

Serum oxidative stress and vasoactive biomarkers in women with preeclampsia: a comparative cross-sectional study

Biomarker Stres Oksidatif Dan Vasoaktif Serum Pada Ibu Hamil Dengan Preeklampsia: Studi Potong Lintang Komparatif

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ARTICLE HISTORY Received [29 July 2026] Revised [10 August 2026] Accepted [18 Sept 2026]	ABSTRAK Latar belakang: Preeklampsia berkaitan dengan stres oksidatif dan perubahan jalur vasoaktif. Penelitian ini membandingkan enam biomarker serum pada ibu hamil dengan preeklampsia dan ibu hamil normotensif di Irak. Metode: Studi potong lintang komparatif dilakukan pada Februari–Juni 2026 dengan melibatkan 40 ibu hamil dengan preeklampsia dan 20 kontrol ibu hamil sehat. Kadar koenzim Q10 (CoQ10), malondialdehid (MDA), renin, angiotensin-converting enzyme (ACE), kalikrein-1 (KLK1), dan bradikinin (BK) diukur menggunakan ELISA. Analisis meliputi perbandingan antarkelompok, korelasi Pearson, dan kurva receiver operating characteristic (ROC) secara eksploratif. Hasil: Rerata kadar MDA ($5,97 \pm 0,45$ vs. $2,67 \pm 0,35$ nmol/mL), renin ($2,35 \pm 0,29$ vs. $1,86 \pm 0,54$ pg/mL), ACE ($1,08 \pm 0,37$ vs. $0,76 \pm 0,16$ U/L), dan KLK1 ($1,44 \pm 0,49$ vs. $1,10 \pm 0,36$ pg/mL) lebih tinggi pada kelompok preeklampsia. Sebaliknya, CoQ10 ($22,44 \pm 20,56$ vs. $39,43 \pm 13,83$ µg/mL) dan BK ($0,72 \pm 0,22$ vs. $0,99 \pm 0,27$ ng/mL) lebih rendah. MDA menunjukkan AUC 1,00 pada sampel penelitian, sedangkan KLK1 berkorelasi positif dengan BK pada kelompok preeklampsia ($r = 0,55$). Kesimpulan: Profil biomarker stres oksidatif dan vasoaktif berbeda antara kedua kelompok; pemanfaatan diagnostiknya memerlukan validasi pada populasi yang lebih besar dan representatif.
KEYWORDS Preeclampsia; Oxidative Stress; Coenzyme Q10; Kallikrein–Kinin System; Renin–Angiotensin System	ABSTRACT Background: Preeclampsia is associated with oxidative imbalance and altered vasoactive pathways. This study compared six serum biomarkers between women with preeclampsia and normotensive pregnant controls in Iraq. Methods: In a comparative cross-sectional study conducted from February to June 2026, 40 women with preeclampsia and 20 healthy pregnant controls were enrolled. Serum coenzyme Q10 (CoQ10), malondialdehyde (MDA), renin, angiotensin-converting enzyme (ACE), kallikrein-1 (KLK1), and bradykinin (BK) were measured using ELISA. Group comparisons, Pearson correlations, and exploratory receiver operating characteristic (ROC) analyses were performed. Results: Mean MDA (5.97 ± 0.45 vs. 2.67 ± 0.35 nmol/mL), renin (2.35 ± 0.29 vs. 1.86 ± 0.54 pg/mL), ACE (1.08 ± 0.37 vs. 0.76 ± 0.16 U/L), and KLK1 (1.44 ± 0.49 vs. 1.10 ± 0.36 pg/mL) were higher in the preeclampsia group. CoQ10 (22.44 ± 20.56 vs. 39.43 ± 13.83 µg/mL) and BK (0.72 ± 0.22 vs. 0.99 ± 0.27 ng/mL) were lower. MDA yielded an area under the ROC curve of 1.00 within the study sample, and KLK1 correlated positively with BK among cases ($r = 0.55$). Conclusion: Oxidative stress and vasoactive biomarker profiles differed between groups; their diagnostic relevance requires validation in larger, representative cohorts.

