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The prognostic nutritional index is associated with preeclampsia in twin pregnancies

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Abstract

Objective We aimed to investigate the relationship between the prognostic nutritional index (PNI) during the third trimester and the risk of preeclampsia (PE) in twin pregnancies.

Method A total of 2998 twin pregnancies were enrolled in Fujian Maternal and Child Health Hospital from January 2015 to December 2021, including preeclampsia group ($n=421$) and control group ($n=2577$). The significance of the characteristic variables in predicting PE in twin pregnancies were calculated using the random forest algorithm (Boruta package) and the correlation between PNI and PE in twin pregnancies was examined in three distinct models using multivariable logistic regression corrected for confounders. Receiver operating characteristics (ROC) curves were used to evaluate the ability for PNI to predict PE in twin pregnancies.

Results PNI (37.92 ± 3.86 vs. 40.57 ± 3.63, $P<0.001$) was significantly lower in the PE group than in the control group. After adjusting for all covariates, the PNI was negatively associated with PE in twin pregnancies (OR = 0.780; 95% CI: 0.753, 0.808). Meanwhile, the higher PNI remained an independent protective factor for PE in twin pregnancies compared to lower PNI (OR, 95% CI: 0.410, 0.438–0.530; 0.144, 0.103–0.201) in sensitivity analysis. ROC curve analysis revealed an area under curve (AUC) of 0.691 for PNI and the cut-off value of PNI was 40.162.

Conclusion PNI was negatively correlated with the risk of PE in twin pregnancies, which may help in risk assessment for twin pregnancies.

Clinical trial number Not applicable.

Keywords Prognostic nutritional index, Preeclampsia, Twin pregnancies, Multivariable logistic regression, The random forest algorithm

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Introduction

Preeclampsia (PE), a pregnancy-related hypertensive disorder, affects 2–8% of pregnancies globally and is a leading cause of significant maternal and perinatal morbidity and mortality [1, 2]. The underlying mechanisms contributing to the pathophysiology of preeclampsia remain poorly understood, as it is a complex disease process that originates at the maternal-fetal interface and affects multiple organ systems [3]. It is thought to involve abnormal placental vascular development, characterized by defective deep placentation and inadequate spiral artery.

Recent studies have shown that the nutrition and the release of inflammatory factors play an important role in placental endothelial function and oxidative stress [4, 5]. Therefore, the significance of serum inflammatory markers as predictive indicators for preeclampsia has been extensively studied [6, 7]. As pregnant women encounter a wide range of nutritional challenges throughout their pregnancy, there is an increasing number of studies exploring the predictive value of inflammatory-nutritional markers in adverse pregnancy outcomes [8, 9]. Malnutrition, in conjunction with poor health behavior, is one of the most significant factors responsible for preeclampsia among pregnant women [10, 11]. Body mass index (BMI), calculated based on pre-pregnancy weight, is often used to assess nutritional status [12]. Whlie, relying solely on a single nutritional index represents an oversimplified and clinically unreliable evaluation method. The prognostic nutritional index (PNI), which is calculated by using serum albumin (ALB) concentration and peripheral blood lymphocyte count, has been proposed as a marker of immune-nutrition and reflects the chronic inflammation, immune status, and nutrition of the individual [13]. Recently, as an easily accessible and non-invasive biomarker, PNI has attracted more attention and has been extensively used for the clinical evaluation of the prognosis in patients with adverse cardiovascular events and tumor [14, 15]. However, its application in obstetrics has been explored in only a limited number of studies. A recent study found that the PNI is lower in patients with early-onset PE than in normotensive pregnant patients [16]. Besides, Songquan Wei et al. reported that high PNI score at admission was associated with reduced in-hospitalization risk of adverse events in patients with PE [17]. Nevertheless, the association between PNI and PE in twin pregnancies remains uncertain.

Twin pregnancy rates have increased in the past 30 years, particularly in high-income or middle-income countries, owing to an increased use of assisted reproductive techniques [18]. Twin pregnancies are associated with maternal and fetal adverse outcomes, including severe maternal morbidity (SMM) and neonatal near-miss (NNM) [19]. Besides, the risk of PE in twin pregnancies is 3–4 times higher than in singleton pregnancies [20]. The underlying mechanisms may involve the expanded placental mass, hemodynamic overload, endothelial dysfunction, oxidative stress, and immune dysregulation characteristic of twin pregnancies [21, 22]. The maternal outcomes could also be led by changes in inflammation and nutritional status that are more pronounced than in singleton pregnancies. While there is insufficient evidence regarding the relationships of PNI with PE in twin pregnancies.

