

Original Research

Received 04 June 2026

Revised 22 July 2026

Accepted 06 Aug 2026

Natural Resources for Human Health 2026, Vol. 6 (15s): 1094–1102

KEYWORDS:

Chronic kidney disease; Oxidative stress; Biomarkers; Coenzyme Q10; Advanced glycation end-products; Glutathione peroxidase.

Progressive Alterations in Oxidative Stress Biomarkers across Chronic Kidney Disease Stages

Harith S. Aziz¹, Ammar Lateef Hussein¹, Mohamed Ghalib Zakari², Ghazwan Mohammed Radhi³, Mohsen Hamoud Jasim^{4*}

¹Department of Biochemistry, College of Medicine, Tikrit University, Tikrit, Iraq

²Department of Medicine, College of Medicine, Tikrit University, Tikrit, Iraq

³Department of Pathological Sciences, College of Science, Dijlah University, Baghdad, Iraq

⁴Ibn Khaldoun University College, Baghdad, Iraq

ORCID: Aziz 0009-0009-9560-3472; Hussein 0000-0002-1210-3635; Zakari 0000-0001-7784-1850; Jasim 0009-0001-7879-562X; Radhi 0009-0007-6683-391X

*Corresponding author: Mohsen Hamoud Jasim, Ibn Khaldoun University College, Baghdad, Iraq. E-mail: mohsen07829431518@gmail.com;

ABSTRACT: Chronic kidney disease (CKD) is characterised by progressive redox imbalance, yet it remains unclear which oxidative-stress markers track disease severity rather than merely distinguishing disease from health. In this cross-sectional study, five oxidative-stress and antioxidant biomarkers — coenzyme Q10 (CoQ10), F2-isoprostane, advanced glycation end-products (AGEs), 8-hydroxy-2'-deoxyguanosine (8-OHdG) and glutathione peroxidase (GPx) — were measured in 60 male controls and 120 male patients with CKD stratified into five stages (n = 24 per stage; total N = 180). Groups were compared by Kruskal–Wallis and Bonferroni-corrected Mann–Whitney U tests, diagnostic performance by receiver operating characteristic (ROC) analysis, and associations by Spearman correlation. All five biomarkers differed significantly across groups ($p < 0.001$). CoQ10 declined progressively from control to Stage 5 (7.26 ± 2.16 to 2.29 ± 0.19 ng/mL), while F2-isoprostane, AGEs and 8-OHdG rose progressively (all $\rho \geq 0.90$). These four markers correlated strongly with estimated glomerular filtration rate (eGFR) and creatinine ($|\rho| \geq 0.90$) and discriminated CKD from control well (AUC 0.82–1.00). GPx was markedly higher in every CKD stage than in control ($p < 0.001$) but did not differentiate the stages (Stage 1 vs Stage 5, $p = 0.847$) and was uncorrelated with eGFR within the CKD group ($\rho = -0.13$, $p = 0.150$), indicating an early, saturating rather than severity-tracking response. CoQ10, F2-isoprostane, AGEs and 8-OHdG therefore track CKD severity in a graded, diagnostically useful manner, whereas GPx elevation appears to be an early threshold response to renal impairment rather than a marker of progression.

1. INTRODUCTION

Chronic kidney disease (CKD) affects a substantial proportion of the global population and is associated with markedly increased cardiovascular morbidity and all-cause mortality, much of which is not explained by traditional risk factors alone (Himmelfarb et al., 2002; Tonelli et al., 2006). Over two decades ago, Himmelfarb and colleagues proposed oxidative stress as a unifying mechanism linking uremia to accelerated cardiovascular disease, a concept that has since been extended to the progression of kidney injury itself (Daenen et al., 2019; Himmelfarb et al., 2002). As renal function declines, the balance between

reactive oxygen species (ROS) generation and antioxidant defence is progressively disturbed, driven by reduced renal clearance of oxidised species, mitochondrial dysfunction, chronic low-grade inflammation, and dialysis-related factors in advanced disease (Daenen et al., 2019; Ratliff et al., 2016; Sung et al., 2013).

