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Investigation of serum phoenixin-14 and phoenixin-20 levels in pregnant women with preeclampsia

Vyšetření sérových hladin fénixinu-14 a fénixinu-20 u těhotných žen s preeklampsií

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Summary: **Objective:** Phoenixin has endothelial protective and anti-inflammatory properties, but has been associated with the development of hypertension. Given that endothelial dysfunction plays a significant role in the pathophysiology of preeclampsia, we aimed to investigate the serum levels of phoenixin-14 and phoenixin-20 in pregnant women diagnosed with preeclampsia. **Materials and methods:** In this cross-sectional case-control study, 45 pregnant women diagnosed with preeclampsia comprised the preeclampsia group, while 45 healthy pregnant women, matched to the preeclampsia group by age, body mass index, and gestational age, served as the control group. Commercial kits were used to analyze phoenixin-14 and phoenixin-20 levels in serum samples. **Results:** Serum phoenixin-14 level was 390.3 pg/mL in the preeclampsia group and 393.2 pg/mL in the control group (P = 0.434). While the serum phoenixin-20 level was 346.6 pg/mL in the preeclampsia group, it was 379.9 pg/mL in the control group (P = 0.278). When the preeclampsia group was divided into subgroups according to the severity of the disease and the onset of the disease and compared with the control group, no significant difference was found between the groups regarding serum phoenixin-14 and phoenixin-20 levels. **Conclusion:** In this study, serum levels of phoenixin-14 and phoenixin-20 were similar in both the preeclampsia and control groups. Although the sample size is too small to draw a definitive conclusion, findings suggest that phoenixin-14 and phoenixin-20 do not play a role in the pathophysiology of preeclampsia.

Key words: phoenixin-14 – phoenixin-20 – preeclampsia – pregnancy

Souhrn: **Cíl:** Fénixin má endoteliální ochranné a protizánětlivé vlastnosti a je spojován s rozvojem hypertenze. Vzhledem k tomu, že endoteliální dysfunkce hrají významnou roli v patofyziologii preeklampsie, zaměřili jsme se na vyšetření sérových hladin fénixinu-14 a fénixinu-20 u těhotných žen s diagnostikovanou preeklampsií. **Materiál a metody:** V této průřezové případové studii tvořilo 45 těhotných žen s diagnostikovanou preeklampsií skupinu preeklampsie, zatímco 45 zdravých těhotných žen, které odpovídaly skupině preeklampsie věkem, indexem tělesné hmotnosti a gestačním věkem plodu, sloužilo jako kontrolní skupina. Pro analýzu hladin fénixinu-14 a fénixinu-20 ve vzorcích séra byly použity komerční soupravy. **Výsledky:** Bylo zjištěno, že ve skupině s preeklampsií byla hladina fénixinu-14 v séru 390,3 pg/ml, zatímco v kontrolní skupině byla 393,2 pg/ml (p = 0,434). Hladina fénixinu-20 v séru ve skupině s preeklampsií byla 346,6 pg/ml a v kontrolní skupině 379,9 pg/ml (p = 0,278). Když byla skupina s preeklampsií rozdělena do podskupin podle závažnosti onemocnění a počátku onemocnění a porovnána s kontrolní skupinou, v hladinách sérového fénixinu-14 a fénixinu-20 mezi skupinami nebyl nalezen žádný významný rozdíl. **Závěr:** V této studii byly sérové hladiny fénixinu-14 a fénixinu-20 u preeklampsie a u kontrolní skupiny podobné. Ačkoli je velikost vzorku příliš malá na to, aby bylo možné vyvodit definitivní závěr, zjištění naznačují, že fénixin-14 ani fénixin-20 v patofyziologii preeklampsie nehraje roli.

Klíčová slova: fénixin-14 – fénixin-20 – preeklampsie – těhotenství

Introduction

Preeclampsia is a condition in which hypertension occurs after the 20th week of pregnancy and is accompanied by proteinuria or renal failure, liver involvement, and some neurological and hematological complications. It is reported that preeclampsia complicates 2–8% of all pregnancies [1]. Although it is still the leading cause of maternal and fetal morbidity and mortality, especially in underdeveloped countries, the

pathophysiology of the disease has not yet been fully elucidated. It is thought that placental development is impaired due to maternal-fetal immune incompatibility during early pregnancy. This compromised placentation results in the release of various inflammatory cytokines from the placenta into the maternal bloodstream. These mediators cause endothelial dysfunction and hemodynamic alterations, ultimately leading to preeclampsia's clinical manifestations [2].

