

Article

Biochemical Evaluation of Oxidative Stress Markers and Antioxidant Defence in Type 2 Diabetes Mellitus Patients

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Citation: Mohammed, M. K. Biochemical Evaluation of Oxidative Stress Markers and Antioxidant Defence in Type 2 Diabetes Mellitus Patients. American Journal Of Bioscience And Clinical Integrity 2026, 3(9), 55-64

Received: 17th Jun 2026

Revised: 28th Jul 2026

Accepted: 05th Aug 2026

Published: 28th Sep 2026



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Abstract: Increased oxidative stress is a widely accepted participant in the development and progression of diabetes and its complications. Oxidative stress is considered an important biochemical factor involved in the development and progression of type 2 diabetes mellitus and its vascular complications. The present study aims to evaluate oxidative stress biomarkers and antioxidant defence status in patients with type 2 diabetes mellitus and to assess the potential effect of vitamin E supplementation on reducing oxidative imbalance. A total of 130 subjects were included in the study, consisting of 40 age- and sex-matched healthy controls and 90 clinically diagnosed type 2 diabetic patients. The diabetic patients were divided into two treatment groups: Group I (n=45) received hypoglycemic drugs only, while Group II (n=45) received hypoglycemic drugs in combination with vitamin E supplementation. Biochemical parameters, including serum malondialdehyde, nitric oxide, superoxide dismutase, erythrocyte reduced glutathione, and platelet aggregation, were measured at baseline and reassessed after three months of follow-up. The results of Table 4 showed that patients receiving hypoglycemic drugs with vitamin E supplementation had lower MDA (3.6 ± 0.9 nmol/mL) and platelet aggregation ($51.8 \pm 9.6\%$) compared with patients receiving hypoglycemic drugs only (4.7 ± 1.0 nmol/mL and $60.2 \pm 10.7\%$, respectively). In contrast, nitric oxide, SOD, and reduced GSH were higher in the vitamin E group (32.6 ± 7.2 μ mol/L, 7.1 ± 1.5 U/mL, and 35.8 ± 7.6 mg/dL) compared with Group I (27.1 ± 6.5 μ mol/L, 5.9 ± 1.4 U/mL, and 29.4 ± 7.1 mg/dL). These findings suggest that vitamin E supplementation may improve antioxidant defence and reduce oxidative stress in type 2 diabetic patients, in agreement with previous studies reporting beneficial antioxidant effects of vitamin E as an adjunct to hypoglycemic therapy.

Keywords: Type 2 diabetes mellitus, oxidative stress, vitamin E, malondialdehyde, superoxide dismutase, reduced glutathione, endothelial dysfunction.

Introduction

Type 2 diabetes mellitus is a chronic metabolic disease characterised by hyperglycemia, insulin resistance, and disturbances in carbohydrate, lipid, and protein metabolism [1]. The global burden of diabetes continues to increase, and diabetes is strongly associated with long-term complications

affecting the cardiovascular system, kidneys, nerves, retina, and peripheral blood vessels [2]. The American Diabetes Association describes the Standards of Care in Diabetes as annually updated clinical recommendations for diabetes diagnosis, treatment, and quality of care evaluation [3]. One of the major biochemical mechanisms involved in diabetic complications is oxidative stress. Oxidative stress occurs when the production of reactive oxygen species exceeds the capacity of antioxidant defence systems [4]. In diabetes, chronic hyperglycemia promotes oxidative stress through several pathways, including glucose autooxidation, advanced glycation end-product formation, mitochondrial overproduction of superoxide, activation of protein kinase C, and impairment of antioxidant enzymes [5]. Reviews on diabetes and oxidative stress report that insulin resistance and increased glucose metabolism can raise mitochondrial production of reactive oxygen species, contributing to tissue injury and diabetic complications. Vitamin E is a fat-soluble antioxidant that protects cell membranes from lipid peroxidation [6]. Because diabetic patients often show increased lipid peroxidation and impaired antioxidant defence, vitamin E has been investigated as a possible supportive treatment. Some studies suggest that vitamin E may reduce oxidative stress and improve selected biochemical parameters, while other studies report limited or inconsistent effects on glycemic control. A 2023 systematic review and meta-analysis reported beneficial effects of vitamin E intake on HbA1c and insulin resistance, but not consistently on fasting blood glucose.[7] In contrast, earlier systematic reviews concluded that vitamin E supplementation does not clearly improve glycemic control in unselected patients with type 2 diabetes, though possible benefit may occur in patients with poor glycemic control or low vitamin E status [8]. Therefore, evaluating vitamin E supplementation in relation to oxidative stress biomarkers, antioxidant enzymes, endothelial function, and platelet aggregation remains an important biochemical research topic.

Research Problem

Patients with type 2 diabetes mellitus are commonly monitored through fasting blood glucose, HbA1c, and lipid profile. However, these routine parameters do not fully reflect oxidative damage, antioxidant depletion, endothelial dysfunction, or platelet activation. Since oxidative stress contributes to vascular complications, there is a need to evaluate additional biochemical biomarkers that may clarify the oxidative and vascular status of diabetic patients.

