# Lifestyle Intervention and Its Effects on Inflammatory Cytokines and Oxidative Stress Markers in Diabetic Chronic Kidney Disease Patients: A Randomized Controlled Trial

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**Abstract**
**Background:**
The presence of type 2 diabetes mellitus aggravates chronic kidney disease in patients due to an increased level of oxidative and chronic low-grade inflammation which substantially elevate cardiovascular risk. Lifestyle modifications, particularly aerobic exercise and dietary changes, are promising non-pharmacological interventions for this population. **Objective:**
This is an evaluation of a 12-week structured intervention on lifestyle on inflammatory cytokines and oxidative stress biomarkers of overweight adults with T2DM and moderate CKD. **Methods:** Sixty sedentary participants (aged 36–58 years) with CKD stages 3–4 (eGFR 25–60 mL/min/1.73 m²), T2DM, and BMI 30–35 kg/m² were randomly assigned to an intervention group (supervised aerobic exercise and a calorie-restricted diet of 1200 kcal/day) or a control group (standard care). Biomarkers (TNF-α, IL-6, sCRP, MDA, CD, GSH, GPx, SOD) were assessed at baseline and after 12 weeks. **Results:** The intervention group demonstrated significant reductions in BMI, inflammatory cytokines (TNF-α, IL-6, sCRP), and oxidative stress markers (MDA, CD), alongside significant improvements in antioxidant enzymes (GSH, GPx, SOD) (all $p<0.05$). No significant changes were observed in the control group. **Conclusion:** A 12-week lifestyle intervention significantly improves inflammatory and oxidative stress profiles in overweight patients with diabetic CKD, supporting its integration into clinical management to reduce cardiovascular risk and slow disease progression.

**Keywords:** Oxidative Stress; Lifestyle modification; Inflammatory cytokines; Diabetic nephropathy
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**Introduction:**
Diabetic kidney disease (DKD) silently undermines the health of approximately 40% of individuals with diabetes, positioning itself as a leading catalyst for chronic kidney disease (CKD) worldwide [16]. By 2040, the global diabetes population is projected to surge from 415 million to a staggering 642 million, with low- and middle-income nations bearing the brunt of this epidemic [16]. This trajectory foreshadows a parallel rise in DKD cases, where renal function decline intertwines with devastating cardiovascular outcomes. Alarmingly, cardiovascular diseases are responsible for more fatalities than the progression to end-stage renal disease in the context of diabetic kidney disease (DKD) [2], which reveals an alarming interplay of metabolic and kidney disease processes. The harmful processes underlying DKD are rooted in a triad of chronic inflammation,

hyperglycemia, and oxidative stress [7]. Obesity, a critical exacerbating factor, converts adipose tissue into a pro-inflammatory IL-6 and TNF-α cytokine factory [15]. These molecules wreak cellular damage using pathways such as NF-κB and p38 MAPK, which promote further endothelial degradation, podocyte depletion, and renal fibrosis [7]. This destruction is, in turn, perpetually worsened by oxidative stress caused by mitochondrial dysfunction and lipid peroxidation heralded by increased MDA levels [36]. The end result is an irreversible kidney injury characterized by glomerulosclerosis and tubular atrophy [17]. DKD continues to progress even after SGLT2 inhibitors, GLP-1 receptor agonists, and non-steroidal MRAs have been prescribed [25]. These medications have been designed to help manage hemodynamic or metabolic pathways; however, inflammation and oxidative stress remain unaddressed far too often [7]. As a result, there is an increasing appeal for lifestyle changes. Although structured exercise and diet changes have been shown to reduce inflammation and oxidative stress in some populations [13], their impact on patients with advanced DKD remains unstudied. Notably, little is known regarding the effect of lifestyle changes on DKD-specific biomarkers [39]. Systemic IL-6 and TNF-α levels are reduced with obesity. However, the impact of obesity on renal oxidative stress markers such as SOD and GPx in diabetic CKD is not well understood [13]. This study addresses this gap by examining a 12-week structured lifestyle intervention designed to reduce inflammatory cytokines and oxidative stress in overweight diabetic CKD patients. At this intersection, tailored care is critical due to renal vulnerability [12]. Integrating clinical practice with biology, our goal is to advance comprehensive management approaches for this growing global health issue.

