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Original Article

The relationship between vitamin A and E levels and the severity of disease and oxidative stress injury in patients with preeclampsia

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Abstract: Objective: To explore the correlation of vitamin A (VA) and vitamin E (VE) levels with preeclampsia (PE) severity and oxidative stress injury in patients. Methods: Clinical data from 93 PE patients who established health records and delivered newborns at Xingtai People's Hospital between January 2017 and September 2019 were retrospectively analyzed. The patients were categorized into mild a PE group (n = 51) and severe a PE group (n = 42) based on the severity of their condition, and also into an early-onset PE group (n = 38, gestational weeks < 34) and a late-onset PE group (n = 55, gestational weeks ≥ 34) by the timing of onset. Additionally, 50 healthy pregnant women undergoing routine prenatal check-ups during the same period were selected as the control group. Pearson's correlation was used to analyze the correlation of VA and VE levels with blood lipids, liver and kidney functions, and oxidative stress injury indices in PE patients. Receiver operator characteristic (ROC) curves were plotted to assess the value of serum VA and VE levels in evaluating early-onset PE and adverse pregnancy outcomes in PE patients. Results: Pearson correlation analysis revealed that VA and VE levels in PE patients had negative correlation with total cholesterol (r = -3.426, -4.812), triglycerides (r = -3.862, -5.321), low-density lipoprotein (r = -4.065, -4.916), serum creatinine (r = -4.967, -5.437), blood urea nitrogen (r = -5.074, -4.653), uric acid (r = -4.716, -5.384), advanced oxidation protein products (AOPP) (r = -6.132, -5.876), myeloperoxidase (r = -6.812, -6.732), nicotinamide adenine dinucleotide phosphate (r = -5.862, -4.762), and reactive oxygen species levels (r = -3.716, -4.352, all P < 0.05), and they had a positive correlation with high-density lipoprotein (r = 5.132, 4.932), catalase (r = 4.165, 3.135), and superoxide dismutase levels (r = 5.621, 4.997, all P < 0.05). ROC curve analysis showed that the area under the curve (AUC) values for predicting early-onset PE were 0.847 for VA, 0.891 for VE, and 0.908 for the combination. For predicting adverse pregnancy outcomes in PE, the AUC values were 0.897, 0.924, and 0.931, respectively. Conclusions: Serum VA and VE levels are closely related to PE severity, lipid levels, renal function, AOPP, and other oxidative stress injury markers in PE patients. Combined detection of VA and VE levels can help assess early-onset PE and adverse pregnancy outcomes.

Keywords: Preeclampsia, vitamin A, vitamin E, advanced oxidation protein products, condition of disease

Introduction

Severe preeclampsia (PE) can affect many organs, including the liver and kidneys, and increase the risk of adverse pregnancy outcomes such as fetal respiratory distress, asphyxia, and malnutrition [1-4]. Currently, there are no specific tests for PE. Clinical evaluation primarily involves monitoring clinical risk assessment, blood pressure, mean arterial pressure (MAP), and their fluctuations in order to assess the severity of a patient's condition. Blood flow is observed using a color Doppler ultrasound examination of the uterine artery pulsatility index (PI). However, the accuracy of clinical risk assessment predictions is low, especially for first-time pregnancies, as many high-risk factors are not evident in the early stages. Biomarker detection, including placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1), may be influenced by individual variations and different stages of pregnancy. Additionally, the high cost of detection limits its widespread use. Ultrasound and Doppler examinations of fetal and placental blood flow require specialized equipment and technology,

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relying heavily on the operator's experience and skill level. Therefore, while serological indices, MAP, and uterine artery blood flow spectrum, combined with clinical history and physical signs, have some value in predicting PE [4], they still suffer from low specificity and accuracy.

The pathogenesis of PE is not fully understood but is believed to be related to placental ischemia, oxidative stress, and vascular endothelial dysfunction [5]. Ischemia-hypoxia-reperfusion injury of the placenta can trigger oxidative stress factors such as advanced oxidation protein products (AOPP) and myeloperoxidase (MPO), leading to systemic artery spasms and endothelial dysfunction [6]. Thus, oxidative stress injury plays a pivotal role in the progression of PE. Vitamin A (VA) and vitamin E (VE) are fat-soluble antioxidants that reduce vascular endothelial dysfunction and damage, defend against oxidative stress injury, and are essential for maintaining normal metabolism and body function [7, 8]. Clinical studies have found that VA and VE deficiencies in postpartum women, combined with oxidative stress injury, may elevate the risk of PE by influencing maternal nutritional status and fetal growth and development [8]. Research [9] has also shown lower expression levels of VA and VE in PE and postpartum renal injury, with the latter demonstrating higher sensitivity and specificity. These vitamins were negatively correlated with renal injury markers such as kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), uric acid (UA), and serum creatinine (SCr), suggesting they could serve as promising indicators for clinical prediction. The correlation between maternal serum VA and VE levels and PE severity, as well as their diagnostic value, still requires further investigation.