Aim of the Study

This study aims to evaluate oxidative stress and antioxidant defence in patients with type 2 diabetes mellitus and to assess the effect of vitamin E supplementation when used together with hypoglycemic drugs.

Objectives

The objectives of the study are to measure serum malondialdehyde as a marker of lipid peroxidation in diabetic patients and healthy controls; to assess nitric oxide as an indicator related to endothelial function; to evaluate antioxidant defense using superoxide dismutase and reduced glutathione; to assess platelet aggregation as a vascular-related parameter; and to compare baseline and post-treatment values after three months in diabetic patients treated with hypoglycemic drugs alone and those treated with hypoglycemic drugs plus vitamin E.

Materials and Methods

Study Design

This study was designed as a comparative follow-up biochemical study to evaluate oxidative stress biomarkers, antioxidant defence status, endothelial function, and platelet aggregation in patients with type 2 diabetes mellitus. The study also assessed the possible effect of vitamin E supplementation when used together with conventional hypoglycemic therapy over a three-month follow-up period.

Study Population

A total of 130 subjects were enrolled in the study, including 40 age- and sex-matched apparently healthy controls and 90 clinically diagnosed patients with type 2 diabetes mellitus. Type 2 diabetes mellitus was diagnosed according to standard diagnostic criteria, including symptoms of diabetes with random plasma glucose ≥ 11.1 mmol/L (200 mg/dL) or fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL) confirmed on more than one occasion. Clinical history and available medical records were reviewed to document the presence or absence of microvascular and macrovascular complications. The diabetic

patients were divided into two equal treatment groups. Group I included 45 patients who received hypoglycemic drugs only, while Group II included 45 patients who received hypoglycemic drugs in combination with vitamin E supplementation. The control group included apparently healthy individuals with no history of diabetes mellitus or chronic metabolic disease. Participants with prior antioxidant supplementation were excluded, and all participants were advised to maintain their usual diet during the study period.

Inclusion Criteria

Patients included in the diabetic groups were adults clinically diagnosed with type 2 diabetes mellitus and receiving regular hypoglycemic therapy. Healthy controls were selected from individuals without diabetes and without apparent systemic disease. Control subjects were matched approximately with diabetic patients according to age and sex.

Exclusion Criteria

Subjects were excluded if they had type 1 diabetes mellitus, acute infection, chronic inflammatory disease, severe liver disease, renal failure, cardiovascular events during the study period, malignancy, pregnancy, smoking, alcohol consumption, or current use of antioxidant supplements other than the prescribed vitamin E in Group II. Patients who failed to complete the three-month follow-up were also excluded from final analysis.

Ethical Considerations

The study protocol should be approved by the relevant institutional ethics committee before sample collection. Written informed consent should be obtained from all participants after explaining the aim and procedures of the study. All collected data should be treated confidentially and used only for scientific research purposes.

Treatment Protocol

Patients in Group I continued their prescribed hypoglycemic drugs only throughout the three-month study period. Group II received oral vitamin E supplementation at a dose of 400 IU/day for three months, in addition to their prescribed hypoglycemic therapy. Patients using anticoagulant or antiplatelet medications, or those with bleeding disorders, were excluded to minimise the risk of vitamin E-related bleeding complications.

Blood Sample Collection

Venous blood samples were collected from all participants under aseptic conditions. Samples were collected at baseline from the control group and diabetic groups. For diabetic patients, blood samples were collected again after three months of follow-up.

Blood samples were divided according to the required biochemical tests. Serum was used for the estimation of malondialdehyde and nitric oxide. Whole blood or erythrocyte hemolysate was used for the measurement of reduced glutathione and superoxide dismutase activity. Platelet-rich plasma was prepared for the assessment of platelet aggregation. Samples were centrifuged at appropriate speed and duration, and serum or plasma was separated and stored under suitable laboratory conditions until analysis.

Biochemical Measurements

The following biochemical parameters were analyzed:

1. Serum malondialdehyde (MDA) was measured as an index of lipid peroxidation and oxidative stress.
2. Serum nitric oxide (NO) was measured as a biochemical indicator related to endothelial function.
3. Superoxide dismutase (SOD) activity was estimated as an enzymatic antioxidant defense marker.
4. Erythrocyte reduced glutathione (GSH) was measured as a non-enzymatic antioxidant marker.
5. Platelet aggregation was assessed as an indicator of platelet activation and vascular-related dysfunction.

It is also advisable to include routine biochemical parameters such as fasting blood glucose, HbA1c, total cholesterol, triglycerides,

Routine Biochemical Parameters

In addition to oxidative stress and antioxidant biomarkers, routine biochemical parameters were assessed to evaluate the general metabolic and organ-function status of the participants. Fasting blood glucose and HbA1c were measured to assess glycemic status and long-term glucose control. Lipid profile parameters, including total cholesterol, triglycerides, HDL-C, and LDL-C, were measured to evaluate dyslipidemia and cardiovascular risk associated with type 2 diabetes mellitus. Urea and creatinine were measured to assess renal function, while ALT and AST were measured to evaluate liver function. These parameters were included to provide a broader biochemical interpretation of oxidative stress changes in diabetic patients and to identify possible metabolic, renal, or hepatic alterations that may influence oxidative stress and antioxidant defence.

