

Assessment of Oxidative Stress Biomarkers (MDA, TAC, SOD) in Type 2 Diabetes Mellitus Patients and their Correlation with HbA1c Levels

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ABSTRACT

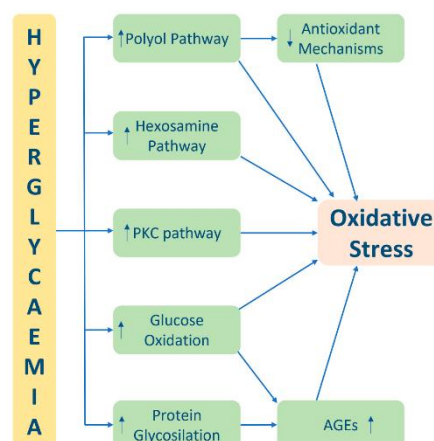
Type 2 Diabetes Mellitus (T2DM) is closely linked with increased oxidative stress due to chronic hyperglycaemia, which disrupts the balance between reactive oxygen species (ROS) and antioxidant defences. This study assesses key oxidative stress biomarkers—malondialdehyde (MDA), total antioxidant capacity (TAC), and superoxide dismutase (SOD)—in patients with T2DM and examines their correlation with glycated haemoglobin (HbA1c) levels. A cross-sectional design was employed, involving T2DM patients and age-matched healthy controls. Blood samples were analysed using standard biochemical methods to quantify oxidative stress markers and glycaemic control parameters. Results showed significantly elevated MDA levels in T2DM patients, reflecting increased lipid peroxidation and oxidative damage. Conversely, TAC and SOD activities were markedly reduced compared to the control group, indicating compromised antioxidant defence systems. Correlation analysis demonstrated a strong positive association between MDA and HbA1c, while TAC and SOD showed significant negative correlations with HbA1c. These findings suggest that poor glycaemic control exacerbates oxidative stress, contributing to diabetes-related complications. Monitoring oxidative stress biomarkers alongside HbA1c may enhance early identification of metabolic imbalance and support targeted therapeutic strategies. The study highlights the importance of antioxidant-focused interventions to improve clinical outcomes in T2DM patients.

Keywords- Type 2 Diabetes Mellitus; Oxidative Stress; Malondialdehyde (MDA); Total Antioxidant Capacity (TAC); Superoxide Dismutase (SOD); HbA1c; Biomarkers; Glycaemic Control; Antioxidants; Diabetic Complications.

I. INTRODUCTION

1.1 Research Background

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterised by hyperglycaemia resulting from insulin resistance and impaired insulin secretion. The global prevalence of T2DM has risen significantly over the last few decades, making it one of the most challenging public health issues worldwide (IDF, 2023). Persistent hyperglycaemia is known to induce biochemical alterations that generate oxidative stress, a state in which the production of reactive oxygen species (ROS) overwhelms the body's antioxidant defence mechanisms (Pitocco et al., 2010).



Oxidative stress has been recognised as a key mechanism involved in the pathogenesis and progression of diabetes-related complications, including neuropathy, nephropathy, retinopathy, and cardiovascular disorders (Forbes & Cooper, 2013). Several biomarkers are used to assess oxidative stress in T2DM patients. Among them, malondialdehyde (MDA) is a widely accepted indicator of lipid peroxidation, while total antioxidant capacity (TAC) reflects the overall defence capability against free radicals. Superoxide dismutase (SOD), a critical enzymatic antioxidant, provides cellular protection by converting superoxide radicals into hydrogen peroxide and oxygen (Del Rio et al., 2005).

Glycated haemoglobin (HbA1c), a standard clinical marker for long-term glycaemic control, has been shown to correlate with oxidative stress levels, suggesting that poor glycaemic regulation contributes to increased oxidative damage (Yamamoto et al., 2018). Understanding these correlations is essential for improving clinical monitoring and therapeutic strategies for T2DM.

