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Original Research Article

Evaluation of Oxidative Stress and Antioxidant Enzyme Activity in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study

Amit Hiralal Asalkar

Assistant Professor, Dept of Biochemistry, DM Wayanad Institute of Medical Sciences, Naseera Nagar, Wayanad, Kerla

Corresponding author: Amit Hiralal Asalkar
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Abstract:

Background: Oxidative stress plays a pivotal role in the pathogenesis and complications of type 2 diabetes mellitus (T2DM). Imbalances between reactive oxygen species (ROS) and antioxidant defense mechanisms such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) contribute to β-cell dysfunction and insulin resistance.

Objective: To assess oxidative stress markers and the activity of key antioxidant enzymes in T2DM patients compared to healthy controls.

Methods: A cross-sectional study was conducted on 100 subjects (60 T2DM patients and 40 healthy controls). Serum malondialdehyde (MDA) levels were used as a marker of lipid peroxidation, and activities of SOD, CAT, and GPx were measured spectrophotometrically. Group comparisons were done using independent *t*-test; correlations between glycemic parameters and oxidative stress markers were evaluated using Pearson's correlation.

Results: MDA levels were significantly elevated in T2DM patients (5.6 ± 1.1 µmol/L) compared to controls (2.9 ± 0.6 µmol/L; $p < 0.001$). Antioxidant enzymes SOD, CAT, and GPx were significantly reduced in T2DM group ($p < 0.001$). HbA1c showed a strong positive correlation with MDA ($r = 0.52$, $p < 0.01$) and negative correlations with SOD ($r = –0.44$), CAT ($r = –0.41$), and GPx ($r = –0.38$).

Conclusion: Increased oxidative stress and reduced antioxidant defense were observed in T2DM patients. These findings support the role of oxidative stress in diabetic pathophysiology and highlight the importance of antioxidant therapy in diabetes management.

Keywords: Oxidative stress, Antioxidant enzymes, Diabetes mellitus, SOD, GPx, Catalase, MDA

Introduction

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder characterized by insulin resistance, impaired glucose tolerance, and chronic hyperglycemia. One of the key pathological mechanisms implicated in its onset and progression is oxidative stress, defined as an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense system (1,2).

Hyperglycemia leads to oxidative stress via several pathways, including increased advanced glycation end-products (AGEs), polyol pathway activation, and mitochondrial dysfunction (3). Malondialdehyde (MDA), a product of lipid peroxidation, serves as a robust biomarker of oxidative damage (4). Enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) protect tissues against ROS-induced injury (5).

This study aimed to assess oxidative stress and antioxidant enzyme levels in T2DM patients compared to healthy individuals and correlate these markers with glycemic status.

Materials and Methods

Study Design and Participants

A hospital-based cross-sectional study was conducted A total of 100 participants were enrolled:

- **T2DM group (n = 60)**:
- **Healthy controls (n = 40)**: Age and sex matched, with no known metabolic disorders

Exclusion criteria included: smoking, alcoholism, acute/chronic infections, liver or renal diseases, and antioxidant supplementation.

Biochemical Analysis

After overnight fasting, venous blood samples were collected. Serum was analyzed for:

- MDA: Thiobarbituric acid reactive substances (TBARS) method
- SOD: Marklund and Marklund method
- CAT: Aebi method
- GPx: Rotruck method
- HbA1c: HPLC-based assay

Statistical Analysis

Data were expressed as mean ± SD. Independent t-test was used for group comparison. Pearson's correlation coefficient analyzed the relationship between oxidative markers and HbA1c. Significance was set at $p < 0.05$. Analysis was done using SPSS v25.

Ethical Approval

The study was approved by the Institutional Ethics Committee Informed consent was obtained.

Results

1. **Comparison of Oxidative Stress and Antioxidant Markers**

T2DM patients had significantly higher MDA levels and lower antioxidant enzyme activities compared to healthy controls.