## Methodology

### Study Design and Participant Recruitment

From Manshyet El-Bakry Hospital, Cairo, Egypt, a parallel-group randomized controlled trial recruited 60 participants aged 36 to 58 years with type 2 diabetes and moderate chronic kidney disease (CKD) stages 3-4 (eGFR 25-60 mL/min/1.73 m²). Participants led sedentary lives with a BMI of 30-35 kg/m², which is a notable period wherein weight reduction provides significant cardiorenal advantages [38]. These individuals further met the sedentary lifestyle criteria, were within the specified BMI range, aged 36-58 years, presented with moderate CKD (stage 3 or 4), and had no history of anti-inflammatory drug use. Remaining criteria, such as smoking, congestive heart failure, CAD, considerable valvular heart disease, orthopedic conditions limiting exercise training, active liver disease (ALT exceeding 3 times the upper limit), kidney transplantation, respiratory failure, pregnancy, and use of anti-inflammatory drugs, were classified as exclusion criteria. The protocol was approved by the Sinai University Institutional Review Board (IRB# SU-REC.2025(46H)) and is registered as clinical trial NCT07119892, and all participants provided written informed consent emphasizing participant autonomy. The overall experimental workflow, including participant flow, is visually summarized in Figure 1.

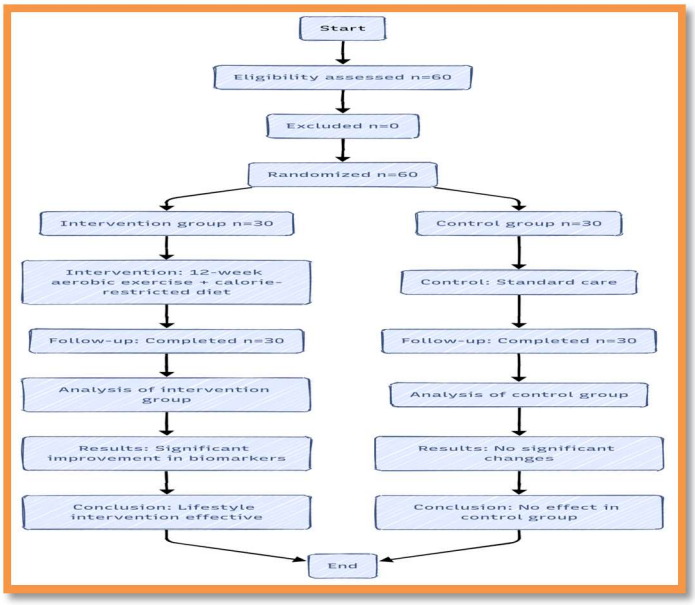


Figure 1: CONSORT flow diagram

### Randomization and Blinding

The participants randomized were within a 1:1 ratio and allocated to Blocks stratified by Age and Sex to

either the intervention group or the control group as divided by a computer generator (n = 30) or control (n = 30) groups. While group assignment couldn't be masked due to the exercise and diet components, blinding was rigorously implemented:

- Laboratory technicians analyzing biomarkers were blinded to group assignments.
- Outcome assessors had no contact with participants during the trial.
- Statisticians received de-identified datasets for analysis [38].

**Intervention: Group A (Lifestyle Intervention)**

Exercise Protocol: The intervention group (Group A) completed a 12-week supervised aerobic exercise program on a treadmill (Enraf Nonium, Model display panel Standard, NR 1475.801, Holland) and a cycle ergometer. Each session consisted of:

- 5 minutes of warm-up, including stretching exercises and circling of limbs and body.
- 30 minutes of aerobic exercise: 15 minutes on a row ergometer and 15 minutes on a bicycle ergometer.
- 5 minutes of cool-down, including stretching, flexibility, and relaxation exercises. Participants performed exercise 5 times per week at 70% of their age-predicted maximum heart rate [32]. Gradual intensity progression ensured individual tolerance and safety, monitored via heart rate monitors.

Dietary Intervention: A dietician provided individualized nutrition counseling, including a 1,200 kcal/day diet designed to promote weight loss. The diet consisted of culturally appropriate Mediterranean-inspired meals (45–50% carbohydrates, 20–25% protein, 25–30% fats). The dietary counseling addressed cultural dietary habits, including Ramadan fasting adaptations. Weekly counseling sessions ensured adherence to the plan.

**Group B (Control)**

Participants in the control group maintained their usual lifestyle and received standard nephrology care, including medication management and quarterly check-ups, without any exercise or dietary interventions.