This study aimed to observe the correlation of serum VA and VE levels with PE severity, lipid levels, renal function, AOPP, and other oxidative stress injury markers, demonstrating that their combination can effectively predict early-onset PE and adverse pregnancy outcomes.

Materials and methods

Clinical data

Clinical data from 93 PE patients who had established health records and delivered their babies at Xingtai People's Hospital between January 2017 and September 2019 were retrospectively analyzed. The patients were aged 23-34 years, with an average age of (28.2±2.9) years and an average gestational age of (30.31±3.46) weeks.

Inclusion criteria: the diagnostic criteria for severe PE followed the American College of Obstetricians and Gynecologists (ACOG) guidelines [10]. Severe PE was confirmed by the presence of any of the following conditions: (1) Sustained elevation of blood pressure: systolic ≥ 160 mmHg and/or diastolic ≥ 110 mmHg [10]; (2) 24-hour proteinuria ≥ 5.0 g or random urine protein ≥ (+++) qualitatively; (3) Persistent headaches, visual disturbances, or other cerebral neurological symptoms; (4) Pulmonary edema or hepatic dysfunction; (5) Persistent epigastric or right upper abdominal pain; (6) Persistent decline in platelet count below 100×10^9/L; (7) Fetal growth restriction; (8) Pregnancy with a single live fetus; (9) No significant liver and kidney function abnormalities before pregnancy; (10) Complete clinical data.

Exclusion criteria: (1) Previous habits, such as alcohol consumption, smoking, and drug use; (2) Metabolic diseases such as gestational diabetes and thyroid disease; (3) Infectious diseases such as hepatitis B and tuberculosis; (4) Rheumatoid diseases, acute and chronic nephritis, and autoimmune diseases; (5) Coagulation dysfunction. Another 50 healthy pregnant women undergoing routine prenatal check-ups during same period were selected as the control group. These women were aged 22-34 years, with an average age of (28.1±3.2) years and an average gestational age of (29.86±4.64) weeks. The women in the control group did not have PE and were in good health condition. Following the ACOG guidelines [10], 93 cases of PE patients were categorized into two groups: 51 patients with mild PE and 42 patients with severe PE. Additionally, patients were grouped according to the timing of PE onset. Among these, 38 pregnant women with PE onset before 34 weeks of gestation were classified as the early-onset PE group, and 55 pregnant women with PE onset at or after 34 weeks of gestation were classified as the late-onset PE group. This study was approved by the Ethics Committee of Xingtai People's Hospital.

The sample size was determined based on power analysis to ensure the study possessed

adequate statistical power to detect the expected differences. According to previous similar studies and clinical experience, the sample sizes for the three groups were established as 93, 42, and 150, respectively. These numbers were sufficient to identify significant correlations of serum levels of VA and VE with the severity of PE and oxidative stress injury. Similar sample sizes in referenced literature further validate the rationality of these sample sizes.

Study methods

This study was a retrospective case-control analysis. Data from clinical records that met the inclusion and exclusion criteria were selected for analysis. The following indicators were compared.

(1) Severity of PE condition. According to the ACOG guidelines, mild PE: Random proteinuria ≥ (+) or systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg after 20 weeks of gestation. Severe PE: Random proteinuria ≥ (++) or urinary protein level ≥ 2.0 g/24 h, SBP ≥ 160 mmHg and/or DBP ≥ 110 mmHg after 20 weeks of gestation.

(2) Different types of PE. Early-onset PE: Onset < 34 weeks of gestation. Late-onset PE: Onset ≥ 34 weeks of gestation.

(3) VA, VE, and oxidative stress injury indicators. Three mL of fasting venous blood was collected from all subjects at 20 weeks of gestation and centrifuged for 10 min (r = 6 cm, 3000 r/min). The serum was separated, and the supernatant was stored at -80°C for testing. The levels of VA, VE and AOPP were determined by high performance liquid chromatography (Beijing Ita Biotechnology Co., Ltd.) using the UPLC1290 high performance liquid chromatograph (Nekman Coulter Co.). The levels of MPO, nicotinamide adenine dinucleotide phosphate (NADPH), catalase (CAT), superoxide dismutase (SOD), and reactive oxygen species (ROS) were measured.