Phoenixin (PNX) was discovered in 2013 by Yosten et al. as a novel peptide produced in the hypothalamus with direct effects on pituitary gonadotrophs [3]. PNX is cleaved from the C-terminal small integral membrane protein 20 and converted into peptides PNX-14 and PNX-20, the most prevalent active isoforms [4]. PNX is a neuropeptide expressed not only in the hypothalamus, but also in peripheral tissues such as the heart, thymus, stomach, small and large intestines, pancreas, ovaries, skin, and adipose tissues [5].

When PNX was initially discovered, it was believed to be a neuropeptide that regulates the reproductive system. However, its expression in peripheral tissues indicated that its functions extend beyond that. Besides promoting the secretion of gonadotropins and steroid hormones, PNX has been found to contribute to memory, behavior, food consumption, glucose and lipid metabolism, and fluid homeostasis [6]. PNX also exhibits cardioprotective, endothelial protective, and anti-inflammatory effects [7,8]. Given that endothelial cell dysfunction underlies the pathophysiology of preeclampsia, this study aimed to examine the levels of PNX-14 and PNX-20 in the serum of women diagnosed with preeclampsia.

Materials and methods

This cross-sectional case-control study was conducted between April 2023 and April 2024 at Umraniye Training and Research Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey. The preeclampsia group consisted of 45 pregnant women with a singleton pregnancy, aged between 18 and 40 years, who were diagnosed with preeclampsia. The control group consisted of 45 healthy pregnant women with singleton pregnancies who were matched with the preeclampsia group in terms of age, body mass index (BMI), and gestational week.

Gestational age of the participants was determined by the last menstrual period and confirmed with the measurement of crown-rump length in the first trimester. Preeclampsia was diagnosed according to the gestational hypertension and preeclampsia practice bulletin of the American College of Obstetricians and Gynecologists (ACOG) [9]. Accordingly, new hypertension occurring after the 20th week of pregnancy accompanied by proteinuria was considered preeclampsia. In the absence of proteinuria, new-onset hypertension occurring after the 20th week of gestation, when accompanied by thrombocytopenia, abnormal liver function functions, renal failure, pulmonary edema, persistent headache unresponsive to medications that cannot be attributed to alternative diagnoses, or visual disturbances, is also diagnosed as preeclampsia. Relevant ACOG guidelines for the diagnosis of mild and severe or early and late preeclampsia were also followed [9].

Smokers, alcohol consumers, those under 18 and over 40 years of age, those with any pregestational or gestational disease, those with congenital uterine anomalies, and those who conceived with assisted reproductive techniques were not included in the control group. In addition to those listed above, those who had any other pregnancy-related disease other than preeclampsia were not included in the preeclampsia group.

Participants' demographic characteristics, examination and ultrasonography findings, laboratory results, and perinatal outcomes were recorded.

Peripheral venous blood samples were taken from the participants in the morning after an 8-hour fast to measure serum PNX-14 and PNX-20 levels. In the preeclampsia group, blood samples were taken before the initiation of antihypertensive treatment. Blood samples in biochemistry tubes were kept at room temperature for 20 min and then centrifuged at 2,000 rpm for 20 min. After centrifugation, the remaining serum in the upper part of the biochemistry tube was transferred to Eppendorfs and stored at –80 degrees. PNX-14 levels in serum samples were determined with the Human Phoenixin-14 ELISA Kit (SunRed Biotechnology Company, Catalog number: 201-12-9271). Measurement range for the Human Phoenixin-14 ELISA Kit used in the study was between 10 pg/mL and 3,000 pg/mL and the sensitivity of the kit was 8.758 pg/mL. PNX-20 levels in serum samples were determined with the Human Phoenixin-20 ELISA Kit (SunRed Biotechnology Company, Catalog number: 201-12-9216). Measurement range for the Human Phoenixin-20 ELISA Kit used in the study was between 10 pg/mL and 3,000 pg/mL and the sensitivity of the kit was 8.722 pg/mL.

The Umraiye Training and Research Hospital Local Ethics Committee approved this study (Approval Number: B.10.1.TKH.4.34.H.GP.0.01/102, Date: 22/03/2023). The study was conducted per the Declaration of Helsinki and followed the country's ethical standards. Informed and written consent was obtained from all participants.