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INTRODUCTION

Preeclampsia is a hypertensive disorder of pregnancy characterized by new-onset hypertension after 20 weeks of gestation, with proteinuria and/or evidence of maternal organ or uteroplacental dysfunction. Proteinuria is not required when other recognized diagnostic features are present (Vera-Ponce et al., 2025; Khan et al., 2022; American College of Obstetricians and Gynecologists [ACOG], 2020). It remains a major contributor to maternal and perinatal morbidity.

Normal pregnancy requires trophoblast invasion and remodeling of the maternal spiral arteries to establish a low-resistance uteroplacental circulation. Defective vascular remodeling and placental hypoxia

are implicated in the endothelial disturbance and oxidative injury associated with preeclampsia (Haram et al., 2020; Aouache et al., 2018; Colson et al., 2021). Placental oxidative stress and systemic endothelial dysfunction can adversely affect vascular adaptation and maternal organ function (Schoots et al., 2018; Boeldt & Bird, 2017).

Malondialdehyde (MDA), a product of lipid peroxidation, provides an indirect indication of oxidative damage, although it is not specific to preeclampsia. The relevance of oxidative stress biomarkers to pregnancy complications has been discussed in general reviews and disease-specific studies (Kiran et al., 2023; Liu et al., 2025). Systematic reviews also support investigation of their clinical relevance while highlighting heterogeneity between populations and assays (Freire et al., 2023; Afrose et al., 2022).

Coenzyme Q10 (CoQ10) contributes to mitochondrial electron transport and antioxidant defense. Reports have investigated its circulating concentration, redox biology, and potential role in preeclampsia (Roland et al., 2010; Teran et al., 2003; Teran et al., 2018; Deer et al., 2025). Broader studies address CoQ10 supplementation or its association with markers of inflammation and oxidative stress (Shaikh et al., 2021; Dabbaghi Varnousfaderani et al., 2023), while the review by Kudalkar (2025) discusses its systemic biochemical functions.

Vascular homeostasis during pregnancy is also influenced by the renin–angiotensin system (RAS) and the kallikrein–kinin system (KKS). These pathways participate in the regulation of vascular tone, inflammation, and permeability, but their circulating measurements cannot be assumed to represent activity throughout all tissues (Lumbers & Pringle, 2014; Bekassy et al., 2022). Research on ACE2 and placental RAS components, as well as studies of placental angiotensin metabolism, illustrates the complexity of these pathways in preeclampsia (Tamanna et al., 2020; Sun et al., 2021; Stettner-Kołodziejska et al., 2022). Investigations of kallikrein generation further suggest changes in the contact-system pathway (Godtfredsen et al., 2022), although this measure differs from serum kallikrein-1 (KLK1).

Evidence remains limited on the joint serum profile of oxidative stress markers and selected RAS and KKS components among Iraqi pregnant women. The present study therefore compared CoQ10, MDA, renin, ACE, KLK1, and bradykinin (BK) between women clinically classified with preeclampsia and normotensive pregnant controls. It also explored within-group biomarker correlations and their apparent ability to distinguish the two study groups. The study hypothesized that oxidative stress and vasoactive marker distributions would differ between groups; the correlation and ROC analyses were exploratory.

RESEARCH METHOD

A comparative cross-sectional study was conducted from February to June 2026 among 60 pregnant women attending private outpatient clinics in Iraq. The sample included 40 women diagnosed with preeclampsia and 20 normotensive pregnant controls. The preeclampsia group was identified through physician-recorded diagnoses after 24 weeks of gestation; ACOG Practice Bulletin No. 222 guided interpretation of the clinical diagnostic framework (ACOG, 2020). Women with preexisting chronic hypertension, diabetes mellitus, or chronic kidney disease were excluded. Age, body mass index (BMI), gestational age, blood pressure, and proteinuria were obtained from questionnaires and available clinical records.

