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ORIGINAL RESEARCH

# Pan-Immune-Inflammation Value and Risk of Hypertensive Disorders of Pregnancy: A Cross-Sectional Study

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**Objective:** This research sought to investigate the connection between pan-immune-inflammation value (PIV) and hypertensive disorders of pregnancy (HDP).

**Methods:** This retrospective cross-sectional study included 1002 pregnant women who delivered in Women's Hospital, Zhejiang University School of Medicine from January to February 2024.Their basic information and laboratory values during the second trimester (24–28 weeks of gestation) were collected from medical records and the hospital information management system, and PIV values were calculated. We explored the relationship between PIV and the risk of developing HDP via univariate and multivariate logistic regression analyses. Receiver operating characteristic (ROC) curve analysis was used to evaluate the ability of PIV to predict the risk of developing HDP. Since preeclampsia (PE) is an important disease of HDP, we also explored the relationship between PIV and the risk of developing PE.

**Results:** Patients with HDP presented higher PIV levels ($P < 0.001$). PIV, a risk factor, was significantly associated with HDP and PE according to the univariate regression analysis ($P < 0.001$). Even after adjusting for potential confounding factors, the risk of developing HDP and PE remained significantly greater. According to subgroup analysis, PIV was significantly and positively associated with the development of HDP and PE among pregnant women aged < 35 years and with normal pre-pregnancy body mass index ($P < 0.05$). ROC curve analyses indicated that PIV had a high predictive value for both HDP and PE ($P < 0.001$).

**Conclusion:** Increased PIV levels are associated with a greater risk of developing HDP and PE, suggesting that PIV is an independent risk factor for the development of HDP and PE.

**Keywords:** pan-immune-inflammation value, hypertensive disorders of pregnancy, preeclampsia, risk, receiver operating characteristic

## Introduction

Hypertensive disorders of pregnancy (HDP) remain a leading cause of maternal-fetal morbidity and mortality, affecting 14.0% of pregnancies globally.[1,2] The World Health Organization (WHO) estimates that the incidence of HDP in developing countries is 2.8% of live births, whereas it is 0.4% in developed countries.[1] The prevalence of HDP varies globally, with 116 per 100,000 women of childbearing age affected. Africa has the highest prevalence at 335 per 100,000, followed by Southeast Asia and the Middle East. The Western Pacific region reports the lowest prevalence at 16 per 100,000 women of childbearing age.[3] The numerous complications associated with HDP include placental abruption, early induction of labor or cesarean section, often resulting in preterm birth. The negative outcomes for fetuses and newborns during the perinatal period include low birth weight, fetal growth restriction, stillbirth, etc.[4] Furthermore, preeclampsia (PE) is a multifaceted and potentially life-threatening condition that poses a significant challenge to

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maternal health, impacting 2–4% of all pregnancies.[5] All women with PE, regardless of the time of onset, are at risk of rapid progression and severe disease. Although there is currently a significant international research effort into the management of HDP risk factor control, yet the prevalence of HDP has not declined significantly in recent decades. This suggests that there are still some potential risk factors that may not be systematically explored and managed.

Recently we reported that systemic inflammation has an important role in the pathogenesis of HDP and PE.[6] For instance, Seyhanli et al reported the value of the systemic inflammation response index (SIRI) in predicting PE in a retrospective analysis involving 276 eligible pregnancies.[7] Aydoğan et al conducted a retrospective cohort study of 148 newborns of mothers with PE and reported that the systemic immune-inflammation index (SII) and neutrophil-to-lymphocyte ratio (NLR) were significant in predicting mortality in infants of mothers with PE.[8] While Singh et al demonstrated the predictive value of the C-reactive protein (CRP) levels for HDP via a cross-sectional study of 200 participants.[9] We found that the pan-immune-inflammation value (PIV), a less established inflammatory marker compared to SII, SIRI, and CRP,[7–9] plays a role in the progression of HDP and PE.[10] Therefore, despite being less researched, PIV should not be overlooked. In addition, no systematic studies were conducted to explore their correlation recently. Therefore, we assume that PIV is significantly associated with the risk of HDP and PE. In this single-center retrospective cross-sectional study, we aimed to explore the relationship between PIV and the risk of HDP and PE. This research was conducted on the basis of the aforementioned hypothesis and background study, with the goal of offering new insights and a theoretical foundation for the clinical management of HDP and PE.

# Methods

## Study Participants

This retrospective cross-sectional study was conducted at a single center, the Women's Hospital, Zhejiang University School of Medicine, from January to February 2024. The study participants consisted of 1358 singleton pregnant women who met the following inclusion criteria: (1) routine antenatal visits and deliveries were performed; (2) more than or equal to 18 years old; (3) the diagnoses of HDP and PE were clear and the assessment information was complete. Moreover, we excluded 356 pregnant women using the following criteria: (1) less than 18 years old; (2) missing full data on laboratory tests or clinical information; (3) multiple pregnancies; (4) gestational weeks at delivery ≤ 28 weeks; (5) abortion or stillbirth; (6) diabetes mellitus or chronic hypertension before pregnancy; (7) severe blood system, heart, liver or kidney diseases; (8) autoimmune disorders; (9) malignancy; (10) severe infectious and chronic toxic disease. Finally, a total of 1002 individuals were included in this study, comprising pregnant women without HDP (N = 828) and pregnant women with HDP (N = 174). Furthermore, the pregnant women with HDP were categorized into two groups: pregnant women without PE (all pregnant women with gestational hypertension) (N = 108) and pregnant women with PE (N = 66). Figure 1 illustrated the study design and the flowchart of the participants. Ethical approval was obtained from the local ethics committee (approval number: IRB-20250161-R). The requirement for informed consent was waived as anonymous patient records were used. The study complied with the guidelines of the Declaration of Helsinki.

## Data Collection and Measurements

Demographic data, past history, comorbidities, and anthropometric data were collected from medical records and the hospital information management system in this study. We gathered demographic information from the participants, including maternal age and education (which was divided into four groups: primary school and below, middle and high school, college, and postgraduate or above). In addition, the past history included assisted reproduction (yes or no), gravidity (= 1, = 2, ≥ 3), parity (= 1, = 2, ≥ 3), gestational weeks of delivery, pre-pregnancy body mass index (pre-pregnancy BMI), systolic pressure, and diastolic pressure at 24–28 weeks of gestation.

Laboratory parameters were measured using standardized protocols and obtained at 24–28 weeks of gestation. The laboratory values included white blood cell (WBC), neutrophil, lymphocyte, monocyte, hemoglobin, platelet, albumin (ALB), alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c), high-density lipoprotein-cholesterol (HDL-c), uric acid (UA), blood urea nitrogen (BUN), creatinine (Cre), fasting plasma glucose (FPG), glycated hemoglobin A1c (HbA1c) and fibrinogen (FIB).