(4) Blood lipids, liver and kidney function indicators. Three mL of fasting venous blood was extracted from all subjects at 20 weeks of gestation and centrifuged to collect the supernatant. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), hepatic and renal function indices, SCr, blood urea nitrogen (BUN), and UA levels were measured using Pumay INFORS-YSI 2900 Biochemistry Analyzer [Precision Medicine Technology (Beijing) Co., Ltd.].

(5) Follow-up: Patients were followed up until delivery. Adverse pregnancy outcomes included postpartum hemorrhage, low amniotic fluid, premature rupture of membranes, fetal growth restriction, neonatal asphyxia, fetal distress, and low birth weight. Patients presenting with any of these conditions were classified into the poor pregnancy group, and the rest were classified into the good pregnancy group. The diagnostic criteria for fetal distress [11] included an Apgar score of ≤ 7 within 1-5 min after birth, fetal movement ≤ 10 times/12 h during pregnancy, and fetal heart rate ≤ 120 beats/min or ≥ 160 beats/min.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) 23.0 was used for data processing, and the Shapiro-Wilk test was used for the assessment of normality. Measurement data conforming to a normal distribution were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was used for comparisons between multiple groups, and Least Significant Difference (LSD)-t test was used for pairwise comparisons. Pearson correlation analysis was performed. Receiver operator characteristic (ROC) curves were plotted to analyze the predictive value of serum VA and VE levels for early-onset PE and adverse pregnancy outcomes in PE. A *p*-value of less than 0.05 indicated statistical significance.

Results

Comparison of baseline data

There were no statistically significant differences in baseline data, including age, gestational weeks, gravidity, parity, and education level, among the control, mild PE, and severe PE groups ($P > 0.05$). The severe PE group had higher BMI, SBP and DBP compared to the mild PE and control groups, and mild PE group also had higher BMI, SBP and DBP compared to the

control group, with statistically significant differences ($P < 0.05$) (**Table 1**).

Comparison of VA, VE, and lipid levels

The severe PE group showed lower serum VA, VE, HDL levels, and higher TC, TG, LDL levels compared to the mild PE and control groups ($P < 0.05$). Similarly, the mild PE group, compared with the control group, exhibited lower serum VA, VE, HDL levels, and higher TC, TG, LDL levels, with statistically significant differences ($P < 0.05$) (**Figure 1**).

Comparison of liver and kidney function indicators

There were no statistically significant differences in ALT and AST among the control, mild PE, and severe PE groups ($P > 0.05$). However, the severe PE group had significantly higher levels of SCr, BUN and UA compared to the mild PE and control groups ($P < 0.05$). The mild PE group also had higher levels of SCr, BUN and UA compared to the control group, with statistically significant differences ($P < 0.05$) (**Figure 2**).

Comparison of oxidative stress injury indices

The severe PE group had higher AOPP, MPO, NADPH, ROS levels and lower CAT and SOD levels compared to the mild PE and control groups ($P < 0.05$). The mild PE group also had higher AOPP, MPO, NADPH, ROS levels and lower CAT and SOD levels compared to the control group, with statistically significant differences ($P < 0.05$) (**Figure 3**).

Correlation of VA and VE levels with blood lipids, liver and kidney function, and oxidative stress injury indices

Pearson correlation analysis indicated that VA levels in PE patients were negatively correlated with TC, TG, LDL, SCr, BUN, UA, AOPP, MPO, NADPH, and ROS (r = -3.426, -3.862, -4.065, -4.967, -5.074, -4.716, -6.132, -6.812, -5.862, -3.716, $P < 0.05$) and positively correlated with HDL, CAT, and SOD (r = 5.132, 4.165, 5.621, $P < 0.05$). VE levels in PE patients were negatively correlated with TC, TG, LDL, SCr, BUN, UA, AOPP, MPO, NADPH, and ROS (r = -4.812, -5.321, -4.916, -5.437, -4.653, -5.384, -5.876, -6.732, -4.762, -4.352, $P < 0.05$) and positively correlated with HDL, CAT, and SOD (r = 4.932, 3.135, 4.997, $P < 0.05$) (**Table 2**).

Comparison of VA and VE levels in patients with various types of PE and pregnancy outcomes

The age of patients in the early-onset PE group was higher than that in the late-onset PE group, with a statistically significant difference ($P < 0.05$). However, there were no statistically significant differences between the early-onset and late-onset PE groups in terms of gravidity, parity, BMI, SBP, and DBP ($P > 0.05$) (**Table 3**). Among the 93 patients with PE, a total of 13 cases of adverse pregnancy outcome were observed, including 1 case of postpartum hemorrhage, 3 cases of hypohydramnios, 3 cases of premature rupture of membranes, 1 case of fetal growth restriction, 1 case of neonatal asphyxia, 2 cases of fetal distress, and 2 cases of low birth weight. The serum VA and VE levels in the early-onset PE group were lower than those in the late-onset PE group, and the serum VA and VE levels in the poor pregnancy group were lower than those in the good pregnancy group ($P < 0.05$) (**Table 4**).