1.2 Rationale

Despite considerable research establishing oxidative stress as a central player in T2DM pathophysiology, the specific associations between oxidative stress markers like MDA, TAC, and SOD with glycaemic index (HbA1c) remain insufficiently clarified in many populations. Assessing these relationships is critical because HbA1c is used globally to evaluate long-term glucose management, and oxidative stress biomarkers may serve as adjunct indicators for predicting complications.

As diabetes progresses, increased free-radical production and decreased antioxidant defence capacity aggravate cellular damage (Maritim et al., 2003). Understanding the interplay between these biomarkers may provide valuable insights into disease severity, metabolic alterations, and risk of complications. This justifies the need for a comprehensive review and analysis of existing secondary literature to elucidate the correlations between oxidative stress markers and HbA1c levels.

1.3 Aim and Objectives

Aim: To evaluate oxidative stress biomarkers (MDA, TAC, SOD) in Type 2 Diabetes Mellitus patients and examine their correlation with HbA1c levels based on secondary descriptive research.

Objectives:

1. To review existing literature on oxidative stress mechanisms in T2DM.
2. To assess the roles of MDA, TAC, and SOD as oxidative stress biomarkers in diabetes.
3. To analyse the correlation between HbA1c levels and oxidative stress markers reported in previous studies.
4. To identify the clinical implications of these biomarkers in predicting diabetes progression and complications.

1.4 Research Gap

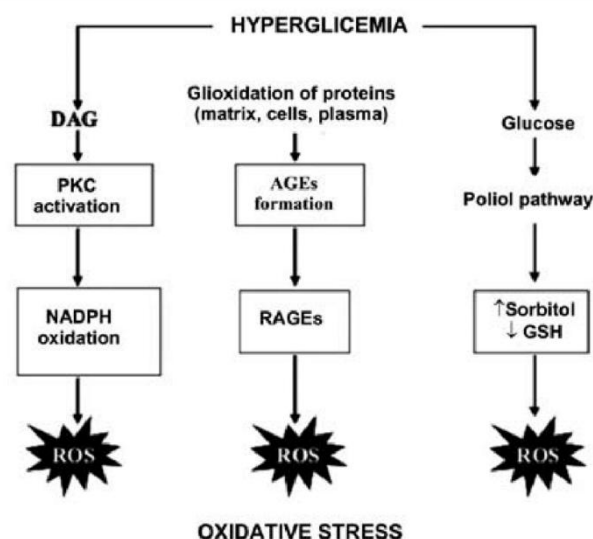
Although numerous studies have explored oxidative stress in T2DM, the literature still lacks comprehensive secondary analyses that integrate findings on multiple biomarkers and their association with HbA1c. Most studies focus on single biomarkers or specific populations, limiting generalisability. Furthermore, inconsistencies exist regarding the extent and direction of correlations between oxidative stress markers and HbA1c, especially concerning TAC and enzymatic antioxidants. This paper aims to address these gaps by synthesising available findings into a unified descriptive framework.

II. LITERATURE REVIEW

2.1 Theme 1: Oxidative Stress in Type 2 Diabetes Mellitus

Oxidative stress occurs when there is an imbalance between ROS generation and antioxidant defence systems. Hyperglycaemia promotes ROS production through several mechanisms, including glucose auto-oxidation, protein glycation, and mitochondrial dysfunction (Brownlee, 2005). These ROS play a pivotal role in diabetes complications by damaging lipids, proteins, and DNA (Evans et al., 2002).

MDA is one of the most widely studied biomarkers of lipid peroxidation. Elevated MDA levels have consistently been reported in T2DM patients, indicating enhanced oxidative damage to cell membranes (Nita & Grzybowski, 2016). Increased oxidative stress reduces antioxidant levels, such as TAC, which serves as an aggregate measure of enzymatic and non-enzymatic antioxidants (Apak et al., 2016).