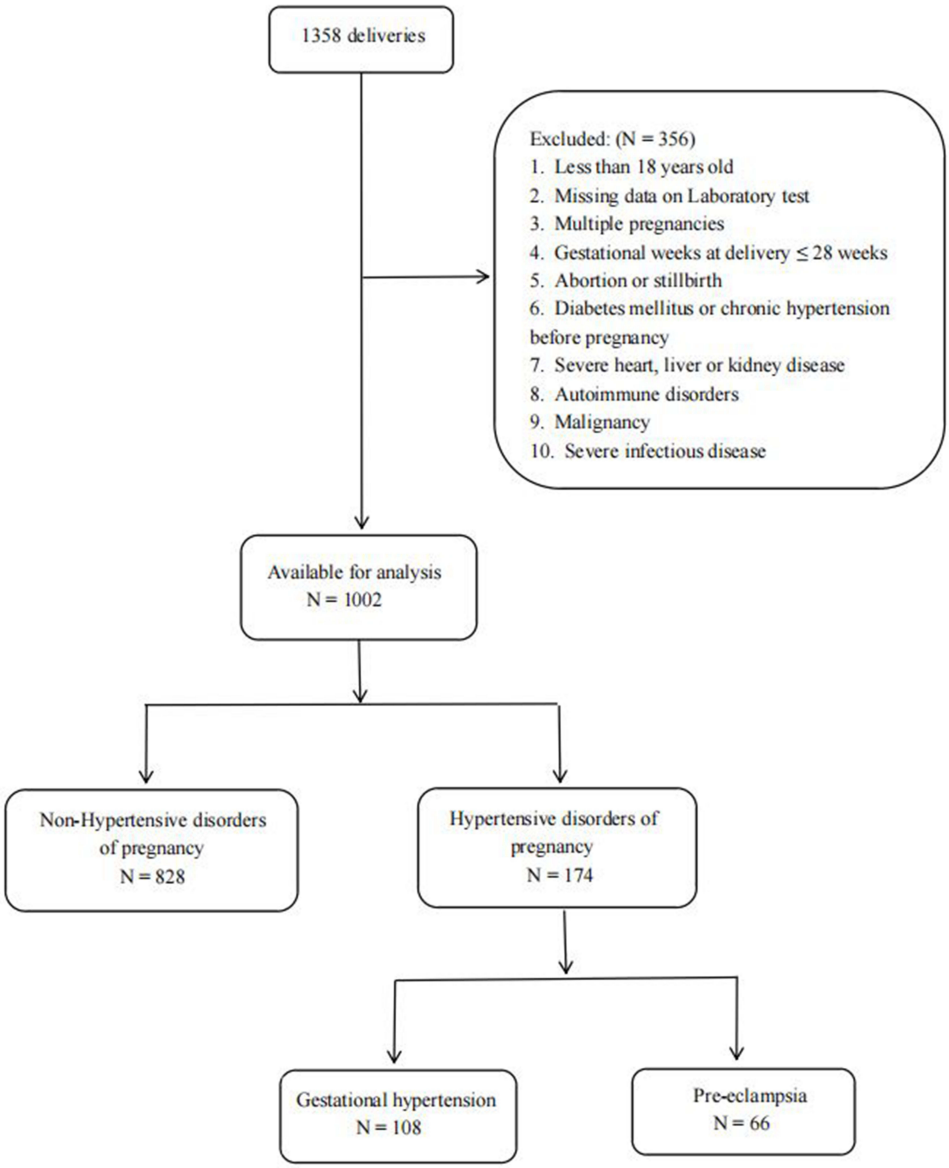


**Figure 1** Flowchart of participant enrollment and group assignment.

The pre-pregnancy BMI was calculated as the ratio of a woman's pre-pregnancy weight (kg) to her height squared ($m^2$). The categories were assigned according to Chinese classification standards as follows: underweight (< 18.5 kg/$m^2$), normal (18.5 kg/$m^2$ ≤ BMI < 24.0 kg/$m^2$), overweight (24.0 kg/$m^2$ ≤ BMI < 28.0 kg/$m^2$), and obese (≥ 28.0 kg/$m^2$).[11]

## Calculation and Evaluation of PIV

PIV was calculated as follows: PIV = neutrophil ($10^3$/μL) × platelet ($10^3$/μL) × monocyte ($10^3$/μL) / lymphocyte ($10^3$/μL).[12] Since PIV was not normally distributed, lnPIV which was converted to normal distribution was used to fit regression risk in the study. In addition, we standardized PIV to fit the risk of each rising standard deviation (SD) for comparative analysis. The standardized PIV was calculated as follows: standardized PIV = (PIV - mean) / SD. We also categorized the participants into two, three, and four groups on the basis of the median, tertiles, and quartiles of PIV. The two groups were named low-PIV (≤ 463.91, N = 501) and high-PIV (> 463.91, N = 501). The three groups were named T1 (≤ 375.57, N = 334), T2 (375.57–569.35, N = 334), and T3 (> 569.35, N = 334). The four groups were named Q1 (≤ 325.57, N = 250), Q2 (325.57–463.91, N = 251), Q3 (463.91–669.78, N = 251) and Q4 (> 669.78, N = 250).


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## Assessment Criteria for HDP and PE

HDP constitute a broad term that comprises different entities, such as PE, eclampsia, chronic hypertension, gestational hypertension, and chronic hypertension with superimposed PE.[13–15] The International Society for the Study of Hypertension in Pregnancy characterizes hypertension during pregnancy as a condition in which the systolic blood pressure reaches or exceeds 140 mmHg and/or the diastolic blood pressure reaches or exceeds 90 mmHg, as verified by two distinct measurements.[15–17] PE is defined as the emergence of hypertension after the 20th week of pregnancy, accompanied by proteinuria or one or more of the following clinical indicators: renal insufficiency, impaired hepatic function, pulmonary edema, persistent headache unresponsive to treatment, thrombocytopenia, or visual disturbances. In contrast, gestational hypertension is identified as the onset of hypertension after the 20th week of gestation in individuals who previously exhibited normal blood pressure levels without above complications.[18–20] In this study, the participants with HDP and PE were assessed on the basis of the above criteria. The sample was composed of pregnant women without HDP (N = 828) and with HDP (N = 174). Furthermore, the pregnant women with HDP were divided into two distinct groups: those without PE, all of whom had gestational hypertension (N = 108), and those with PE (N = 66).

## Statistical Analysis

Statistical analysis was performed via IBM SPSS Statistics version 29.0 (IBM Corp, Armonk, NY, USA). We used the Shapiro–Wilk test and the shape of the histogram to check normality. Continuous variables that followed a normal distribution are presented as the means ± SDs. Independent sample *t* test was used to compare continuous variables between two groups, whereas one-way analysis of variance (ANOVA) was used for comparisons among four groups. Continuous variables that did not follow a normal distribution are reported as medians with interquartile ranges (25th–75th percentiles). The Mann–Whitney *U*-test was applied to compare non-normally distributed continuous variables between two groups, and the Kruskal–Wallis *H*-test was used for comparisons among four groups. The categorical variables are presented as frequencies and proportions (n, %), and the chi-square test was used to compare them between two groups and four groups. We used univariate logistic regression analysis to assess the factors associated with HDP and PE separately. Variables with $P < 0.05$ were included in multivariate logistic regression analysis of HDP and PE separately. Logistic regression analysis was performed with partial or all adjustments for potential covariates. We also performed subgroup analysis to assess the associations between PIV and the risk of HDP and PE. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Receiver operating characteristic (ROC) curves were used to calculate the area under the curve (AUC) to evaluate the diagnostic value of PIV for predicting HDP and PE. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

# Results

## Baseline Characteristics

Table 1 showed the clinical baseline characteristics of the participants after they were grouped according to HDP. The participants were divided into two groups: pregnant women without HDP (N = 828) and pregnant women with HDP (N = 174). Significant differences in assisted reproduction, parity, gestational week of delivery, pre-pregnancy BMI, systolic pressure, and diastolic pressure were detected between the two groups (all $P < 0.05$). The laboratory test results also revealed significant differences in WBC, neutrophil, lymphocyte, monocyte, hemoglobin, platelet, PIV, lnPIV, standardized PIV, ALT, TG, BUN, FPG, HbA1c, and FIB levels (all $P < 0.05$).

The baseline characteristics of the participants based on the quartiles of the PIV values were shown in Table 2. Significant differences were observed in gravidity, parity, pre-pregnancy BMI, systolic pressure, and diastolic pressure among the four groups (all $P < 0.05$). The laboratory test results also revealed significant differences in WBC, neutrophil, monocyte, platelet, ALT, TBIL, TG, BUN, Cre, FPG, HbA1c, and FIB levels (all $P < 0.05$).

Table 2 also showed the prevalence of HDP among the pregnant women in this study. Specifically, Q1 had an prevalence of 3.09% (31 out of 1002). Q2 had an prevalence of 3.29% (33 out of 1002). Q3 had an prevalence of 4.89% (49 out of 1002). Compared with the first three groups, the Q4 subgroup had a significantly greater prevalence of 6.09% (61 out of 1002) ($P < 0.001$).