Five milliliters of venous blood were collected in plain plastic tubes without anticoagulant and allowed to clot at room temperature for approximately 10 minutes. Specimens were centrifuged at 3,000 rpm for 15 minutes, and serum was transferred to microcentrifuge tubes and stored at -20°C . Samples were thawed once before analysis; a protease inhibitor to reduce peptide degradation. Serum biomarkers were measured with SUNLONG Biotech (China) ELISA kits: CoQ10 (SL2187Hu), MDA (SL1135Hu), renin (SL1528Hu), ACE (SL0120Hu), KLK1 (SL1023Hu), and BK (SL0370Hu). Assays were performed according to the manufacturer's instructions. Urinary protein was assessed by dipstick and recorded as 1+, 2+, or 3+ in women with preeclampsia.

The primary grouping variable was the physician-recorded diagnosis of preeclampsia. Biomarker measurements were analyzed as continuous variables. All enrolled participants were included in the reported analyses, and the study reported no missing values for variables in the final analytical dataset. The study followed the principles of the Declaration of Helsinki. Ethical approval was granted by a local ethics committee (approval No. 2390; 31 January 2026), and participant consent was obtained before sampling.

Data were analyzed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean $\pm$ standard deviation (SD), and categorical data as counts and percentages. Group comparisons used independent-samples tests; Table 2 specifically reports Welch's t-test for between-group biomarker comparisons. Pearson correlation coefficients (r) were used for pairwise biomarker associations within each group. Exploratory ROC analyses estimated the area under the curve

(AUC), thresholds, sensitivity, and specificity. All reported tests were two-sided, with $p < 0.05$ indicating statistical significance. Because multiple tests were performed in a small sample without reported multiplicity adjustment or independent validation, nominal p-values and ROC estimates require cautious interpretation. The presentation of this observational study was informed by STROBE principles. Its exploratory discrimination analysis is reported descriptively rather than as a clinically validated diagnostic accuracy study.

RESULTS AND DISCUSSION

Participant Characteristics

Women with preeclampsia were slightly older than controls (29.5 ± 4.11 vs. 27.4 ± 3.01 years; $p = 0.029$). Systolic and diastolic blood pressure were higher in the preeclampsia group (both $p < 0.001$), whereas BMI and gestational age were not significantly different in the unadjusted comparisons. Among women with preeclampsia, dipstick proteinuria was 1+ in seven (17.5%), 2+ in eight (20.0%), and 3+ in 25 (62.5%) participants. Proteinuria was not recorded in the control group (Table 1).

Table 1. Demographic and clinical characteristics of women with preeclampsia and healthy pregnant controls.

Variable	Dipstick	Preeclampsia (n = 40)	Controls (n = 20)	p-value
Age (years)	—	29.5 ± 4.11	27.4 ± 3.01	0.029
BMI (kg/m ²)	—	29.22 ± 1.33	28.6 ± 1.40	0.099
SBP (mmHg)	—	161.6 ± 20.8	111.0 ± 15.4	< 0.001
DBP (mmHg)	—	109.5 ± 16.0	72.4 ± 13.0	< 0.001
Gestational age (weeks)	—	26.55 ± 5.24	24.65 ± 7.99	0.343
Proteinuria (n, %)	1+	7 (17.5%)	0	—
	2+	8 (20.0%)	0	—
	3+	25 (62.5%)	0	—

Values are mean $\pm$ SD or n (%). BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Serum Oxidative Stress and Vasoactive Biomarkers

The preeclampsia group had higher mean MDA, ACE, KLK1, and renin values than healthy pregnant controls. Conversely, mean CoQ10 and BK values were lower in the preeclampsia group. All six between-group comparisons reached nominal significance (Table 2). These findings describe cross-sectional group differences rather than changes over time.