Several circulating biomarkers capture different facets of this redox imbalance. Coenzyme Q10 (CoQ10) is a lipid-soluble component of the mitochondrial electron transport chain and a key endogenous antioxidant; plasma CoQ10 concentrations are consistently reported to be reduced in CKD, reflecting both impaired synthesis and increased consumption in quenching free radicals (Gutierrez-Mariscal et al., 2020; Yeung et al., 2015). F2-isoprostanes are stable, specific products of non-enzymatic lipid peroxidation of arachidonic acid and are widely regarded as one of the most reliable indices of *in vivo* oxidative stress, with elevated levels reported across stages of renal impairment (Lim et al., 2002; Oberg et al., 2004; Sung et al., 2013). Advanced glycation end-products (AGEs) accumulate in CKD both because of increased formation under oxidative and carbonyl stress and because of reduced renal clearance, and have been linked to vascular calcification, inflammation and mortality risk in CKD cohorts (Dozio et al., 2023; Rabbani and Thornalley, 2018; Stingham et al., 2016). 8-hydroxy-2'-deoxyguanosine (8-OHdG) is a sensitive marker of oxidative DNA damage that rises with the severity of renal impairment (Oberg et al., 2004; Sung et al., 2013). Glutathione peroxidase (GPx), by contrast, is an antioxidant enzyme whose behaviour in CKD is less consistent across the literature, with some studies reporting compensatory elevation and others reporting exhaustion at advanced stages (Daenen et al., 2019; Sung et al., 2013).

Most published work has compared a single CKD group against controls, or examined oxidative markers in dialysis populations only, leaving it unclear whether these markers change in proportion to the severity of renal impairment across the full spectrum of CKD stages, or instead simply signal the presence versus absence of disease. Distinguishing between these two patterns has direct implications for whether a marker is suited to staging and monitoring versus screening. The aim of the present study was therefore to (i) compare CoQ10, F2-isoprostane, AGEs, 8-OHdG and GPx across a control group and five CKD stages; (ii) quantify their diagnostic performance for CKD by ROC analysis; and (iii) examine their correlation with each other and with conventional renal function indices (estimated glomerular filtration rate [eGFR] and serum creatinine) to determine which markers track disease severity as opposed to merely disease presence.

2. MATERIALS AND METHODS

2.1 Study Design and Population

This case-control study was conducted in Baghdad Governorate, Iraq, between February and July 2026. It included 120 male patients with chronic kidney disease (CKD), stratified into five stages ($n = 24$ per stage) based on estimated glomerular filtration rate (eGFR) calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation 2021 (Inker et al., 2021), and 60 apparently healthy male control subjects, for a total of 180 male participants aged 20–60 years. Patients were recruited from Al-Kadhimiya Teaching Hospital and several affiliated external medical laboratories in Baghdad, in coordination with a consultant nephrologist.

The diagnosis and clinical assessment of CKD were established by a specialist nephrologist based on the patients' clinical history, laboratory findings and renal function assessment. Urinary microprotein (microproteinuria) was also evaluated as an important laboratory indicator supporting the assessment of renal impairment and was considered alongside the specialist physician's clinical diagnosis. Eligible cases were male patients aged 20–60 years with a confirmed diagnosis of CKD at any stage.

Individuals with acute kidney injury or a history of kidney transplantation, pregnancy, cardiovascular disease, liver disease, diabetes mellitus or malignancy were excluded to reduce confounding from these comorbidities. Demographic and clinical data were collected using a structured, researcher-administered questionnaire covering age and relevant medical history. Written informed consent was obtained from all participants, and confidentiality was maintained throughout. eGFR was not measured in the control group and was therefore excluded from between-group comparisons involving control subjects.

2.2 Sample Collection and Biochemical Analyses

Six millilitres of venous blood were withdrawn from each participant using a sterile, single-use syringe into a plain gel tube, allowed to clot at room temperature, and centrifuged at 3000 rpm for 10 min. The separated serum was aliquoted into 1 mL Eppendorf tubes and stored at -20°C until biochemical analysis.

Serum urea, creatinine, sodium and potassium were measured on the ARCHITECT c4000 clinical chemistry analyser (Abbott, USA): urea by an enzymatic urease/glutamate dehydrogenase kinetic method (340 nm); creatinine by the kinetic alkaline picrate method (500 nm); and sodium and potassium by indirect ion-selective electrode. eGFR was calculated using the CKD-EPI creatinine equation 2021 (Inker et al., 2021).