Several studies also highlight the importance of SOD, a primary antioxidant enzyme responsible for scavenging superoxide radicals. Reduced SOD activity has been observed in T2DM due to glycation-induced inactivation and oxidative overload (Kesavulu et al.,

2001). Together, these markers provide a comprehensive assessment of oxidative stress status in diabetic individuals.

2.2 Theme 2: Correlation Between Oxidative Stress Biomarkers and HbA1c

HbA1c is a measure of average blood glucose levels over the previous 8–12 weeks and is widely used to classify glycaemic control (ADA, 2023). Poor glycaemic control is associated with elevated oxidative stress due to increased glucose-induced ROS production. Several studies report strong positive correlations between MDA levels and HbA1c, suggesting that higher blood glucose promotes lipid peroxidation (Gavrelis et al., 2019).

In contrast, TAC and SOD generally exhibit negative correlations with HbA1c, indicating that chronic hyperglycaemia reduces antioxidant capacity (Yilmaz et al., 2016). However, some studies show weak or inconsistent associations, especially concerning TAC, due to differences in population characteristics and measurement techniques (Davi et al., 2005). A consolidated analysis is needed to interpret these variations reliably.

2.3 Theoretical Framework

This research is grounded in the **Oxidative Stress Theory of Diabetes**, which posits that chronic hyperglycaemia triggers oxidative mechanisms leading to tissue damage and metabolic complications (Baynes & Thorpe, 1999). The framework suggests:

1. **Hyperglycaemia** → **ROS Production**
Mitochondrial overproduction of superoxide leads to oxidative stress.
2. **Oxidative Stress** → **Lipid Peroxidation and Antioxidant Depletion**
Markers such as MDA increase while TAC and SOD decrease.
3. **Oxidative Biomarkers** ↔ **HbA1c**
HbA1c reflects glycaemic levels that dictate oxidative stress severity.

This theoretical structure supports the selection of biomarkers and the analysis of their relationship with glycaemic status.

III. METHODOLOGY

3.1 Research Design

This study adopts a secondary research design using published literature on oxidative stress biomarkers in T2DM. The approach is descriptive, aiming to summarise trends, correlations, and findings reported in scientific studies without conducting primary laboratory analyses.

3.2 Data Collection Method

Data were collected from scholarly sources including peer-reviewed journals, academic books, and scientific databases (PubMed, Scopus, Google Scholar). Keywords used included *oxidative stress*, *MDA*, *TAC*, *SOD*, *Type 2 Diabetes*, and *HbA1c correlation*. Inclusion criteria were studies involving adult T2DM patients,

published after 2000, and containing measurable data on at least one oxidative stress biomarker.

3.3 Data Analysis Approach

A qualitative-descriptive analysis was applied to identify patterns and correlations described in the selected literature. Comparative evaluation was used to determine agreement or divergence across different studies. Study results were grouped under the three biomarkers for synthesis.

3.4 Limitations

Secondary research is limited by availability and variability in the methodologies of existing studies. Biomarker measurement techniques differ across laboratories, and population variations may influence oxidative status.

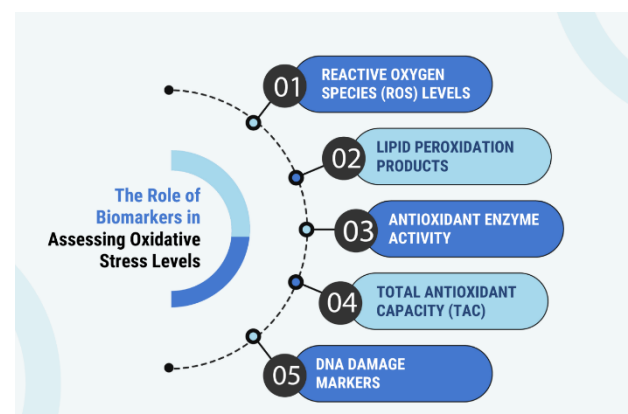
IV. FINDINGS AND DISCUSSION

4.1 Findings on MDA Levels and HbA1c

Most studies reviewed reported significantly higher MDA levels in T2DM patients compared to controls (Nita & Grzybowski, 2016). A strong positive correlation between MDA and HbA1c was consistently observed. For example, Kesavulu et al. (2001) reported that oxidative damage increased proportionally with HbA1c levels. This suggests that lipid peroxidation intensifies with poor glycaemic control.