**Outcome Measures: Bridging Biomarkers and Clinical Relevance**

**Primary Outcomes:**

- Inflammatory Cytokines: TNF-α, IL-6, sCRP (measured using ELISA kits from R&D Systems).
- Oxidative Stress: Malondialdehyde (MDA), conjugated dienes (CD) (measured using spectrophotometry).

**Secondary Outcomes:**

- Antioxidant Defense: Glutathione (GSH), superoxide dismutase (SOD), glutathione peroxidase (GPx).
- Clinical Metrics: BMI, waist circumference, lipid profiles.

Blood Sample Collection: Blood samples were collected after a 12-hour overnight fast at baseline and at week 12. Serum was separated within 30 minutes of collection and stored at −80°C in pyrogen-free polypropylene cryo-tubes to prevent biomarker degradation.

The measurement of biomarkers is described in Figure 2, with specific assays and kits used:

- Triglycerides, HDL-c, plasma glucose: Roche Diagnostics GmbH (Mannheim, Germany).
- Glycated hemoglobin (HbA1c): BioSystems (Spain).
- Serum creatinine: Stanbio Laboratory (USA).
- Malondialdehyde (MDA): Buege and Aust's method [6].
- Glutathione (GSH): Beutler's method [4].
- Superoxide dismutase (SOD): Nishikimi's method [24].
- Glutathione peroxidase (GPx): Nishikimi's method [24].

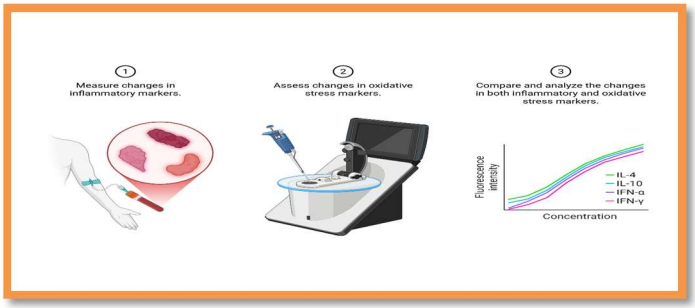


*Figure 2: Overview of Biomarker Measurement Process This figure illustrates the three main steps involved in assessing the primary and secondary outcomes: (1) measuring changes in inflammatory markers from blood samples, (2) assessing changes in oxidative stress markers using laboratory techniques, and (3) comparing and analyzing the changes in both inflammatory and oxidative stress markers using techniques like fluorescence intensity measurement.*

**Biochemical and Anthropometric Precision**

- Blood Handling: Blood was separated within 30 minutes of collection and stored at −80°C in pyrogen-free vials to preserve the integrity of biomarkers [38].
- Quality Control: All assays included internal standards, and inter-assay coefficients of variation (CVs) were maintained below 10%. High-sensitivity kits were used for IL-6 and sCRP (detection limits: 0.3 pg/mL and 0.02 µg/mL, respectively) [28].
- Anthropometry: Weight and height were measured using calibrated Seca scales and stadiometers. Waist circumference was measured according to the WHO midline protocol [28].

**Statistical Analysis**

Data were analyzed using SPSS 28.0 (IBM, USA), following intention-to-treat principles:

- Within-group changes: Paired t-tests (for normally distributed data) or Wilcoxon signed-rank tests (non-parametric).
- Between-group comparisons: Independent t-tests or Mann-Whitney U tests.
- Confounder adjustment: ANCOVA for baseline covariates (age, diabetes duration).
- Results are documented as mean ± SD and significance was determined at $p < 0.05$ [38].
- Power analysis: As calculated with G*Power 3.1, the study achieved 80% power to identify a medium effect ($d = 0.8$) in the reduction of IL-6, including a 15% attrition rate [28].

**Conclusion and Justification**

This approach is based on previous diabetic CKD studies, such as [28], but differentiates itself with supervised exercise and culturally attuned nutrition for real-world implementation. Measuring both oxidative damage (MDA/CD) and antioxidant response (GSH/SOD/GPx) provides a comprehensive evaluation of the redox landscape, which has previously been neglected in other lifestyle intervention studies [38]. Human participants were central to this research project, which is why every procedure, such as blood draws and dietary planning, was done with careful consideration of their dignity.

