Sarcouncil Journal of Medicine and Surgery

ISSN(Online): 2945-3534

Volume- 04| Issue- 09| 2025

Research Article **Received:** 20-07-2025 | **Accepted:** 20-08-2025 | **Published:** 09-09-2025

Relationship between Oxidative Stress and Diabetes Mellitus Complications

Dr. Rusul Mahdi Abid[1] and Dr. Muthanna Thiab Fendi[2]

[1]M.B.Ch.B., F.I.C.M.S. \ (Internal Medicine) Iraqi Ministry of Higher Education and Scientific Research, Thi Qar University, Medical College, Thi Qar, Iraq. Iraqi Ministry of Health, Thi Qar Health Directorate, Al-Nasiriyah Teaching Hospital, Thi Qar, Iraq.

[2]M.B.Ch.B., F.I.C.M.S. \ (Internal Medicine) Iraqi Ministry of Health, Thi Qar Health Directorate, Respiratory Department, Al-Nasiriyah Teaching Hospital, Thi Qar, Iraq.

Abstract: Background: Diabetes mellitus (DM) is a multifactorial metabolic disorder characterized by chronic hyperglycemia and associated with significant microvascular and macrovascular complications and. Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defenses, plays a pivotal role in the pathogenesis of diabetes-related complications as well as found in Our study designed A descriptive cross-sectional study was conducted involving 50 diabetic patients from different hospitals from Iraq with study period between 12-5-2024 to 4-6-2025 where Data collected included demographic characteristics, symptom presentation, diagnostic methods, medication regimens, insulin usage, and HbA1c monitoring frequencies, while that Malondialdehyde (MDA) levels, a biomarker of oxidative stress, were measured in patients and compared to healthy controls, where in our study the finding were found mean (Sd)53.1 ± 9.9,(slight female predominance (54%)) in addition to found The duration of diabetes exceeded 10 years in 32% of the cohort, also was Polyuria the predominant symptom at diagnosis (42%), with 90% diagnosed by glucose tolerance testing, where Oral hypoglycemic drugs were used by 74%, with a mean of 1.1 ± 0.9 agents per patient; 68% were not on insulin therapy in addition to found HbA1c monitoring was inadequate, with 68% of patients lacking regular assessment during the year, and 24% demonstrating levels >7%, indicating poor glycemic control, even that were Significantly elevated MDA levels were observed in diabetic patients (3.20 ± 0.57 µmol/L) compared to healthy controls (1.70 ± 0.35 µmol/L), with a large effect size (Cohen's d = 3.20), reflecting increased oxidative stress, for this results we concluded The study highlights suboptimal glycemic monitoring and control among diabetic patients, alongside markedly elevated oxidative stress, suggesting its critical role in the development and progression of diabetic complications.

Keywords: Diabetes Mellitus, Oxidative Stress, Malondialdehyde, Glycemic Control, Oral Hypoglycemic Agents, Insulin Therapy, Diabetes Complications, HbA1c Monitoring.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease with long-term hyperglycaemia due to disorders in insulin secretion, its action, macrovascular (cardiovascular disease) complications primarily responsible for affecting morbidity and mortality rates in diabetics (Magliano, D. J. *et al.*, 2021) and with Processes for these complications are complex; however, mounting evidence points to oxidative stress as an indispensable factor connecting hyperglycemia with cell damage and malfunction (Ceriello, A. 2006) through antioxidants. ROS, which include free radicals such as the superoxide anion (O2−), the hydroxyl radical (−OH), and non-radical derivatives including the hydrogen peroxide (H2O2), are highly reactive molecules with the potential to cause damages on lipids, proteins, as well as DNA (Forbes, J. M., & Cooper, M. E. 2013) so In diabetes, chronic hyperglycemia causes the over-production of ROS through numerous biochemical mechanisms including the glucose auto-oxidation, the production of advanced glycation end products (AGEs), polyol pathway flux, and disruption involving the mitochondria (Manna, I. *et al.*, 2023).