Therefore, this cohort study employed the random forest algorithm to identify potential predictors of preeclampsia, followed by multivariate logistic regression to assess the association between third-trimester PNI and PE in twin pregnancies The aim was to determine whether lower PNI levels are associated with an elevated risk of PE in this population.

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Materials and methods

Patients and participants

This study is a retrospective cohort study. We retrospectively included twin pregnancies who had regular checkups and delivered at Fujian Maternal and Child Health Hospital from January 2015 to December 2021. The patients were categorized into the control group and the preeclampsia group (Fig. 1).

Exclusion criteria: (1) Essential hypertension or gestational hypertension; (2) Acute or chronic inflammatory conditions; (3) Miscarriage before 28 weeks of pregnancy.

Diagnostic criteria

The diagnosis of PE was determined according to the guidelines for the diagnosis and treatment of hypertensive disorders in pregnancy (2020) issued by Chinese Medical Association Obstetrics and Gynecology Branch [23]: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg after 20 weeks of gestation with any of the following item: urinary protein quantification ≥ 0.3 g/24 h, or urinary protein/creatinine ratio ≥ 0.3, or random urinary protein ≥ (+); Without proteinuria but with any one of the following organs or systems involved: heart, lung, liver, kidney and other vital organs, or abnormal changes in the blood system, digestive system, nervous system, placenta-fetus affected.

Monochorionic and dichorionic twins are classified primarily based on placental chorionicity, which is determined by examining the intertwin membrane at its junction with the placenta during early pregnancy [24].

Research method

Clinical information was collected from hospital electronic medical records for both groups of pregnant women, including:

