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Trends and adverse pregnancy outcomes associated with preeclampsia: a multi-centre cross-sectional study in Hebei, China

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Abstract

Objective This study aimed to assess the incidence, trends, and adverse pregnancy outcomes associated with preeclampsia (PE), while further investigating whether these adverse outcomes differ by parity and the type of pregnancy—twin or singleton.

Materials and methods A multicenter cross-sectional study was conducted in Hebei, China, spanning the years 2013 to 2022, enrolling a total of 455,456 women. The incidence rates and trends of PE and its subtypes were analyzed utilizing joinpoint regression analysis, while modified Poisson regression was employed to assess the association between PE and adverse pregnancy outcomes. Effect modification by parity, twin or singleton pregnancy was also evaluated.

Results The prevalence of PE and its stratification by singleton pregnancies and parity (primiparas versus multiparas) exhibited upward trends, with no statistically significant changes observed in the incidence of twins affected by PE from 2013 to 2022 in Hebei Province. After adjusting for sociodemographic characteristics and other comorbidities during pregnancy, patients with PE experienced significantly elevated risks of cesarean section (adjusted relative risk [aRR], 4.78; 95% confidence interval [CI], 4.54–5.02), postpartum hemorrhage (aRR, 1.97; 95% CI, 1.75–2.21), placental abruption (aRR, 1.52; 95% CI, 1.37–1.69), preterm birth (aRR, 5.35; 95% CI, 5.14–5.56), small for gestational age (SGA) newborns (aRR, 2.48; 95%CI, 2.38–2.58), maternal near-miss events (MNM) (aRR, 1.18; 95% CI, 1.01–1.38), and admission to the neonatal intensive care unit (NICU) (aRR, 1.27; 95% CI, 1.11–1.44). In contrast, the risk of placenta previa was significantly lower (aRR, 0.26; 95% CI, 0.21–0.32). The risks of cesarean section, postpartum hemorrhage, and preterm birth ascribable to PE were conspicuously augmented in twin pregnancies; conversely, the risk of placental abruption was more notable in singletons. The influence on cesarean delivery was pronounced in primiparas, while the risks of MNM, placental abruption, and preterm birth related to PE escalated in multiparas.

Conclusions The incidences of PE in overall, singletons, primiparas and multiparas exhibited upward trends in Hebei from 2013 to 2022. Women afflicted with PE demonstrated a conspicuously augmented risk of adverse pregnancy outcomes and the magnitude of the influence of PE varied with singleton or twin pregnancies and parity.

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Keywords Preeclampsia, Prevalence, Adverse pregnancy outcome, Twin, Parity

Introduction

Preeclampsia (PE) is a hypertensive disorder of pregnancy characterized by compromised placental perfusion and subsequent multi-organ dysfunction, contributing to approximately 14% of maternal mortality and 10–25% of perinatal morbidity worldwide [1]. Increasing evidences support that PE is associated with a substantial elevation in long-term cardiovascular and metabolic risks for both the mother and offspring [2]. In recent years, notwithstanding considerable breakthroughs in preeclampsia research, the global prevalence of PE remains at 4.6%, while the incidence and maternal mortality rates associated with PE in developing countries continue to alarmingly elevated [3]. This may be ascribed to the presence of various subtypes of PE and the heterogeneity inherent in its clinical manifestations [4].

It is imperative to consider the diverse classifications of PE to investigate potential subtypes, thereby facilitating tailored management strategies for the diagnosis and prevention of PE, which has profound implications for its progression [4, 5]. Both twin gestations and primiparity are recognized risk factors for PE; however, marked disparities prevail in the pathogenetic mechanisms of PE, thereby making it imprudent to consolidate these high-risk cohorts [5]. Twin pregnancies with PE might be correlated with augmented placental mass and demand, along with escalated production of anti-angiogenic factors, whereas primiparity is affiliated with a greater immunological mismatch between the fetus and the mother [6–8]. Although the association between PE and adverse pregnancy outcomes has been extensively validated, significant geographical variations persist across different regions. Furthermore, the existing research on whether this interrelationship is associated with parity and its impact on singleton versus twin pregnancies remain relatively sparse.

Employing population-based datasets, this study systematically addressed the trends of PE incidence and its correlation with adverse pregnancy outcomes, and assessed whether the influence affected by maternal characteristics. By elucidating the distinctive characteristics of various PE populations, this study would establish a foundation for enhancing the management of PE and mitigating complications.

Materials and methods

Study population and data collection

Data collected from the Hebei Maternal Near Miss Surveillance System (MNMSS) between January 2013 and December 2022 encompassed 22 hospitals (tertiary, secondary, and primary) across Hebei province, capturing information on a total of 491,182 maternal cases. The dataset included maternal socio-demographic characteristics, obstetric history, delivery facilities and modalities, pregnancy outcomes, as well as complications occurring during pregnancy or the postpartum period. The definitions of the indicators and the data collection protocols adhered to World Health Organization standards, while the methodology for data acquisition has been comprehensively documented in prior literature [9]. Each monitoring hospital assigns trained professionals, who have completed standardized training, to fill out and report maternal data. The submitted data must undergo strict review by professional staff to ensure its accuracy. This study encompassed pregnant women with a gestation of ≥ 28 weeks and live-born neonates. Meanwhile, incomplete or inaccurately recorded data were excluded, ultimately covering information of 455,456 pregnant women(Fig. 1). This study was authorized by the Health Center for Women and Children of Hebei Province to use the database and approved by the Ethics Review Committee of Hebei General Hospital, following the principles of the Helsinki Declaration. Given the retrospective design of this study, the Ethics Review Committee of Hebei General Hospital opted to waive the requirement for informed consent.