**Table 1** Clinical Baseline Characteristics of the Participants After Grouping According to HDP

| Characteristics | All | Non-HDP | HDP | *P* Value |
|---|---|---|---|---|
| N | 1002 | 828 | 174 | |
| Maternal age (years) | 31.85 ± 4.08 | 31.85 ± 4.06 | 31.87 ± 4.20 | 0.959 |
| Education, n (%) | | | | 0.168 |
| Primary or below | 10 (1.0) | 8 (1.0) | 2 (1.1) | |
| Middle and high school | 287 (28.6) | 233 (28.1) | 54 (31.0) | |
| College | 518 (51.7) | 422 (51.0) | 96 (55.2) | |
| Postgraduate or above | 187 (18.7) | 165 (19.9) | 22 (12.6) | |
| Assisted reproduction, n (%) | | | | 0.034 |
| No | 921 (91.9) | 768 (92.8) | 153 (87.9) | |
| Yes | 81 (8.1) | 60 (7.2) | 21 (12.1) | |
| Gravidity, n (%) | | | | 0.162 |
| 1 | 499 (49.8) | 401 (48.4) | 98 (56.3) | |
| 2 | 285 (28.4) | 243 (29.3) | 42 (24.1) | |
| ≥ 3 | 218 (21.8) | 184 (22.2) | 34 (19.5) | |
| Parity, n (%) | | | | 0.017 |
| 1 | 686 (68.5) | 553 (66.8) | 133 (76.4) | |
| 2 | 267 (26.6) | 229 (27.7) | 38 (21.8) | |
| ≥ 3 | 49 (4.9) | 46 (5.6) | 3 (1.7) | |
| Gestational week of delivery (weeks) | 38.39 ± 1.33 | 38.49 ± 1.25 | 37.89 ± 1.56 | < 0.001 |
| Pre-pregnancy BMI (kg/m²) | 21.47 ± 2.99 | 21.17 ± 2.78 | 22.87 ± 3.51 | < 0.001 |
| Pre-pregnancy BMI category, n (%) | | | | < 0.001 |
| Underweight | 129 (12.9) | 120 (14.5) | 9 (5.2) | |
| Normal | 704 (70.3) | 594 (71.7) | 110 (63.2) | |
| Overweight | 133 (13.3) | 94 (11.4) | 39 (22.4) | |
| Obese | 36 (3.6) | 20 (2.4) | 16 (9.2) | |
| Systolic pressure (mmHg) | 108.65 ± 12.18 | 106.26 ± 10.70 | 120.03 ± 12.41 | < 0.001 |
| Diastolic pressure (mmHg) | 67.69 ± 8.51 | 66.14 ± 7.64 | 75.05 ± 8.60 | < 0.001 |
| WBC ($10^3$/μL) | 9.39 ± 2.02 | 9.28 ± 1.97 | 9.91 ± 2.17 | < 0.001 |
| Neutrophil ($10^3$/μL) | 6.99 ± 1.71 | 6.91 ± 1.69 | 7.40 ± 1.78 | < 0.001 |
| Lymphocyte ($10^3$/μL) | 1.70 ± 0.41 | 1.69 ± 0.40 | 1.77 ± 0.45 | 0.017 |
| Monocyte ($10^3$/μL) | 0.56 ± 0.20 | 0.55 ± 0.20 | 0.60 ± 0.18 | 0.004 |
| Hemoglobin (g/L) | 115.04 ± 8.72 | 114.61 ± 8.42 | 117.10 ± 9.80 | 0.002 |
| Platelet ($10^3$/μL) | 213.38 ± 48.22 | 211.31 ± 47.14 | 223.24 ± 52.08 | 0.003 |
| PIV ($10^6$/μL$^2$) | 463.91 (325.57, 669.78) | 444.12 (318.23, 643.02) | 532.85 (390.93, 751.94) | < 0.001 |
| LnPIV | 6.13 ± 0.55 | 6.10 ± 0.54 | 6.26 ± 0.58 | < 0.001 |
| Standardized PIV | −0.21 (−0.65, 0.44) | −0.27 (−0.67, 0.35) | 0.01 (−0.44, 0.70) | < 0.001 |
| ALB (g/L) | 38.09 ± 2.26 | 36.07 ± 2.36 | 36.19 ± 1.73 | 0.506 |
| ALT (U/L) | 14.00 (10.00, 21.00) | 15.00 (10.00, 22.00) | 13.00 (10.00, 18.00) | 0.025 |
| AST (U/L) | 18.00 (15.00, 22.00) | 18.00 (15.00, 22.00) | 17.00 (15.00, 21.00) | 0.086 |
| TBIL (μmol/L) | 7.07 ± 2.13 | 7.11 ± 2.19 | 6.89 ± 1.85 | 0.198 |
| TG (mmol/L) | 2.33 ± 0.89 | 2.28 ± 0.82 | 2.56 ± 1.12 | 0.002 |
| TC (mmol/L) | 6.30 ± 1.03 | 6.30 ± 1.00 | 6.32 ± 1.12 | 0.827 |
| LDL-c (mmol/L) | 3.51 ± 0.69 | 3.51 ± 0.68 | 3.52 ± 0.74 | 0.858 |
| HDL-c (mmol/L) | 2.14 ± 0.37 | 2.15 ± 0.37 | 2.12 ± 0.38 | 0.343 |
| UA (μmol/L) | 250.88 ± 49.01 | 249.44 ± 47.00 | 257.74 ± 57.26 | 0.075 |
| BUN (mmol/L) | 2.90 ± 0.69 | 2.93 ± 0.70 | 2.75 ± 0.61 | 0.001 |
| Cre (μmol/L) | 45.41 ± 6.06 | 45.46 ± 6.10 | 45.16 ± 5.88 | 0.554 |
| FPG (mmol/L) | 4.32 ± 0.39 | 4.30 ± 0.37 | 4.42 ± 0.44 | 0.001 |
| HbA1c (%) | 5.20 ± 0.33 | 5.17 ± 0.32 | 5.30 ± 0.35 | < 0.001 |
| FIB (g/L) | 3.99 ± 0.61 | 3.94 ± 0.58 | 4.21 ± 0.72 | < 0.001 |

**Abbreviations**: HDP, hypertensive disorders of pregnancy; WBC, white blood cell; PIV, pan-immune-inflammation value; ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; TG, triglyceride; TC, total cholesterol; LDL-c, low-density lipoprotein-cholesterol; HDL-c, high-density lipoprotein-cholesterol; UA, uric acid; BUN, blood urea nitrogen; Cre, creatinine; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; FIB, fibrinogen.


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**Table 2** The Baseline Characteristics Based on the Quartiles of the PIV Values