Serum concentrations of F2-isoprostane (8-iso-PGF₂ α ; Cat. No. ELK8402), AGEs (Cat. No. ELK1890), 8-OHdG (Cat. No. ELK10848) and CoQ10 (Cat. No. ELK9177) were measured using commercially available competitive enzyme-linked immunosorbent assay (ELISA) kits, and GPx (GPX1; Cat. No. ELK1928) was measured using a sandwich ELISA kit (all ELK Biotechnology, China), according to the manufacturers' instructions, with absorbance read at 450 nm on a microplate reader. Standard curve ranges were 31.25–2000 pg/mL for F2-isoprostane, 125–8000 ng/mL for AGEs, 1.57–100 ng/mL for 8-OHdG, 0.78–50 ng/mL for CoQ10 and 3.13–200 ng/mL for GPx. For the four competitive assays, absorbance is inversely proportional to analyte concentration; for the GPx sandwich assay, absorbance is directly proportional to analyte concentration. All concentrations were interpolated from the respective kit standard curves.

2.3 Statistical Analysis

Data were analysed in Python (SciPy, statsmodels, scikit-learn). Normality of distribution was assessed per variable within each group using the Shapiro–Wilk test. Because all five oxidative-stress biomarkers were non-normally distributed in at least one group, between-group comparisons were performed using the Kruskal–Wallis H test, with epsilon-squared (ϵ^2) as the effect size. Where the omnibus test was significant, pairwise post-hoc comparisons were performed using the Mann–Whitney U test with Bonferroni correction for the number of pairwise comparisons; groups not sharing a common superscript letter in the tables differ significantly ($p < 0.05$). Associations between biomarkers, and between biomarkers and renal function indices, were assessed using Spearman's rank correlation coefficient. Diagnostic performance for discriminating CKD (all stages combined) from control was evaluated by receiver operating characteristic (ROC) curve analysis; the area under the curve (AUC) and its 95% confidence interval were computed by the Hanley–McNeil method, and the optimal cutoff was selected using the Youden index. A two-tailed $p < 0.05$ was considered statistically significant throughout.

2.4 Ethical Approval

This study was approved by the Scientific Committee of the College of Medicine, Tikrit University, which had adopted the study protocol in coordination with Al-Kadhimiya Teaching Hospital and affiliated external laboratories in Baghdad. Written informed consent was obtained from all participants prior to enrolment.

3. RESULTS AND DISCUSSION

3.1 Between-Group Comparison of Oxidative-Stress Biomarkers

All five oxidative-stress biomarkers differed significantly across the control and five CKD stage groups (Kruskal–Wallis, all $p < 0.001$; Table 1, Table 2; Figure 1). CoQ10 declined progressively and monotonically from control (7.26 ± 2.16 ng/mL) to Stage 5 (2.29 ± 0.19 ng/mL), with every pairwise comparison reaching statistical significance (all $p < 0.001$), giving the largest effect size of the five markers ($\epsilon^2 = 0.946$). F2-isoprostane, AGEs and 8-OHdG each rose progressively with advancing stage ($\epsilon^2 = 0.934$, 0.925 and 0.902 , respectively), and nearly all pairwise stage-to-stage comparisons were significant, indicating that these three markers track disease severity in a graded fashion rather than merely separating CKD from control. A notable exception within this pattern was AGEs, for which Stage 1 (1068.67 ± 56.03 ng/mL) was significantly lower than control (1246.99 ± 110.89 ng/mL; $p < 0.001$) before rising progressively from Stage 2 onward — a non-monotonic dip discussed further below.

GPx showed a qualitatively different pattern. Mean GPx rose sharply from control (53.01 ± 8.86 ng/mL) to Stage 1 (83.49 ± 6.57 ng/mL; $p < 0.001$) but did not differ significantly among Stages 1 through 5 (all pairwise $p \geq 0.847$), giving a smaller effect size ($\epsilon^2 = 0.669$) driven almost entirely by the control-versus-CKD contrast rather than by a stage-dependent gradient.