Table 2. Serum oxidative stress and vasoactive biomarkers in women with preeclampsia and healthy pregnant controls.

Biomarker	Preeclampsia (n = 40)	Controls (n = 20)	Difference (95% CI)	p-value
CoQ10 (μ g/mL)	22.44 ± 20.56	39.43 ± 13.83	-16.99 (-25.99 to -7.99)	0.0004
MDA (nmol/mL)	5.97 ± 0.45	2.67 ± 0.35	3.30 (3.09 to 3.51)	< 0.001
ACE (U/L)	1.08 ± 0.37	0.76 ± 0.16	0.32 (0.18 to 0.46)	0.00002
BK (ng/mL)	0.72 ± 0.22	0.99 ± 0.27	-0.27 (-0.41 to -0.13)	0.00049
KLK1 (pg/mL)	1.44 ± 0.49	1.10 ± 0.36	0.34 (0.12 to 0.56)	0.004
Renin (pg/mL)	2.35 ± 0.29	1.86 ± 0.54	0.49 (0.22 to 0.76)	0.00085

Values are mean $\pm$ SD. Differences are calculated as preeclampsia minus controls. The original analysis reports 95% confidence intervals and Welch's t-tests.

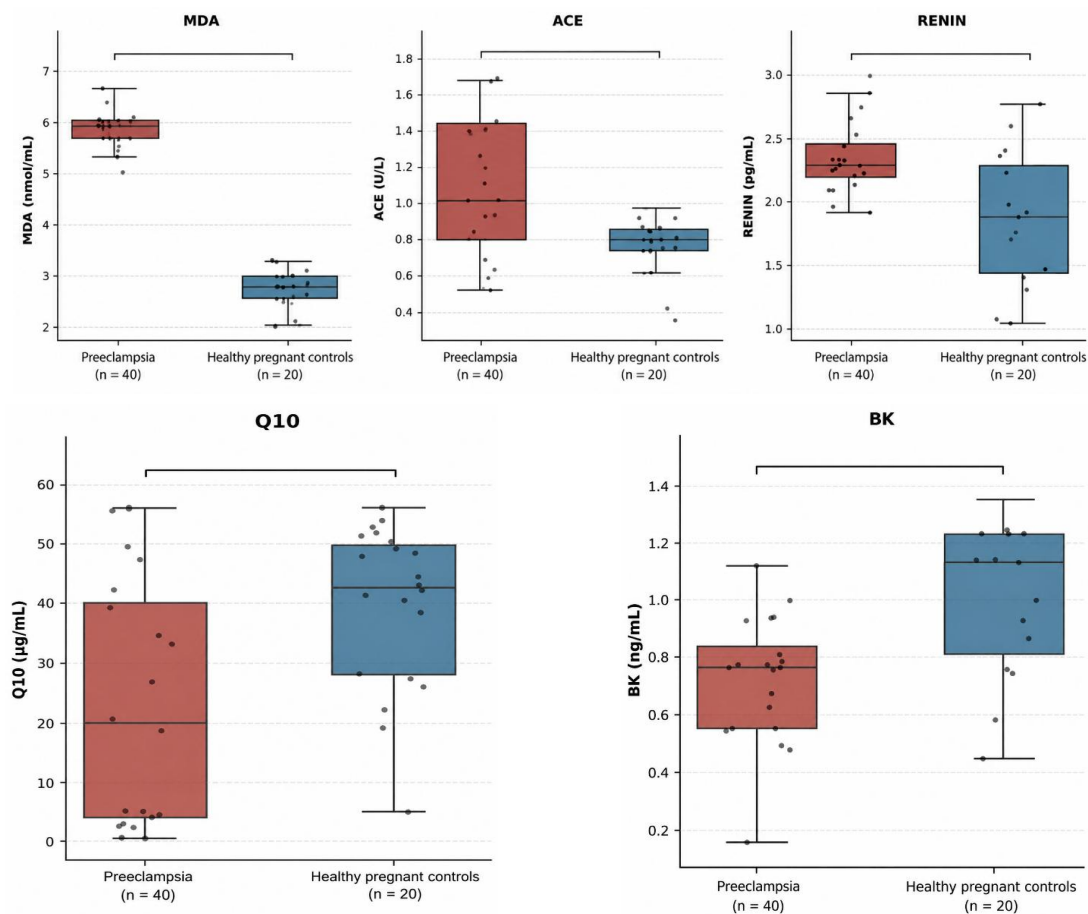


Figure 1. Distribution of selected serum oxidative stress and vasoactive biomarkers in women with preeclampsia and healthy pregnant controls.

Within-Group Correlations

In the preeclampsia group, KLK1 and BK were positively correlated ($r = 0.55$; $p = 0.00024$), while CoQ10 and MDA also showed a positive correlation ($r = 0.44$; $p = 0.0045$). ACE and renin exhibited a weaker