Definition of variables

We selected variables associated with preeclampsia (PE), including marital status, hospital level (tertiary, secondary, primary), educational attainment (≤ 6 years, 7–9 years, ≥ 10 years), maternal age at delivery (≤ 24 years, 25–29 years, 30–34 years, and ≥ 35 years), gravidity encompassing the current pregnancy (1, 2, ≥ 3), parity (0 or ≥ 1), number of previous cesarean deliveries (0 or ≥ 1), fetal presentation (cephalic and non-cephalic), and number of fetuses (singleton and twin). Pregnancy comorbidities comprised chronic hypertension, anemia (hemoglobin < 110 g/L), heart disease, gestational diabetes, and kidney disease. According to the 2014 International Society for the Study of Hypertension in Pregnancy (ISSHP) criteria, PE is defined as the onset of hypertension and proteinuria after 20 weeks of gestation, or hypertension accompanied by involvement of at least one organ system [10]. We categorized PE into singleton and twin classifications based on the number of fetuses, further distinguishing it into primiparous and multiparous subtypes according to parity for subsequent analysis. Adverse maternal pregnancy outcomes included: cesarean delivery, postpartum hemorrhage (≥ 500 ml for vaginal delivery and ≥ 1000 ml for cesarean delivery), placental abruption, placenta previa, maternal

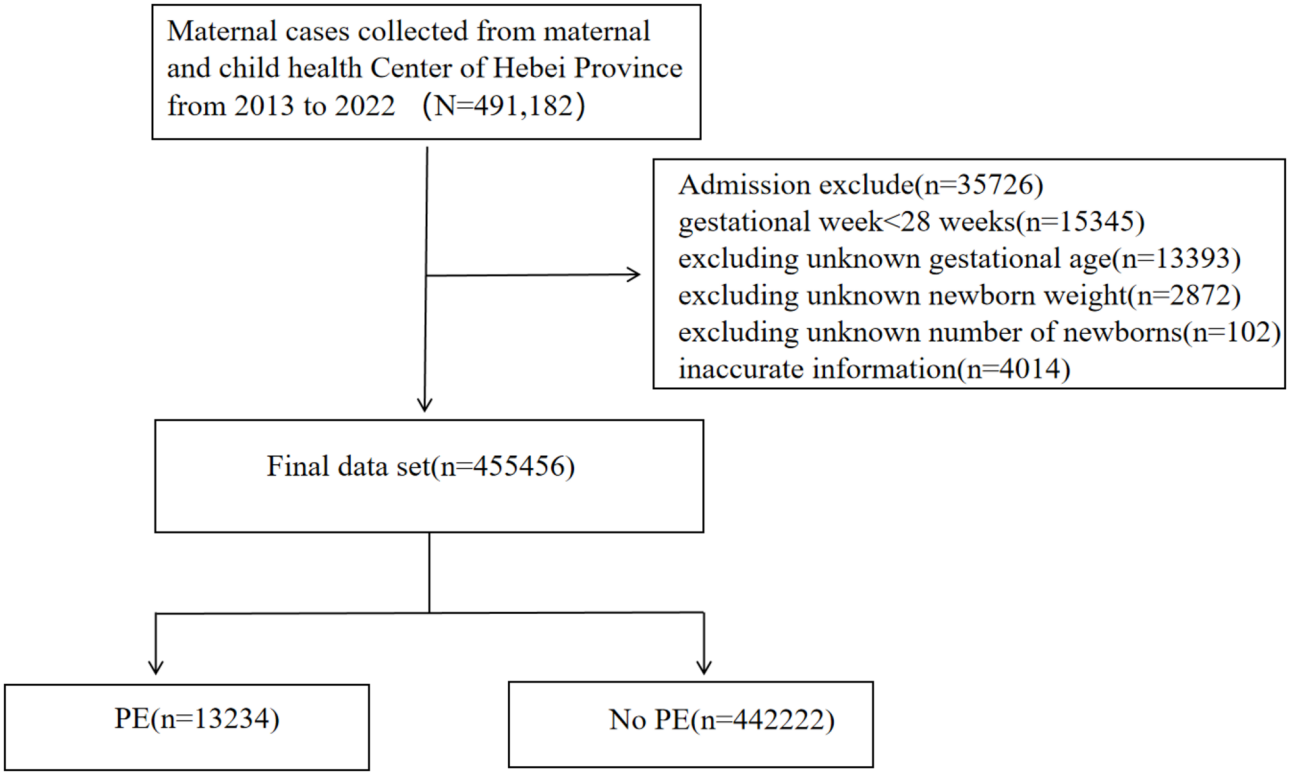

Fig. 1 Flow chart of study population

ICU (intensive care unit) admission, and maternal near-miss (MNM). The estimate of blood loss was based on a combination of the scaled suction canisters for collecting blood, the area of the surgical gauze impregnated with blood, and the weighing of the blood dressing. MNM is a life-threatening complication or comorbidity during pregnancy, delivery and 42 days postpartum, with effective medical intervention for survivors, with criteria defined by the WHO through the identification of markers of organ system dysfunction [11]. Adverse neonatal outcomes are preterm birth (gestational age 28–36^{+6} weeks), neonatal asphyxia (Apgar ≤ 7), admission to Neonatal Intensive Care Unit (NICU), neonatal death, and small-for-gestational-age newborns(SGA). SGA is defined as birthweights less than the 10th percentile of the normal average weight for the same gestational age according to the INTERGROWTH-21st standard [12].