| Characteristics | Q1 | Q2 | Q3 | Q4 | *P* Value |
|---|---|---|---|---|---|
| N | 250 | 251 | 251 | 250 | |
| Maternal age (years) | 32.25 ± 3.89 | 31.67 ± 4.06 | 31.94 ± 4.25 | 31.56 ± 4.10 | 0.229 |
| Education, n (%) | | | | | 0.925 |
| Primary or below | 3 (1.2) | 1 (0.4) | 2 (0.8) | 4 (1.6) | |
| Middle and high school | 65 (26.0) | 73 (29.1) | 77 (30.7) | 72 (28.8) | |
| College | 132 (52.8) | 128 (51.0) | 128 (51.0) | 130 (52.0) | |
| Postgraduate or above | 50 (20.0) | 49 (19.5) | 44 (17.5) | 44 (17.6) | |
| Assisted reproduction, n (%) | | | | | 0.588 |
| No | 234 (93.6) | 229 (91.2) | 227 (90.4) | 231 (92.4) | |
| Yes | 16 (6.4) | 22 (8.8) | 24 (9.6) | 19 (7.6) | |
| Gravidity, n (%) | | | | | 0.003 |
| 1 | 114 (45.6) | 111 (44.2) | 124 (49.4) | 150 (60.0) | |
| 2 | 78 (31.2) | 89 (35.5) | 66 (26.3) | 52 (20.8) | |
| ≥ 3 | 58 (23.2) | 51 (20.3) | 61 (24.3) | 48 (19.2) | |
| Parity, n (%) | | | | | 0.002 |
| 1 | 153 (61.2) | 170 (67.7) | 168 (66.9) | 195 (78.0) | |
| 2 | 83 (33.2) | 67 (26.7) | 66 (26.3) | 51 (20.4) | |
| ≥ 3 | 14 (5.6) | 14 (5.6) | 17 (6.8) | 4 (1.6) | |
| Gestational week of delivery (weeks) | 38.48 ± 1.25 | 38.29 ± 1.40 | 38.51 ± 1.10 | 38.28 ± 1.52 | 0.093 |
| Pre-pregnancy BMI (kg/m²) | 20.77 ± 2.87 | 21.64 ± 3.05 | 21.68 ± 3.12 | 21.76 ± 2.81 | < 0.001 |
| Pre-pregnancy BMI category, n (%) | | | | | 0.010 |
| Underweight | 47 (18.8) | 29 (11.6) | 32 (12.7) | 21 (8.4) | |
| Normal | 175 (70.0) | 181 (72.1) | 171 (68.1) | 177 (70.8) | |
| Overweight | 22 (8.8) | 32 (12.7) | 35 (13.9) | 44 (17.6) | |
| Obese | 6 (2.4) | 9 (3.6) | 13 (5.2) | 8 (3.2) | |
| Systolic pressure (mmHg) | 106.96 ± 12.11 | 107.55 ± 11.43 | 109.87 ± 12.81 | 110.25 ± 12.08 | 0.003 |
| Diastolic pressure (mmHg) | 66.16 ± 7.75 | 67.90 ± 8.01 | 68.15 ± 9.01 | 68.55 ± 9.04 | 0.009 |
| WBC ($10^3$/μL) | 7.60 ± 1.34 | 8.93 ± 1.30 | 9.79 ± 1.34 | 11.23 ± 2.03 | < 0.001 |
| Neutrophil ($10^3$/μL) | 5.40 ± 1.08 | 6.55 ± 1.07 | 7.39 ± 1.10 | 8.63 ± 1.64 | < 0.001 |
| Lymphocyte ($10^3$/μL) | 1.68 ± 0.43 | 1.73 ± 0.41 | 1.69 ± 0.38 | 1.71 ± 0.44 | 0.547 |
| Monocyte ($10^3$/μL) | 0.41 ± 0.09 | 0.52 ± 0.09 | 0.58 ± 0.12 | 0.74 ± 0.26 | < 0.001 |
| Hemoglobin (g/L) | 115.58 ± 8.71 | 114.50 ± 8.69 | 115.25 ± 8.00 | 114.84 ± 9.46 | 0.537 |
| Platelet ($10^3$/μL) | 178.60 ± 37.03 | 204.97 ± 37.75 | 218.26 ± 38.96 | 251.72 ± 47.29 | < 0.001 |
| ALB (g/L) | 36.10 ± 1.83 | 36.28 ± 3.15 | 35.82 ± 1.90 | 36.15 ± 1.86 | 0.130 |
| ALT (U/L) | 12.00 (10.00, 19.00) | 16.00 (11.00, 22.00) | 14.00 (10.00, 21.00) | 16.00 (12.00, 23.00) | < 0.001 |
| AST (U/L) | 18.00 (15.00, 22.00) | 18.00 (15.00, 23.00) | 18.00 (15.00, 21.00) | 18.00 (16.00, 22.00) | 0.279 |
| TBIL (μmol/L) | 7.49 ± 2.43 | 7.06 ± 2.08 | 7.05 ± 2.01 | 6.70 ± 1.93 | < 0.001 |
| TG (mmol/L) | 2.15 ± 0.77 | 2.29 ± 0.91 | 2.43 ± 0.95 | 2.45 ± 0.88 | < 0.001 |
| TC (mmol/L) | 6.35 ± 1.07 | 6.24 ± 1.02 | 6.26 ± 1.07 | 6.35 ± 0.93 | 0.485 |
| LDL-c (mmol/L) | 3.53 ± 0.72 | 3.47 ± 0.68 | 3.50 ± 0.72 | 3.54 ± 0.64 | 0.734 |
| HDL-c (mmol/L) | 2.17 ± 0.39 | 2.15 ± 0.39 | 2.11 ± 0.34 | 2.15 ± 0.37 | 0.244 |
| UA (μmol/L) | 247.38 ± 46.16 | 252.06 ± 50.52 | 255.02 ± 49.59 | 249.05 ± 49.58 | 0.314 |
| BUN (mmol/L) | 2.98 ± 0.70 | 2.93 ± 0.67 | 2.89 ± 0.73 | 2.81 ± 0.64 | 0.040 |
| Cre (μmol/L) | 46.72 ± 5.92 | 45.63 ± 5.92 | 44.87 ± 6.15 | 44.41 ± 6.01 | < 0.001 |
| FPG (mmol/L) | 4.26 ± 0.37 | 4.33 ± 0.38 | 4.35 ± 0.37 | 4.37 ± 0.43 | 0.013 |
| HbA1c (%) | 5.10 ± 0.30 | 5.18 ± 0.34 | 5.21 ± 0.29 | 5.28 ± 0.36 | < 0.001 |
| FIB (g/L) | 3.78 ± 0.57 | 3.95 ± 0.58 | 4.01 ± 0.58 | 4.21 ± 0.66 | < 0.001 |
| HDP, n (%) | 31 (3.09) | 33 (3.29) | 49 (4.89) | 61 (6.09) | < 0.001 |

**Abbreviations**: HDP, hypertensive disorders of pregnancy; WBC, white blood cell; ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; TG, triglyceride; TC, total cholesterol; LDL-c, low-density lipoprotein-cholesterol; HDL-c, high-density lipoprotein-cholesterol; UA, uric acid; BUN, blood urea nitrogen; Cre, creatinine; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; FIB, fibrinogen.

## Univariate Logistic Regression Analysis of HDP and PE

Assisted reproduction, parity, pre-pregnancy BMI, neutrophil, lymphocyte, monocyte, hemoglobin, platelet, PIV, ALT, TG, UA, BUN, FPG, HbA1c, and FIB were significantly associated with HDP in the univariate logistic regression analysis (all $P < 0.05$). Furthermore, parity, ALT and BUN are protective factors, and assisted reproduction, pre-pregnancy BMI, neutrophil, lymphocyte, monocyte, hemoglobin, platelet, PIV, TG, UA, FPG, HbA1c and FIB were risk factors (Table 3).