Table 1. Serum oxidative-stress biomarkers in control subjects and patients with chronic kidney disease, Stages 1–5 (mean $\pm$ SD).

Biomarker	Control	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Coenzyme Q10 (ng/mL)	7.26 $\pm$ 2.16 ^a	3.74 $\pm$ 0.18 ^b	3.31 $\pm$ 0.06 ^c	2.90 $\pm$ 0.08 ^d	2.67 $\pm$ 0.08 ^e	2.29 $\pm$ 0.19 ^f
F2-isoprostane (pg/mL)	122.27 $\pm$ 33.24 ^f	180.13 $\pm$ 15.21 ^e	195.26 $\pm$ 4.12 ^d	210.30 $\pm$ 5.73 ^c	228.58 $\pm$ 5.15 ^b	251.66 $\pm$ 11.78 ^a
AGEs (ng/mL)	1246.99 $\pm$ 110.89 ^e	1068.67 $\pm$ 56.03 ^f	1442.24 $\pm$ 25.74 ^d	1585.20 $\pm$ 44.42 ^c	1827.90 $\pm$ 26.50 ^b	1900.37 $\pm$ 21.06 ^a
8-OHdG (ng/mL)	7.38 $\pm$ 2.15 ^f	9.63 $\pm$ 2.20 ^e	12.11 $\pm$ 0.80 ^d	14.31 $\pm$ 0.61 ^c	16.51 $\pm$ 0.78 ^b	18.58 $\pm$ 0.71 ^a
GPx (ng/mL)	53.01 $\pm$ 8.86 ^b	83.49 $\pm$ 6.57 ^a	84.28 $\pm$ 8.51 ^a	83.74 $\pm$ 7.46 ^a	83.96 $\pm$ 7.30 ^a	87.27 $\pm$ 7.30 ^a

Values are mean $\pm$ SD (n = 60 control; n = 24 per CKD stage). Within each row, values not sharing a common superscript letter differ significantly ($p < 0.05$, Mann–Whitney U test with Bonferroni correction). AGEs, advanced glycation end-products; CKD, chronic kidney disease; GPx, glutathione peroxidase; SD, standard deviation; 8-OHdG, 8-hydroxy-2'-deoxyguanosine.

Table 2. Kruskal–Wallis omnibus test statistics for oxidative-stress biomarkers across the six study groups.

Biomarker	H statistic	ϵ^2	p-value	Post-hoc test
Coenzyme Q10 (ng/mL)	169.62	0.946	< 0.001	Mann–Whitney U (Bonferroni)
F2-isoprostane (pg/mL)	167.48	0.934	< 0.001	Mann–Whitney U (Bonferroni)
AGEs (ng/mL)	165.88	0.925	< 0.001	Mann–Whitney U (Bonferroni)
8-OHdG (ng/mL)	162.02	0.902	< 0.001	Mann–Whitney U (Bonferroni)
GPx (ng/mL)	121.33	0.669	< 0.001	Mann–Whitney U (Bonferroni)

ϵ^2 , epsilon-squared effect size; AGEs, advanced glycation end-products; GPx, glutathione peroxidase; 8-OHdG, 8-hydroxy-2'-deoxyguanosine.

3.2 Diagnostic Performance (ROC Analysis)

When discriminating all CKD patients (Stages 1–5 combined) from control subjects, GPx achieved the highest diagnostic accuracy (AUC = 1.000, 95% CI 0.998–1.000), followed by CoQ10 (AUC = 0.997) and F2-isoprostane (AUC = 0.991); both exceeded the conventional threshold for excellent discrimination (AUC $\geq$ 0.90), as did 8-OHdG (AUC = 0.961). AGEs showed good but comparatively lower diagnostic performance (AUC = 0.817). Full diagnostic performance characteristics, including optimal cutoffs derived from the Youden index, are shown in Table 3, and the corresponding ROC curves in Figure 2.

Table 3. Diagnostic performance of oxidative-stress biomarkers for discriminating chronic kidney disease (Stages 1–5 combined) from control by ROC analysis.