Statistical analysis

First, the National Cancer Institute Surveillance Research Program's Joint Point Regression Program 5.0.2 (May 2023) was applied to determine the annual percentage change (APC) and average annual percentage change (AAPC) in the occurrence of PE and subgroups of PE. Therein, AAPC represented the disease trend for the entire period 2013–2022; APC indicated the disease trend for each segment/period identified by the joint-point regression software. Second, the obstetric characteristics (including sociodemographic characteristics and maternal comorbidities) were presented as frequencies (percentages), and intergroup comparisons were conducted by $\chi 2$ or Fisher's exact test, a multivariate modified Poisson regression analysis with robust error variances was used to calculate of adverse pregnancy outcomes in PE and its subtypes. In model A, we adjusted for maternal age, education, parity, delivery hospital, fetal presentation, multiple pregnancies. In model B, we extra-adjusted for chronic hypertension, anemia, heart disease, gestational diabetes, and kidney disease. Of these, the overall PE group added an interaction term to the Poisson regression model to test for an interaction effect between parity and multiple pregnancies. All analyses were undertaken using SPSS 22 (IBM Corporation, Chicago, USA) and R version 4.2.2 (R Project for Statistical Computing), and a difference of $P < 0.05$ was considered statistically significant.

Results

During the period, 455,456 pregnant women were eventually enrolled in the study. As shown in Fig. 2, the prevalence of PE was 2.91% ($n = 13234$), and in the subgroup analysis, the probability of PE was 2.76% in singletons ($n = 12386$) and the highest risk of PE in twins at 12.67% ($n = 6695$). Additionally, the subgroups divided by

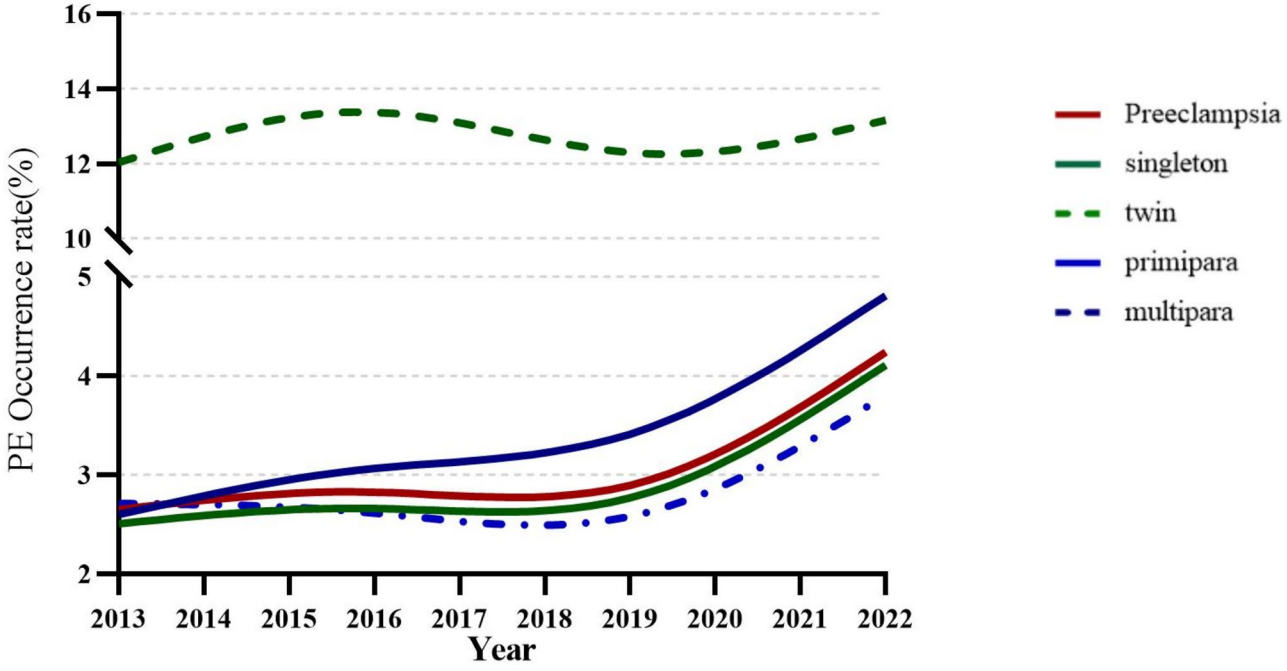

Fig. 2 The prevalence of preeclampsia in overall, singletons, twins, primiparas and multiparas in Hebei from 2013 to 2022. Note: The break symbol in the ordinate indicated that the axis had been segmented, specifically omitting the incidence data between 5% and 10%

Table 1 Trends of preeclampsia in overall, singletons, twins, primiparas and multiparas based on joinpoint regression analysis in Hebei from 2013 to 2022

Variables and segments	Year	APC (95% CI)	*P*
PE			
Trend1	2013–2019	0.79(-7.29,3.82)	0.92
Trend2	2019–2022	14.85(5.42,30.09)	< 0.001*
AAPC (95% CI)	2013–2022	5.27(2.57,7.25)	< 0.001*
PE in singletons			
Trend1	2013–2019	0.89(-8.59,4.50)	0.98
Trend2	2019–2022	15.77(5.33,32.89)	< 0.001*
AAPC (95% CI)	2013–2022	5.63(2.60–7.89)	< 0.001*
PE in twins			
Trend (AAPC)	2013–2022	0.17(-3.57,3.23)	0.94
PE in primiparas			
Trend (AAPC)	2013–2022	6.19(1.77,10.10)	0.01*
PE in multiparas			
Trend1	2013–2019	-1.69(-13.02,2.84)	0.32
Trend2	2019–2022	16.49(3.51,37.05)	0.01*
Trend (AAPC)	2013–2022	4.03(0.37,6.74)	0.03*