**Table 3** Univariate Logistic Regression Analysis of HDP and PE

| Variable | HDP | | | PE | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* Value | OR | 95% CI | *P* Value |
| Maternal age | 1.001 | 0.962–1.042 | 0.959 | 1.003 | 0.942–1.067 | 0.932 |
| Education | | | | | | |
| Primary or below | Ref | | | Ref | | |
| Middle school | 0.927 | 0.191–4.490 | 0.925 | 0.790 | 0.095–6.596 | 0.827 |
| College | 0.910 | 0.190–4.353 | 0.906 | 0.645 | 0.078–5.306 | 0.683 |
| Postgraduate or above | 0.553 | 0.106–2.674 | 0.445 | 0.388 | 0.043–3.489 | 0.398 |
| Assisted reproduction | 1.757 | 1.038–2.974 | 0.036 | 2.286 | 1.110–4.707 | 0.025 |
| Gravidity | | | | | | |
| 1 | Ref | | | Ref | | |
| 2 | 0.707 | 0.476–1.050 | 0.086 | 0.592 | 0.315–1.113 | 0.104 |
| ≥ 3 | 0.756 | 0.493–1.159 | 0.200 | 0.726 | 0.379–1.394 | 0.726 |
| Parity | | | | | | |
| 1 | Ref | | | Ref | | |
| 2 | 0.690 | 0.466–1.021 | 0.064 | 0.676 | 0.367–1.247 | 0.676 |
| ≥ 3 | 0.271 | 0.083–0.885 | 0.031 | 0.481 | 0.1132.040 | 0.321 |
| Pre-pregnancy BMI | 1.190 | 1.129–1.254 | < 0.001 | 1.219 | 1.132–1.313 | < 0.001 |
| WBC | 1.017 | 0.987–1.048 | 0.267 | 1.174 | 1.045–1.318 | 0.007 |
| Neutrophil | 1.177 | 1.073–1.292 | < 0.001 | 1.189 | 1.036–1.365 | 0.014 |
| Lymphocyte | 1.589 | 1.084–2.329 | 0.018 | 1.390 | 0.772–2.503 | 0.272 |
| Monocyte | 2.875 | 1.234–6.698 | 0.014 | 2.799 | 1.061–7.382 | 0.038 |
| Hemoglobin | 1.034 | 1.014–1.054 | < 0.001 | 1.038 | 1.008–1.069 | 0.013 |
| Platelet | 1.005 | 1.002–1.008 | 0.003 | 1.009 | 1.004–1.014 | < 0.001 |
| PIV | 1.001 | 1.000–1.001 | < 0.001 | 1.001 | 1.001–1.002 | < 0.001 |
| LnPIV | 1.709 | 1.257–2.324 | < 0.001 | 2.363 | 1.474–3.786 | < 0.001 |
| Standardized PIV | 1.289 | 1.112–1.495 | < 0.001 | 1.436 | 1.182–1.744 | < 0.001 |
| ALB | 1.023 | 0.956–1.095 | 0.506 | 1.037 | 0.947–1.136 | 0.434 |
| ALT | 0.983 | 0.966–0.999 | 0.038 | 0.990 | 0.967–1.013 | 0.394 |
| AST | 0.983 | 0.958–1.010 | 0.213 | 0.997 | 0.962–1.035 | 0.889 |
| TBIL | 0.948 | 0.874–1.028 | 0.198 | 0.940 | 0.829–1.066 | 0.338 |
| TG | 1.369 | 1.159–1.617 | < 0.001 | 1.380 | 1.073–1.775 | 0.012 |
| TC | 1.018 | 0.868–1.194 | 0.826 | 1.191 | 0.935–1.518 | 0.158 |
| LDL-c | 1.022 | 0.807–1.294 | 0.858 | 1.295 | 0.907–1.849 | 0.156 |
| HDL-c | 0.807 | 0.518–1.257 | 0.343 | 1.103 | 0.568–2.140 | 0.773 |
| UA | 1.003 | 1.000–1.007 | 0.043 | 1.004 | 0.999–1.009 | 0.141 |
| BUN | 0.654 | 0.504–0.848 | 0.001 | 0.681 | 0.457–1.014 | 0.058 |
| Cre | 0.992 | 0.965–1.019 | 0.554 | 0.976 | 0.936–1.018 | 0.258 |
| FPG | 2.085 | 1.393–3.121 | < 0.001 | 2.415 | 1.323–4.411 | 0.004 |
| HbA1c | 3.097 | 1.866–5.141 | < 0.001 | 2.023 | 0.925–4.422 | 0.077 |
| FIB | 2.022 | 1.557–2.626 | < 0.001 | 2.522 | 1.718–3.702 | < 0.001 |

**Abbreviations**: HDP, hypertensive disorders of pregnancy; PE, preeclampsia; OR, odds ratio; CI, confidence interval; WBC, white blood cell; PIV, pan-immune-inflammation value; ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; TG, triglyceride; TC, total cholesterol; LDL-c, low-density lipoprotein-cholesterol; HDL-c, high-density lipoprotein-cholesterol; UA, uric acid; BUN, blood urea nitrogen; Cre, creatinine; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; FIB, fibrinogen.


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We also performed univariate logistic regression analysis of PE. As shown in Table 3, assisted reproduction, pre-pregnancy BMI, WBC, neutrophil, monocyte, hemoglobin, platelet, PIV, TG, FPG, and FIB were significantly associated with PE (all $P < 0.05$).

## Multivariate Logistic Regression Analysis of PIV and the Risk of HDP and PE

In Table 4, to ascertain the stability of this relationship under various conditions, we constructed two additional models for verification. In Model 1, the variables adjusted for were basic characteristics, including assisted reproduction, parity, and pre-pregnancy BMI. Logistic regression analysis revealed that whether as a continuous variable or multiple categorical variables, PIV was associated with the risk of HDP ($P < 0.05$). In Model 2, hemoglobin, ALT, TG, UA, BUN, FPG, HbA1c, and FIB were added as covariates, alongside assisted reproduction, parity, and pre-pregnancy BMI. Similar results were obtained for this model, except for lnPIV and four-category PIV. We found that the risk of HDP increased by 0.1% for every unit elevated and increased by 19.9% for every SD elevated ($P < 0.05$). The risk of HDP in the high PIV group was 1.546 times greater than that in the low PIV group [OR: 1.546 (95%: 1.078–2.217) $P < 0.05$]. Compared with the reference T1 group, the T3 group was significantly associated with the risk of HDP [OR: 1.592 (95%: 1.015–2.497) $P < 0.05$].

Additionally, we constructed two models of PE. In Model 1, the variables adjusted for were basic characteristics, including assisted reproduction and pre-pregnancy BMI. Logistic regression analysis revealed that whether as a continuous variable or multiple categorical variables, PIV was associated with the risk of PE (all $P < 0.05$). In Model 2, hemoglobin, TG, FPG, and FIB were added as covariates, in addition to assisted reproduction and pre-pregnancy BMI. We found that the risk of PE increased by 0.1% for PIV every elevated unit and increased by 37.9% for every elevated SD (all $P < 0.05$). The risk of PE increased by 101.1% for lnPIV at every elevated unit ($P < 0.05$). Among the tertile groups, Group T3 had a greater adjusted OR for developing PE compared to the reference Group T1 [OR: 3.015 (95%: 1.465–6.204) $P < 0.05$]. Compared with the reference Group Q1, Group Q4 had a greater adjusted OR for developing PE [OR: 4.420 (95%: 1.755–11.134), $P < 0.05$] (Table 4).

## Subgroup Analysis Exploring the Associations Between PIV and the Risk of HDP and PE

Subgroup analysis by maternal age, gravidity, parity, and pre-pregnancy BMI was conducted, as presented in Table 5. PIV, lnPIV, standardized PIV, high PIV (vs low PIV), T3 (vs T1), and Q4 (vs Q1) were significantly associated with the

**Table 4** Multivariate Logistic Regression Analysis of PIV and the Risk of HDP and PE

| | PIV and HDP | | | | PIV and PE | | | |
|---|---|---|---|---|---|---|---|---|
| | Model 1 | | Model 2 | | Model 1 | | Model 2 | |
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| PIV[a] | 1.001 (1.000–1.001) | 0.003 | 1.001 (1.000–1.001) | 0.026 | 1.001 (1.001–1.002) | < 0.001 | 1.001 (1.000–1.002) | 0.001 |
| LnPIV[a] | 1.551 (1.124–2.141) | 0.008 | 1.333 (0.950–1.870) | 0.097 | 2.376 (1.452–3.890) | < 0.001 | 2.011 (1.212–3.335) | 0.007 |
| Standardized PIV[b] | 1.259 (1.081–1.466) | 0.003 | 1.199 (1.022–1.407) | 0.026 | 1.461 (1.200–1.777) | < 0.001 | 1.379 (1.132–1.681) | 0.001 |
| Low PIV | Ref | | Ref | | Ref | | Ref | |
| High PIV | 1.746 (1.233–2.473) | 0.002 | 1.546 (1.078–2.217) | 0.018 | 2.897 (1.632–5.141) | < 0.001 | 2.474 (1.387–4.415) | 0.002 |
| T1 | Ref | | Ref | | Ref | | Ref | |
| T2 | 1.308 (0.833–2.053) | 0.243 | 1.211 (0.764–1.919) | 0.415 | 1.572 (0.718–3.445) | 0.258 | 1.510 (0.690–3.306) | 0.303 |
| T3 | 1.899 (1.237–2.915) | 0.003 | 1.592 (1.015–2.497) | 0.043 | 3.632 (1.788–7.378) | < 0.001 | 3.015 (1.465–6.204) | 0.003 |
| P for trend | | 0.011 | | 0.115 | | < 0.001 | | 0.005 |
| Q1 | Ref | | Ref | | Ref | | Ref | |
| Q2 | 0.871 (0.506–1.499) | 0.618 | 0.868 (0.498–1.512) | 0.617 | 1.611 (0.580–4.476) | 0.360 | 1.652 (0.598–4.564) | 0.333 |
| Q3 | 1.451 (0.875–2.404) | 0.149 | 1.298 (0.772–2.184) | 0.325 | 2.571 (0.982–6.732) | 0.055 | 2.410 (0.917–6.337) | 0.074 |
| Q4 | 1.799 (1.101–2.942) | 0.019 | 1.519 (0.900–2.562) | 0.117 | 5.297 (2.137–13.130) | < 0.001 | 4.420 (1.755–11.134) | 0.002 |
| P for trend | | 0.011 | | 0.127 | | < 0.001 | | 0.003 |

**Notes**: [a]per unit; [b]per SD. For HDP, Model 1: was adjusted only for assisted reproduction, parity and pre-pregnancy BMI; Model 2: was adjusted for assisted reproduction, parity, pre-pregnancy BMI, hemoglobin, ALT, TG, UA, BUN, FPG, HbA1c and FIB. For PE, Model 1: was adjusted only for assisted reproduction and pre-pregnancy BMI; Model 2: was adjusted for assisted reproduction, pre-pregnancy BMI, hemoglobin, TG, FPG and FIB.

