

The Role of Oxidative Stress and Antioxidant Therapy in the Progression of Type 2 Diabetes Mellitus: An Experimental and Clinical Study

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ABSTRACT:

Background: Oxidative stress is increasingly recognized as a key factor in the pathogenesis of Type 2 Diabetes Mellitus (T2DM). Free radical accumulation damages pancreatic β -cells, reduces insulin secretion, and exacerbates insulin resistance. However, the therapeutic benefit of antioxidant supplementation in T2DM remains unclear. **Objective:** To investigate the role of oxidative stress markers in T2DM patients and evaluate the efficacy of antioxidant therapy in improving glycemic control and reducing oxidative burden. **Methods:** A two-part study was conducted. (1) Clinical Study: 120 patients with T2DM and 60 healthy controls were assessed for oxidative stress biomarkers (MDA, SOD, GSH, and TAC) and glycemic indices (FBS, HbA1c, HOMA-IR). (2) Experimental Study: Male Wistar rats were divided into 4 groups: control, diabetic, diabetic + vitamin E, and diabetic + vitamin C. Biochemical assays, histopathology of pancreatic tissues, and insulin levels were measured after 8 weeks. **Results:** T2DM patients exhibited significantly elevated MDA levels ($p < 0.001$) and reduced antioxidant enzymes compared to controls. Antioxidant supplementation in patients resulted in a 15% reduction in HbA1c and significant improvement in TAC. In experimental rats, vitamin E and C restored pancreatic islet structure, reduced oxidative stress, and improved insulin secretion. **Conclusion:** Oxidative stress plays a pivotal role in T2DM progression. Antioxidant therapy, particularly vitamin E, demonstrates significant protective effects on β -cell integrity and improves glycemic control. Antioxidants may serve as adjunctive therapy in T2DM management.

Keywords: Type 2 Diabetes Mellitus, Oxidative Stress, Antioxidants, Vitamin E, Pancreatic β -cells

INTRODUCTION:

Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder characterized by chronic hyperglycemia, impaired insulin secretion, and insulin resistance. While genetic and lifestyle factors contribute to disease progression, oxidative stress has emerged as a key pathological mechanism. Excess reactive oxygen species (ROS) impair pancreatic β -cell function, induce apoptosis, and worsen insulin resistance.

Several studies have reported elevated oxidative markers and reduced antioxidant defenses in T2DM patients. Despite this evidence, the clinical role of antioxidant therapy in diabetes remains debated, with conflicting results across populations.

This study aims to:

- Evaluate oxidative stress markers in T2DM patients compared to healthy individuals.
- Assess the therapeutic potential of antioxidant supplementation in both patients and experimental models of diabetes.

MATERIALS AND METHODS:

Clinical Study Design:

- **Population:** 120 T2DM patients (diagnosed ≥ 2 years) and 60 age-matched healthy controls.
- **Exclusion criteria:** Patients on antioxidant therapy, liver/kidney disorders, or acute infections.
- **Parameters measured:**
 - Glycemic indices: FBS, HbA1c, HOMA-IR

- Oxidative stress markers: Malondialdehyde (MDA), Superoxide dismutase (SOD), Glutathione (GSH), Total antioxidant capacity (TAC)
- **Intervention:** 60 diabetic patients received daily antioxidant supplementation (Vitamin E 400 IU + Vitamin C 500 mg) for 12 weeks; 60 remained on standard therapy.

Experimental Animal Study:

- **Subjects:** 40 male Wistar rats (200–250g)
- **Groups:**
 1. Control (saline)
 2. Diabetic (streptozotocin-induced)
 3. Diabetic + Vitamin E (100 mg/kg/day)
 4. Diabetic + Vitamin C (200 mg/kg/day)
- **Assessments:**
 - Blood glucose, serum insulin
 - Oxidative markers (MDA, SOD, GSH)
 - Histopathology of pancreatic islets

Statistical Analysis:

Data analyzed using SPSS v26. Results expressed as mean $\pm$ SD. Student's *t*-test and ANOVA used for comparison. *p* < 0.05 considered significant.

RESULTS:

Clinical Study:

- T2DM patients showed **significantly higher MDA** (4.8 ± 0.6 vs 2.1 ± 0.4 $\mu\text{mol/L}$, *p* < 0.001) and **lower TAC** (0.78 ± 0.09 vs 1.45 ± 0.12 mmol/L, *p* < 0.001) compared to controls.
- Antioxidant therapy led to:
 - **HbA1c reduction** ($8.9\% \rightarrow 7.6\%$, *p* < 0.01)
 - **Increase in TAC** ($0.82 \pm 0.10 \rightarrow 1.10 \pm 0.14$ mmol/L, *p* < 0.01)

Experimental Study:

- Diabetic rats showed marked pancreatic islet damage, reduced insulin levels, and increased MDA.
- Antioxidant-treated rats exhibited:
 - Restoration of β -cell structure (confirmed by histology)
 - Reduced oxidative damage
 - Improved insulin secretion (Vitamin E > Vitamin C)

Table 1. Changes in Oxidative Stress Markers in T2DM Patients Before and After Antioxidant Therapy (n = 60)

Parameter	Before Therapy (Mean $\pm$ SD)	After Therapy (Mean $\pm$ SD)	% Change	<i>p</i> -value
Malondialdehyde (MDA, $\mu\text{mol/L}$)	4.82 ± 0.65	3.41 ± 0.54	↓ 29%	<0.001
Superoxide Dismutase (SOD, U/mL)	2.15 ± 0.41	3.02 ± 0.46	↑ 40%	<0.01
Glutathione (GSH, $\mu\text{mol/g Hb}$)	3.85 ± 0.55	4.92 ± 0.61	↑ 28%	<0.01
Total Antioxidant Capacity (TAC, mmol/L)	0.82 ± 0.10	1.10 ± 0.14	↑ 34%	<0.01
HbA1c (%)	8.9 ± 0.8	7.6 ± 0.7	↓ 15%	<0.01

Note: Values are presented as mean $\pm$ SD. ↓ = decrease, ↑ = increase. Statistical significance calculated by paired *t*-test.

DISCUSSION:

Our study confirms that oxidative stress is significantly elevated in T2DM patients and contributes to disease progression. Antioxidant supplementation improved both biochemical markers and glycemic control in patients, consistent with previous findings (Ceriello et al., 2019).

The animal study provided mechanistic insights, demonstrating that antioxidants protect pancreatic β -cells from ROS-induced damage and enhance insulin secretion. Vitamin E was found to be more effective than Vitamin C, likely due to its lipid-soluble nature, which protects cell membranes from oxidative injury.

These findings suggest that **antioxidant therapy could serve as an adjunct in T2DM treatment**, especially in patients with poor glycemic control and elevated oxidative burden. However, large-scale randomized trials are required to validate long-term benefits and safety.

CONCLUSION:

Oxidative stress is a major contributor to the pathogenesis of T2DM. Antioxidant therapy, particularly

vitamin E, offers promising protective effects by reducing oxidative burden and preserving pancreatic β -cell integrity. Incorporation of antioxidants into diabetes management may enhance therapeutic outcomes.

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Conflict of Interest: None

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