APC: annual percentage change, AAPC: average annual percent change, CI: confidence interval

parity had incidences of PE of 3.15% ($n = 6764$) and 2.69% ($n = 6470$) in primiparas and multiparas, respectively. Over the 10-year study period from 2013 to 2022, the prevalence of PE in primiparas continuously increased by 73.30% [AAPC 6.19% (95%CI: 1.77,10.10)]. Concurrently, the incidences of PE in overall, singletons, and multiparas exhibited similar patterns. These trends remained stable from 2013 to 2019(P_{APC}>0.05), before increasing significantly from 2019 to 2022(P_{APC} < 0.05), but the overall trend were upward(P_{APCC} < 0.05). Meanwhile the prevalence of PE in twins was relatively stable with no statistically significant difference(P_{APC}>0.05) (Table 1).

The demographic characteristics were summarized in Table 2. The comparison of socio-demographic characteristics in the study population revealed that marital status was not statistically significant in both PE and subgroup analyses. In contrast to the non-eclampsia cohort, the PE cohort demonstrated a markedly elevated rate of deliveries in tertiary care institutions, distinguished by a higher prevalence of primiparous women, multiple gestations, advanced maternal age, prior cesarean sections, abnormal fetal positioning, and an increased propensity for concomitant pregnancy-related comorbidities including chronic hypertension, anemia, heart disease, gestational diabetes, and kidney disease ($P < 0.05$). In the two subgroup analyses, no statistically significant differences were observed in pregnancies complicated by gestational diabetes and kidney disease($P > 0.05$). Similarly, the presence of heart disease did not demonstrate any substantial effects in the analyses involving primiparous and multiparous women with PE ($P > 0.05$)(Additional Table 1). Finally, no statistically significant interaction between parity and multiparity were found ($P > 0.05$).

The clinical analysis of adverse pregnancy outcomes associated with PE and its subgroups were detailed in Table 3. In the PE group, there was a pronounced increase in the incidences of cesarean section, postpartum hemorrhage, placental abruption, maternal ICU

Table 2 Maternal clinical characteristics of women with PE and its subgroups stratified in Hebei Province, China, from 2013–2022

Characteristic (*N*, %)	Overall		PE stratified by singleton or twins		PE stratified by parity	
	No PE (*n* = 442222)	PE (*n* = 13234)	Singletons (*n* = 12386)	Twins (*n* = 848)	Primiparas (*n* = 6764)	Multiparas (*n* = 6470)
Marital status						
Single	1931(0.44)	69 (0.52)	62(0.50)	7 (0.83)	50 (0.74)	19(0.29)
Married	440,291(99.56)	13,165 (99.48)	12,324 (99.50)	841 (99.17)	6714 (99.26)	6451 (99.71)
Education (year)						
≤ 6	138,837 (31.40)	4080 (30.83)	3856 (31.13)	224 (26.42)	1598 (23.63)	2482 (38.36)
7–9	132,193 (29.89)	4444 (33.58)	4133 (33.37)	311 (36.67)	2237 (33.07)	2207 (34.11)
≥ 10	171,192 (38.71)	4710 (35.59)	4397 (35.50)	313 (36.91)	2929 (43.30)	1781 (27.53)
Maternal age (y)						
≤ 24	67,994 (15.38)	1966 (14.86)	1845 (14.90)	121 (14.27)	1744 (25.78)	222 (3.43)
24–29	188,283 (42.58)	4672 (35.30)	4341 (35.05)	331 (39.03)	3171 (46.88)	1501 (23.20)
30–34	131,011 (29.63)	3979 (30.07)	3704 (29.90)	275 (32.43)	1408 (20.82)	2571 (39.74)
≥ 35	54,934 (12.42)	2617 (19.77)	2496 (20.15)	121 (14.27)	441 (6.52)	2176 (33.63)
Gravidity						
1	164,091 (37.11)	5098 (38.52)	4685 (37.82)	413 (48.70)	5098 (75.37)	-
2	161,562 (36.53)	3809 (28.78)	3595 (29.02)	214 (25.24)	1166 (17.24)	2643 (40.85)
≥ 3	116,569 (26.36)	4327 (32.70)	4106 (33.15)	221 (26.06)	500 (7.39)	3827 (59.15)
Parity						
0	208,118 (47.06)	6764 (51.11)	6214 (50.17)	550 (64.86)	-	
≥ 1	234,104(52.94)	6470 (48.89)	6172 (49.83)	298(35.14)	-	
Cesarean section history						
0	336,696 (76.14)	9595 (72.50)	8907 (71.91)	688 (81.13)	6764 (100.00)	2831 (43.76)
≥ 1	105,526 (23.86)	3639 (27.50)	3479 (28.09)	160 (18.87)	0 (0.00)	3639 (56.24)
Delivery hospital						
Tertiary hospital	215,633 (48.76)	9347 (70.63)	8623 (69.62)	724 (85.38)	5013 (74.11)	4334 (66.99)
Secondary hospital	219,234 (49.58)	3783 (28.59)	3661 (29.56)	122 (14.39)	1718 (25.40)	2065 (31.92)
Primary Hospital	7355 (1.66)	104 (0.79)	102 (0.82)	2 (0.24)	33 (0.49)	71 (1.08)
Multiple pregnancies						
Yes	5847 (1.32)	848 (6.41)			550 (8.13)	298 (4.61)
No	436,375 (98.68)	12,386 (93.59)			6214 (91.87)	6172 (95.39)
Abnormal fetal position						
Yes	12,342 (2.79)	794 (6.00)	588(4.75)	206(24.29)	407 (6.02)	387 (5.98)
No	429,880 (97.21)	12440(94.00)	11798(95.25)	642(75.71)	6357 (93.98)	6083 (94.02)
Maternal complications during pregnancy						
Chronic hypertension	3419 (0.77)	534 (4.04)	519 (4.19)	15 (1.77)	189 (2.79)	345 (5.33)
Anaemia	142,120 (32.14)	4661 (35.22)	4288 (34.62)	373 (43.99)	2326 (34.39)	2335 (36.09)
Cardiopathy	1081 (0.24)	162 (1.22)	144 (1.16)	18 (2.12)	86 (1.27)	76 (1.17)
Nephropathy	1207 (0.27)	149 (1.13)	135 (1.09)	14 (1.65)	83 (1.23)	66 (1.02)
Gestational diabetes	26,670 (6.03)	1483 (11.21)	1394 (11.25)	89 (10.50)	747 (11.04)	736 (11.38)