**Abbreviations**: PIV, pan-immune-inflammation value; HDP, hypertensive disorders of pregnancy; PE, preeclampsia; OR, odds ratio; CI, confidence interval.

**Table 5** Subgroup Analysis Exploring the Association Between PIV and the Risk of HDP

| | PIV[a] | LnPIV[a] | Standardized PIV[b] | PIV (High vs Low) | PIV (T2 vs T1) | PIV (T3 vs T1) | PIV (Q2 vs Q1) | PIV (Q3 vs Q1) | PIV (Q4 vs Q1) |
|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* |
| Maternal age | | | | | | | | | |
| < 35 years | 1.001 (1.000–1.002) < 0.001 | 1.921 (1.303–2.834) < 0.001 | 1.405 (1.169–1.688) < 0.001 | 1.755 (1.169–2.634) 0.007 | 1.466 (0.856–2.511) 0.163 | 2.144 (1.291–3.561) 0.003 | 1.159 (0.608–2.208) 0.654 | 1.558 (0.833–2.913) 0.165 | 2.255 (1.246–4.081) 0.007 |
| ≥ 35 years | 1.000 (0.999–1.001) 0.745 | 0.901 (0.484–1.677) 0.742 | 0.942 (0.657–1.351) 0.745 | 1.487 (0.724–3.054) 0.280 | 0.941 (0.387–2.288) 0.893 | 1.218 (0.498–2.979) 0.666 | 0.568 (0.177–1.816) 0.340 | 1.352 (0.536–3.412) 0.523 | 0.971 (0.343–2.746) 0.955 |
| Gravidity | | | | | | | | | |
| 1 | 1.000 (0.999–1.001) 0.703 | 1.104 (0.706–1.726) 0.665 | 1.042 (0.841–1.292) 0.703 | 1.388 (0.843–2.286) 0.197 | 1.594 (0.828–3.070) 0.163 | 1.698 (0.911–3.162) 0.095 | 0.822 (0.378–1.787) 0.621 | 1.332 (0.656–2.702) 0.427 | 1.190 (0.591–2.396) 0.625 |
| ≥ 2 | 1.001 (1.000–1.002) 0.008 | 1.783 (1.067–2.981) 0.027 | 1.420 (1.098–1.836) 0.008 | 1.706 (1.003–2.901) 0.049 | 0.852 (0.436–1.664) 0.639 | 1.438 (0.732–2.826) 0.292 | 0.858 (0.379–1.942) 0.714 | 1.170 (0.533–2.568) 0.695 | 1.951 (0.875–4.349) 0.102 |
| Parity | | | | | | | | | |
| 1 | 1.000 (0.999–1.001) 0.192 | 1.268 (0.851–1.889) 0.244 | 1.133 (0.939–1.367) 0.192 | 1.808 (1.198–2.728) 0.005 | 1.307 (0.753–2.267) 0.341 | 1.757 (1.034–2.985) 0.037 | 0.762 (0.393–1.478) 0.422 | 1.356 (0.738–2.490) 0.326 | 1.396 (0.762–2.556) 0.281 |
| ≥ 2 | 1.001 (1.000–1.002) 0.023 | 1.499 (0.777–2.891) 0.227 | 1.421 (1.051–1.922) 0.023 | 1.381 (0.676–2.819) 0.376 | 0.963 (0.401–2.311) 0.932 | 1.210 (0.500–2.928) 0.673 | 1.045 (0.364–2.998) 0.935 | 1.067 (0.374–3.041) 0.903 | 1.956 (0.685–5.584) 0.210 |
| Pre-pregnancy BMI | | | | | | | | | |
| Normal | 1.001 (1.000–1.001) 0.009 | 1.588 (1.087–2.320) 0.017 | 1.257 (1.059–1.492) 0.009 | 1.805 (1.180–2.762) 0.006 | 1.226 (0.703–2.137) 0.472 | 1.637 (0.946–2.832) 0.078 | 0.644 (0.326–1.274) 0.206 | 1.327 (0.726–2.427) 0.358 | 1.362 (0.731–2.537) 0.331 |
| Abnormal* | 1.000 (0.999–1.001) 0.889 | 1.129 (0.597–2.135) 0.708 | 1.027 (0.704–1.500) 0.889 | 1.291 (0.654–2.551) 0.462 | 1.257 (0.532–2.968) 0.602 | 1.491 (0.649–3.425) 0.347 | 1.678 (0.572–4.922) 0.346 | 1.454 (0.503–4.200) 0.489 | 2.153 (0.754–6.151) 0.152 |

**Notes**: [a]per unit; [b]per SD. Subgroup analysis adjusted for assisted reproduction, parity, pre-pregnancy BMI, hemoglobin, ALT, TG, UA, BUN, FPG, HbA1c and FIB. *Abnormal of pre-pregnancy BMI includes underweight (< 18.5 kg/m²), overweight (24.0–28.0 kg/m²) and obese (≥ 28.0 kg/m²).

**Abbreviations**: PIV, pan-immune-inflammation value; OR, odds ratio; CI, confidence interval.

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risk of HDP among pregnant women aged < 35 years (all $P < 0.05$). PIV, lnPIV, standardized PIV, and high PIV (vs low PIV) were significantly associated with the risk of HDP among pregnant women with gravidity ≥ 2 and normal pre-pregnancy BMI. High PIV (vs low PIV) and T3 (vs T1) were significantly associated with the risk of HDP among primiparas, and there was a significant correlation between PIV and standardized PIV with the risk of HDP among multiparas (all $P < 0.05$).

In the subgroup analysis of PE, PIV, lnPIV, standardized PIV, high PIV (vs low PIV), T2 (vs T1), T3 (vs T1), Q3 (vs Q1), and Q4 (vs Q1) were significantly associated with the risk of PE among pregnant women aged < 35 years (all $P < 0.05$). In the quartile groups, the risk of PE in Group Q4 was 11.994 times greater than that in Group Q1 [OR: 11.994 (95%: 2.726–52.779) $P < 0.05$]. PIV, lnPIV, standardized PIV, high PIV (vs low PIV), T3 (vs T1), and Q4 (vs Q1) were significantly associated with the risk of PE among pregnant women with normal pre-pregnancy BMI (all $P < 0.05$). Notably, the risk of PE in Group Q4 was 7.060 times greater than that in Group Q1 in the quartile groups [OR: 7.060 (95%: 2.043–24.394) $P < 0.05$]. PE risk in different PIV groups varied slightly in gravidity and parity subgroups ($P < 0.05$) (Table 6).

## ROC Curve Analyses of PIV to Predict HDP and PE

As shown in Figure 2, the ROC curve analyses indicated that PIV had a high predictive value for both HDP and PE. The AUC for PIV in predicting HDP was 0.594 (95% CI: 0.547–0.641 $P < 0.001$), whereas the AUC for PIV in predicting PE was 0.652 (95% CI: 0.582–0.722 $P < 0.001$).