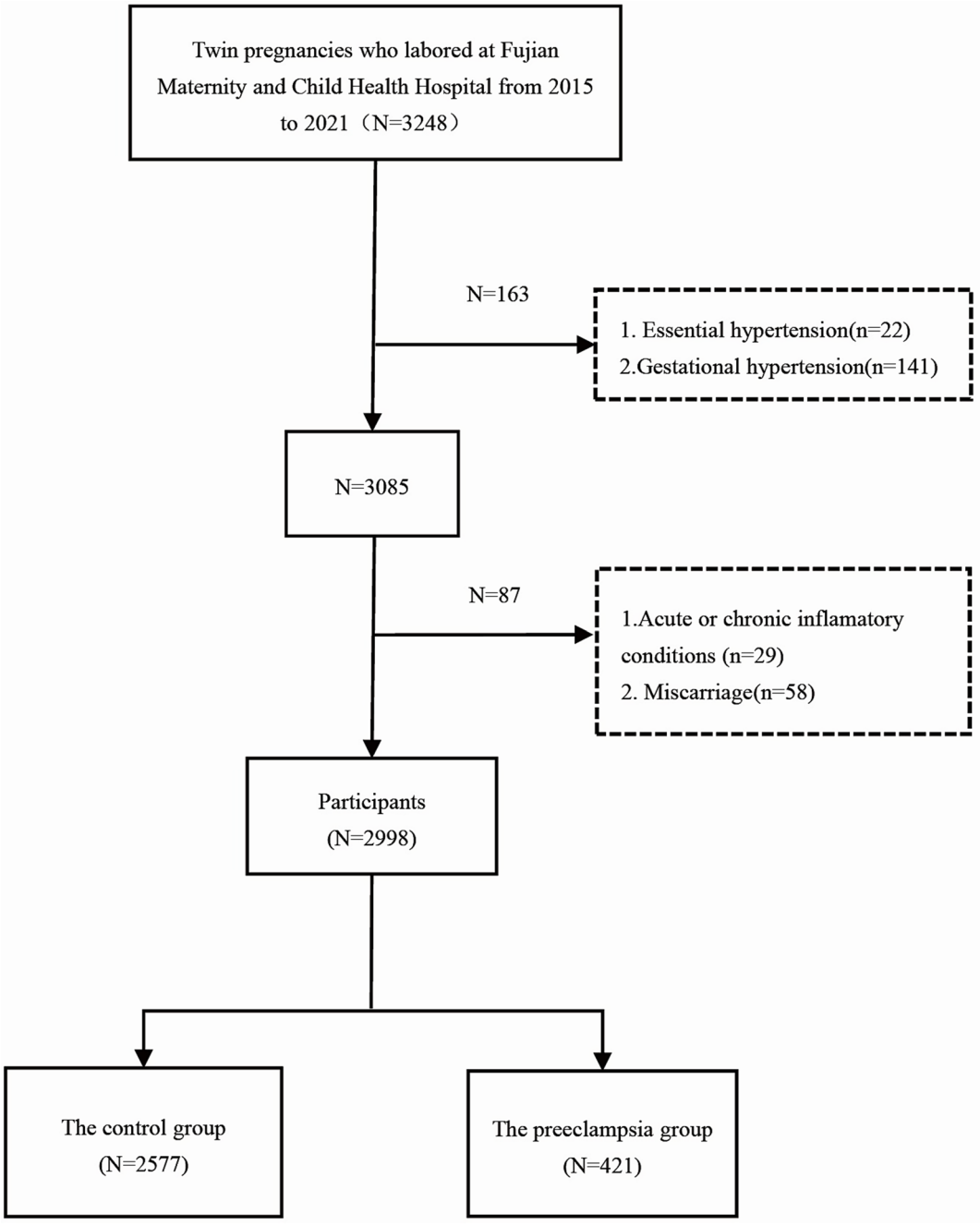

Fig. 1 Flow chart of the sample collection

(1) General information, such as age, pre-pregnancy body mass index (BMI), education level, gravidity, parity, chronicity, gestational age and in vitro fertilization–embryo transfer.
(2) Maternal complications, such as gestational diabetes mellitus (GDM), scarred uterus, intrahepatic cholestasis of pregnancy (ICP), oligohydramnios, hydramnios and hepatitis B virus infection.
(3) Laboratory indicators upon admission for delivery in the third trimester (from 28 weeks of gestation until delivery). The clinical examination parameters from peripheral blood samples were measured using a Sysmex XN-1000Q automated blood analyzer. Lymphocyte, neutrophil, platelet counts, high-density lipoprotein cholesterol, albumin and Fib were analyzed. We calculated the SIRI (systemic inflammation response index), SII (systemic immune inflammation index), AISI (the aggregate index of systemic inflammation), NHR (neutrophil to high-density lipoprotein cholesterol ratio), MHR

(monocyte to high-density lipoprotein cholesterol ratio (MHR), PHR (platelet-to-HDL-C ratio), LHR (lymphocyte to HDL-C ratio), MLR (monocyte-to-lymphocyte ratio), PLR (platelet-to-lymphocyte ratio), PNI, FARI (fibrinogen-albumin-ratio index) and NPAR (neutrophil-percentage-to-albumin ratio) according to the following equations: SIRI = (neutrophil count × monocyte count)/ lymphocyte count, SII =(neutrophil count × platelet count)/ lymphocyte count, AISI = neutrophil count ×platelet count ×monocyte count/ lymphocyte count, NHR = neutrophil counts/high-density lipoprotein cholesterol (HDL-C), MHR = monocyte counts/HDL-C, PHR = platelet counts/HDL-C, LHR = lymphocyte counts/HDL-C, MLR = monocyte counts/lymphocyte count, PLR = platelet count/ lymphocyte count, PNI = 5× lymphocyte count (10^9/L) + serum albumin (g/L), FARI = Fib (g/L)/ serum albumin (g/L), NPAR = Neutrophil percentage (in total WBC count) (%) × 100/Albumin (g/dL).

Statistical methods

The R software (V3.6.2) package was used to analyse the data. The measurement data that conforms to the normal distribution were expressed as mean ± standard deviation (x ± s) and the difference in means between groups were compared by t-test. For measurement data that does not conform to the normal distribution were expressed as the median (interquartile range) [M (P 25, P 75)] and the non-parametric test (Mann-Whitney U test) was used to compare the differences between the two groups. Count data were expressed as n (%) and analyzed using the $\chi 2$ test, corrected chi-square test or Fisher's exact probability method. The significance of the characteristic variables in predicting PE in twin pregnancies were calculated using the random forest algorithm (Boruta package). The correlation between PNI and PE in twin pregnancies was examined in three distinct models using multivariable logistic regression corrected for confounders to adjust for the odds ratio (OR) and 95% confidence interval (CI), with $P < 0.05$ being a statistically significant difference. We tested the robustness of our results by doing a sensitivity analysis using PNI converted from a continuous variable to a categorical variable (tertiles). Then we used the generalized additive models (GAM) to draw smooth curve fitting to visualize the relationship between PE and PNI. We further constructed receiver operating characteristic (ROC) analysis for PNI and other albumin-inflammatory biomarkers (NPAR and FARI). The best cutoff point was defined as that which maximized the Youden index. The area under the curve (AUC) was computed for each biomarkers, and the differences in AUC were statistically compared using bootstrap resampling ($n = 2000$ iterations).