admissions, and MNM, while the incidence of placenta previa was relatively lower ($P < 0.05$).(Additional Table 2). Simultaneously, the probabilities of adverse neonatal outcomes such as preterm birth, SGA, NICU admission, neonatal asphyxia, and neonatal death were conspicuously augmented ($P < 0.05$) (Additional Table 2). As shown in Table 4; Fig. 3,after adjusting for sociodemographic characteristics and pregnancy-related comorbidities, patients with PE exhibited significantly higher risks of cesarean section (adjusted relative risk [aRR], 4.78; 95% confidence interval [CI], 4.54–5.02), postpartum hemorrhage (aRR, 1.97; 95% CI, 1.75–2.21), placental abruption (aRR, 1.52; 95% CI, 1.37–1.69), preterm birth (aRR, 5.35; 95% CI, 5.14–5.56), SGA (aRR, 2.48; 95%CI, 2.38–2.58), MNM (aRR, 1.18; 95% CI, 1.01–1.38), and NICU (aRR, 1.27; 95% CI, 1.11–1.44). In contrast, the risk of placenta previa was significantly lower (aRR, 0.26; 95% CI, 0.21–0.32). Concurrently, we observed that the risks of maternal ICU admission (aRR, 1.28; 95% CI, 0.93–1.78), neonatal asphyxia (aRR, 1.04; 95% CI, 0.90–1.21), and neonatal death (aRR, 1.04; 95% CI, 0.78–1.38) were not statistically significant. Adjusting for the various covariates did not significantly impact the estimates, as models A and B yielded comparable results (Table 4).

Table 3 Adverse maternal and fetal outcomes in PE and PE stratified by parity and twin or Singleton

Outcomes (*N*, %)	Overall		PE stratified by singleton or twins		PE stratified by parity	
	No PE (*n* = 442222)	PE (*n* = 13234)	Singletons (*n* = 12386)	Twins (*n* = 848)	Primiparas (*n* = 6764)	Multiparas (*n* = 6470)
Maternal outcomes						
Cesarean delivery	230,583 (52.14)	11,468 (86.66)	10,650 (85.98)	818 (96.46)	5797 (85.70)	5671 (87.65)
PPH	4937 (1.12)	292 (2.21)	237 (1.91)	55 (6.49)	163 (2.41)	129 (1.99)
Placeta previa	1880 (0.43)	80 (0.60)	68 (0.55)	12 (1.42)	27 (0.40)	53 (0.82)
Placental abruption	914 (0.21)	295 (2.23)	290 (2.34)	5 (0.59)	109 (1.61)	186 (2.87)
Maternal ICU	118 (0.03)	43 (0.32)	38 (0.31)	5 (0.59)	15 (0.22)	28 (0.43)
MNM	703 (0.16)	169(1.28)	154 (1.24)	15 (1.77)	59 (0.87)	110 (1.70)
Fetal outcomes						
Preterm birth	23,605 (5.34)	5003 (37.80)	4415 (35.65)	588 (69.34)	2278 (33.68)	2725 (42.12)
SGA	26,757 (6.05)	2403 (18.16)	2238 (18.07)	165 (19.46)	1257 (18.58)	1146 (17.71)
NICU	4466 (1.01)	663 (5.01)	599 (4.84)	64 (7.55)	274 (4.05)	389 (6.01)
Neonatal death	326 (0.07)	44 (0.33)	40 (0.32)	4 (0.47)	17 (0.25)	27 (0.42)
Neonatal asphyxia	3419 (0.77)	498 (3.76)	458 (3.70)	40 (4.72)	200 (2.96)	298 (4.61)

Abbreviation: PE: preeclampsia, PPH: postpartum hemorrhage, ICU: intensive care unit, MNM: maternal near-miss, SGA: small-for-gestational-age, NICU: neonatal Intensive Care Unit

Table 4 Adjusted risk ratios for maternal and fetal adverse outcomes associated with PE and its subgroups