# Discussion

This retrospective study systematically demonstrated a strong relationship between PIV with DHP and PE. The study revealed that patients with HDP had higher PIV values. The prevalence of HDP increased significantly with increasing PIV in the quartile group. In particular, Group Q4 had a significantly greater prevalence of 6.09% (61 out of 1002) compared to the first three groups ($P < 0.001$). According to the univariate logistic regression analysis, PIV was a risk factor for developing HDP and PE ($P < 0.001$). Even after adjusting for partial or all potential confounding factors, PIV maintained independent predictive significance for both HDP and PE. In the subgroup with age < 35 years and normal pre-pregnancy BMI, a higher PIV was significantly associated with a greater risk of HDP and PE. The ROC curve analyses indicated that PIV had a high predictive value for both HDP and PE. These findings suggest that PIV is a simple but valuable predictor of both HDP and PE.

Considering the profound effects of HDP and PE on maternal and perinatal health outcomes worldwide, there is a pressing need to develop reliable predictive tests for HDP and PE. These tests should be crucial for facilitating early detection, focused monitoring, and prompt intervention. Research indicates that maternal systemic inflammation is correlated with an increased risk of HDP and PE.[21] Recently, markers of systemic inflammation, calculated from complete blood count (CBC) analysis, have been suggested as early indicators of HDP and PE. For instance, Kang et al proposed that the NLR has significant predictive value in patients with severe PE.[22] Conversely, Urtoglu E et al reported no statistically significant association between the NLR and the severity of PE.[23] The platelet-to-lymphocyte ratio (PLR) has been previously examined as an inflammatory marker for predicting PE and its severity, yet the results have been inconsistent.[24,25] In addition, the SII has been studied as a potential predictor of PE[26] but has not been used as a practical clinical marker. PIV, recognized as a novel biomarker for the immune-inflammatory response, is a recently established scoring system that encompasses neutrophils, platelets, monocytes, and lymphocytes in peripheral blood.[27] It has shown considerable effectiveness as a prognostic biomarker in particular malignancies.[28,29] However, the relationship between PIV and HDP has not yet been systematically investigated. Our results corroborated and extended previous observations linking systemic inflammation to HDP and PE pathogenesis. The results of this study indicated that peripheral PIV levels were significantly increased in pregnant women with HDP and PE. Notably, lnPIV, which was converted to a normal distribution, and standardized PIV were both strongly correlated with HDP and PE risk. Logistic regression analysis revealed that PIV was independently correlated with HDP and PE after adjusting for potential confounders. The ROC curve analyses also indicated that PIV had a high predictive value for HDP and PE risk. These findings have important implications for the prediction and management of HDP and PE.

**Table 6** Subgroup Analysis Exploring the Association Between PIV and the Risk of PE

| | PIV[a] | LnPIV[a] | Standardized PIV[b] | PIV (High vs Low) | PIV (T2 vs T1) | PIV (T3 vs T1) | PIV (Q2 vs Q1) | PIV (Q3 vs Q1) | PIV (Q4 vs Q1) |
|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* | OR (95% CI) *P* |
| Maternal age | | | | | | | | | |
| < 35 years | 1.002 (1.001–1.003) < 0.001 | 4.133 (2.212–7.722) < 0.001 | 1.743 (1.364–2.227) < 0.001 | 3.156 (1.534–6.493) 0.002 | 2.953 (1.008–8.652) 0.048 | 6.568 (2.401–17.968) < 0.001 | 3.495 (0.723–16.895) 0.120 | 5.628 (1.218–25.994) 0.027 | 11.994 (2.726–52.779) 0.001 |
| ≥ 35 years | 1.000 (0.999–1.001) 0.911 | 0.776 (0.334–1.801) 0.555 | 1.024 (0.679–1.545) 0.911 | 1.479 (0.522–4.196) 0.462 | 0.674 (0.176–2.577) 0.564 | 1.389 (0.406–4.751) 0.601 | 0.913 (0.185–4.497) 0.911 | 1.016 (0.236–4.380) 0.983 | 2.031 (0.489–8.438) 0.329 |
| Gravidity | | | | | | | | | |
| 1 | 1.001 (1.000–1.001) 0.136 | 2.248 (1.152–4.387) 0.018 | 1.220 (0.940–1.584) 0.136 | 4.432 (1.798–10.926) 0.001 | 2.933 (0.732–11.750) 0.129 | 7.362 (2.063–26.279) 0.002 | 1.672 (0.293–9.543) 0.563 | 4.262 (0.864–21.013) 0.075 | 7.628 (1.671–34.819) 0.009 |
| ≥ 2 | 1.001 (1.000–1.002) 0.006 | 1.611 (0.747–3.474) 0.224 | 1.557 (1.134–2.137) 0.006 | 1.471 (0.639–3.385) 0.365 | 1.043 (0.382–2.852) 0.934 | 1.398 (0.504–3.882) 0.520 | 1.642 (0.457–5.901) 0.448 | 1.456 (0.397–5.337) 0.571 | 2.738 (0.766–9.792) 0.121 |
| Parity | | | | | | | | | |
| 1 | 1.001 (1.000–1.002) 0.008 | 2.183 (1.185–4.020) 0.012 | 1.360 (1.083–1.706) 0.008 | 3.423 (1.621–7.225) 0.001 | 2.077 (0.749–5.760) 0.160 | 4.027 (1.540–10.532) 0.005 | 1.600 (0.395–6.480) 0.511 | 3.711 (1.006–13.690) 0.049 | 5.531 (1.563–19.566) 0.008 |
| ≥ 2 | 1.001 (1.000–1.003) 0.029 | 1.725 (0.676–4.407) 0.254 | 1.559 (1.047–2.321) 0.029 | 1.634 (0.562–4.749) 0.367 | 0.984 (0.251–3.862) 0.981 | 2.130 (0.614–7.388) 0.234 | 1.675 (0.355–7.908) 0.515 | 1.158 (0.220–6.095) 0.863 | 3.924 (0.851–18.100) 0.080 |
| Pre-pregnancy BMI | | | | | | | | | |
| Normal | 1.001 (1.000–1.002) < 0.001 | 3.155 (1.699–5.857) < 0.001 | 1.529 (1.218–1.918) < 0.001 | 4.063 (1.826–9.040) < 0.001 | 3.064 (0.967–9.707) 0.057 | 5.694 (1.918–16.901) 0.002 | 1.167 (0.378–6.915) 0.517 | 3.593 (0.964–13.390) 0.057 | 7.060 (2.043–24.394) 0.002 |
| Abnormal* | 1.000 (0.999–1.002) 0.665 | 1.137 (0.492–2.627) 0.765 | 1.112 (0.668–1.796) 0.665 | 1.543 (0.613–3.887) 0.357 | 0.652 (0.189–2.252) 0.499 | 1.750 (0.599–5.116) 0.306 | 1.720 (0.380–7.781) 0.482 | 1.648 (0.379–7.172) 0.505 | 2.770 (0.656–11.693) 0.165 |

**Notes**: [a]per unit; [b]per SD. Subgroup analysis adjusted for assisted reproduction, pre-pregnancy BMI, hemoglobin, TG, FPG and FIB. *Abnormal of pre-pregnancy BMI includes underweight (< 18.5 kg/m²), overweight (24.0–28.0 kg/m²) and obese (≥ 28.0 kg/m²).