The formula used to estimate the incidence of an event in the population within certain margins of error and to calculate the required sample size is as follows:

$$n = \frac{(Z_{\frac{\alpha}{2}})^2 p(1-p)}{E^2}$$

(α = type 1 error probability, z_(α/2) = z value at α error level, p = probability of occurrence of the event, E = margin

Tab. 1. Comparison of demographic characteristics between the control group and preeclampsia group.
Tab. 1. Srovnání demografických charakteristik mezi kontrolní skupinou a skupinou s preeklampsií.

		Control group (N = 45) mean ± SD, median (Min.–Max.), N (%)	Preeclampsia group (N = 45) mean ± SD, median (Min.–Max.), N (%)	P
Age (years)		29.8 ± 5.2	29.9 ± 5.2	0.920[a]
BMI (kg/m²)		32.4 ± 5.2	32.9 ± 5.3	0.714[a]
Weight gained during pregnancy (kg)		9.8 ± 5	9.6 ± 7	0.877[a]
Parity	nulliparous	21 (46.6)	20 (44.4)	1.000[b]
	multiparous	24 (53.4)	25 (55.6)	

[a] Independent T-test, [b] Chi-Square test
BMI – body mass index, N – number, SD – standard deviation

Tab. 2. Comparison of control and preeclampsia groups in terms of laboratory results and ultrasound findings.
Tab. 2. Porovnání kontrolní skupiny a skupiny preeklampsie z hlediska laboratorních výsledků a ultrazvukového nálezu.

		Control group (N = 45) mean ± SD, median (Min.–Max.), N (%)	Preeclampsia group (N = 45) mean ± SD, median (Min.–Max.), N (%)	P
Systolic blood pressure (mmHg)		119 (104–130)	150 (140–200)	< 0.001[b]
Diastolic blood pressure (mmHg)		72 (60–80)	95 (90–110)	< 0.001[b]
Mean arterial pressure (mmHg)		87.7 (74.7–96.7)	112.7 (106.7–140)	< 0.001[b]
Protein/creatinine in the spot urine sample		0.1 (0.1–0.3)	0.4 (0.3–5.5)	< 0.001[b]
AST (U/L)		15 (9–48)	16 (6–385)	0.385[b]
ALT (U/L)		12 (5–72)	11 (5–263)	0.509[b]
Platelet count (/uL)		24,1711 ± 79,330	22,7022 ± 74,323	0.367[a]
Umbilical artery Doppler PI		1 ± 0.2	1 ± 0.2	0.166[a]
Umbilical artery Doppler RI		0.6 (0.4–2)	0.7 (0.5–0.9)	0.279[b]
Umbilical artery Doppler S/D		2.6 (1.6–5.6)	2.8 (1.9–6.2)	0.104[b]
MCA Doppler PI		1.9 ± 0.5	1.7 ± 0.5	0.053[a]
MCA Doppler RI		0.9 ± 0.1	0.8 ± 0.1	0.011[a]
MCA Doppler S/D		6.8 (2.7–45.6)	4.8 (2.3–111.1)	0.003[b]
FGR	yes	0 (0)	8 (17.8)	0.006[c]
	no	45 (100)	37 (82.2)	

[a] Independent T-test, [b] Mann-Whitney U-test, [c] Chi-Square test
AST – aspartate aminotransferase, ALT – alanine aminotransferase, FGR – fetal growth restriction, MCA – middle cerebral artery, N – number, PI – pulsatility index, RI – resistance index, S/D – systole/diastole, SD – standard deviation

of error). Accordingly, when the type 1 error probability (α) is accepted as 0.05 (95% confidence level), the z value is 1.96. When the prevalence value we predicted for preeclampsia admitted to our clinic is calculated as (0.05%), the margin of error (E) is accepted as 0.1 unit (small effect). Using the formula stated above, it was determined that the minimum sample size required to estimate the prevalence in the hospital at a 95% confidence level was 18 participants for each group. Since the Human Phoenixin-14 and Phoenixin-20 ELISA Kits used in the study allowed blood samples of 90 participants to be examined, we conducted the study on 90 participants, 45 in the preeclampsia group and 45 in the control group.