Predictive value of serum VA and VE levels for early-onset PE and adverse pregnancy outcomes

ROC curves indicated that the AUCs for VA, VE and their combination in predicting early-onset PE were 0.847 (95% CI: 0.769-0.925), 0.891 (95% CI: 0.825-0.957) and 0.908 (95% CI: 0.848-0.968), respectively. For predicting adverse pregnancy outcome in PE, the AUCs for VA, VE, and their combination were 0.897 (95% CI: 0.814-0.980), 0.924 (95% CI: 0.852-0.996), and 0.931 (95% CI: 0.864-0.997), respectively (**Table 5**; **Figures 4**, **5**).

Discussion

The results of this study indicated that serum VA and VE levels in the severe PE group were significantly lower than those in the mild PE and control groups. Serum VA and VE levels were negatively correlated with TC, TG, LDL, SCr, BUN and UA and positively correlated with HDL in PE patients. The AUCs of VA, VE, and their combination in predicting early-onset PE were 0.847, 0.891 and 0.908, respectively. The AUCs for predicting adverse pregnancy outcomes in PE were 0.897, 0.924 and 0.931, respectively. Research showed a significant decrease in VE levels in PE women [12]. It was

Table 1. Comparison of baseline data (n, $\bar{x}\pm s$)

Group	Number of cases	Age (years)	Gestational week (weeks)	Gravidity (times)	Parity (times)	BMI (kg/m^2)	SBP (mmHg)	DBP (mmHg)	Education level
									A/B/C
Control group	50	28.1±3.2	29.86±4.64	1.97±0.34	1.37±0.27	20.34±2.25	120.56±4.75	87.26±2.45	18/21/11
Mild PE group	51	27.9±2.8	30.27±5.42	1.76±0.28	1.46±0.33	22.99±1.38$^{\#}$	147.26±5.02$^{\#\#\#}$	98.64±4.15$^{\#\#\#}$	16/20/15
Severe PE group	42	28.3±4.1	30.79±5.14	1.86±0.34	1.41±0.29	24.87±1.57$^{\#\#\#,**}$	169.85±4.85$^{\#\#\#,***}$	117.43±5.78$^{\#\#\#,***}$	10/19/13
χ^2/F		0.164	0.383	2.552	1.153	75.542	126.610	52.760	2.115
P		0.849	0.682	0.082	0.319	< 0.001	< 0.001	< 0.001	0.715

Note: A is junior high school and below, B is high school or secondary school, C is college and above. PE: preeclampsia; BMI: body mass index; SBP: systolic blood pressure; SDP: diastolic blood pressure. Compared to the control group, $^{\#}P < 0.05$, $^{\#\#\#}P < 0.001$; compared to the mild PE group, $^{**}P < 0.01$, $^{***}P < 0.001$.

