent with the findings of previous studies [40, 41]. Placental hypoxia and endothelial dysfunction promote PE in twin pregnancies, the etiology of which has been proposed to be related to increased uteroplacental demand and relative placental insufficiency [42–44].

Pregnancy with ICP showed more than 3-fold risk for PE in this study. Wikström et al. first reported a significant association between ICP and PE in 2013 [45], and recent a meta study had shown that ICP is associated with a higher incidence of PE [46]. However, these reports are limited to small samples and lack of Chinese population, whereas this large retrospective study provides robust data and clinically beneficial risk assessment, which showed a more comprehensive and reliable basis for ICP as a risk factor for PE of Chinese population. High bile acid levels in ICP cause placental antioxidant system dysfunction and oxidative stress, which facilitate the formation of various vasoactive mediators, such as endoglin-1 and soluble fms-like tyrosine kinase receptor, which are also increased in PE [47–49]. Similarly, we also found GDM was also a significant risk factor for PE in this study, consistent with previous major findings [50]. hyperglycemia induces oxidative stress and inflammation through the formation of advanced glycation end products to promote PE [51, 52]. Additionally, over activated neutrophils in GDM release excessive neutrophil extracellular traps, leading to placental ischemia, which is associated with PE [50, 53, 54]. Lastly, we comprehensively analyzed the associations between PE and perinatal outcomes of singleton as well as twin pregnancies. We observed a significant correlation between PE in singleton pregnancies and adverse perinatal outcomes, including an increased risk of preterm birth, cesarean section, stillbirth, low birth weight, fetal distress, neonatal unit admission, and neonatal asphyxia. The risk of preterm birth, cesarean section, neonatal unit admission were in accordance with the results of previous studies, whereas stillbirth, low birth weight remains contradictory in reports from different studies [8, 9, 55–57],. A

Table 2 Factors associated with the incidence of PE by multivariate logistic regression models. Note. PE, preeclampsia; ICP, intrahepatic cholestasis pregnancy; BMI, body mass index; IVF, in vitro fertilization; OR, odds ratio

	Crude OR	*P* value	Adjusted OR	*P* value
Maternal Age category [n (%)], years				
< 25	1.11(0.96–1.28)	0.148	1.09(0.93–1.29)	0.297
25–34	1		1	
≥ 35	1.61(1.39–1.87)	0.000	1.44(1.18–1.75)	< 0.001
Pre-pregnancy BMI [n (%)] (kg/m^2)				
Underweight (< 18.5)	0.50(0.40–0.64)	0.000	0.65(0.41–0.72)	0.000
Normal weight (18.5–24.9)	1		1	
Overweight (25.0-29.9)	3.11(2.61–3.70)	0.000	2.34(1.26–2.79)	< 0.001
Obesity(≥ 30)	7.55(5.33–10.72)	0.000	5.67(3.23-8.00)	< 0.001
Maternal education [n (%)]				
Low	1.22(1.12–2.54)	0.002	1.15(0.54–2.45)	0.719
Medium	0.69(0.30–1.83)	0.434	0.81(0.38–1.74)	0.592
High	1		1	
Gestational weight gain [n (%)]				
Inadequate	0.97(0.80–1.18)	0.751	0.98(0.81–1.20)	0.866
Adequate	1		1	
Excessive	2.54(2.13–3.04)	0.000	2.11(1.67–2.44)	< 0.001
Parity [n (%)]				
Primiparous	1		1	
Multiparous	0.70(0.61–0.79)	0.000	0.46(0.38–0.54)	< 0.001
Number of pregnancy [n (%)]				
Singleton pregnancy	1		1	
Twin pregnancy	3.33(2.77–4.02)	0.000	2.00(1.57–2.54)	< 0.001
IVF [n (%)]				
No	1		1	
Yes	2.49(2.12–2.91)	0.000	1.58(1.29–1.93)	< 0.001
Caesarean history [n (%)]				
No	1		1	
Yes	4.63(4.03–5.33)	0.000	3.82(3.24–4.51)	< 0.001
Abortion history [n (%)]				
0	1		1	
1	1.00(0.86–1.15)	0.972	0.89(0.75–1.05)	0.164
≥2	1.22(1.02–1.47)	0.029	0.91(0.73–1.14)	0.417
GDM [n (%)]				
No	1		1	
Yes	1.57(1.37–1.76)		1.45(1.23–1.70)	< 0.001
ICP [n (%)]				
No	1		1	
Yes	3.00(2.46–3.67)		2.26(1.77–2.88)	< 0.001