Boruta is a feature selection algorithm that randomly disrupts each real feature in order, evaluates the importance of each feature, and iteratively removes features with low correlation to find the best variable. The Boruta reduces overfitting via shadow features and statistical testing. The Boruta algorithm compares the importance of original features with that of shadow features. If the importance of an original feature is significantly higher than the maximum importance of all shadow features, it is considered "confirmed". If its importance is lower than the maximum importance of shadow features, it is considered "rejected". For those whose importance cannot be clearly determined, the algorithm marks them as "tentative".

Ethical approval

This retrospective cohort study was approved by the ethical committee of the Fujian Maternity and Child Health Hospital (2024KY275). As there were no interventions to the patients' care at any stage, the need for ethical approval and written informed consent was waived.

Results

Participants characteristics at baseline

A total of 2998 twin pregnancies included in the study, including preeclampsia group ($n = 421$) and control group ($n = 2577$). Among the 421 pregnant women with preeclampsia, there were 58 cases of early-onset preeclampsia (delivery < 34 weeks) and 363 cases of late-onset preeclampsia (delivery ≥ 34 weeks). The mean gestational age at onset was 34.94 weeks. The baseline characteristics are presented in Table 1. In general, twin pregnancies in the preeclampsia group had lower gravidity, parity, PLR, PNI, FARI and higher values of MHR, NHR, LHR, NLR and NPAR. There was no statistically significant difference in age and education level between the two groups. The proportion of women with advanced maternal age and primipara in the PE group were significantly higher than those in the control group. PE group showed a significantly higher prevalence of ICP compared with control group ($P < 0.05$; Table 1).

Importance of the inflammation-related characteristic variables in predicting PE in twin pregnancies

The Boruta algorithm of random forest was used to assess the importance of the characteristic inflammation-related variables in predicting PE in twin pregnancies. The characteristic inflammation-related variables were ranked according to their importance scores (Fig. 2). As shown in the Fig. 3, these inflammation-related variables are all important predictors of preeclampsia. Among them, PNI was the top-ranked important predictor variables.

Table 1 Comparison of basic characteristics between control group and preeclampsia group in the twin pregnancies

	Control group (*n* = 2577)	Preeclampsia (*n* = 421)	*P*-value
Age (y)	30.08 (4.32)	30.35 (4.70)	0.250
Advanced maternal age (n(%))#			
NO	2188 (84.9)	341 (81.0)	0.048
YES	389 (15.1)	80 (19.0)	
Gestational week at delivery (week)	36.86 [35.14, 37.43]	36.29 [35.00, 37.14]	0.003
Education level			
Primary school or below (n(%))	18 (0.7)	4 (1.0)	0.412
Junior school (n(%))	408 (15.8)	78 (18.5)	
Senior high school (n(%))	549 (21.3)	80 (19.0)	
College or higher (n(%))	1602 (62.2)	259 (61.5)	
Pre-pregnancy BMI (kg/m^2)	21.07 (2.89)	21.32 (2.94)	0.090
Gravidity	2.00 [1.00, 2.00]	1.00 [1.00, 2.00]	0.013
Parity	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.001
Primipara (n(%))			
NO	938 (36.4)	117 (27.8)	0.001
YES	1639 (63.6)	304 (72.2)	
Chorionicity (n(%))			
Monochorionic	847 (32.9)	150 (35.6)	0.289
Dichorionic	1730 (67.1)	271 (64.4)	
IVF-ET (n(%))			
NO	1548 (60.1)	243 (57.7)	0.391
YES	1029 (39.9)	178 (42.3)	
Gestational Diabetes Mellitus (n(%))			
NO	1970 (76.4)	310 (73.6)	0.233
YES	607 (23.6)	111 (26.4)	
Oligohydramnios (n(%))			
NO	2553 (99.1)	417 (99.0)	1
YES	24 (0.9)	4 (1.0)	
Hydramnios (n(%))			
NO	2514 (97.6)	413 (98.1)	0.611
YES	63 (2.4)	8 (1.9)	
ICP (n(%))	2505 (97.2)	394 (93.6)	<0.001
	72 (2.8)	27 (6.4)	
SIRI	4.16 ± 2.45	4.26 ± 2.41	0.433
SII	1126.73 ± 573.03	1084.99 ± 544.41	0.163
AISI	838.70 ± 602.40	792.30 ± 569.31	0.140
MHR	0.47 ± 0.20	0.52 ± 0.20	<0.001
NHR	5.58 ± 2.27	6.50 ± 2.68	<0.001
PHR	131.63 ± 50.21	136.15 ± 54.30	0.090
LHR	1.05 ± 0.43	1.16 ± 0.46	<0.001
PLR	133.98 ± 48.58	124.93 ± 45.64	<0.001
NLR	5.71 ± 2.32	5.99 ± 2.46	0.022
MLR	0.48 ± 0.17	0.47 ± 0.17	0.813
NPAR	26.97 ± 8.93	29.75 ± 9.79	<0.001
PNI	40.57 ± 3.63	37.92 ± 3.86	<0.001
FARI	13.86 ± 2.92	13.01 ± 3.56	<0.001