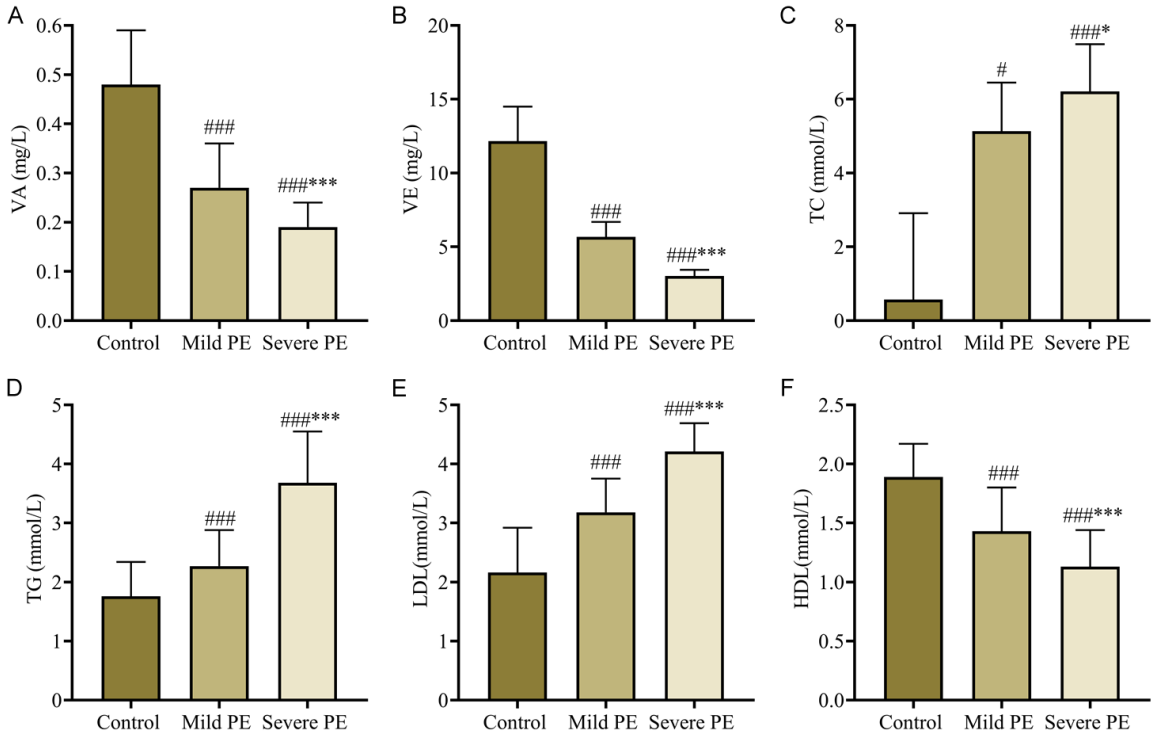

Figure 1. Comparison of VA, VE, and lipid levels among control group, mild PE group, and severe PE group. A: Vitamin A (VA); B: Vitamin E (VE); C: Total cholesterol (TC); D: Triglycerides (TG); E: Low-density lipoprotein (LDL); F: High-density lipoprotein (HDL). Note: PE: preeclampsia. Compared to the control group, $^{\#}P < 0.05$, $^{\#\#\#}P < 0.001$; compared to the mild PE group, $^{*}P < 0.05$, $^{***}P < 0.001$.

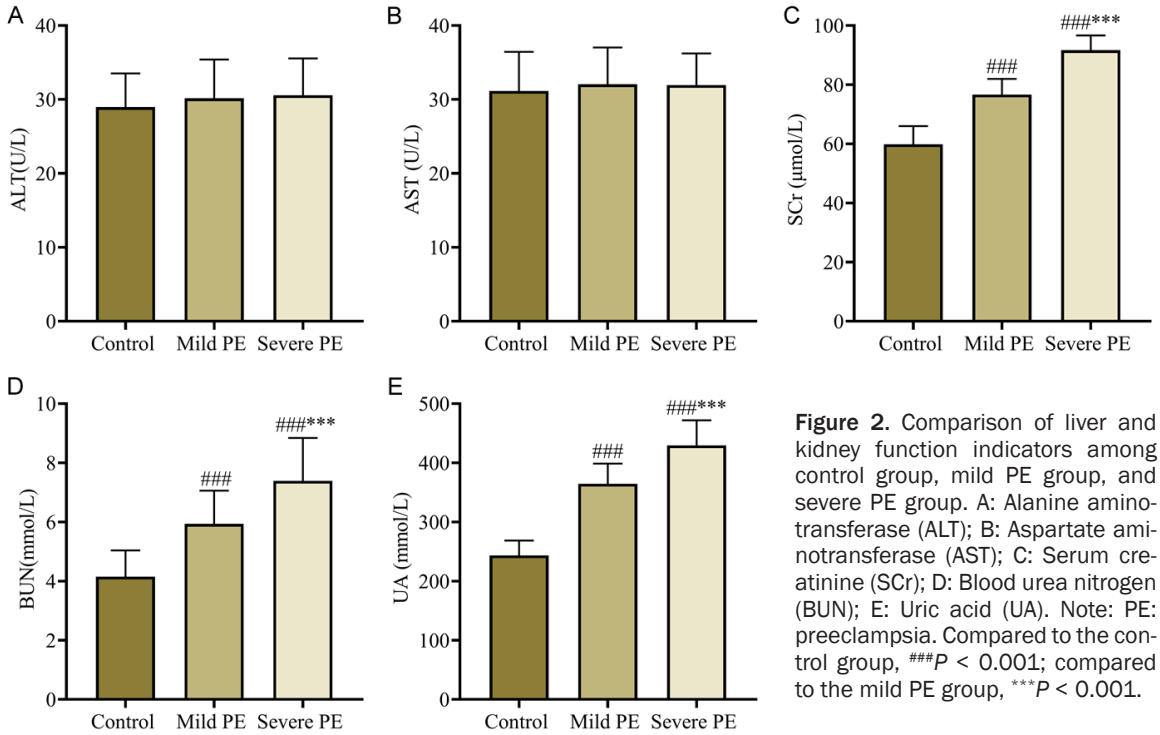

Figure 2. Comparison of liver and kidney function indicators among control group, mild PE group, and severe PE group. A: Alanine aminotransferase (ALT); B: Aspartate aminotransferase (AST); C: Serum creatinine (SCr); D: Blood urea nitrogen (BUN); E: Uric acid (UA). Note: PE: preeclampsia. Compared to the control group, $^{\#\#\#}P < 0.001$; compared to the mild PE group, $^{***}P < 0.001$.