Outcome	Model A [aRR (95% CI)]			Model B [aRR (95% CI)]		
	PE vs. No PE	Twin vs. Singletons	Primiparas vs. Multiparas	PE vs. No PE	Twin vs. Singletons	Primiparas vs. Multiparas
Maternal outcomes						
Cesarean delivery	4.88(4.64–5.13)*	3.09 (2.13–4.48)*	1.05(1.01–1.09)*	4.78(4.54–5.02)*	3.13 (2.16–4.54)*	1.05(1.01–1.09)*
PPH	2.08(1.85–2.33)*	3.91(3.14–4.89)*	1.03(0.94–1.14)	1.97(1.75–2.21)	3.32(2.62–4.19)*	1.05(0.96–1.16)
Placeta previa	0.25(0.20–0.31)*	1.26(0.75–2.13)	0.82(0.62–1.07)	0.26(0.21–0.32)*	1.25(0.75–2.09)	0.82(0.63–1.07)
Placental abruption	1.50(1.35–1.66)*	0.16(0.07–0.40)*	0.82(0.71–0.94)*	1.52(1.37–1.69)*	0.15(0.06–0.37)*	0.83(0.72–0.95)*
Maternal ICU	1.35(0.99–1.84)	1.48(0.60–3.70)	0.81(0.56–1.18)	1.28(0.93–1.78)	1.54(0.62–3.78)	0.81(0.56–1.18)
MNM	1.21(1.03–1.42)*	0.83(0.52–1.33)	0.79(0.67–0.94)*	1.18(1.01–1.38)*	0.79(0.50–1.23)	0.80(0.67–0.95)*
Neonatal outcomes						
Preterm	5.45(5.25-5.70)*	3.06(2.60–3.60)*	0.85(0.82–0.88)*	5.35(5.14–5.56)*	3.17(2.69–3.73)*	0.85(0.82–0.88)*
SGA	2.46(2.37–2.57)*	0.85(0.72–1.01)	1.01(0.98–1.05)	2.48(2.38–2.58)*	0.88(0.74–1.05)	1.01(0.98–1.05)
NICU	1.31(1.15–1.50)*	1.30(0.89–1.91)	1.03(0.88–1.20)	1.27(1.11–1.44)*	1.34(0.92–1.95)	1.03(0.88–1.20)
Neonatal asphyxia	1.01(0.87–1.17)	0.63(0.39–1.02)	0.97(0.81-1.17)	1.04(0.90–1.21)	0.65(0.40–1.05)	0.97(0.81–1.17)
Neonatal death	1.06(0.81–1.40)	0.88(0.34–2.31)	0.90(0.67–1.20)	1.04(0.78–1.38)	0.92(0.35–2.41)	0.90(0.67–1.21)

Model A adjusted for age, education, gravidity, parity, delivery hospital, multiple pregnancy and abnormal fetal position

Model B adjusted for all maternal complications during pregnancy in addition to covariates in model A

Abbreviation: PE: preeclampsia, ICU: intensive care unit, MNM: maternal near-miss, NICU: neonatal Intensive Care Unit

* $P < 0.05$

The subgroup analysis further substantiated that, in contrast to PE in singletons, the probabilities of cesarean section (aRR,3.13; 95%CI, 2.16–4.54), postpartum hemorrhage (aRR, 3.32; 95% CI, 2.62–4.19), and preterm birth (aRR, 3.17; 95% CI, 2.69–3.73) were augmented in twins, concomitantly with a diminished risk of placental abruption (aRR, 0.15; 95% CI, 0.06–0.37). Similarly, in subgroups stratified by parity, primiparas afflicted with PE manifested elevated a risk of cesarean delivery (aRR, 1.05; 95%CI, 1.01–1.09), alongside reduced risks of MNM (aRR, 0.80; 95% CI, 0.67–0.95), placental abruption (aRR, 0.83; 95% CI, 0.72–0.95)and preterm birth (aRR, 0.85; 95% CI, 0.82–0.88) in comparison to those with multiparas controls.

Discussion

Employing extensive and high-quality data from MNMSS, this research disclosed that from 2013 to 2022, the prevalence of PE and its associated subtypes in Hebei Province demonstrated upward trends, with the exception of PE in twins. Women with PE were exposed to significantly augmented risks of SGA and admission to NICU, while the risk of placenta previa was reduced. These outcomes were unaffected by parity or whether the pregnancy was singleton or twin. Cesarean section, postpartum hemorrhage, placental abruption, MNM and preterm birth- these adverse outcomes of PE varied in accordance with twin or singleton and parity.