#Advanced maternal age (AMA) is defined as pregnant women aged 35 years or older

Correlation between PNI and PE in twin pregnancies

We first screened for confounding factors based on the results of univariate analysis and clinical significance ($P < 0.1$). Then we assessed the relationships between PNI and PE in twin pregnancies using three different models (Table 2). In model 1, univariate logistic regression suggested that lower PNI was signifcantly related to the risk of PE (OR = 0.817; 95% CI: 0.793, 0.843). In model 2, after accounting for confounding variables (primipara, pre-pregnancy BMI, women with advanced maternal age), lower PNI remained an independent risk factor for PE in twin pregnancies (OR = 0.818; 95% CI: 0.792, 0.843). In the fully adjusted model, after accounting for confounding variables (primipara, pre-pregnancy BMI, women with advanced maternal age, gravidity, parity, intrahepatic cholestasis of pregnancy, MHR, NHR, PHR, LHR, PLR, NLR, NPAR, FARI), PNI was strongly correlated with PE (OR = 0.780; 95% CI: 0.753, 0.808).

We tested the robustness of our results by doing a sensitivity analysis using PNI converted from a continuous variable to a categorical variable (tertiles). The higher PNI remained an independent protective factor for PE in twin pregnancies compared to lower PNI (OR, 95% CI: 0.410, 0.438–0.530; 0.144, 0.103–0.201). After conducting sensitivity analysis, we found a trend of consistency (P for trend <0.001). Notably, low PNI maintained its association with increased PE risk in all sensitivity analyses and model specifications, even after comprehensive adjustment for potential confounders, confirming the robustness of this relationship.

Generalized additive models were used to visually assess functional relationships between the continuous covariates (PNI) and the risk of PE in twin pregnancies. This analysis was conducted using both logarithmic transformed and untransformed data. Log (relative risk) can be converted to a relative risk by taking antilog. For example, a log (relative risk) of 0 implies the relative risk of 1 (no impact on the probability of PE in twin pregnancies), whereas a log (relative risk) of 1 implies the relative risk of 2.71 (2.71-fold increase in the probability of PE in twin pregnancies). As shown in the Fig. 3, a negative linear correlation was observed between PNI and the risk of PE in twin pregnancies (Fig. 3A-B).