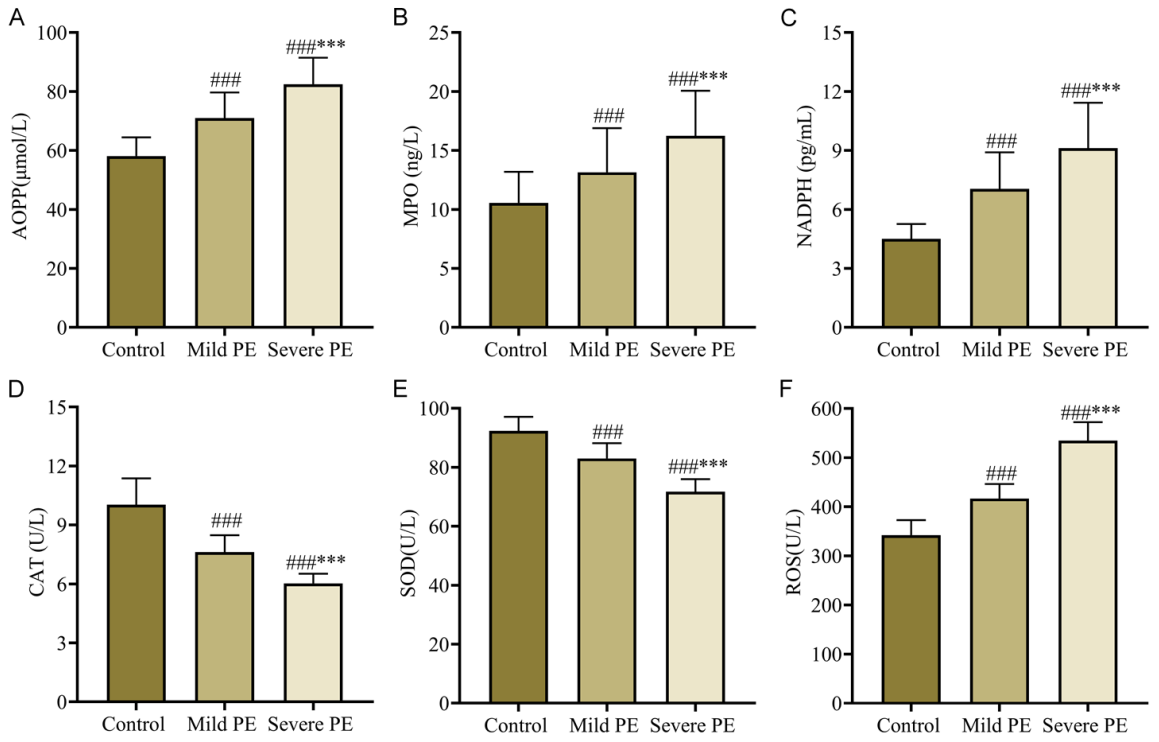

Figure 3. Comparison of oxidative stress injury indicators among control group, mild PE group, and severe PE group. A: Advanced oxidation protein products (AOPP); B: Myeloperoxidase (MPO); C: Nicotinamide adenine dinucleotide phosphate (NADPH); D: Catalase (CAT); E: Superoxide dismutase (SOD); F: Reactive oxygen species (ROS). Note: PE: preeclampsia. Compared to the control group, $^{###}P < 0.001$; compared to the mild PE group, $^{***}P < 0.001$.

reported that 12.3% of 2,824 pregnant women had abnormal serum VA levels, and among women with PE risk factors (within 20-40 weeks) who received 400 IU of VE supplementation daily, the incidence of PE was 5.0%, compared to 17.5% in the control group without VE supplementation [13]. These results align with the present study. The findings suggest that decreased VA and VE levels in PE patients are closely related to the severity of PE, and combined detection of these vitamins can help assess early-onset PE and adverse pregnancy outcomes. This may be due to the accumulation of excessive oxidative products in PE patients, with VA and VE deficiencies further aggravating oxidative stress, damaging vascular endothelial cells, and potentially leading to cell apoptosis. This process directly promotes the occurrence and progression of PE.