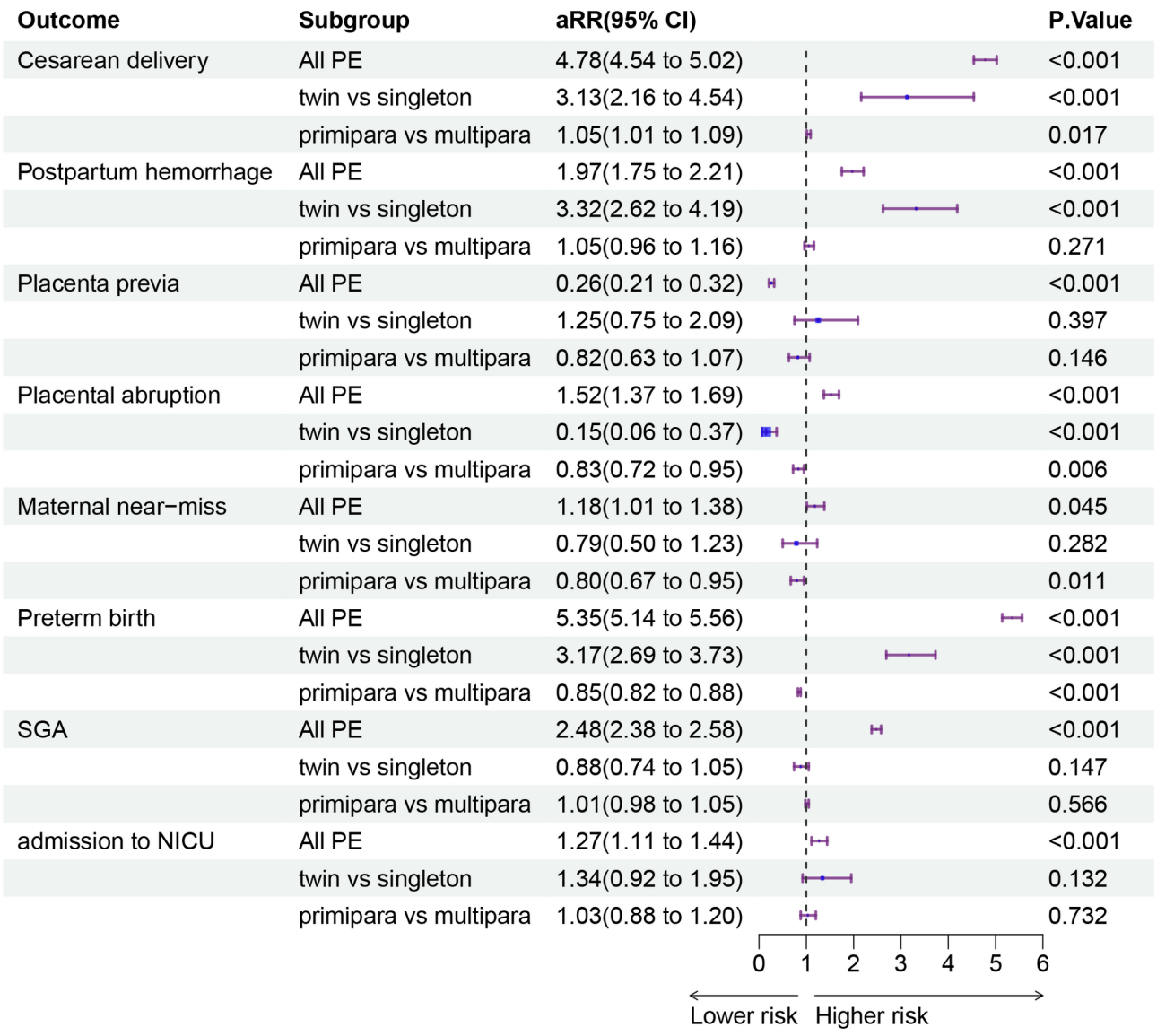

Fig. 3 Multivariable Poisson regression analysis of maternal and fetal adverse outcomes associated with PE and its subgroups after controlling for sociodemographic characteristics and other comorbidities during pregnancy.

In this study, the overall prevalence of PE in Hebei Province was found to be 2.91%, aligning with the results of a cross-sectional survey conducted by Yang et al. in 2021, which divulged a prevalence ratio of 2.3% among 79,243 individuals across China [13]. Over the past decade, coinciding with the relaxation of China's "two-child" family planning policy, the incidence of hypertensive disorders in pregnancy escalated from 5.22% in 2011 to 6.40% during the period from 2014 to 2018 in China [14]. Although our results indicated an overall upward trend in PE incidence over the past decade, it exhibited a pattern of initial stability followed by an increase. The aforementioned findings may be attributed to two factors. First, the Hebei Province Statistical Yearbook revealed a steady economic and healthcare development in Hebei Province from 2013 to 2022 [15]. This suggested that despite the adjustments to China's fertility policies during this period, the high quality of maternal and child healthcare services in Hebei Province likely contributed to the stable incidence of PE. Second, accumulating literatures have substantiated the hypothesis that maternal infection with COVID-19 may elevate the risk of PE, potentially owing to the substantial overlap in endothelial, vascular, and immune functions between the two diseases [16]. The period from 2019 to 2022 marked the peak of the COVID-19 pandemic, which may account for the observed rise in PE incidence. Unexpectedly, the incidence of PE in twin pregnancies did not demonstrate a substantial augmentation in our study. This finding warrants further investigation to elucidate its underlying

causes, but it also supports the heterogeneity of the pathogenesis of PE in twin pregnancies [8]. It is crucial to emphasize that across different birth policy periods, while the proportion of primiparous women had progressively diminished, the associated incidence of preeclampsia had paradoxically escalated in the study (Additional Table 3). This may be attributed to the global trend of first-birth postponement, which is closely associated with an increased risk of PE [17–19]. Such results motivated obstetricians and scholars to work together to reverse the rising trend of preeclampsia and ameliorate the pregnancy outcomes of PE.