Statistical analyses were performed using the Statistical Package for the Social Sciences 25.0 program (SPSS Inc.; Chicago, IL, USA). The Kolmogorov-Smirnov test was used to check whether the data were normally distributed. Descriptive statistical methods (mean, SD – standard deviation, median, IQR – interquartile range, frequency, ratio) were used to evaluate the study data. An Independent T-test was used for two-group comparisons showing parametric distribution, and the Mann-Whitney U-test was used for two-group comparisons showing non-parametric distribution. Kruskal-Wallis H-test was used for comparisons of more than three groups.

Tab. 3. Comparison of control and preeclampsia groups in terms of perinatal outcomes.
Tab. 3. Srovnání kontrolní skupiny a skupiny preeklampsie z hlediska perinatálních výsledků.

		Control group (N = 45) mean ± SD, median (Min.–Max.), N (%)	Preeclampsia group (N = 45) mean ± SD, median (Min.–Max.), N (%)	P
Thrombocytopenia	yes	0 (0)	5 (11.1)	0.056[b]
	no	45 (100)	40 (89.9)	
HELLP syndrome	yes	0 (0)	4 (8.8)	0.117[b]
	no	45 (100)	41 (91.2)	
Visual symptoms	yes	0 (0)	20 (44.4)	< 0.001[b]
	no	45 (100)	25 (55.6)	
Pulmonary edema	yes	0 (0)	2 (4.4)	0.494[b]
	no	45 (100)	43 (95.6)	
Eclampsia	yes	0 (0)	5 (11.1)	0.056[b]
	no	45 (100)	40 (88.9)	
Placental abruption	yes	0 (0)	11 (24.4)	< 0.001[b]
	no	45 (100)	34 (75.6)	
Gestational week at birth		38 (37–41)	37 (27–39)	< 0.001[a]
Mode of delivery	vaginal birth	23 (51.1)	4 (8.8)	< 0.001[b]
	cesarean section	22 (48.9)	41 (91.2)	
Birth weight (g)		3,250 (3,000–4,360)	2,790 (580–3,720)	< 0.001[a]
1st min Apgar score		8 (6–9)	8 (3–9)	< 0.001[a]
5th min Apgar score		10 (8–10)	9 (5–10)	< 0.001[a]
Emergency Caesarean section	yes	11 (24,4)	28 (62.2)	< 0.001[b]
	no	34 (75.6)	17 (37.8)	
Meconium Stained Amnion	yes	5 (11.1)	5 (11.1)	1.000[b]
	no	40 (88.9)	40 (88.9)	
Preterm delivery	yes	0 (0)	19 (42.2)	< 0.001[b]
	no	45 (100)	26 (57.8)	
Gender of the newborn	female	22 (48.8)	26 (57.7)	0.398[b]
	male	23 (51.2)	19 (42.3)	
NICU Admission	yes	0 (0)	18 (40)	< 0.001[b]
	no	45 (100)	27 (60)	

[a] Mann-Whitney U-test, [b] Chi-Square test
HELLP – hemolysis, elevated liver enzymes, and low platelet, N – number, NICU – neonatal intensive care unit, SD – standard deviation

Statistical significance was accepted as $P < 0.05$ for all variables.

Results

Preeclampsia and control groups were similar in terms of age, BMI, weight gained during pregnancy, and parity ($P > 0.05$, for each) (Tab. 1).

Systolic, diastolic, and mean arterial pressure were significantly higher in the preeclampsia group than in the control group ($P < 0.001$, for each). The protein/creatinine ratio in a spot urine sample was significantly higher in the preeclampsia group, but aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels and platelet count were similar in both groups ($P < 0.001$, $P = 0.385$, $P = 0.509$, $P = 0.367$, resp.). The umbilical artery pulsatility index (PI), resistance index (RI), and systole/diastole (S/D) ratio were similar in both groups ($P > 0.05$, for each). While middle cerebral artery Doppler PI was similar in both groups, RI and S/D were significantly lower in the preeclampsia group than in the control group ($P = 0.053$, $P = 0.011$, $P = 0.003$, resp.). While fetal growth restriction (FGR) developed in 8 pregnant women in the preeclampsia group, no pregnant woman in the control group developed FGR ($P = 0.006$) (Tab. 2).