A previous study exposed trophoblast cells to AOPP and found that AOPPs were highly expressed in PE placenta, increasing apoptosis in trophoblast cells via the NADPH oxidase pathway [14]. It was also found that AOPP levels were negatively correlated with the severity of PE [15]. VA and VE can reduce vascular endothelial damage and dysfunction in various ways, while their deficiency directly promotes the development of PE. VE supplementation at 16-22 weeks of gestation can effectively prevent PE; VE deficiency directly leads to oxidative stress-induced apoptosis in PE patients, so timely supplementation is beneficial for prevention [16]. Another study indicated that timely VA and VE supplementation during pregnancy for PE could effectively reduce perinatal complications and significantly improve blood lipid levels [17]. The present study indicated that serum VA and VE levels were related to oxidative stress injury markers in PE patients, suggesting that reduced VA and VE levels may lead to oxidative stress injury, thereby promoting the progression of PE. However, whether VA and VE supplementation can help elevate serum VA and VE levels, reduce oxidative stress injury, and improve the prognosis of PE patients requires further validation through large cohort prospective studies. A meta-analysis [18] searched PubMed, Embase, and sev-

Table 2. Correlation of VA and VE levels with blood lipids, liver and kidney function, and oxidative stress damage indicators in PE patients

Indicator	Coefficient	TC	TG	LDL	HDL	SCr	BUN	UA	AOPP	MPO	NADPH	ROS	CAT	SOD
VA	*r*	-3.426	-3.862	-4.065	5.132	-4.967	-5.074	-4.716	-6.132	-6.812	-5.862	-3.716	4.165	5.621
	P	0.007	0.004	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.005	0.000	0.000
VE	*r*	-4.812	-5.321	-4.916	4.932	-5.437	-4.653	-5.384	-5.876	-6.732	-4.762	-4.352	3.135	4.997
	P	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.011	< 0.001

VA: vitamin A; VE: vitamin E; TC: total cholesterol; TG: triglycerides; LDL: low-density lipoprotein; HDL: high-density lipoprotein; SCr: serum creatinine; BUN: blood urea nitrogen; UA: uric acid; AOPP: advanced oxidation protein products; MPO: myeloperoxidase; NADPH: nicotinamide adenine dinucleotide phosphate; ROS: reactive oxygen species; CAT: catalase; SOD: superoxide dismutase.

Table 3. Comparison of clinical data of different types of PE patients

Group	Number of cases	Age (years)	Gravidity (times)	Parity (times)	BMI (kg/m^2)	SBP (mmHg)	DBP (mmHg)
Early-onset PE group	38	33.68±4.15	1.77±0.37	1.48±0.28	23.73±2.36	153.63±5.09	92.25±2.83
Late-onset PE group	55	30.29±3.22	1.85±0.31	1.42±0.35	24.39±2.55	154.64±5.22	93.09±3.59
t		4.431	1.130	0.880	1.264	0.927	1.206
P		< 0.001	0.262	0.381	0.209	0.357	0.231

PE: preeclampsia; BMI: body mass index; SBP: systolic blood pressure; SDP: diastolic blood pressure.

Table 4. Comparison of VA and VE levels in patients with different types of PE and different pregnancy outcomes ($\bar{x}$±s, mg/L)

Type	Number of cases	VA	VE
Early-onset PE group	38	0.17±0.07###	3.68±0.85###
Late-onset PE group	55	0.29±0.08	5.14±0.75
Good pregnancy group	80	0.31±0.09	5.12±0.84
Poor pregnancy group	13	0.19±0.05***	3.43±0.82***
F		31.004	42.760
P		< 0.001	< 0.001

Note: PE: preeclampsia; VA: vitamin A; VE: vitamin E. Compared to the late-onset PE group, ###*P* < 0.001; compared to the good pregnancy group, ****P* < 0.001.

Table 5. Predictive value of serum VA and VE levels on the occurrence of early-onset PE and adverse pregnancy outcomes

Objective	Indicator	Cut-off value	Sensitivity	Specificity	Jorden index	AUC	Standard error	*P*-value	95% CI
Early-onset PE	VA	0.245 mg/L	0.782	0.789	0.571	0.847	0.040	< 0.001	0.769-0.925
	VE	4.290 mg/L	0.836	0.783	0.619	0.891	0.034	< 0.001	0.825-0.957
	Joint	-	0.873	0.852	0.725	0.908	0.031	< 0.001	0.848-0.968
Adverse pregnancy outcomes	VA	0.220 mg/L	0.838	0.769	0.607	0.897	0.042	< 0.001	0.814-0.980
	VE	4.240 mg/L	0.863	0.802	0.665	0.924	0.037	< 0.001	0.852-0.996
	Joint	-	0.888	0.923	0.811	0.931	0.034	< 0.001	0.864-0.997

PE: preeclampsia; VA: vitamin A; VE: vitamin E; AUC: area under the curve.