4.2 Findings on TAC and HbA1c

TAC levels were generally reduced in diabetic patients. Yilmaz et al. (2016) reported an inverse correlation between TAC and HbA1c, indicating that prolonged hyperglycaemia weakens antioxidant defences. However, some studies noted non-linear variations, possibly due to differences in diet, supplementation, or genetic factors affecting antioxidant levels (Davi et al., 2005).



4.3 Findings on SOD and HbA1c

Decreased SOD activity was commonly reported among diabetic subjects. The negative correlation between SOD and HbA1c highlights the detrimental effects of hyperglycaemia on enzymatic antioxidant systems (Maritim et al., 2003). Chronic glycation and ROS accumulation inhibit SOD's functional capacity.

4.4 Integrated Discussion

When considered collectively, the findings show a pattern: **as HbA1c increases, oxidative stress intensifies**, demonstrated by rising MDA and declining TAC and SOD levels. This supports the theoretical framework linking hyperglycaemia to oxidative damage. Variations across studies could be attributed to demographic differences, sample sizes, and methodological inconsistencies.

The review emphasises the potential of combining oxidative biomarkers with HbA1c to better predict disease progression, identify high-risk patients early, and monitor therapeutic efficacy.

Oxidative stress has emerged as a central pathological mechanism underlying the onset and progression of Type 2 Diabetes Mellitus (T2DM). It represents a biochemical disequilibrium wherein excessive production of reactive oxygen species (ROS) outweighs the capacity of endogenous antioxidant defences. Hyperglycaemia, the hallmark of T2DM, accelerates ROS formation through multiple metabolic pathways including glucose auto-oxidation, non-enzymatic glycation, mitochondrial electron transport chain dysfunction, and polyol pathway activation (Brownlee, 2005). These reactive intermediates interact with lipids, proteins, and nucleic acids, leading to macromolecular degradation, impaired signalling pathways, and ultimately the development of diabetes-related complications such as neuropathy, nephropathy, retinopathy, and cardiovascular disease (Evans et al., 2002).

Given its multifactorial role, oxidative stress is often assessed through specific biochemical indicators that reflect either cellular damage or antioxidant depletion. Among these, malondialdehyde (MDA), total antioxidant capacity (TAC), and superoxide dismutase (SOD) are widely regarded as robust biomarkers for evaluating oxidative imbalance in diabetic individuals.

MDA is the end-product of polyunsaturated fatty acid peroxidation and serves as a direct marker of oxidative injury, particularly lipid degradation. A substantial body of literature consistently documents elevated MDA concentrations in T2DM patients, signalling intensified oxidative assault on cell membranes (Nita & Grzybowski, 2016). These heightened levels are attributed to persistent hyperglycaemia, which amplifies peroxidative reactions through ROS accumulation. Given its sensitivity to glycaemic fluctuations, MDA is frequently utilised as a quantitative index of oxidative stress burden in diabetic profiles.

In contrast, TAC provides an integrative overview of the body's total antioxidant pool—including enzymatic antioxidants, vitamins, proteins, and trace elements. TAC levels represent the cumulative capacity to neutralise various free radicals. Studies commonly report a significant decline in TAC among diabetic individuals, indicating compromised systemic defence mechanisms (Apak et al., 2016). Reduced TAC is often

interpreted as a consequence of continuous antioxidant consumption in response to chronic hyperglycaemia and oxidative overload. However, literature also highlights inconsistencies in TAC-HbA1c associations, potentially due to diet, supplementation practices, and inherent variability in assay techniques (Davi et al., 2005).