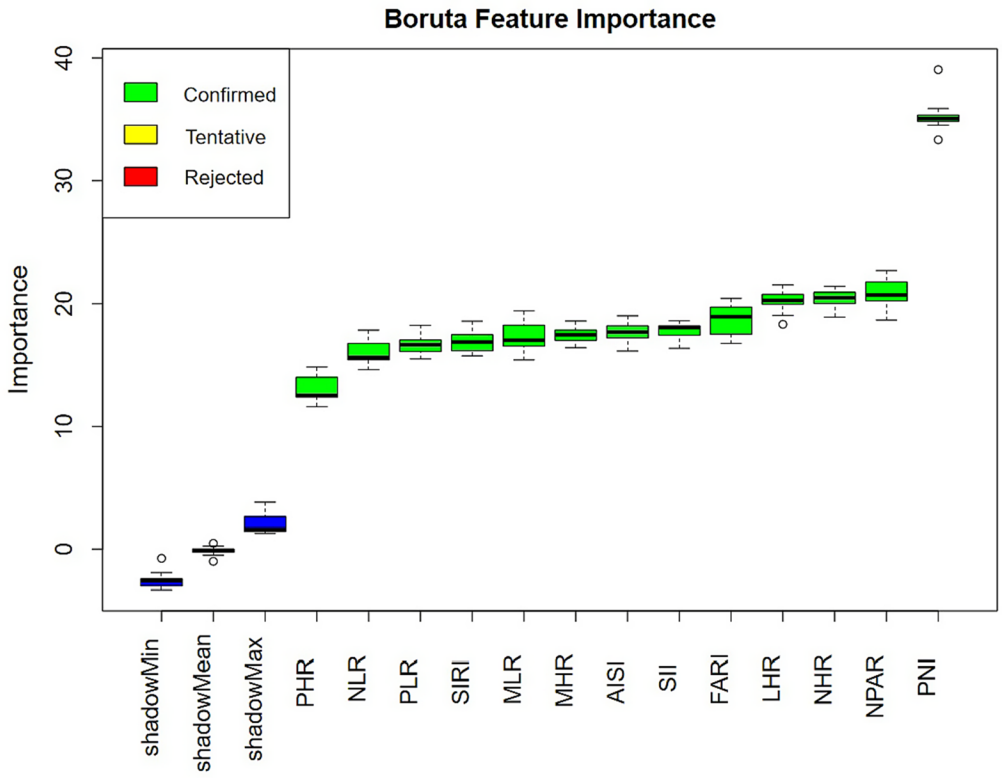

Fig. 2 Schematic diagram for assessing the importance of variables (The horizontal axis is the characteristic variable predicting PE in twin pregnancies, the vertical axis is the importance score, green is the important variable, red is the insignificant variable, blue is the shadow variable and yellow is the Tentative variable.)

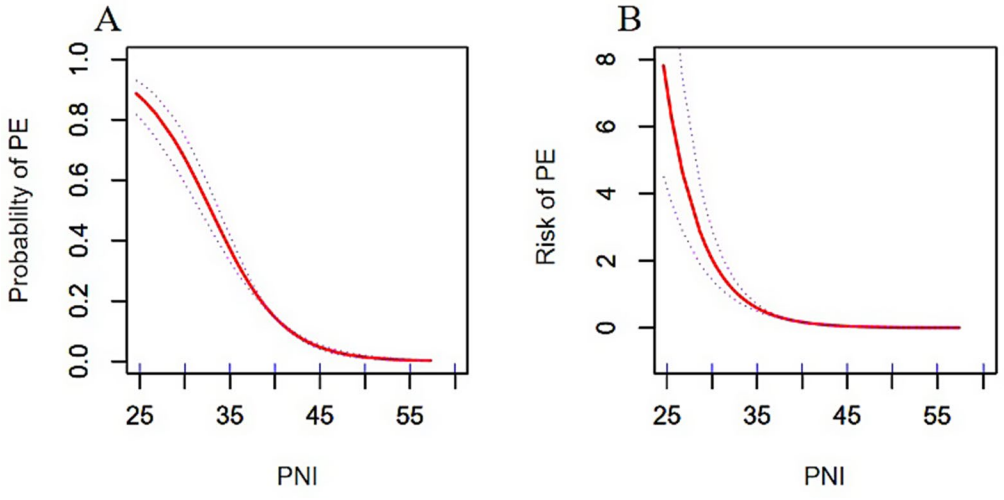

Fig. 3 The correlation between PNI and PE. **A**: General additive models demonstrate the relationship between PNI and the probablilty of PE. **B**: General additive models demonstrate the relationship between PNI and the risk of PE. The resulting figures show the predicted log (relative risk) in the y-axis and the PNI in the x-axis

ROC analysis of PNI in predicting PE in twin pregnancies

In the ROC analyses, the cut-off value of PNI score was 40.162. ROC curve analysis revealed an area under curve (AUC) of 0.691 (sensitivity: 72.7%, specificity: 46.1%) for PNI score. Although the AUC of 0.691 indicates discriminative ability superior to random chance (AUC = 0.5), below the optimal threshold, it may still serve for preliminary screening or risk stratification of preeclampsia. PNI showed a higher AUC (0.691) for predicting PE in twin pregnancies compared to NPAR