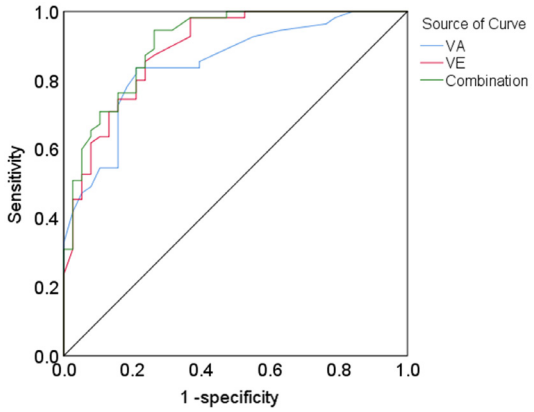

Figure 4. ROC plots of serum VA, VE and the combination of both for predicting early-onset PE. PE: preeclampsia; VA: vitamin A; VE: vitamin E; ROC: receiver operator characteristic.

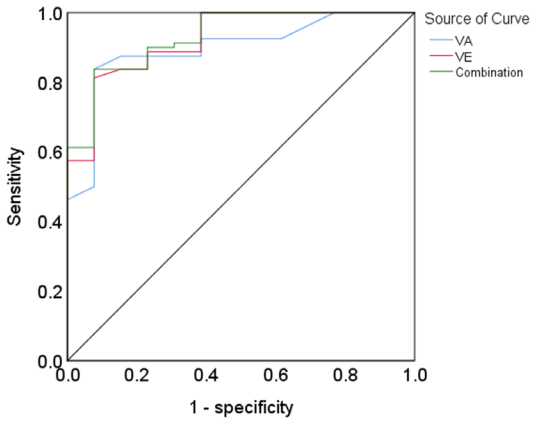

Figure 5. ROC plots of serum VA, VE and the combination of both for predicting adverse pregnancy outcomes in PE. PE: preeclampsia; VA: vitamin A; VE: vitamin E; ROC: receiver operator characteristic.

eral other databases from 1970 to 2013 for observational studies measuring levels of non-enzymatic antioxidants (vitamins A, C, E, and carotenoids) in maternal blood during pregnancy or within 72 h postpartum. The results indicated that among 64 studies, the standardized mean differences of vitamins A, C, and E were significantly negatively correlated with the overall incidence of PE, which were similar to the findings of the present research; however, the meta-analysis also noted that most included studies were small in scale and had a high risk of bias, highlighting the need for large-scale prospective cohort studies.

The results of this study indicated that there was no statistically significant difference in ALT and AST levels among the control group, the mild PE group, and the severe PE group. This may be due to an insufficient sample size, the

complex pathology of PE, the influence of multiple factors on liver enzyme levels, and the limitations of statistical analysis methods. These factors combined may obscure minor differences between groups. In future research, the sample size should be increased, and the mechanisms of liver enzyme level changes in PE patients should be further explored. Additionally, research should consider other factors that may affect liver enzyme levels, such as diet, genetics, and other health conditions, to comprehensively understand the impact of PE on liver function.

In conclusion, serum VA and VE levels are closely related to the severity of disease, lipid levels, renal function, AOPP, and other markers of oxidative stress injury in PE patients. Their combination can help assess early-onset PE and adverse pregnancy outcomes in PE. The sample size determined for this study was based on power analysis and drew from previous literature and clinical experience, ensuring the reliability and statistical validity of the results. Although this is a preliminary study with a relatively small sample size, which may introduce some bias, the number of cases will be increased in subsequent research to achieve more comprehensive and accurate conclusions. Additionally, the specific concentration levels of VA and VE in relation to PE and their specific signaling pathways that promote oxidative stress were not calculated in this study. To ensure that factors like age do not influence the study outcomes, women of childbearing age were selected, leading to a small sample size. Additionally, the effect of advanced age on VA and VE expression was not explored. The aforementioned shortcomings of this study will be addressed in the next phase of study. Furthermore, another limitation of this research is the lack of separate analysis of VA and VE levels in the early-onset and late-onset PE groups. Due to the preliminary nature and small sample size, thorough grouped analysis of VE and VA levels in various pregnancy outcomes in the early-onset PE group was not conducted. In subsequent research, the sample size will be expanded to enhance the analysis.

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Disclosure of conflict of interest

None.

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