Given the limitations of small sample sizes or racial disparities, and the inconclusive or inconsistent findings in previous literature regarding pregnancy outcomes in twins affected by PE, we aimed to investigate investigate the disparities in adverse pregnancy outcomes between singleton and twin pregnancies with PE [20, 21] In comparison to non-PE patients, our findings revealed a greater than four-fold increase in the risk of preterm birth among pregnant women with PE. Furthermore, subgroup analysis indicated that twins affected by PE disclosed a higher propensity for preterm birth compared to singletons counterparts. Notably, we observed a lower prevalence of extremely preterm births in twins with PE compared to singletons (13.61% vs. 26.59%), which markedly differed by gestational age at delivery, thereby reaffirming the etiological discrepancies between PE in twin and singleton pregnancies [22]. Emerging researches underscore that while PE is more prevalent in twins than in singletons, the associated risks of adverse pregnancy outcomes have not been significantly elevated [20, 23]. The propensity for cesarean section and postpartum hemorrhage was decidedly greater in twins as opposed to singletons in the study, most likely ascribable to the preexisting augmented risk affiliated with twin pregnancies [23]. Furthermore, we ascertained that singletons afflicted with PE were more prone to placental abruption compared to twins. This intriguing finding was also corroborated by a study conducted in Japan [24]. This result may be attributed to the increased attention given to twin pregnancies following the issuance of risk warnings in clinical guidelines [25]. Additionally, the high caesarean section rate in twin pregnancies reduces the risk of placental abruption occurring after the first fetus is delivered vaginally. Such findings will empower obstetricians to offer more precise guidance during antenatal consultations for women with PE in twin pregnancies.

MNM is emerging as an imperative indicator of standardized outcomes for assessing and improving the quality of obstetric care, necessitating the identification of factors associated with adverse maternal outcomes [26]. The primary cause of MNM in southern Ghana was preeclampsia/eclampsia, accounting for 41.0%, and women afflicted with PE manifested an eightfold escalation in the incidence of MNM in contrast to those devoid of these conditions [27, 28]. Notwithstanding our findings affirmed PE as a hazard factor for MNM, the effect estimate obtained (1.18 times) was relatively modest. The observed discrepancy may be attributed to the fact that previous studies were conducted during an earlier period (2004–2008) with a preeclamptic population. While our cohort was more up-to-date, potentially allowing for a higher prevalence of low-dose oral aspirin use among high-risk PE patients, this may have mitigated the risk of MNM events associated with PE. [29]. Simultaneously, it was discerned in the subgroup analysis that the prevalence of MNM induced by PE in multiparas was 1.20 times higher than that in primiparas. Moreover, our findings indicated that multiparas with PE were more predisposed to preterm birth and placental abruption compared to primiparas. Previous studies have documented an association between parity and adverse pregnancy outcomes. However, there is a lack of research on the specific effects of parity on adverse pregnancy outcomes related to PE [30–32]. These findings may be attributed to the elevated risk of multiple pregnancy complications and comorbidities observed among multiparas, which subsequently results in more severe adverse pregnancy outcomes in cases complicated by PE [33]. Additionally, primipara with PE were more frequently subjected to cesarean delivery in our study, which may be related to the higher proportion of primipara requesting cesarean section. These results emphasize the necessity for clinicians to appropriately encourage primipara to pursue vaginal delivery. Simultaneously, efforts should focus on mitigating severe obstetric complications and preventing subsequent maternal mortality by addressing modifiable risk factors in multipara.

The strengths of this study lie in its large sample size and multicenter design, encompassing 455,456 representative pregnant women. This enabled a systematic investigation of PE and its rare pregnancy outcomes, thereby ensuring the reliability and significance of our findings in clinical practice. Moreover, despite the regional nature of our study, our findings were influenced by global factors such as delayed childbearing and the COVID-19 pandemic. Therefore, the latest trends in PE incidence identified in our study provided valuable insights for international research on PE. Finally, this study provided an in-depth analysis of how different stratified types influenced PE-related adverse outcomes, which hold crucial implications for preventing severe complications associated with PE in pregnancy care regimens.

However, this study still has some limitations. First, the treatment standard for PE in this study followed the ISSHP management criteria, but detailed treatment protocols, frequency of PE assessment, history of COVID-19

infection, history of PE, gestational age at onset of preeclampsia, socioeconomic status, lifestyle behaviors, genetic predispositions, and blood pressure status were not collected, which in turn could have contributed to potential biases in the results and the inability to classify more subtypes. Second, Although our statistical methods and data collection strategies aimed to account for temporal factors, the study still has limitations in fully capturing the dynamic effects of time-related changes. The dynamic changes in the individuals we failed to follow in the study prevented us from combining longitudinal approaches to strengthen causal inferences. Third, In clinical practice for PE, individualized treatment regimens may be employed. Due to the absence of specific treatment protocols in our data, we cannot rule out the potential bias introduced by variations in treatment approaches on study outcomes.

Conclusion

In conclusion, the incidences of PE in Hebei Province exhibited upward trends over the past decade, both overall and among women with singleton, primiparas and multiparas. Women afflicted with PE demonstrated a conspicuously augmented risk of adverse pregnancy outcomes and the magnitude of the influence of PE varied with singleton or twin pregnancies and parity. These findings will hold substantial significance for the risk assessment and management of PE, providing a basis for targeted intervention measures.

Abbreviations

PE	Preeclampsia
SGA	Small for gestational age
MNM	Maternal near-miss
NICU	Neonatal intensive care unit
APC	Annual percentage change
AAPC	Average annual percentage change
ICU	Intensive care unit
PPH	Postpartum hemorrhage

Supplementary Information

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Supplementary Material 1

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Author contributions

RFW: Designed study, analyzed data, and wrote the manuscript. LYD: data collection. JYD and LL: data organization. YD, WNL, SXL, and YH: analyzed data. DDY: statistical analysis, revised and proofread the manuscript.

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Data availability

Data available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate

This study was authorized by the Health Center for Women and Children of Hebei Province to use the database and approved by the Ethics Review Committee of Hebei General Hospital, following the principles of the Helsinki Declaration. Given the retrospective design of this study, the Ethics Review Committee of Hebei General Hospital opted to waive the requirement for informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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