It is also established by the evidence of elevated oxidative biomarkers, such as malondialdehyde (MDA), but lower antioxidants in diabetics when compared with normal controls (Fatima Rehman, F. *et al.*,) in addition to Elevated MDA, the end product of lipid peroxidation, reflects cell membrane damages caused by ROS and is widely used as an indicator for the presence of oxidative stress while also Higher oxidative damages have been connected with the progression of the diabetic complication such as neuropathy, nephropathy, and cardiovascular diseases (Caturano, A. *et al.*, 2025) furthermore Mechanistically, endothelial function impairment, inflammation, and apoptosis are regulated by oxidative stress, hence inducing tissue damage in diabetes. ROS induce the commencement of mitochondrial DNA damage and the enhancement in the formation of pro-inflammatory cytokines, aggravating vessel damage in diabetic tissues (Manna, I. *et al.*, 2023), where Diabetes mellitus is a metabolic disorder that occurs in various forms and is characterized by abnormal regulation of glucose metabolism. In diabetic patients, tissue repair is a sequence of events involving

***Corresponding Author:** Dr. Rusul Mahdi Abid

DOI- https://doi.org/10.5281/zenodo.18091893

inflammation, angiogenesis, remodeling, and complete tissue repair and according to Several molecular mechanisms have been proposed to account for these pathological effects also was In particular, two mechanisms are important in the progression of diabetic periodontal disease (PD): the accumulation of advanced glycation end products (AGEs) in cells exposed to chronic hyperglycemia, and the damage caused by oxidative stress resulting from the overproduction of reactive oxygen species (ROS) although in research oxidative stress induces key signal transduction pathways such as the nuclear factor-kappa B (NF-κB), an adhesion molecule and inflammatory mediator upregulated, hence driving the progression of diabetic complications (Al Khuzaee, M. F. *et al*., 2025; Cecerska-Heryć, E. *et al*., 2025) even that antioxidative defences, including the enzymic components like superoxide dismutase (SOD), catalase, and glutathione peroxidase, and the non-enzymic molecules like vitamin C and vitamin E, are often defective in diabetes, hence speeding up oxidative damages further (Al Khuzaee, M. F. *et al*., 2025) Oxidative damage happens when antioxidant defenses are weakened or when the concentration of oxidizing chemicals, whether endogenous or foreign, rises. Because they can produce oxidative states or impact the production or recovery efficiency of antioxidant systems, metabolic illnesses like diabetes mellitus have a high likelihood of involving oxidative elements in their genesis, progression, or consequences (Cecerska-Heryć, E. *et al*., 2025).then concluded imbalance between ROS formation and antioxidative ability is central to the pathophysiology of diabetic complication where Oxidative stress therapies have also been explored as treatments, so finally of background Research demonstrates that supplementation with antioxidants or agents improving the functioning of the mitochondria decrease oxidative damage and prevent or reduce diabetic complications in animal studies and human trials (Chen, X. *et al*., 2025; Roy, B. 2025; Płóciniczak, A. *et al*., 2025; Chung, S. S. *et al*., 2003).

MATERIAL AND METHOD

The research was conceptualized as a cross-sectional observational study to examine the association between oxidative stress and the complications of diabetes mellitus where our Patients who actively present for follow-up in the diabetic outpatient department are managed and monitored for diabetes and Approval for the institutional review board had been obtained, with all the participants also having issued informed written consent before inclusion in the study as well as The study involved adult patients who had been diagnosed with diabetes mellitus, who came for visitation at the clinic between days defined by the predetermined period. Participants had to be 18 years or above with an internationally recognized diagnosis of diabetes mellitus according to the World Health Organization (WHO)'s guidelines. However, a number of related requirements must be satisfied—many of which are not—in order to categorize oxidative involvement in a disease. This keeps the illness from being categorized as an oxidative disease; therefore, antioxidant therapy cannot be advised as a preventative measure or to stop or slow the progression of the illness. The oxidizing agent must be present and detectable at the damage site; there must be a logical relationship between the oxidant's generation and the damage; the damage must be lessened or eliminated when the oxidizing agent is removed; and antioxidants must be able to mitigate the damage in order for the association to be established. The mechanisms of oxidative damage, the involvement of pro-oxidant agents, the development, persistence, and characteristics of oxidative stress and the antioxidant response, as well as the advantages of using various schemes and agents to establish antioxidant therapies and obtain, if applicable, the therapeutic and diagnostic recommendation protocols, are all still being investigated for a number of diseases that are in the exploration phase to determine whether or not they are oxidative diseases (Roy, B. 2025; Płóciniczak, A. *et al*., 2025).