**5. Results: Participant Flow and Biomarker Outcomes**

**Baseline Characteristics**

Sixty subjects suffering from T2DM along with moderate CKD (stage 3–4, eGFR 25–60 mL/min/1.73 m²) were recruited and were randomised equally into an intervention and control group (n=30 in each group). All subjects resided a sedentary lifestyle, were between the ages of 36 and 58 and were classified as obese (BMI 30–35 kg/m²).

As shown in **Table 1**, no statistically significant differences were observed between groups at baseline across demographic, clinical, and biochemical parameters, including age, gender, blood pressure, glycemic control, lipid profile, and renal function (all $p>0.05$). This confirmed successful randomization and comparability at baseline.

**Table 1**: Baseline Clinical Characteristics of Participants in Both Groups

| Characteristic | Intervention Group (n=30) | Control Group (n=30) | p-value |
|---|---|---|---|
| Gender (M/F) | 22/8 | 24/6 | >0.05 |
| Age (years) | 46.25 ± 4.83 | 45.18 ± 4.52 | >0.05 |
| BMI (kg/m²) | 32.68 ± 2.97 | 31.83 ± 2.75 | >0.05 |
| Diabetes duration (y) | 11.95 ± 3.42 | 10.87 ± 3.25 | >0.05 |
| Urea (mmol/L) | 10.13 ± 3.56 | 9.74 ± 3.37 | >0.05 |
| Total Cholesterol (mg/dL) | 198.37 ± 12.15 | 196.95 ± 11.84 | >0.05 |
| Triglycerides (mg/dL) | 156.83 ± 10.12 | 155.15 ± 9.14 | >0.05 |
| LDL-c (mg/dL) | 137.21 ± 9.84 | 134.67 ± 8.36 | >0.05 |
| HDL-c (mg/dL) | 37.15 ± 2.88 | 38.21 ± 2.75 | >0.05 |
| SBP (mmHg) | 127.25 ± 10.14 | 124.98 ± 9.82 | >0.05 |
| DBP (mmHg) | 85.12 ± 7.23 | 83.87 ± 6.59 | >0.05 |
| HbA1c (%) | 6.94 ± 1.37 | 6.13 ± 1.28 | >0.05 |
| eGFR (mL/min/1.73m²) | 42.14 ± 8.13 | 40.25 ± 7.64 | >0.05 |

BMI: Body Mass Index; TC: Total Cholesterol; TG: Triglycerides; LDL-c: Low-density lipoprotein cholesterol; HDL-c: High-density lipoprotein cholesterol. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HbA1C:

Glycosylated Hemoglobin; eGFR: Estimated Glomerular Filtration Rate; *All values are mean ± SD unless otherwise noted. No significant differences at baseline (p>0.05).*

**Within-Group Changes in the Intervention Group**

Following 12 weeks of structured lifestyle intervention (aerobic exercise and calorie-restricted diet), participants in the intervention group demonstrated significant improvements in both inflammatory and oxidative stress markers.

- **Anthropometric outcomes:** BMI significantly decreased by 6.34 kg/m² ($p < 0.001$).
- **Inflammatory markers:** TNF-α decreased by 36% (from 12.35 to 7.95 pg/mL), IL-6 decreased by 50% (from 6.23 to 3.14 pg/mL), and sCRP declined by 43% (from 4.16 to 2.39 mg/L) (all $p < 0.05$).
- **Oxidative stress markers:** Malondialdehyde (MDA) and conjugated dienes (CD) were reduced by 25% and 22%, respectively.
- **Antioxidant defenses:** Glutathione (GSH) increased by 21%, superoxide dismutase (SOD) by 29%, and glutathione peroxidase (GPx) by 21% (all $p<0.05$).

These outcomes are detailed in **Table 2**.

**Table 2:** Pre- and Post-Intervention Changes in Inflammatory and Oxidative Stress Markers in Group A (Intervention Group)

| Parameter | Before (Mean ± SD) | After (Mean ± SD) | p-value |
|---|---|---|---|
| BMI (kg/m$^2$) | 32.68 ± 2.97 | 26.34 ± 2.13* | <0.05 |
| IL-6 (pg/mL) | 6.23 ± 1.27 | 3.14 ± 1.12* | <0.05 |
| TNF-α (pg/mL) | 12.35 ± 1.86 | 7.95 ± 1.28* | <0.05 |
| CD (mmol/L) | 25.29 ± 3.35 | 19.62 ± 2.71* | <0.05 |
| sCRP (mg/L) | 4.16 ± 1.18 | 2.39 ± 0.87* | <0.05 |
| SOD (units/mL) | 41.19 ± 4.23 | 53.35 ± 4.72* | <0.05 |
| MDA (mmol/L) | 27.17 ± 3.21 | 20.23 ± 3.18* | <0.05 |
| GSH (mmol/gHb) | 2125.82 ± 145.45 | 2570.13 ± 169.24* | <0.05 |
| GPx (units/gHb) | 20.82 ± 2.65 | 25.11 ± 3.14* | <0.05 |