Note. PE, preeclampsia; ICP, intrahepatic cholestasis pregnancy; BMI, body mass index; IVF, in vitro fertilization; OR, odds ratio

similar significant correlation between PE in twin pregnancies and adverse perinatal outcomes, except for stillbirth and neonatal asphyxia, was also observed, which has rarely been reported. No significant association was found between PE and meconium amniotic fluid, postpartum hemorrhage and macrosomia of singleton as well as twin pregnancies. However, previous studies have shown that PE contributes to postpartum hemorrhage [8]. The differences in clinical pregnancy management and confounding variables of the studies may resulted in this inconsistency, this large sample study of the Chinese population provides a reliable basis for clinicians to manage pregnancy.

Although several studies have reported risk factors and adverse perinatal outcomes for PE, comprehensive reporting these in Chinese population is rare. The strengths of the present study is that We firstly reported the prevalence in eastern Chinese, assessed risk factors and adverse perinatal outcomes for PE this large retrospective cohort, especially after adjusting for confounding variables such as baseline characteristics and pregnancy complications. However, the study has several limitations. First, this is a single-center retrospective study, which may lack certain information, such as the treatment of PE. Hence, there is a risk of selection and information bias. Second, the relationship between the onset time and risk of PE could not be established because the timing of PE diagnosis was unavailable in the present study. Third, the association between PE severity and adverse perinatal outcomes was not assessed because of a lack of data. Therefore, a multi-center prospective study on PE will help to improve our understanding of PE.

Conclusion

Maternal age > 35 years, pre-pregnancy overweight/obesity, excessive GWG, multiparity, twin pregnancy, IVF, cesarean section history, times of abortion history ≥ 2, and pregnancy with GDM or ICP were significant risk factors of PE. Furthermore, PE was significantly associated with a higher risk of adverse perinatal outcomes in singleton and twin pregnancies. The present study provides comprehensive and useful evidence for clinicians managing women at risk of PE to decrease its prevalence and improve perinatal outcomes.

Table 3 Adverse perinatal outcomes of singleton pregnancy associated with PE

	PE (994 women 994 newborns)	non-PE (37022 women 37022 newborns)	*P*	Crude OR (95%CI)	Adjusted OR (95%CI)
Maternal outcome					
Caesarean section	734(73.84)	14,677(39.64)	0.000	4.30(3.73–4.96) [a]	3.89(3.16–4.33) [a]
PROM	103(10.36)	7896(21.33)	0.000	0.43(0.35–0.52) [a]	0.64(0.51–0.80)[b]
Preterm birth	387(38.93)	3348(9.04)	0.000	6.41(5.62–7.32) [a]	4.98(4.18–5.92) [a]
Abruptio placentae	36(3.62)	704(1.90)	0.000	1.94(1.38–2.73) [b]	1.68(0.98–2.57)
Meconium amniotic fluid	2(0.20)	252(0.68)	0.233	0.81(0.61–1.41)	0.92(0.72–1.54)
Postpartum hemorrhage	55(5.53)	1750(4.72)	0.238	1.18(0.90–1.56)	1.07(0.76–1.44)
Neonatal outcome					
Stillbirth	34(3.42)	416(1.12)	0.000	3.12(2.18–4.45) [a]	4.32(2.44–7.63) [a]
Macrosomia	37(3.72)	1831(4.95)	0.078	0.74(0.55–1.04)	0.89(0.70–1.32)
LBW	67(6.74)	369(1.00)	0.000	7.18(5.49–9.39) [a]	7.40(5.28–10.38) [a]
Fetal distress	209(21.03)	5880(15.88)	0.000	1.41(1.21–1.65) [b]	1.20(1.06–1.48) [b]
Neonatal asphyxia	30(3.02)	325(0.88)	0.000	3.51(2.40–5.14) [a]	2.11(1.22–3.62) [a]
Neonatal unit admission	451(45.33)	5453(14.73)	0.000	5.96(3.80–7.69) [a]	5.21(3.15–6.87) [a]