In our study, we collected 50 people with diabetes who participated in this study using a convenience sampling method. In addition, the control group consisting of healthy participants, age- and sex-matched, who did not suffer from diabetes or other chronic diseases, was recruited for serving the baseline values for oxidative stress markers in addition to Estimation for the sample size was also carried out using the expected variances for malondialdehyde (MDA) values considering the preliminary data and previously available literature for the assurance on statistical power for detecting the significant differences further more were The data collection process comprised demographic variables, clinical profile, duration of diabetes, treatment strategies, and laboratory parameters also Age, gender, marital status, educational level, duration of diabetes, and age on diagnosis of diabetes were obtained through structured

Publisher: SARC Publisher

interviews with the help of patient medical records. Information regarding the presence of symptoms at the time of diagnosis and diagnostic procedures used, for instance, Glucose Tolerance Test (GTT) or HbA1c estimations, was noted in a systematic fashion.

As per the treatment, the information on the used oral hypoglycemic drug (OHD), the type and dosage of insulin used, and the rate of monitoring the HbA1c over the past 1 year were received, and it showed the clinical management plan, along with the current status of glycaemic control of the patient. Malondialdehyde (MDA) was the main oxidative-stress biomarker that was measured, a known end-product of lipid peroxidation, and an indicator of oxidative cell membrane damage. The blood was collected after an overnight fast and separated and stored at -20 o C, awaiting assay. Thio barbituric acid reactive substances (TBARS) method was used to measure MDA concentrations with the use of standardised protocols to provide reproducibility and precision. To measure the level of oxidative stress level in diabetes, the MDA levels in diabetic patients were compared with the of normal controls. The assay specificity and sensitivity were checked by having the inclusion of corresponding controls and calibration standards of each analytical batch.

Statistical Analysis

Descriptive statistics were created both on demographic and clinical variables, including means and standard deviations of the continuous variables and frequencies with percentages of the categorical data.

The use of an independent t-test to perform a comparative analysis of the MDA levels of diabetic patients and normal controls indicates that the data is parametric.

The effect size was calculated using Cohen 3 -D, which consequently depicted the size of the differences that were observed among the groups.

Mathematical analysis. The correlation between MDA levels and clinical parameters (glycaemia (HbA1c), age at diagnosis, disease duration, and symptoms at diagnosis) was analyzed by the use of the correlation coefficient.

This method helped to find the possible correlations between oxidative-stress load and disease development or complications.

All the statistical tests were done in SPSS, and the results with p less than 0.05 were considered as significant.

RESULTS

Table 1- Assessment outcomes of patients according to Demographic Characteristics

Parameter	**Category**	**F**	**P%**	**M±SD**
Age (years)	-	-	-	53.1 ± 9.9
Sex Distribution	M	23	46.0	-
	F	27	54.0	-
Marital Status	Married	38	76.0	-
	Widowed	10	20.0	-
	Divorced	1	2.0	-
	Single	1	2.0	-
Education Level	6 primary schools	13	26.0	-
	Illiterate	8	16.0	-
	6 high schools	6	12.0	-
	2 institute	5	10.0	-
	3 high schools	5	10.0	-
	4th college	4	8.0	-
	5 primary schools	4	8.0	-
	Other levels	5	10.0	-
Duration of DM	5 years	12	24.0	-
	1-4 years	9	18.0	-
	6-10 years	11	22.0	-
	>10 years	16	32.0	-
	First visit	2	4.0	-
Age at Diagnosis	-	-	-	46.7 ± 10.5