**Abbreviations**: PIV, pan-immune-inflammation value; OR, odds ratio; CI, confidence interval.

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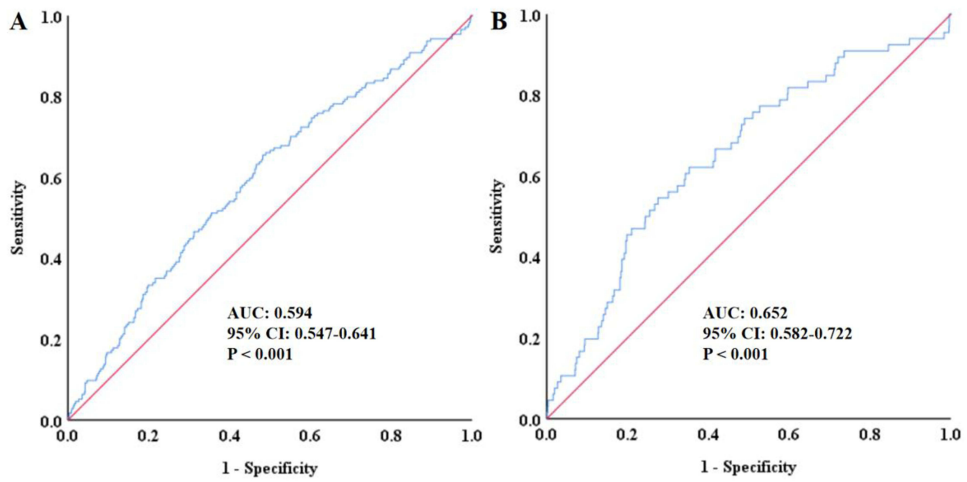


**Figure 2** ROC curve analyses of the ability of PIV to predict HDP and PE. (**A**) ROC curve analyses of PIV to predict HDP; (**B**) ROC curve analyses of PIV to predict PE. **Abbreviations**: PIV, pan-immune-inflammation value; HDP, hypertensive disorders of pregnancy; PE, preeclampsia; AUC, area under the curve; CI, confidence interval.

HDP include a variety of conditions, and PE is a major and relatively prevalent disease within this classification.[15] PE is a multifaceted disorder with complex origins that affects the brain, liver, heart, and kidneys.[30] Despite the breadth of research conducted, the specific mechanisms underlying the development of PE remain largely elusive. A growing body of research has shown that inflammation plays a significant role in the pathophysiological mechanisms of HDP and PE. The more accepted hypothesis is the two-stage hypothesis:[31] (1) Abnormal Placentation: In early pregnancy in PE, insufficient extravillous trophoblast invasion and spiral artery remodeling are insufficient due to genetic predisposition, reduced human leukocyte antigen G expression, or dysfunction between uterine NK cells and trophoblast cells, leading to reduced placental perfusion and hypoxia.[32,33] (2) Maternal systemic inflammatory response and oxidative stress: The production of pro-inflammatory cytokines during placental ischemia and hypoxia induces a systemic inflammatory response in PE, resulting in endothelial damage.[34] The activation of inflammatory cells releases excess reactive oxygen species and pro-inflammatory mediators, sustaining the cycle of endothelial injury and oxidative stress.[35] Systemic inflammation is characterized by persistent immune activation and increased levels of inflammatory cytokines, which play a significant role in the pathogenesis of PE.[31] Interleukin-6 (IL-6) stimulates neutrophil proliferation, maturation and activation, IL-8 stimulates neutrophil degranulation and neutrophil recruitment to the endometrium,[36] and IL-17A stimulates the expression of neutrophil chemokines in vascular smooth muscle, which subsequently increases neutrophil production.[37] Furthermore, elevated pro-inflammatory mediators such as IL-1β, IL-6, and mononuclear chemotactic protein-1 shift macrophage differentiation from the M2 (anti-inflammatory) phenotype to the M1 (pro-inflammatory) phenotype.[38] Ma et al reported that the number of CD14+CD11c+CD163- (M1) monocytes in women with PE was significantly greater. Specifically, the study revealed a reduction in the number of anti-inflammatory (classical) monocytes and a notable increase in the number of pro-inflammatory (intermediate and non-classical) monocytes in PE women. This shift resulted in an elevated monocyte count and an increased monocyte / lymphocyte ratio in pregnant women with PE.[39] These pro-inflammatory cytokines can directly or indirectly suppress regulatory T cell (Treg) proliferation and function, and may even drive their differentiation into other T cell subsets, such as Th17 cells, consequently aggravating the Treg/Th17 imbalance.[40] All these pro-inflammatory mediators play a role in endothelial dysfunction by upregulating adhesion molecule expression and diminishing the bioavailability of nitric oxide.[21] Endothelial dysfunction in PE further leads to uncontrolled platelet activation and consumption, and an increase in platelets could be a response to the inflammatory state at the onset of PE.[41]

The observed correlation between PIV levels and an increased risk of HDP and PE provides further evidence for the significant role of systemic immuno-inflammatory responses in the pathophysiological mechanisms of these conditions. Consequently, we propose immunological interventions as a potentially important therapeutic strategy for HDP and PE. Currently, low-dose aspirin, exerting its effects through antiplatelet aggregation and anti-inflammatory mechanisms, is

widely used for PE prophylaxis in high-risk populations, typically initiated in early pregnancy.[42] Elevated levels of oxidative stress markers and decreased levels of antioxidants (such as vitamin E, vitamin C, and lycopene) in PE patients suggest that antioxidant supplementation may represent a simple and effective therapeutic approach.[43,44] In recent years, monoclonal antibodies targeting cytokines such as tumor necrosis factor-α, IL-6, and IL-17 have demonstrated efficacy in other inflammatory diseases; however, their investigation in PE remains in the early stages.[45–47] Some studies have indicated that intravenous immunoglobulin may improve clinical symptoms in a subset of PE patients,[48] but its safety profile during pregnancy, particularly concerning potential infusion reactions, necessitates cautious evaluation. In conclusion, immunological interventions has shown some potential in the treatment of HDP and PE, but it is still in the early stage of research. In the future, more basic research and clinical trials are needed to explore safer and more effective immunotherapy strategies.

The current study appeared to be a systematic report of the relationship between PIV and the risk of HDP and PE. Our study revealed that PIV had important implications for the prediction and management of HDP. Meanwhile, subgroup analyses identified vulnerable populations, revealing that younger women (< 35 years) and those with normal pre-pregnancy BMI exhibited amplified PIV-related risks, which may inform targeted screening strategies. The possible reasons are younger women exhibit higher metabolic rates, as well as elevated levels of inflammation and oxidative stress. Pregnant women with a normal pre-pregnancy BMI likely have more balanced nutrition and metabolism, thus the relationship between PIV and the risk of HDP and PE is more pronounced. Conversely, metabolic imbalances in pregnant women with abnormal pre-pregnancy BMI (including underweight, overweight, and obese) may attenuate the effect of PIV on the risk of developing HDP and PE.

Despite the merits and innovations of our study, several limitations must be acknowledged. First, we need to collect sufficient information about the participants, such as their dietary and exercise factors, medical interventions, or other unknown and complex factors that may act as confounders. Second, our analysis was based on the small sample size of a single center, which likely introduced selection bias and limited the generalizability of the results. Therefore, further multicenter and future studies are needed to investigate the utility of PIV in predicting HDP in different ethnicities and gestational ages. Third, we did not include pregnant women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome or eclampsia. So that it narrowed the clinical applicability of findings, as these conditions often exhibit distinct inflammatory properties. Fourth, owing to the small number of PE cases, pregnant women with PE were not further classified into mild PE and severe PE groups; therefore, further research is needed.

This study confirmed that PIV was significantly associated with HDP and PE. These findings suggest that PIV, an inflammatory marker, may have significant clinical value in the risk monitoring and prognostic assessment of HDP and PE. More large-sample, multicenter clinical studies are needed to further explore these associations in the future.

## Conclusions

This study demonstrates that PIV serves as a robust biomarker for predicting HDP, particularly PE. These parameters can provide less expensive monitoring indicators and valuable advice for healthcare personnel. Thus they can help them identify women in “high-risk” groups and implement tailored prenatal surveillance, with the potential to reduce complications associated with HDP and PE and facilitate early identification and rapid processing of HDP and PE.

## Data Sharing Statement

The data are available from the corresponding author (Zhenghui Cui) upon reasonable request.

## Ethical Approval and Informed Consent

This research was reviewed and approved by the Ethics Committee of Women’s Hospital, Zhejiang University School of Medicine (approval number: IRB-20250161-R). The research protocol complied with the Declaration of Helsinki in 1964 and its current amendments. This research was a retrospective analysis, and all the data were collected from previous clinical records. The Ethics Committee of Women’s Hospital, Zhejiang University School of Medicine approved the informed consent exemption due to anonymous patient records.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no conflicts of interest.

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