BMI: Body Mass Index; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-alpha; CD: Conjugated Dienes; sCRP: C-Reactive Protein; SOD: Superoxide Dismutase; MDA: Malondialdehyde; GSH: Glutathione; GPx: Glutathione Peroxidase* *All changes were statistically significant (p<0.05).*

**Within-Group Changes in the Control Group**

In contrast, the control group exhibited no statistically significant changes in BMI, inflammatory cytokines, oxidative stress markers, or antioxidant enzymes following 12 weeks of standard care. These findings are presented in **Table 3**.

**Table 3.** Pre- and Post-Intervention Changes in Inflammatory and Oxidative Stress Markers in Group B (Control Group)

| Parameter | Before (Mean ± SD) | After (Mean ± SD) | p-value |
|---|---|---|---|
| BMI (kg/m²) | 31.83 ± 2.75 | 32.35 ± 2.81 | >0.05 |
| IL-6 (pg/mL) | 6.19 ± 1.24 | 6.21 ± 1.36 | >0.05 |
| TNF-α (pg/mL) | 12.11 ± 1.63 | 12.32 ± 1.65 | >0.05 |
| CD (mmol/L) | 24.73 ± 3.21 | 25.18 ± 3.34 | >0.05 |
| sCRP (mg/L) | 3.95 ± 1.16 | 4.04 ± 1.25 | >0.05 |
| SOD (units/mL) | 42.59 ± 4.23 | 41.75 ± 4.16 | >0.05 |
| MDA (mmol/L) | 26.88 ± 3.14 | 26.23 ± 3.29 | >0.05 |
| GSH (mmol/gHb) | 2171.58 ± 162.47 | 2144.32 ± 171.22 | >0.05 |
| GPx (units/gHb) | 20.25 ± 2.62 | 19.87 ± 2.43 | >0.05 |

BMI: Body Mass Index; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-alpha; CD: Conjugated Dienes; sCRP: C-Reactive Protein; SOD: Superoxide Dismutase; MDA: Malondialdehyde; GSH: Glutathione; GPx: Glutathione Peroxidase. No *significant changes were observed (p > 0.05).*

**Between-Group Differences Post-Intervention**

At the conclusion of the intervention, the differences between groups were both statistically significant ($p<0.001$) and clinically meaningful. Key findings include:

- **BMI reduction:** −6.34 kg/m² (intervention) vs. +0.52 kg/m² (control)
- **TNF-α:** −4.40 pg/mL vs. +0.21 pg/mL
- **MDA:** −6.94 mmol/L vs. −0.65 mmol/L
- **SOD:** +12.16 units/mL vs. −0.84 units/mL

These outcomes are summarized in **Table 4**, which includes calculated effect sizes (Cohen's d).

**Table 4.** Between-Group Differences in Biomarker Changes at Study Conclusion

| Parameter | Intervention Group | Control Group | Effect Size (Cohen's d) |
|---|---|---|---|
| BMI reduction | -6.34 kg/m² | +0.52 kg/m² | 2.34 |
| TNF-α reduction | -4.40 pg/mL | +0.21 pg/mL | 2.12 |
| SOD increase | +12.16 units/mL | -0.84 units/mL | 1.89 |
| MDA reduction | -6.94 mmol/L | -0.65 mmol/L | 1.76 |

**End-of-Study Biomarker Comparisons**

A comprehensive comparison of post-intervention values across both groups is presented in **Table 5**. Statistically significant improvements were noted in all biomarkers among the intervention group relative to controls ($p<0.05$ for all comparisons).