positive association ($r = 0.32$; $p = 0.0441$). Other pairwise coefficients were smaller or were not statistically significant at the nominal threshold (Table 3). Figure 2 illustrates the positive KLK1–BK association in participants with preeclampsia.

Table 3. Pearson correlations among serum biomarkers in women with preeclampsia ($n = 40$).

biomarkers	CoQ10	MDA	ACE	BK	KLK1	Renin
CoQ10	1.00	0.44 $p = 0.0045$	0.04 $p = 0.806$	-0.21 $p = 0.193$	-0.16 $p = 0.3240$	0.09 $p = 0.5807$
MDA	0.44 $p = 0.0045$	1.00	0.10 $p = 0.5392$	-0.10 $p = 0.5393$	0.16 $p = 0.3240$	-0.28 $p = 0.0801$
ACE	0.04 $p = 0.806$	0.10 $p = 0.5392$	1.00	-0.14 $p = 0.3889$	-0.10 $p = 0.5392$	0.32 $p = 0.0441$
BK	-0.21 $p = 0.193$	-0.10 $p = 0.5393$	-0.14 $p = 0.3889$	1.00	0.55 $p = 0.00024$	-0.04 $p = 0.8064$
KLK1	-0.16 $p = 0.3240$	0.16 $p = 0.3240$	-0.10 $p = 0.5392$	0.55 $p = 0.00024$	1.00	-0.01 $p = 0.9511$
Renin	0.09 $p = 0.5807$	-0.28 $p = 0.0801$	0.32 $p = 0.0441$	-0.04 $p = 0.8064$	-0.01 $p = 0.9511$	1.00

Cells show Pearson r and the corresponding nominal p -value. CoQ10: coenzyme Q10; MDA: malondialdehyde; ACE: angiotensin-converting enzyme; BK: bradykinin; KLK1: kallikrein-1.