In the preeclampsia group, thrombocytopenia developed in 5 patients, HELLP syndrome in 4 patients, visual symptoms in 20 patients, pulmonary edema in 2 patients, eclampsia in 5 patients, and placental abruption in

Tab. 4. Comparison of control and preeclampsia groups in terms of serum PNX-14 and PNX-20 levels.
Tab. 4. Srovnání kontrolní skupiny a skupiny s preeklampsií z hlediska sérových hladin PNX-14 a PNX-20.

	Control group (N = 45) mean ± SD, median (Min.–Max.), N (%)	Preeclampsia group (N = 45) mean ± SD, median (Min.–Max.), N (%)	P
Gestational week at blood sampling	33 (24–38)	33 (24–38)	0.984[a]
Serum PNX-14 level (pg/mL)	393.2 (193.3–21,808.3)	390.3 (205.2–21,508.2)	0.434[a]
Serum PNX-20 level (pg/mL)	379.9 (168.7–4,484.4)	346.6 (246.5–2,689.5)	0.278[a]

[a] Mann-Whitney U-test
N – number, PNX – phoenixin

Tab. 5. Comparison of control, mild preeclampsia, and severe preeclampsia groups in terms of serum PNX-14 and PNX-20 levels.
Tab. 5. Srovnání kontrolní skupiny, mírné preeklampsie a těžké preeklampsie z hlediska sérových hladin PNX-14 a PNX-20.

	Control group (N = 45) median (Min.–Max.)	Mild preeclampsia group (N = 30) median (Min.–Max.)	Severe preeclampsia group (N = 15) median (Min.–Max.)	P
Serum PNX-14 level (pg/mL)	393.2 (193.3–21,808.3)	410.2 (205.2–21,508.2)	344.2 (207.1–9,992.9)	0.281[a]
Serum PNX-20 level (pg/mL)	379.9 (168.7–4,484.4)	343.9 (247.7–2,689.5)	346.6 (246.5–1,990.2)	0.547[a]

[a] Kruskall-Walis H-test
N – number, PNX – phoenixin

Tab. 6. Comparison of control, early-onset preeclampsia, and late-onset preeclampsia groups in terms of serum PNX-14 and PNX-20 levels.
Tab. 6. Srovnání kontrolní skupiny, preeklampsie s časným nástupem a preeklampsie s pozdním nástupem z hlediska sérových hladin PNX-14 a PNX-20.

	Control group (N = 45) median (Min.–Max.)	Early-onset preeclampsia group (N = 21) median (Min.–Max.)	Late-onset preeclampsia group (N = 24) median (Min.–Max.)	P
Serum PNX-14 level (pg/mL)	393.2 (193.3–21,808.3)	408.5 (205.2–8,767.2)	373.1 (208.1–21,508.2)	0.718[a]
Serum PNX-20 level (pg/mL)	379.9 (168.7–4,484.4)	340.7 (270.1–1,737.8)	351.2 (246.5–2,689.5)	0.481[a]

[a] Kruskall-Walis H-test
N – number, PNX – phoenixin

11 patients. Gestational week at birth, birth weight, and 1st, and 5th min Apgar scores were significantly lower in the preeclampsia group than in the control group ($P < 0.001$, for each). Cesarean delivery and the need for emergency cesarean section were significantly higher in the preeclampsia group than in the control group ($P < 0.001$, for each). The incidence of meconium-stained amnion and newborn gender were similar in both groups, whereas preterm delivery and neonatal intensive care unit admission were significantly higher in the preeclampsia group ($P = 1.000$, $P = 0.398$, $P < 0.001$, $P < 0.001$, resp.) (Tab. 3).

Gestational week at blood sampling for serum PNX-14 and PNX-20 was similar in the two groups ($P = 0.984$). The median serum PNX-14 level was 390.3 pg/mL in the preeclampsia group and 393.2 pg/mL in the control group ($P = 0.434$). While the median serum PNX-20 level was 346.6 pg/mL in the preeclampsia group, it was 379.9 pg/mL in the control group ($P = 0.278$) (Tab. 4).

When the preeclampsia group was divided into subgroups according to the severity of the disease and the onset of the disease and compared with the control group, no significant difference was found between the groups in terms of serum PNX-14 and PNX-20 levels (Tab. 5, 6).

Discussion

In this study, serum PNX-14 and PNX-20 levels were investigated in the preeclampsia group and the control group, and serum PNX-14 and PNX-20 levels were found to be similar in both groups.