Publisher: SARC Publisher

Table 2- Rate of Symptoms and Complications at Diagnosis and Diagnostic Methods

Symptom/Complication	Frequency (n)	Percentage (%)
Polyuria (alone)	21	42.0
Polyuria + thirst + dry mouth	6	12.0
Polyuria + fatigue	3	6.0
Fatigue + dizziness	3	6.0
Gestational DM	2	4.0
Other combinations	15	30.0
Diagnostic Method	**Frequency (n)**	**Percentage (%)**
Glucose Tolerance Test (GTT)	45	90.0
HbA1c	5	10.0

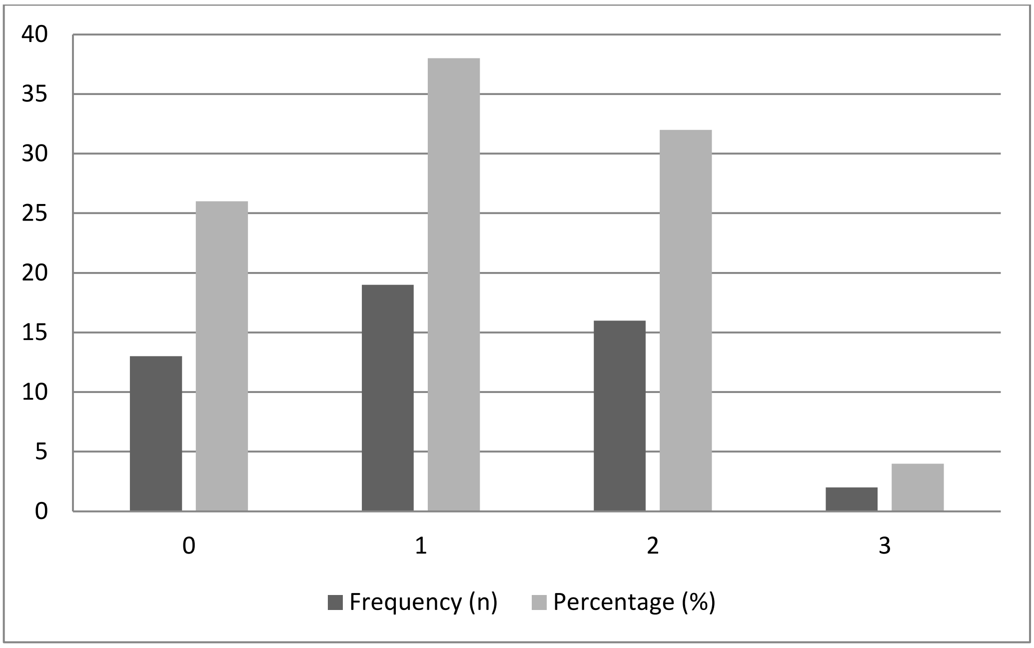

Figure 1- Distribution of patients according to the Number of Oral Hypoglycemic Drug (OHD) Items

Table 3- Evaluate Outcomes of Relationship Between Insulin Type and Insulin Dose

Insulin Type	Number of Patients	Mean Dose ± SD (units/day)
No insulin (0)	34	0.0 ± 0.0
Insulin mixtard	13	55.0 ± 21.5
Insulin soluble	1	20.0 ± 0.0
Insulin glargine	1	30.0 ± 0.0
Insulin lente	1	16.0 ± 0.0

Table 4 – Find value of HbA1c Monitoring

Monitoring Frequency per Year	Number of Patients	Percentage (%)
0 times	34	68.0
1 time	6	12.0
2 times	4	8.0
3 times	1	2.0
4 times	5	10.0
HbA1c >7% Last Year Status	**Number of Patients**	**Percentage (%)**
No monitoring (0)	34	68.0
Yes	12	24.0
Unknown	2	4.0
No	2	4.0
Statistic	**Value**	
Mean HbA1c ± SD (decimal)	0.1 ± 0.0	

Publisher: SARC Publisher

Range of values	0.071 - 0.12	

Table 5- Outcomes of patients according to MDA (Malondialdehyde) Levels - Oxidative Stress Marker

Group	MDA Level (µmol/L) Mean ± SD
Diabetes Patients	3.20 ± 0.57
Healthy Controls	1.70 ± 0.35
Difference	1.50 µmol/L
Effect Size	3.20 (Cohen's d)