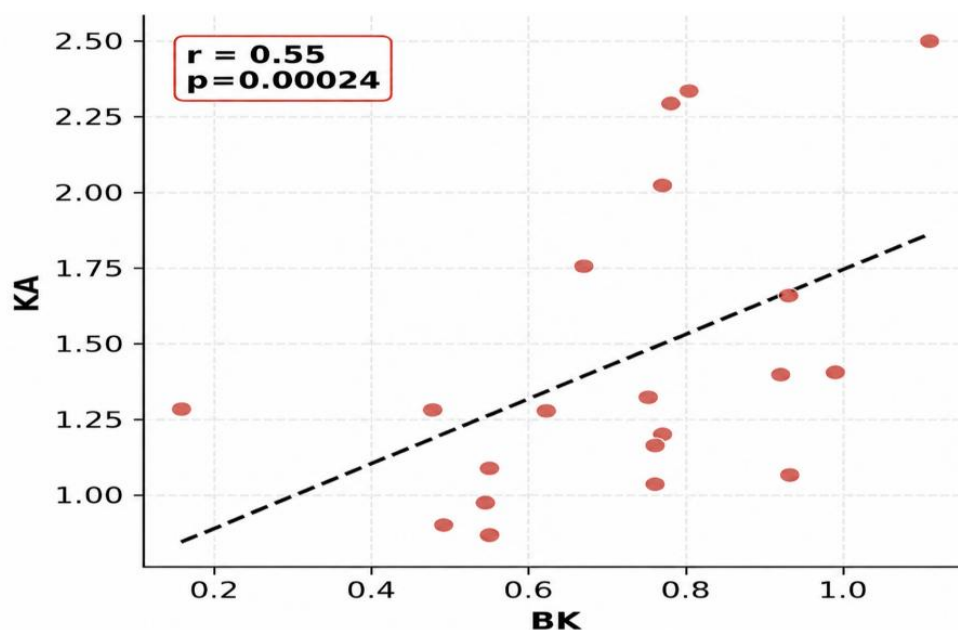


Figure 2. Positive correlation between serum bradykinin and kallikrein-1 in women with preeclampsia.

In healthy pregnant controls, CoQ10 and BK were inversely correlated ($r = -0.57$; $p = 0.0086$), as shown in Table 4 and Figure 3. No other pairwise correlations reached the nominal $p < 0.05$ threshold within the control group. These analyses were exploratory and did not establish causal relationships between biomarkers.

Table 4. Pearson correlations among serum biomarkers in healthy pregnant controls ($n = 20$).

Biomarker	CoQ10	MDA	ACE	BK	KLK1	Renin
CoQ10	1.00	-0.32 $p = 0.1690$	0.02 $p = 0.9333$	-0.57 $p = 0.0086$	0.13 $p = 0.5848$	0.19 $p = 0.4223$
MDA	-0.32 $p = 0.1690$	1.00	0.11 $p = 0.6443$	0.34 $p = 0.1424$	-0.26 $p = 0.2682$	0.20 $p = 0.3978$
ACE	0.02 $p = 0.9333$	0.11 $p = 0.6443$	1.00	-0.06 $p = 0.8016$	0.43 $p = 0.0584$	0.24 $p = 0.3081$
BK	-0.57 $p = 0.0086$	0.34 $p = 0.1424$	-0.06 $p = 0.8016$	1.00	-0.30 $p = 0.1987$	-0.40 $p = 0.0805$
KLK1	0.13 $p = 0.5848$	-0.26 $p = 0.2682$	0.43 $p = 0.0584$	-0.30 $p = 0.1987$	1.00	0.30 $p = 0.1987$
Renin	0.19 $p = 0.4223$	0.20 $p = 0.3978$	0.24 $p = 0.3081$	-0.40 $p = 0.0805$	0.30 $p = 0.1987$	1.00

Cells show Pearson r and the corresponding nominal p -value. Values have not been adjusted for multiple testing.