Following the identification of PNX as a multifunctional peptide, recent studies have focused on the endothelial protective and anti-inflammatory properties of PNX. Ling and colleagues studied the effect of PNX-14 on smooth muscle cell-induced endothelial cell dysfunction,

which plays a role in the etiopathogenesis of intracranial aneurysms. PNX-14 was shown to attenuate endothelial cell dysfunction induced by inflammatory smooth muscle cells *in vitro* [10]. Another study published in 2024 supported these findings. Ling et al. examined the role of PNX-14 in the phenotypic change of vascular smooth muscle cells (VSMC) during the pathogenesis of an intracranial aneurysm using both cellular and animal models. The authors showed that H_2O_2 stimulated intracellular reactive oxygen species (ROS) production and induced oxidative stress in VSMCs, while PNX-14 pretreatment reduced intracellular ROS levels in VSMCs exposed to H_2O_2. It was also reported that PNX-14 administration prevented intracranial aneurysm formation and rupture in rat models [11]. Zhang et al. showed that PNX-14 protects human brain vascular endothelial cells against oxygen-glucose deprivation/reoxygenation-induced inflammation and permeability [8].

It was reported that the cytoprotective effect of PNX-14 is not only on the vascular endothelium, but also on the cells of the central nervous system itself. Ma et al. showed that PNX-14 prevents ischemia/reperfusion-induced cytotoxicity in microglia [12]. In a different study, Wang et al. stated that PNX-14 has a protective effect against lipopolysaccharide-induced inflammation and inflammasome activation in astrocytes [13].

Recent studies have also documented the role of PNX in mitigating oxidative stress and preventing inflammation in peripheral tissues. For example, Yılmaz et al. investigated the protective effect of PNX-14 against oxidative damage in gonads. An experimental torsion-detorsion model was performed in pre-pubertal rats. It was revealed that PNX-14 treatment caused a significant decrease in oxidative stress and inflammation and significantly repaired the damage in testicular tissue [14]. In 2024, Chai et al. published a study investigating the effects of PNX-20 in a rat model of experimentally induced pulmonary hypertension. They determined that PNX-20 alleviated pulmonary arterial hypertension by inhibiting oxidative stress and inflammation [15].

In their 2022 study, Akdu et al. examined serum levels of PNX-14 and PNX-20 in 36 hypertensive patients and 36 healthy controls. Serum PNX-14 and PNX-20 levels were found to be significantly lower in the hypertensive group compared to the normotensive group. Negative significant correlations were found between both serum PNX-14 and PNX--20 and the participants' weight, BMI, systolic and diastolic blood pressures. The authors suggested that serum PNX-14 and PNX-20 may serve as new biomarkers for the diagnosis of hypertension [16]. Based on this study and additional literature, we hypothesized that PNX-14 and PNX-20 might contribute to the pathophysiology of preeclampsia. At the outset of our research, we anticipated that serum PNX levels would be lower in preeclamptic pregnant women compared to healthy controls. However, contrary to our hypothesis, we observed that serum levels of PNX-14 and PNX-16 were similar in both the preeclampsia group and the control group.

There is currently no available data on serum PNX levels during healthy pregnancies. Only one study has explored serum PNX levels in pregnancy. This research focused on serum PNX-14 levels in cases of hyperemesis gravidarum, revealing significantly elevated levels in pregnant women affected by this condition [17]. Although no significant results were obtained, to our knowledge, this is the first study in the literature investigating serum PNX levels in preeclampsia.

This single-center study has important limitations. First, the study was conducted with a limited number of participants. Additionally, serum PNX-14 and PNX-20 levels were measured only once in each participant. As a result, these values represent single-point observations and do not capture the dynamic changes in serum levels throughout the entire pregnancy. It is also important to note that the expressions of PNX-14 and PNX-20 in tissues, as well as their interactions with receptors, may differ from their serum levels.

Conclusion

In this investigation, serum levels of PNX-14 and PNX-20 were found to be comparable between the preeclampsia and control groups. Also, no significant differences were observed in the levels of PNX-14 and PNX-20 when subgroup analyses were conducted based on the severity or onset of preeclampsia. Although the sample size in this study was limited, which precludes drawing definitive conclusions, the results suggest that PNX-14 and PNX-20 may not be crucial to the pathophysiology of preeclampsia or may not be influenced by the disease. However, further studies with larger sample sizes are needed to confirm these findings.

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