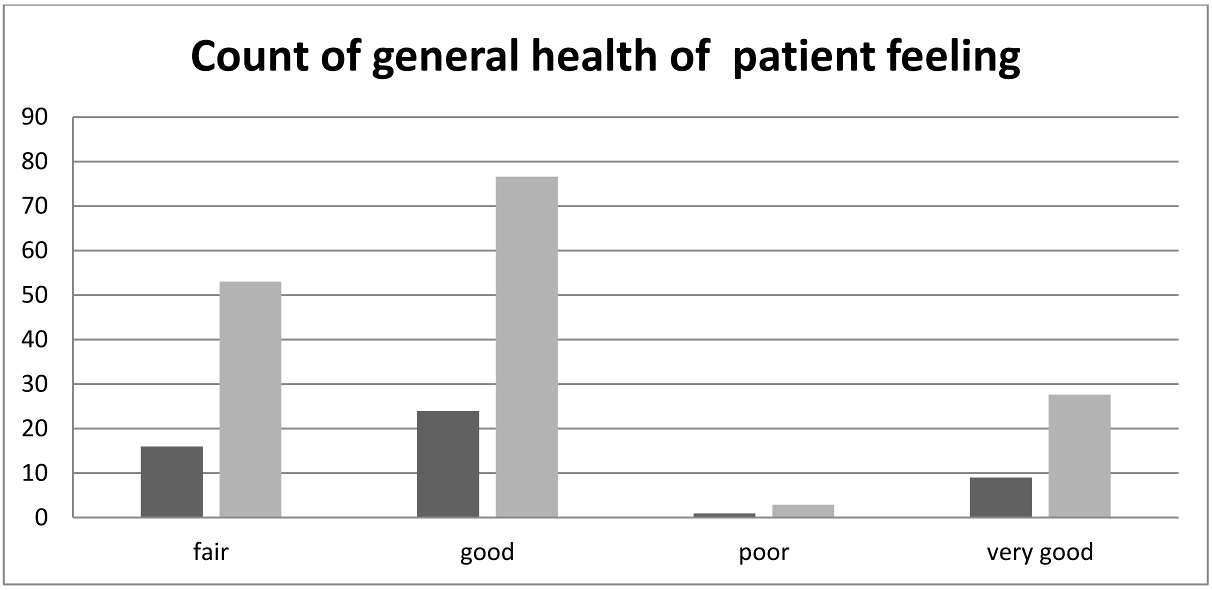

Figure 2- Correlation between the general health of the patient's feelings and MDA.

DISCUSSION

The study population demographic is of a typical middle-aged population with a mean age of about 53 years (SD 9.9), hence it fits well into the age bracket within which type 2 diabetes mellitus (T2DM) is commonest. There is a balance in the sex distribution (some populations have a slight imbalance towards females, 54) or reflecting increased use of healthcare services or a difference in disease prevalence; in our current study, the preponderance of married patients (76) also has the potential to affect social support mechanisms that are crucial in managing chronic diseases.

Education levels are unevenly distributed among the cohort, with a large proportion (42%) having no more than a primary school education, which can affect health literacy and self-management skills. The mean duration of diabetes in the entire population of patients is diverse, with 32 percent of the patients experiencing the condition for over ten years, hence giving a considerable time to develop chronic complications. The average age of diagnosis is approximately 47 years, which is in line with the normal adult-onset of T2DM.

Polyuria, a typical symptom of hyperglycaemia (an osmotic diuresis), is the most frequent symptom as it occurs by itself in 42100 of patients and is accompanied by thirst and dry mouth in another 12100 of patients (see Table 2). Fatigue and dizziness are also mentioned, which could indicate an underlying metabolic imbalance, either hyperglycaemia or hypoglycaemia.

Diagnostic assessment proves that most of the participants (90 %) were diagnosed with the help of the Glucose Tolerance Test (GTT), and only a small fraction (10 %) of participants were diagnosed using the HbA1c, which is a more convenient test and reflects longer-term glycaemic control.