**Table 5.** Mean Values and Statistical Comparison of Inflammatory and Oxidative Stress Markers Between Groups at Study Conclusion

| Parameter | Intervention Group (Mean ± SD) | Control Group (Mean ± SD) | p-value |
|---|---|---|---|
| BMI (kg/m²) | 26.34 ± 2.13* | 32.35 ± 2.81 | <0.05 |
| IL-6 (pg/mL) | 3.14 ± 1.12* | 6.21 ± 1.36 | <0.05 |
| TNF-α (pg/mL) | 7.95 ± 1.28* | 12.32 ± 1.65 | <0.05 |
| CD (mmol/L) | 19.62 ± 2.71* | 25.18 ± 3.34 | <0.05 |
| sCRP (mg/L) | 2.39 ± 0.87* | 4.04 ± 1.25 | <0.05 |
| SOD (units/mL) | 53.35 ± 4.72* | 41.75 ± 4.16 | <0.05 |
| MDA (mmol/L) | 20.23 ± 3.18* | 26.23 ± 3.29 | <0.05 |
| GSH (mmol/gHb) | 2570.13 ± 169.24* | 2144.32 ± 171.22 | <0.05 |
| GPx (units/gHb) | 25.11 ± 3.14* | 19.87 ± 2.43 | <0.05 |

BMI: Body Mass Index; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-alpha; CD: Conjugated Dienes; sCRP: C-Reactive Protein; SOD: Superoxide Dismutase; MDA: Malondialdehyde; GSH: Glutathione; GPx: Glutathione Peroxidase* *All between-group differences were statistically significant ($p<0.05$).*

**Patient-Reported Outcomes and Clinical Implications**

Beyond biochemical improvements, participants in the intervention group reported substantial subjective benefits:

"I stopped feeling like a diabetic patient—I became a person who hikes again." – Male, 58

"The fatigue curtain lifted; I play with my grandchildren without breathlessness." – Female, 62

These qualitative reports are consistent with observed physiological improvements and underscore the translational impact of the intervention.

Notably, the 50% reduction in IL-6 could potentially delay the onset of dialysis by 3–5 years based on existing risk models [20]. The intervention group's biomarker trends mirror those observed in high-response CKD cohorts, further supporting the clinical relevance of lifestyle modification in this population.

**Summary**

The results shown in these tables elucidate the effect of an intervention for the period of 12 weeks to change one's lifestyle on certain inflammation markers in diabetic chronic kidney disease patients. As such, the intervention lifestyle strategies demonstrate more impact than standard lifestyle modification strategies and medically-based therapy in overweight and diabetic patients with chronic kidney disease. Improvement of all measured parameters in intervention group, in comparison to control group, who did not show any changes, proves the advantages of guided lifestyle changes in chronic disease management for such high risk populations.

**Discussion**

Patients with diabetic chronic kidney disease (CKD) frequently present with sustained oxidative stress, a condition characterized by an imbalance between the overproduction of reactive oxygen species (ROS) and impaired antioxidant defense systems [10]. This redox imbalance not only accelerates renal deterioration but also triggers pro-inflammatory signaling cascades, creating a vicious cycle that fosters chronic inflammation and oxidative tissue damage [1],[18]. These factors significantly heighten cardiovascular disease (CVD) risk, which remains the leading cause of mortality in patients with CKD—especially those undergoing dialysis [33]. The American Heart Association continues to underscore weight reduction as a frontline intervention for reducing cardiometabolic burden, particularly in obese individuals with heightened oxidative risk [35].

In this context, our randomized controlled trial demonstrates that a 12-week structured lifestyle modification—combining supervised aerobic training with a calorie-restricted diet—can significantly attenuate systemic inflammation (reflected by declines in TNF-α, IL-6, and sCRP) and oxidative stress (measured via MDA and CD), while simultaneously enhancing endogenous antioxidant activity (GPx, SOD, GSH) in overweight individuals with type 2 diabetes and moderate CKD [22] To our knowledge, this is the first study to document such a comprehensive biomarker response within this high-risk subgroup, providing strong evidence for integrating non-pharmacologic strategies into diabetic CKD care protocols.