Table 2 Associations between PNI with PE in twin pregnancies

	Model 1	Model 2	Model 3
	OR (95% CI)	AOR (95% CI)	AOR (95% CI)
Continuous	0.817 (0.793,0.843)	0.818 (0.792, 0.843)	0.780 (0.753, 0.808)
Categories			
Tertile 1	Reference	Reference	Reference
Tertile 2	0.466 (0.367, 0.590)	0.476 (0.374, 0.606)	0.410 (0.438, 0.530)
Tertile 3	0.212 (0.157, 0.258)	0.215 (0.159, 0.290)	0.144 (0.103, 0.201)
P for trend	<0.001	<0.001	<0.001

In sensitivity analysis, PNI was converted from continuous variables to categorical variables (tertiles)

Model 1: unadjusted. Model 2: adjusted for primipara, pre-pregnancy BMI, women with advanced maternal age, gravidity, parity, intrahepatic cholestasis of pregnancy Model 3: further adjusted for MHR, NHR, PHR, LHR, PLR, NLR, NPAR, FARI

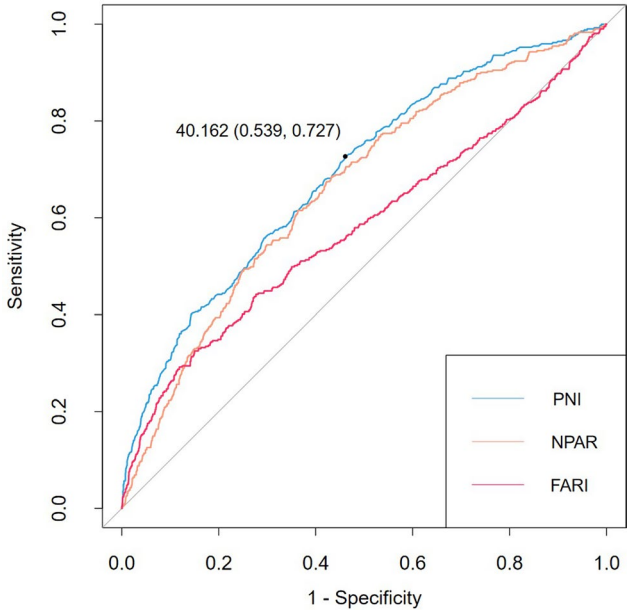

Fig. 4 ROC analysis of PNI, NPAR and FARI to predict PE in twin pregnancies

(0.662) and FARI (0.565), the differences were statistically significant ($P=0.013$ and $P<0.001$, respectively). These results indicate that, in comparison to other albumin-inflammatory biomarkers (NPAR and FARI), PNI has the best discriminative ability and accuracy in predicting PE in twin pregnancies (Fig. 4).

Discussion

In this study, the third-trimester PNI was demonstrated to be an independent predictor of PE in twin pregnancies. Elevated PNI levels were found to be correlated with a decreased incidence of PE in the fully adjusted model among twin pregnancies. As far as we know, this is the first study to highlight the significant correlation between PNI and PE in twin pregnancies. This finding provides important guidance for clinical practice and helps improve quality of life for twin pregnancies.

PNI is calculated as 5 × peripheral lymphocyte count (10^9/L) + serum albumin (g/L), which includes albumin and lymphocyte count, reflecting nutritional and immune status, respectively. In recent years, PNI has been proposed as a novel marker for systemic inflammation, based on its combination with two clinical inflammatory evaluation parameters [25, 26]. In the field of obstetrics, Tak et al. identified PNI as a novel prognostic marker for adverse cardiovascular events in peripartum cardiomyopathy patients [27]. Another study conducted by Seyhanli Z et al. demonstrated that assessing PNI during the first trimester is a valuable indicator for predicting late-onset fetal growth restriction (FGR). Furthermore, low PNI values are associated with composite adverse neonatal outcomes in pregnancies complicated by FGR [9]. Albumin, the predominant protein and major nutrient in human plasma, has been associated with preeclampsia [28, 29]. Oxidative stress plays a vital role in the pathology and development of PE. The reduction in maternal serum albumin levels diminishes the protective mechanisms against oxidative damage, thereby exacerbating the onset and progression of PE. Lymphocytes, which are produced by the lymphoid organs and play a crucial role in the immune response, have been associated with the risk of PE [30]. In preeclampsia, insufficient blood flow perfusion in the placenta triggers a cascade of events that include immunosuppression and the stimulation of pro-inflammatory inhibitors. This disruption in the balance of immune and inflammatory mechanisms ultimately leads to lymphocyte apoptosis. However, relying on a single indicator to assess the overall immune and nutritional status of a patient has limitations. Therefore, in our study, we investigated the predictive value of the PNI in identifying cases of PE in twin pregnancies, which demonstrated the lower value of PNI, the higher risk of developing preeclampsia in twin pregnancies.