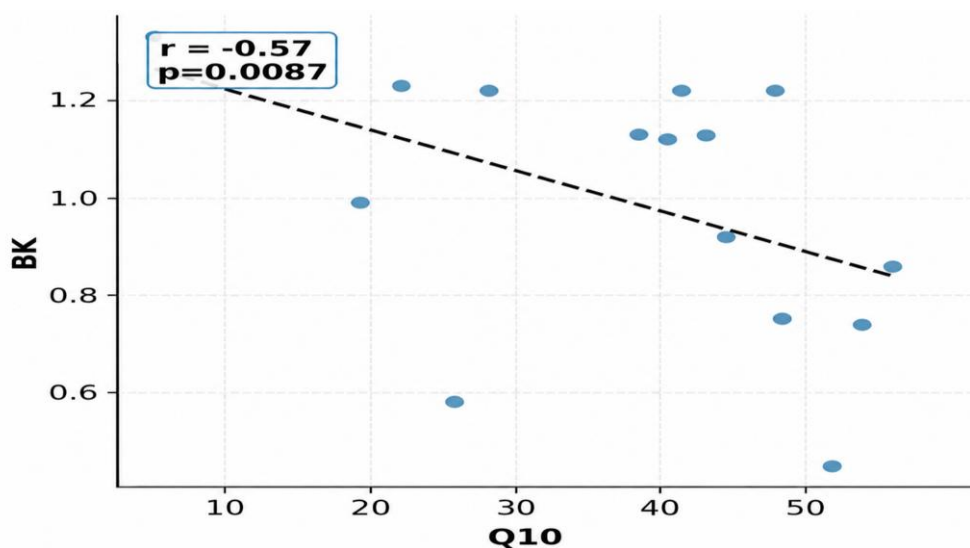


Figure 3. Negative correlation between serum bradykinin and coenzyme Q10 in healthy pregnant controls.

Exploratory ROC Analysis

ROC analysis evaluated the apparent discrimination between the two study groups for each marker. MDA showed perfect separation within this sample (AUC = 1.000; reported sensitivity and specificity = 100% at the selected cutoff of 5.07 nmol/mL). The AUC values for BK, renin, ACE, CoQ10, and KLK1 were 0.777, 0.760, 0.747, 0.746, and 0.680, respectively (Table 5). These performance estimates were obtained from the same dataset used to assess group differences, without external validation, and should not be interpreted as established clinical diagnostic thresholds.

Table 5. Exploratory receiver operating characteristic analysis for individual serum biomarkers.

Biomarker	AUC (95% CI)	p-value	Cutoff	Sensitivity (%)	Specificity (%)
MDA	1.000 (1.000–1.000)	< 0.001	5.07	100	100
BK	0.777 (0.623–0.930)	< 0.001	1.11	100	53
Renin	0.760 (0.602–0.918)	0.001	2.09	90	67
ACE	0.747 (0.585–0.909)	0.003	0.99	55	100
CoQ10	0.746 (0.593–0.900)	0.002	20.50	55	90
KLK1	0.680 (0.503–0.857)	0.047	1.04	85	53

Cutoffs are reported as provided in the original analysis; their selection method was not documented. Units are given in Table 2. These are in-sample exploratory estimates.

Interpretation and Comparison With Previous Studies

The principal finding is a distinct cross-sectional pattern of oxidative stress and vasoactive biomarkers in women with preeclampsia compared with normotensive pregnant controls. Their higher blood pressures are consistent with the clinical phenotype of preeclampsia. The groups also differed in mean age, so age-related influences cannot be excluded. Existing research has examined maternal age, obesity, placental pathology, and clinical management as important aspects of preeclampsia (Sheen et al., 2020; Durst et al., 2016; Weiner et al., 2018; Nirupama et al., 2021). Because the present comparisons were unadjusted, none of the measured group differences should be interpreted as independent of these or other unmeasured clinical factors.

Higher MDA accompanied by lower CoQ10 in the preeclampsia group is compatible with an imbalance between lipid peroxidation and antioxidant defenses. This pattern is consistent with reports of

reduced circulating CoQ10 in preeclampsia (Teran et al., 2003; Teran et al., 2018) and broader evidence connecting oxidative stress markers with the condition (Aouache et al., 2018; Freire et al., 2023; Afrose et al., 2022). Nevertheless, serum MDA is not disease-specific, and total CoQ10 does not directly identify its oxidized-to-reduced redox ratio. Serum biomarker differences therefore support biological investigation but do not prove a specific pathogenic mechanism or the efficacy of CoQ10 supplementation (Shaikh et al., 2021).