Biomarker	AUC	95% CI	Cutoff	Sens. / Spec. (%)	p-value
GPx (ng/mL)	1.000	0.998–1.000	72.00	99.2 / 100.0	< 0.001
Coenzyme Q10 (ng/mL)	0.997	0.990–1.000	4.02	99.2 / 96.7	< 0.001
F2-isoprostane (pg/mL)	0.991	0.978–1.000	184.83	91.7 / 100.0	< 0.001
8-OHdG (ng/mL)	0.961	0.934–0.987	10.76	88.3 / 100.0	< 0.001
AGEs (ng/mL)	0.817	0.756–0.877	1396.16	80.0 / 96.7	< 0.001

AUC, area under the ROC curve; CI, confidence interval (Hanley–McNeil method); Sens., sensitivity; Spec., specificity; the cutoff was selected by the Youden index. AGEs, advanced glycation end-products; GPx, glutathione peroxidase; 8-OHdG, 8-hydroxy-2'-deoxyguanosine.

3.3 Correlation with Renal Function

Within the pooled CKD group (Stages 1–5, $n = 120$), CoQ10, F2-isoprostane, AGEs and 8-OHdG were all strongly correlated with eGFR and serum creatinine ($|r| = 0.90–0.96$, all $p < 0.001$), consistent with the graded, stage-tracking behaviour described above. GPx, in contrast, showed no meaningful correlation with either eGFR ($r = -0.13$, $p = 0.150$) or creatinine ($r = 0.13$, $p = 0.144$) once the analysis was restricted to CKD patients — that is, once the control-versus-CKD contrast was removed from the comparison. This dissociation between a strong control-versus-CKD effect and the absence of a within-CKD gradient supports interpreting the GPx elevation as an early, threshold-type response to the onset of renal impairment rather than a marker of progressive severity. The five oxidative markers were, as expected, also strongly inter-correlated with one another (Table 4), with the exception of GPx, which correlated weakly with the other four markers ($|r| \leq 0.17$).

Table 4. Spearman correlation matrix among oxidative-stress biomarkers in pooled chronic kidney disease patients (Stages 1–5, $n = 120$).

	Coenzyme Q10	F2-isoprostane	AGEs	8-OHdG	GPx
Coenzyme Q10	1.00	−0.97 ^a	−0.98 ^a	−0.99 ^a	−0.17
F2-isoprostane	−0.97 ^a	1.00	0.97 ^a	0.96 ^a	0.14
AGEs	−0.98 ^a	0.97 ^a	1.00	0.97 ^a	0.16
8-OHdG	−0.99 ^a	0.96 ^a	0.97 ^a	1.00	0.17
GPx	−0.17	0.14	0.16	0.17	1.00

Values are Spearman's rho (r). ^aStatistically significant correlation ($p < 0.001$). Correlations involving GPx were not statistically significant ($p > 0.05$). AGEs, advanced glycation end-products; GPx, glutathione peroxidase; 8-OHdG, 8-hydroxy-2'-deoxyguanosine. The correlations of each biomarker with eGFR and serum creatinine are reported in the text and are not shown in this matrix.

3.4 Discussion

This study demonstrates that oxidative-stress biomarkers in CKD do not behave as a homogeneous group: CoQ10, F2-isoprostane, AGEs and 8-OHdG changed in a graded, stage-dependent manner that was strongly correlated with the degree of renal impairment, whereas GPx rose sharply at the transition from health to disease but then plateaued, with no further change or correlation with renal function across CKD stages. This distinction has practical relevance: markers that track severity are candidates for staging and monitoring progression, while markers that merely separate health from disease — however strong their discriminative accuracy — are better suited to screening or case-finding roles.

The progressive decline in CoQ10 is consistent with previous reports of reduced plasma CoQ10 in CKD, attributed to both impaired hepatic and renal synthesis and ongoing consumption of this lipophilic antioxidant in quenching lipid peroxidation products as oxidative burden increases (Gutierrez-Mariscal et al., 2020; Yeung et al., 2015). Because CoQ10 is also an essential component of the mitochondrial electron transport chain, its depletion may compound the mitochondrial dysfunction that is itself implicated in CKD progression (Sureshbabu et al., 2015), and CoQ10 supplementation has been explored as a potential adjunct therapy in this context (Yeung et al., 2015).