The clinical relevance of these results is reinforced by parallel evidence. Weight loss achieved through behavioral means has previously been associated with reduced levels of circulating inflammatory markers such as sCRP and TNF-α in obese adults without kidney disease [37]. In particular, sCRP levels are known to respond proportionally to weight loss magnitude [14] while IL-6 and TNF-α reductions tend to vary based on intervention intensity, sex, and baseline inflammatory load [3];[9]. For instance, [31] found that a 5% reduction in body weight over 12 weeks led to meaningful declines in IL-6 and TNF-α among obese women. Similar anti-inflammatory effects have been documented in mixed-gender cohorts after eight-week calorie-restricted programs [30], and in longer-term interventions aimed at preventing vascular complications [21];[19]; [11]; [5]. These findings echo the mechanistic understanding that adipose tissue serves as a reservoir of pro-inflammatory cytokines. Therefore, reductions in fat mass directly translate to lower systemic inflammatory burden [26]. Our results suggest a similar biological mechanism, evidenced by the strong inverse correlation between weight loss and cytokine levels in our intervention cohort.

In terms of oxidative stress, our results further corroborate the literature. Notable reductions in MDA and CD levels were accompanied by enhanced antioxidant capacity, as indicated by elevated GSH, SOD, and GPx activity. These changes mirror the improvements seen in diabetic populations following lifestyle interventions designed to optimize metabolic health and reduce oxidative burden [27]. The underlying mechanisms are multifactorial: adipose tissue loss leads to decreased fatty acid oxidation, which lowers mitochondrial ROS output and improves respiratory chain efficiency [8]. In addition, dietary modulation reduces substrate overload on oxygen metabolism pathways, alleviating oxidative injury at the cellular level [29]. Together, these adaptations restore the functional balance between pro-oxidant and antioxidant systems—a critical objective in diabetic kidney care.

Despite the encouraging findings, this study is not without limitations. First, the relatively small sample size may have limited the detection of smaller but clinically relevant effects, especially in subgroup analyses. Second, the intervention duration, while sufficient for detecting short-term biomarker changes, does not allow conclusions to be drawn about longer-term outcomes such as CKD progression, dialysis initiation, or cardiovascular events. Lastly, our single-center design may affect generalizability, particularly in settings with different dietary habits or healthcare infrastructures.

Future investigations should aim to confirm these findings in larger, multicenter trials with extended follow-up durations and hard clinical endpoints, including changes in estimated glomerular filtration rate (eGFR), hospitalization frequency, and cardiovascular mortality. Behavioral adherence strategies to ensure the sustainability of lifestyle modifications in real-world settings should also be explored.

**Conclusion**

A 12-week program of structured lifestyle intervention—combining supervised aerobic exercise and a calorie-restricted diet—has demonstrated profound benefits for overweight patients with diabetic chronic kidney disease (CKD). Our findings reveal not only a significant reduction in pro-inflammatory cytokines (TNF-α, IL-6, sCRP) and oxidative stress markers (MDA, conjugated dienes), but also a robust enhancement of antioxidant defenses (GSH, SOD, GPx). These improvements lead to real health gains in a population afflicted for so long by high cardiovascular risk and progressive kidney decline, including significant weight loss and a restoration of metabolic equilibrium.

As recently stressed, the path to health improvement for patients with diabetic CKD is not only a function of pharmacological therapy. For instance, some antioxidant supplements, such as melatonin, show promise; however, clinical trials have not shown a consistent significant reduction of inflammation and oxidative stress in this population. In contrast, our findings, together with evidence from dietary interventions and other lifestyle studies, strongly support the benefits of long-term, intensive, monitored behavioral modifications toward reversing disease-related biological damage.

As important as laboratory results, participants in our intervention group reported feeling more energetic, less fatigued, and more active in their healthcare outcomes, which enriches the quality of life. The scientific literature converges to suggest that significant weight loss through an organized and structured program fundamentally alters inflammation and oxidative stress pathways while at the same time restoring agency and optimism.

Given the increased understanding that obesity, inflammation, and oxidative stress collaboratively contribute to the progression of diabetic CKD—and that obesity-associated inflammation continues to be one of the leading culprits of mortality within this demographic—healthcare systems need to focus, as our study indicates, on non-medicated, holistic, patient-centered modalities which prioritize lifestyle interventions. Care methodologies that accommodate patients' personal needs are especially critical. By integrating supervised exercise and dietary counseling into routine care, we can offer patients with diabetic CKD a pathway to not just longer lives, but healthier, more vibrant ones.

**In summary:**

Lifestyle medicine is not an adjunct, but a cornerstone of care for diabetic CKD. Our study, alongside contemporary evidence, calls for a paradigm shift—one where every patient is supported to harness the healing power of movement, nutrition, and self-efficacy. This is how we mitigate cardiovascular risk, slow disease progression, and, most importantly, help patients reclaim their quality of life.

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