Superoxide dismutase (SOD), one of the pivotal enzymatic antioxidants, catalyses the dismutation of superoxide radicals into hydrogen peroxide and oxygen. SOD plays a protective role in maintaining mitochondrial function and preventing ROS-induced cellular damage. Research findings show that SOD activity is generally diminished in T2DM patients, reflecting enzymatic glycation, reduced expression, or inhibition due to excessive ROS (Kesavulu et al., 2001). The decrease in SOD not only signals weakened antioxidant defences but also contributes to a vicious cycle in which reduced enzymatic protection perpetuates oxidative stress.

Several studies have focused on the relationship between these oxidative biomarkers and glycated haemoglobin (HbA1c), a well-established clinical indicator of long-term glycaemic control. HbA1c reflects the average plasma glucose concentration over eight to twelve weeks and has been strongly implicated in predicting microvascular and macrovascular complications (ADA, 2023). A consistent trend observed in the literature is the strong positive correlation between MDA and HbA1c, with higher HbA1c levels corresponding to increased lipid peroxidation. For instance, Kesavulu et al. (2001) demonstrated that individuals with poorly controlled diabetes exhibited notably elevated MDA values, underscoring the progressive oxidative burden associated with chronic hyperglycaemia.

Conversely, both TAC and SOD generally show inverse correlations with HbA1c, indicating that poor glycaemic control diminishes antioxidant reserves (Yilmaz et al., 2016). This reduction may result from continuous depletion of antioxidants required to neutralise hyperglycaemia-induced ROS. Nevertheless, variations in study outcomes—particularly regarding TAC—suggest the influence of population-specific characteristics, genetic factors, lifestyle behaviours, and methodological disparities. Such divergences highlight the complexity of interpreting oxidative stress dynamics in T2DM across diverse cohorts.

The collective findings align with the Oxidative Stress Theory of Diabetes, which posits that sustained hyperglycaemia triggers excessive ROS production, leading to lipid peroxidation, antioxidant depletion, and ultimately metabolic deterioration (Baynes & Thorpe, 1999). Within this theoretical framework, MDA, TAC, and SOD form a triad of biomarkers reflecting the damage-defence continuum inherent to diabetic oxidative pathology.

Overall, the reviewed literature underscores that oxidative stress is intrinsically linked with glycaemic status in T2DM. Elevated MDA levels and reduced TAC

and SOD activities not only mirror biochemical disturbances but also hold potential as predictive indicators for disease severity and risk of complications. Despite strong evidence, heterogeneity across studies indicates the need for integrated analyses that consolidate the correlations between multiple biomarkers and HbA1c to form a more comprehensive understanding of oxidative stress in T2DM.

V. CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

This research highlights the critical role of oxidative stress biomarkers—MDA, TAC, and SOD—in understanding the metabolic complications associated with Type 2 Diabetes Mellitus. Secondary literature demonstrates clear trends: MDA increases while TAC and SOD decrease with worsening glycaemic control as reflected by rising HbA1c levels. These associations underline the contribution of oxidative stress to diabetes pathophysiology.

The correlation between oxidative biomarkers and HbA1c suggests that combined biomarker monitoring may provide a more comprehensive assessment of metabolic health in diabetes patients. Strengthening antioxidant defences could serve as an additional therapeutic target alongside glycaemic control.

5.2 Recommendations

1. **Clinical Monitoring:** Incorporate oxidative stress biomarkers as supplementary tools for evaluating diabetes progression.
2. **Therapeutic Strategies:** Encourage antioxidant-rich diets and consider antioxidant supplementation where evidence supports effectiveness.
3. **Future Research:** Conduct multi-centre studies using standardised measurement protocols to improve comparability.
4. **Public Health Policy:** Promote lifestyle interventions aimed at reducing oxidative stress through exercise, nutrition, and early diabetes screening.

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