The progressive rise in F2-isoprostane and 8-OHdG is consistent with their established roles as stable, specific indices of lipid peroxidation and oxidative DNA damage, respectively, both of which have previously been shown to increase with declining renal function and to be elevated further in patients receiving renal replacement therapy (Lim et al., 2002; Oberg et al., 2004; Sung et al., 2013). The near-perfect inverse correlation we observed between these markers and eGFR ($|r| > 0.90$) supports their candidacy as quantitative indices of cumulative oxidative burden across the CKD spectrum, rather than simple binary indicators of disease presence.

AGEs also rose progressively from Stage 2 onward, consistent with their well-documented accumulation in CKD due to a combination of increased formation under oxidative and carbonyl stress and reduced renal clearance of AGE free adducts as glomerular filtration declines (Dozio et al., 2023; Rabbani and Thornalley, 2018; Stinghen et al., 2016). The unexpected dip at Stage 1, where AGEs were lower than in control, has, to our knowledge, no clear mechanistic precedent in the reviewed literature and should be interpreted cautiously; possible explanations include early compensatory upregulation of clearance pathways (for example the glyoxalase system) before filtration is meaningfully impaired, cohort-specific dietary or metabolic differences between the control and Stage 1 groups, or sampling variability given the moderate group size ($n = 24$). This finding warrants replication in an independent, larger cohort before firm mechanistic conclusions are drawn.

The plateau observed for GPx after an initial rise is more difficult to reconcile with a single mechanism. GPx is an antioxidant enzyme, and some studies report compensatory upregulation of antioxidant enzyme activity in early CKD as a physiological response to increased ROS generation, while others report progressive exhaustion of antioxidant capacity at more advanced stages or in dialysis populations (Daenen et al., 2019; Sung et al., 2013). Our cross-sectional data are compatible with an early, threshold-type compensatory response that is largely established by Stage 1 and does not scale further with additional loss of renal function; they cannot, however, distinguish this from a ceiling effect of the assay, a difference in disease aetiology across our stage groups, or an antioxidant response that is more closely tied to acute oxidative insult than to eGFR per se. Because GPx nonetheless achieved the highest AUC of the five markers for distinguishing CKD from control, our data suggest a potential screening role for GPx that is distinct from — and should not be conflated with — a staging or monitoring role.

3.5 Limitations

This study has several limitations. First, the cross-sectional design precludes causal or temporal inference regarding the direction of the observed associations. Second, participants were recruited from a single teaching hospital and its affiliated laboratories, and the sample size per stage ($n = 24$), while adequate to detect the large effect sizes observed, limits precision for smaller effects and for exploring subgroups (for example by underlying CKD aetiology). Third, the study was restricted to men, so the findings cannot be generalised to women without further investigation. Fourth, dietary intake, medication use (including antioxidant supplementation) and inflammatory status were not accounted for and may confound oxidative marker levels independently of renal function. Fifth, the unexpected non-monotonic pattern observed for AGEs at Stage 1 requires replication before mechanistic interpretation. Finally, because eGFR was not available for the control group, comparisons involving eGFR were necessarily restricted to CKD patients only.

4. CONCLUSION

Among five oxidative-stress and antioxidant biomarkers assessed across the CKD spectrum, CoQ10, F2-isoprostane, AGEs and 8-OHdG each declined or rose progressively with disease stage and correlated strongly with renal function, supporting their use as candidate markers of oxidative burden that scales with CKD severity. The increased GPx activity in CKD patients may reflect a compensatory antioxidant response to the increased oxidative stress associated with impaired renal function, but it did not track severity. These findings suggest that oxidative-stress biomarkers should not be treated as functionally interchangeable in CKD research or clinical translation, and that marker selection should be guided by whether the intended application is disease screening or severity monitoring.

ACKNOWLEDGEMENTS

The authors thank the staff of Al-Kadhimiya Teaching Hospital and the affiliated medical laboratories in Baghdad for their assistance with participant recruitment and sample collection, and the consultant nephrologist who supervised the clinical assessment and staging of the patients.

AUTHOR CONTRIBUTIONS

Harith S. Aziz: Conceptualization, Methodology, Investigation, Formal Analysis, Writing — Original Draft.