The higher serum renin and ACE values suggest variation in selected RAS components. However, they do not by themselves demonstrate activation of the entire RAS or increased angiotensin II signaling, which was not measured. Pregnancy-related RAS regulation involves circulating and local tissue compartments (Lumbers & Pringle, 2014). Moreover, studies involving ACE2, placental RAS markers, and placental angiotensin metabolism use different biological matrices and assays (Tamanna et al., 2020; Sun et al., 2021; Stettner-Kołodziejska et al., 2022); their results cannot be equated directly with serum ACE measurements.

Women with preeclampsia also had higher KLK1 and lower BK than controls, and these two biomarkers were positively correlated within the affected group. This apparent divergence in group means is not necessarily contradictory to a positive within-group correlation: comparisons between groups and associations within groups describe different statistical relationships. Studies of kallikrein generation and contact activation provide a relevant context (Godtfredsen et al., 2022), but circulating KLK1 concentration and kallikrein-generating capacity are not interchangeable measures. Crosstalk among RAS, KKS, and complement pathways is biologically plausible (Bekassy et al., 2022), yet causation cannot be inferred from these serum data.

The inverse CoQ10–BK correlation observed only among controls should be considered hypothesis-generating. Exploratory analysis of multiple marker pairs increases the chance of nominally significant associations, and the relatively small control group further limits precision. The proteinuria distribution is descriptive rather than a severity classification: dipstick results are semiquantitative and should not independently define preeclampsia severity (Okamoto et al., 2022).

Although MDA achieved an AUC of 1.000, this estimate reflects only the sampled cases and healthy controls. The selected thresholds, potential spectrum differences, and absence of external validation can inflate apparent performance. The lower AUCs of the other markers also do not establish their utility alone or in combination. Future studies should include prospective recruitment, standardized assays, prespecified thresholds, clinically relevant comparator groups, and validation cohorts before diagnostic use is considered.

Study Limitations

This study included only 60 participants from outpatient settings, with an unequal case–control distribution and no reported a priori sample-size justification. The methods did not fully specify recruitment and gestational-age matching, the analysis did not adjust for maternal age or other potential confounders, and multiple comparisons were not corrected. ROC threshold selection and independent validation were not described. The cross-sectional design cannot establish temporal or causal relationships. These limitations restrict generalizability and the interpretation of estimated biomarker performance.

CONCLUSION

Women with preeclampsia had higher serum MDA, renin, ACE, and KLK1 and lower CoQ10 and BK than healthy pregnant controls in this comparative cross-sectional sample. KLK1 and BK were positively correlated among women with preeclampsia, while CoQ10 and BK showed an inverse association among controls. The strong in-sample discrimination observed for MDA warrants replication, not immediate clinical use. Larger, prospectively designed studies with confounder adjustment and independent validation are needed to establish whether these biomarkers provide clinically meaningful information.

ETHICS AND DECLARATIONS

Ethical Approval and Consent

The study followed the Declaration of Helsinki. Ethical approval was reported under No. 2390 (31 January 2026), and informed consent was obtained before specimen collection.

Data Availability

Data may be requested from the corresponding author at the email address provided above.



Competing Interests

The author declared no competing interests.

Funding

No funding was declared.

Author Contributions

Shahad Idrees Mohammed was responsible for the study concept, design, implementation, analysis, and manuscript preparation.

Acknowledgments

No acknowledgments were reported.

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ABBREVIATIONS

Abbreviation	Full name
ACOG	American College of Obstetricians and Gynecologists
ACE	Angiotensin-converting enzyme
AUC	Area under the curve
BK	Bradykinin
BMI	Body mass index
CoQ10	Coenzyme Q10
ELISA	Enzyme-linked immunosorbent assay
KKS	Kallikrein–kinin system
KLK1	Kallikrein-1
MDA	Malondialdehyde
PE	Preeclampsia
RAS	Renin–angiotensin system
ROC	Receiver operating characteristic
SPSS	Statistical Package for the Social Sciences
STARD	Standards for Reporting Diagnostic Accuracy Studies