Preeclampsia is pregnancy-specific, and significantly contributes to maternal, and perinatal morbidity and mortality worldwide. Consequently, early detection and diagnosis are particularly important. Following that, there are many potential novel biomarkers that might improve the prediction of PE [31]. When compared to these time-consuming prognostic tests, serum inflammatory indexes have the advantage of being easily obtained from routine blood and biochemical tests, making it more accessible and cost-effective. For instance, Seyhanli Z et al. revealed that SIRI and PIV hold promise as potential tools for predicting the risk of preeclampsia during the first trimester [6]. Another study by Wang J et al. reported that NLR and MLR offer more effective indicators of clinical assessment, disease severity evaluation, and prognosis evaluation of PE [32]. Nonetheless,

the correlation between PNI and PE remains an underexplored area in scientific research. In a prospective study, the PNI levels were lower in patients with early-onset PE than in those with normal pregnancies [17]. Besides, Esercan A et al. identified a cut-off PNI of 36.30 in the early-onset PE group compared to the normotensive group [16]. Similar to some of the previously mentioned studies, we found that PNI is the top-ranked important predictor variables in predicting PE in twin pregnancies through Boruta algorithm of random forest. Furthermore, ROC demonstrated that the predictive capability of PNI exceeds other albumin-inflammatory biomarkers. To our knowledge, this is the first study to investigate the significant correlation between PNI and PE in twin pregnancies. Twin pregnancies are a risk factor for preeclampsia with a reported incidence of 2–3 times higher than singleton pregnancies [33]. Meanwhile, PE in twins carries a higher risk of maternal/fetal morbidity and mortality including renal failure, stroke, cardiac arrest, pulmonary edema, placental abruption, cesarean delivery, fetal growth restriction, and iatrogenic preterm delivery [34]. Therefore, it is particularly crucial to identify twin pregnancies who exhibit high-risk factors for PE. For this reason, our findings suggested that twin pregnancies with decreased PNI levels are more likely to develop PE and require special attention and medical intervention in clinical practice.

There are certain limitations to our research. First, because this is a retrospective study, it reflects only single-center experience, and relatively limited number of cases. Potential selection bias may exist due to the retrospective study design, particularly regarding the representativeness of the enrolled population. Moreover, our retrospective design precludes definitive causal conclusions. Second, the predictive performance of PNI was 0.691 among twin pregnancies, which is still regarded as poor [35], indicating that PNI alone is insufficient to serve as long-term prognostic markers in twin pregnancies. As a result, large-scale prospective studies must be established to verify conclusions and collect more clinical data to comprehensively evaluate the effects of PNI. Nevertheless, as a tertiary maternal-fetal medicine center in Southeast China, our number of cases is still representative.

Conclusions

In conclusion, our findings demonstrate that twin pregnancies with lower PNI during the third trimester have a higher risk of developing PE, which may provide clinicians with a valuable tool for risk stratification, and enabling more individualized antenatal care in twin pregnancies. As we look to the future, integrating PNI into multifactorial risk models could enhance its predictive value, supporting more targeted interventions for high-risk pregnancies.

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Author contributions
QH and NL conceptualized this study. YTG, XLC and SSZ acquired data. HLZ designed the analyses and SSZ performed the analyses. QH and SSZ drafted the manuscript. All authors read and approved the final draft of the manuscript for important intellectual content.

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Data availability
Data were anonymized, and no patient information was included to preserve confidentiality. All data used to reach the aforementioned conclusions is available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and consent waiver obtained from the institutional ethics committee of Fujian Maternity and Children's Hospital (2024KY275).

Consent for publication
All data were anonymized; therefore, individual consent for publication was not required.

Competing interests
The authors declare no competing interests.

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