Ammar Lateef Hussein: Conceptualization, Methodology, Supervision, Writing — Review & Editing.

Mohamed Ghalib Zakari: Investigation, Clinical Assessment, Resources, Writing — Review & Editing.

Ghazwan Mohammed Radhi: Investigation, Laboratory Analysis, Data Curation, Writing — Review & Editing.

Mohsen Hamoud Jasim: Formal Analysis, Software, Visualization, Writing — Review & Editing.

All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

This study was approved by the Scientific Committee of the College of Medicine, Tikrit University, Iraq, which adopted the study protocol in coordination with Al-Kadhimiya Teaching Hospital and affiliated external laboratories in Baghdad (approval number [NO.10325 IN 19/2/2025]). Written informed consent was obtained from all participants prior to enrolment, and the study was conducted in accordance with the Declaration of Helsinki.

FUNDING

This research received no external funding.

DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work the authors used a generative AI-assisted language tool to improve the readability and language of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

REFERENCES

- [1] Daenen, K., Andries, A., Mekahli, D., Van Schepdael, A., Jouret, F., Bammens, B., 2019. *Oxidative stress in chronic kidney disease*. Pediatric Nephrology 34(6), 975–991.
- [2] Dozio, E., Caldiroli, L., Molinari, P., Castellano, G., Delfrate, N.W., Corsi Romanelli, M.M., et al., 2023. *Accelerated AGEing: the impact of advanced glycation end products on the prognosis of chronic kidney disease*. Antioxidants 12(3), 584.
- [3] Gutierrez-Mariscal, F.M., Arenas-de Larriva, A.P., Limia-Perez, L., Romero-Cabrera, J.L., Yubero-Serrano, E.M., López-Miranda, J., 2020. *Coenzyme Q10 supplementation for the reduction of oxidative stress: clinical implications in the treatment of chronic diseases*. International Journal of Molecular Sciences 21(21), 7870.
- [4] Himmelfarb, J., Stenvinkel, P., Ikizler, T.A., Hakim, R.M., 2002. *The elephant in uremia: oxidant stress as a unifying concept of cardiovascular disease in uremia*. Kidney International 62(5), 1524–1538.
- [5] Inker, L.A., Eneanya, N.D., Coresh, J., Tighiouart, H., Wang, D., Sang, Y., et al., 2021. *New creatinine- and cystatin C-based equations to estimate GFR without race*. New England Journal of Medicine 385(19), 1737–1749.
- [6] Lim, P.S., Chang, Y.M., Thien, L.M., Wang, N.P., Yang, C.C., Chen, T.T., et al., 2002. *8-iso-prostaglandin F2a as a useful clinical biomarker of oxidative stress in ESRD patients*. Blood Purification 20(6), 537–542.

- [7] Oberg, B.P., McMenamin, E., Lucas, F.L., McMonagle, E., Morrow, J., Ikizler, T.A., et al., 2004. *Increased prevalence of oxidant stress and inflammation in patients with moderate to severe chronic kidney disease*. *Kidney International* 65(3), 1009–1016.
- [8] Rabbani, N., Thornalley, P.J., 2018. *Advanced glycation end products in the pathogenesis of chronic kidney disease*. *Kidney International* 93(4), 803–813.
- [9] Ratliff, B.B., Abdulmahdi, W., Pawar, R., Wolin, M.S., 2016. *Oxidant mechanisms in renal injury and disease*. *Antioxidants & Redox Signaling* 25(3), 119–146.
- [10] Stinghen, A.E.M., Massy, Z.A., Vlassara, H., Striker, G.E., Boullier, A., 2016. *Uremic toxicity of advanced glycation end products in CKD*. *Journal of the American Society of Nephrology* 27(2), 354–370.
- [11] Sung, C.C., Hsu, Y.C., Chen, C.C., Lin, Y.F., Wu, C.C., 2013. *Oxidative stress and nucleic acid oxidation in patients with chronic kidney disease*. *Oxidative Medicine and Cellular Longevity* 2013, 301982.
- [12] Sureshbabu, A., Ryter, S.W., Choi, M.E., 2015. *Oxidative stress and autophagy: crucial modulators of kidney injury*. *Redox Biology* 4, 208–214.
- [13] Tonelli, M., Wiebe, N., Culleton, B., House, A., Rabbat, C., Fok, M., et al., 2006. *Chronic kidney disease and mortality risk: a systematic review*. *Journal of the American Society of Nephrology* 17(7), 2034–2047.
- [14] Yeung, C.K., Billings, F.T. 4th, Claessens, A.J., Roshanravan, B., Linke, L., Sundell, M.B., et al., 2015. *Coenzyme Q10 dose-escalation study in hemodialysis patients: safety, tolerability, and effect on oxidative stress*. *BMC Nephrology* 16, 183.