Note. Multivariate analyses were adjusted for Maternal age, pre-pregnancy BMI, GWG, parity, number of pregnancy, in vitro fertilization (IVF), caesarean history, GDM and ICP. The results were presented with an adjusted odds ratio, aOR (95% CI)

PE, preeclampsia; PROM, premature rupture of the membranes; LBW, low birth weight; OR, odds ratio. P was calculated by Pearson's Chi-square or Fisher's exact test, which were used to compare the proportions of maternal and neonatal outcomes between the two groups; [a]$P < 0.01$, [b]$P < 0.05$

Table 4 Adverse perinatal outcomes of twin pregnancy associated with PE

	PE (136 women 272 newborns)	non-PE (1474 women 2948 newborns)	*P*	Crude OR (95%CI)	Adjusted OR (95%CI)
Maternal outcome					
Caesarean section	132(97.06)	1270(86.16)	0.000	5.29(1.94–14.46) [a]	4.30(1.84–10.28) [a]
PROM	5(3.68)	238(16.15)	0.000	0.20(0.08–0.49) [a]	0.26(0.09–0.71) [b]
Preterm birth	113(83.09)	961(65.20)	0.000	2.62(1.66–4.16) [a]	2.90(1.74–4.82) [a]
Abruptio placentae	3(2.21)	40(2.71)	0.839	0.88(0.27–2.92)	0.98(0.40–2.39)
Meconium amniotic fluid	1(0.10)	1(0.07)	0.921	1.21(0.33–3.29)	1.03(0.44–3.95)
Postpartum hemorrhage	12(8.82)	126(8.55)	0.914	1.04(0.56–1.92)	1.00(0.66–1.37)
Neonatal outcome					
Stillbirth	2(0.74)	13(0.44)	0.329	1.22(0.84–2.98)	1.01(0.88–2.33)
Macrosomia	0	0			
LBW	229(84.19)	1764(59.84)	0.000	2.57(1.91–3.46) [a]	2.23(1.50–2.71) [a]
Fetal distress	28(10.29)	182(6.17)	0.005	1.88(1.20–2.55) [a]	1.33(1.13–1.99) [b]
Neonatal asphyxia	8(2.94)	105(3.56)	0.468	0.89(0.66–2.90)	0.92(0.73–2.52)
Neonatal unit admission	172(63.24)	1201(41.11)	0.000	2.58(1.87–3.33) [a]	2.13(1.67–3.03) [a]

Note. Multivariate analyses were adjusted for Maternal age, pre-pregnancy BMI, GWG, parity, number of pregnancy, in vitro fertilization (IVF), caesarean history, GDM and ICP. The results were presented with an adjusted odds ratio, aOR (95% CI). PE, preeclampsia; PROM, premature rupture of the membranes; LBW, low birth weight; OR, odds ratio. P was calculated by Pearson's Chi-square or Fisher's exact test, which were used to compare the proportions of maternal and neonatal outcomes between the two groups; [a]$P < 0.01$, [b]$P < 0.05$

Abbreviations

PE	Pre-eclampsia
pp-BMI	Pre-pregnancy body mass index
IVF	In vitro fertilization
GDM	Gestational diabetes mellitus, ICP, intrahepatic cholestasis of pregnancy
GWG	Gestational weight gain
WHO	World Health Organization
LBW	Low birth weight
CI	Confidence intervals

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Author contributions
KW and BZ conceived, designed and led the implementation of the study. LC, SL, BY and XZ developed the analysis plan and analyzed the data. LC and SL wrote the initial draft of the paper. KW and BZ reviewed the manuscript. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of the hospital approved this study protocol (approval no: IRB-20230095-R).

Consent for publication
All authors consented for this study's publication.

Competing interests
The authors declare no competing interests.

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