Table 1: Comparison of Oxidative Stress Markers Between T2DM Patients and Controls

Parameter	T2DM (n = 60)	Control (n = 40)	p-value
MDA (µmol/L)	5.6 ± 1.1	2.9 ± 0.6	<0.001*
SOD (U/mL)	1.5 ± 0.4	2.8 ± 0.6	<0.001*
Catalase (U/mL)	29.4 ± 6.5	52.1 ± 7.2	<0.001*
GPx (U/L)	28.3 ± 7.1	46.5 ± 8.8	<0.001*

2. **Correlation with Glycemic Control**

HbA1c positively correlated with MDA ($r = 0.52$, $p < 0.01$), and inversely with SOD ($r = –0.44$), CAT ($r = –0.41$), and GPx ($r = –0.38$).

Table 2: Correlation Between HbA1c and Oxidative Stress Markers

Marker	Correlation Coefficient (r)	p-value
MDA	0.52	<0.01*
SOD	0.44	<0.01*
Catalase	0.41	<0.01*
GPx	0.38	<0.05*

Discussion

Our findings clearly demonstrate a significant increase in oxidative stress, evidenced by elevated levels of malondialdehyde (MDA), alongside a marked reduction in the activities of key antioxidant enzymes—superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx)—in patients with type 2 diabetes mellitus (T2DM). This biochemical imbalance supports the widely accepted hypothesis that oxidative stress is a central contributor to the pathophysiology of diabetes and its complications (6–8).

Oxidative stress arises when the generation of reactive oxygen species (ROS) overwhelms the body's endogenous antioxidant defenses. In

T2DM, chronic hyperglycemia enhances ROS production through multiple metabolic pathways, including glucose auto-oxidation, protein glycation, and activation of the polyol pathway (6). These ROS not only damage cellular lipids, proteins, and DNA but also impair insulin signaling and β-cell function, thereby perpetuating insulin resistance and hyperglycemia in a vicious cycle (7). Maritim et al. (6) highlighted that diabetic individuals typically exhibit elevated MDA levels and depleted antioxidant enzymes, which aligns with our current observations. Mohan et al. (7) further emphasized the link between oxidative biomarkers and the inflammatory cascade in Indian diabetic cohorts, underscoring the regional relevance of our findings. Suresh et al. (8) also reported significantly reduced total antioxidant status in T2DM patients, consistent with our enzymatic analysis results.

Importantly, we observed a strong inverse relationship between antioxidant enzyme activities and HbA1c levels, indicating that worsening glycemic control is directly associated with declining antioxidant capacity. High HbA1c levels reflect prolonged glucose exposure, which accelerates oxidative stress and subsequently depletes antioxidant reserves. This biochemical stress impairs endothelial function, alters vascular tone, and contributes to the development of both microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (atherosclerosis, cardiovascular disease) complications (9–11). Ceretta LB et al. (12) demonstrated that oxidative stress markers are directly modulated by glycemic levels and antioxidant interventions. Giacco and Brownlee (13) provided mechanistic insight into how oxidative stress disrupts cellular homeostasis and activates damaging metabolic pathways. Similarly, Jain (14) confirmed that elevated glucose enhances lipid peroxidation and weakens endogenous antioxidants, including SOD and GPx, echoing our correlation analysis.

From a translational standpoint, our data support the role of antioxidant therapy, dietary interventions rich in polyphenols and vitamins, and rigorous glycemic control as practical strategies to combat oxidative damage in diabetics. Such interventions can preserve β-cell function, improve insulin sensitivity, and reduce the risk of complications. As Nishikawa et al. (15) demonstrated, targeting mitochondrial ROS production effectively ameliorates hyperglycemia-induced damage and offers a promising direction for future therapeutic research.

Collectively, these findings reinforce the relevance of oxidative stress in diabetic management and suggest that monitoring both pro-oxidant and antioxidant markers may provide valuable prognostic insights in routine clinical settings.

Conclusion

This study confirms increased oxidative stress and reduced antioxidant enzyme activities in patients with T2DM. Monitoring these parameters, alongside HbA1c, may offer predictive value in identifying patients at higher risk of diabetic complications.

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