FIGURE LEGENDS

Figure 1. Distribution of oxidative-stress biomarkers across control and CKD Stages 1–5. Violin width shows the estimated distribution density; the inset box shows the median and interquartile range; points are individual subjects. Groups not sharing a common letter differ significantly ($p < 0.05$, Kruskal–Wallis followed by Bonferroni-corrected pairwise Mann–Whitney U tests). AGEs, advanced glycation end-products; CKD, chronic kidney disease; GPx, glutathione peroxidase; 8-OHdG, 8-hydroxy-2'-deoxyguanosine.

Figure 2. Receiver operating characteristic (ROC) curves for oxidative-stress biomarkers discriminating CKD patients (Stages 1–5 combined) from control subjects. Red points mark the optimal cutoff (Youden index); the dashed diagonal indicates no discrimination ($AUC = 0.5$). AGEs, advanced glycation end-products; AUC, area under the curve; CKD, chronic kidney disease; GPx, glutathione peroxidase; 8-OHdG, 8-hydroxy-2'-deoxyguanosine.

Figure 1

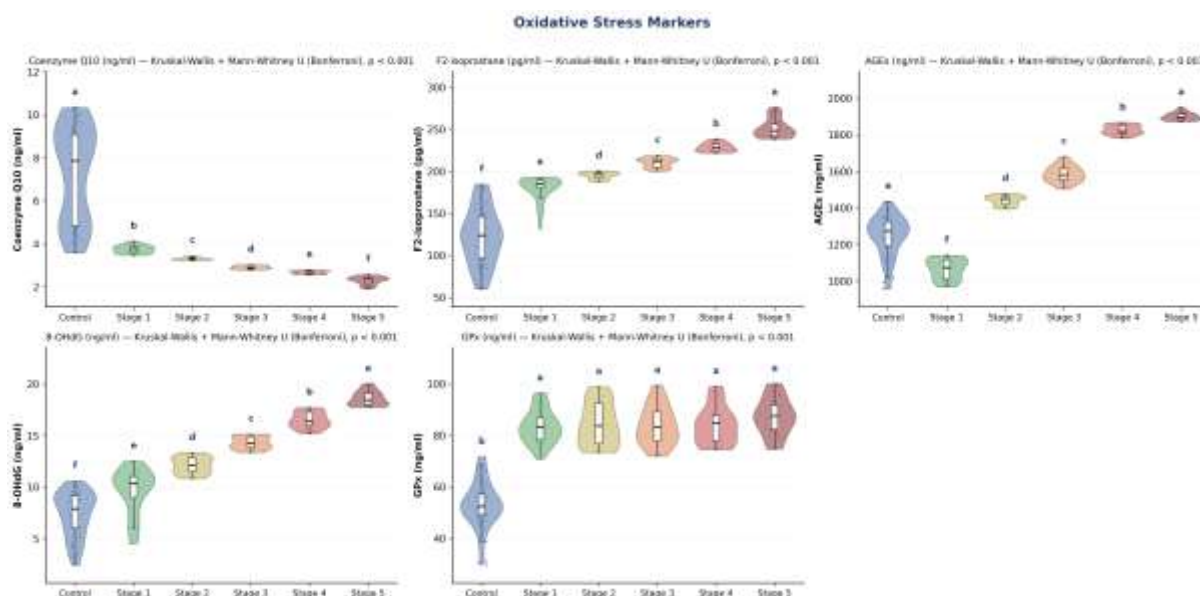


Figure 2