In terms of pharmacologic management, 74 percent of the patients were taking one or more oral hypoglycaemic drugs (OHDs), with mean of 1.1 drugs per patient and a range of 0 to 3; such distribution implies many patients were at the moderate stage of the disease, where most of the treatment is done by oral agents (metformin or sulfonylureas), which is consistent with current treatment guidelines. On the other hand, 26 percent were not taking any oral drugs, which could be a

Publisher: SARC Publisher

new case of the disease, which can be managed with lifestyle changes only, or those who have converted to using insulin.

With regards to insulin treatment, about 68 percent of patients did not use insulin, and this is in line with the general treatment of T2DM, where insulin is only used when the disease is at an advanced stage or when it is uncontrolled. Among insulin users, premixed insulin (Mixtard) was taken by a majority of the patients with a mean of 55 insulin units per day, which is expected of patients with moderate to severe deficiency of insulin.

The glycaemic surveillance, through HbA1c was unsatisfactory in this cohort; 68% were missing HbA1c measurement within the previous year and this is a worrying factor since frequent HbA1c examination is a standard care that should guide treatment, and forecast the risk of complication occurrence where This is probably a consequence of poor monitoring, exemplified by 24 -percent of patients having last-year HbA1c above 70%, which is generally regarded as a sign of poor glycaemic control and higher risks of complications. The reported mean value of HbA1c seems to be abnormally low (0.1 in decimal units, which may be a data entry or a rounding error), but the high percentage with higher values indicates a clear necessity of better surveillance.

The occurrence of oxidative stress, which is a well-known pathogenic process in diabetes complications, was measured using the levels of malondialdehyde (MDA), which is an indicator of lipid peroxidation and oxidative damage. The level of MDA was significantly higher in patients with diabetes (mean 3.20 ug/L +-0.57) than that in healthy individuals (mean 1.70 ug/L +-0.35), and the difference (1.50 ug/L) was significant with a very large effect size (Cohen d=3.20). This observation confirms the large oxidative stress load in diabetic patients, which is one of the determinants that have been identified to initiate and accelerate micro- and macro-vascular complications. High oxidative stress triggers cellular damage through the destruction of lipids, proteins, and DNA, therefore leading to endothelial dysfunction, inflammation, and consequent diabetic complications as well as Approximately half of cardiovascular disease is commonly recognized to be linked with hypoglycaemia as well as hyperglycaemia, regardless of whether it is persistent and chronic or not. Hypoglycaemias are also an established side effect of the process of diabetes management, particularly when insulin or a particular oral hypoglycaemic medication is used.

CONCLUSION

The data provides the evidence on a cohort of middle-aged individuals with diabetes with different durations of the disease and a range of therapeutic interventions reflecting the factual aspects of diabetes treatment in the world, as cited in the literature. It highlights the existing challenges relating to in optimal monitoring and control of glycaemic conditions. Also, it highlights the central role of the oxidative stress in the pathophysiology of diabetes, including significantly increased malondialdehyde levels. These findings support the clinical potential of mitigative interventions that would counter oxidative harm, which would prevent or delay the development of diabetic complications.

REFERENCES

1. Magliano, D. J., Boyko, E. J., & Atlas, I. D. "COVID-19 and diabetes." *IDF DIABETES ATLAS [Internet]. 10th edition*. International Diabetes Federation (2021).
2. Ceriello, A. "Oxidative stress and diabetes-associated complications." *Endocrine Practice* 12 (2006): 60-62.
3. Forbes, J. M., & Cooper, M. E. "Mechanisms of diabetic complications." *Physiological reviews* 93.1 (2013): 137-188.
4. Manna, I., Das, D., Mondal, S., & Bandyopadhyay, M. "Use of nanoparticles in the delivery of plant-based therapeutics." *Advances in phytonanotechnology for the treatment of various diseases*. CRC Press, (2023): 67-126.
5. Fatima Rehman, F., Fatima, E., Fatima, H. S., & Naz, L. "The Interplay of Mitochondrial Dysfunction and Oxidative Stress in the Development of Chronic Diseases in Humans."
6. Caturano, A., Rocco, M., Tagliaferri, G., Piacevole, A., Nilo, D., Di Lorenzo, G., ... & Sasso, F. C. "Oxidative stress and cardiovascular complications in type 2 diabetes: from pathophysiology to lifestyle modifications." *Antioxidants* 14.1 (2025): 72.
7. Manna, I., Das, D., Mondal, S., & Bandyopadhyay, M. "Use of nanoparticles in the delivery of plant-based therapeutics." *Advances in phytonanotechnology for the treatment of various diseases*. CRC Press, (2023): 67-126.

Publisher: SARC Publisher

8. Al Khuzaee, M. F., El Nobey, M. A., El Hamidy, S. M., Al Hunduwan, K., & Al Harthi, A. A. "Synergistic Effects of Green-Synthesized Silver Nanoparticles and Moringa oleifera on Lipid and Renal Function in Diabetic Rats." *Egyptian Academic Journal of Biological Sciences, D. Histology & Histochemistry* 17.1 (2025): 33-45.
9. Cecerska-Heryć, E., Engwert, W., Michałów, J., Marciniak, J., Birger, R., Serwin, N., ... & Dołęgowska, B. "Oxidative stress markers and inflammation in type 1 and 2 diabetes are affected by BMI, treatment type, and complications." *Scientific Reports* 15.1 (2025): 23605.
10. Chen, X., Xie, N., Feng, L., Huang, Y., Wu, Y., Zhu, H., ... & Zhang, Y. "Oxidative stress in diabetes mellitus and its complications: From pathophysiology to therapeutic strategies." *Chinese Medical Journal* 138.1 (2025): 15-27.
11. Roy, B. "Pathophysiological mechanisms of diabetes-induced macrovascular and microvascular complications: the role of oxidative stress." *Medical Sciences* 13.3 (2025): 87.
12. Płóciniczak, A., Bukowska-Olech, E., & Wysocka, E. "The Complexity of Oxidative Stress in Human Age-Related Diseases—A Review." *Metabolites* 15.7 (2025): 479.
13. Chung, S. S., Ho, E. C., Lam, K. S., & Chung, S. K. "Contribution of polyol pathway to diabetes-induced oxidative stress." *Journal of the American Society of Nephrology* 14.suppl_3 (2003): S233-S236.
14. Zhang, Z., Apse, K., Pang, J., & Stanton, R. C. "High glucose inhibits glucose-6-phosphate dehydrogenase via cAMP in aortic endothelial cells." *Journal of Biological Chemistry* 275.51 (2000): 40042-40047.
15. Ii, S., Ohta, M., Kudo, E., Yamaoka, T., Tachikawa, T., Moritani, M., ... & Yoshimoto, K. "Redox state-dependent and sorbitol accumulation-independent diabetic albuminuria in mice with transgene-derived human aldose reductase and sorbitol dehydrogenase deficiency." *Diabetologia* 47.3 (2004): 541-548.
16. Bohren, K. M., Grimshaw, C. E., & Gabbay, K. H. "Catalytic effectiveness of human aldose reductase. Critical role of C-terminal domain." *Journal of Biological Chemistry* 267.29 (1992): 20965-20970.
17. Zhang, J. Z., Gao, L., Widness, M., Xi, X., & Kern, T. S. "Captopril inhibits glucose accumulation in retinal cells in diabetes." *Investigative ophthalmology & visual science* 44.9 (2003): 4001-4005.
18. Reznick, A. Z., Kagan, V. E., Ramsey, R., Tsuchiya, M., Khwaja, S., Serbinova, E. A., & Packer, L. "Antiradical effects in L-propionyl carnitine protection of the heart against ischemia-reperfusion injury: the possible role of iron chelation." *Archives of biochemistry and biophysics* 296.2 (1992): 394-401.
19. Bunn, H. F., & Higgins, P. J. "Reaction of monosaccharides with proteins: possible evolutionary significance." *Science* 213.4504 (1981): 222-224.0

Source of support: Nil; **Conflict of interest:** Nil.

Cite this article as:
Abid, R. M. and Fendi, M. T. " Relationship between Oxidative Stress and Diabetes Mellitus Complications." *Sarcouncil Journal of Medicine and Surgery* 4.9 (2025): pp 1-7.

Publisher: SARC Publisher