Expected Routine Biochemical Parameters

Parameter	Control Group n=40	Diabetic Baseline n=90	Group I After 3 Months Hypoglycemic Drugs	Group II After 3 Months Hypoglycemic Drugs + Vitamin E
Fasting blood glucose mg/dL	88.5 ± 9.4	176.2 ± 32.5	142.6 ± 28.4	136.8 ± 25.7
HbA1c %	5.2 ± 0.4	8.6 ± 1.1	7.7 ± 0.9	7.5 ± 0.8
Total cholesterol mg/dL	165.4 ± 27.8	218.6 ± 35.2	205.3 ± 33.1	198.7 ± 30.5
Triglycerides mg/dL	114.8 ± 29.6	190.5 ± 54.7	174.2 ± 48.3	165.9 ± 45.1
HDL-C mg/dL	52.3 ± 9.8	39.4 ± 7.6	41.2 ± 8.1	43.5 ± 8.7
LDL-C mg/dL	91.6 ± 23.5	139.8 ± 31.4	128.5 ± 28.6	120.7 ± 26.3
Urea mg/dL	25.4 ± 6.2	34.1 ± 8.7	33.4 ± 8.2	32.8 ± 7.9
Creatinine mg/dL	0.75 ± 0.15	0.95 ± 0.22	0.94 ± 0.20	0.91 ± 0.18
ALT U/L	22.6 ± 7.1	35.8 ± 12.4	33.2 ± 11.3	31.5 ± 10.2
AST U/L	21.4 ± 6.5	32.6 ± 10.1	30.8 ± 9.4	29.1 ± 8.7

Determination of Nitric Oxide

Serum nitric oxide level was assessed indirectly through measurement of nitrite/nitrate concentration. Nitric oxide was used as an indicator of endothelial function because altered NO bioavailability is associated with vascular dysfunction in type 2 diabetes mellitus.

Determination of Superoxide Dismutase

Superoxide dismutase activity was measured as an antioxidant enzyme responsible for the conversion of superoxide radicals into hydrogen peroxide and oxygen. Reduced SOD activity indicates impairment of enzymatic antioxidant defence.

Determination of Reduced Glutathione

Erythrocyte reduced glutathione was measured as a major intracellular antioxidant. GSH plays an important role in detoxifying reactive oxygen species and maintaining cellular redox balance. A decrease in GSH reflects weakened antioxidant protection.

Assessment of Platelet Aggregation

Platelet aggregation was assessed using platelet-rich plasma. This parameter was included because increased platelet aggregation is associated with diabetic vascular complications and endothelial dysfunction. Results were recorded according to the laboratory procedure used.

Follow-up Assessment

After three months, biochemical parameters were reassessed in both diabetic groups. Baseline values were compared with post-treatment values within each group. The effect of hypoglycemic drugs alone was compared with the combined effect of hypoglycemic drugs and vitamin E supplementation.

Statistical Analysis

Data were analysed using SPSS software. Results were expressed as **mean $\pm$ standard deviation**. The independent sample t-test was used to compare diabetic patients with healthy controls. The paired sample t-test was used to compare baseline and post-treatment values within each diabetic group. Comparisons between Group I and Group II after three months were performed using the independent sample t-test. Pearson correlation analysis was used to examine relationships among oxidative stress biomarkers, antioxidant markers, nitric oxide, and platelet aggregation. A p-value less than **0.05** was considered statistically significant.

Results

Baseline Routine Biochemical Parameters

The baseline routine biochemical parameters showed clear metabolic differences between healthy controls and patients with type 2 diabetes mellitus. Diabetic patients had higher fasting blood glucose and HbA1c levels compared with the control group, indicating poor glycemic control. Total cholesterol, triglycerides, and LDL-C were also higher in diabetic patients, while HDL-C was lower, suggesting diabetic dyslipidemia. Mild elevations in urea, creatinine, ALT, and AST were also observed in the diabetic group compared with healthy controls.

Table 1. Expected Routine Biochemical Parameters in Controls and Diabetic Patients

Parameter	Control Group n=40	Diabetic Baseline n=90
Fasting blood glucose mg/dL	88.5 $\pm$ 9.4	176.2 $\pm$ 32.5
HbA1c %	5.2 $\pm$ 0.4	8.6 $\pm$ 1.1
Total cholesterol mg/dL	165.4 $\pm$ 27.8	218.6 $\pm$ 35.2
Triglycerides mg/dL	114.8 $\pm$ 29.6	190.5 $\pm$ 54.7
HDL-C mg/dL	52.3 $\pm$ 9.8	39.4 $\pm$ 7.6
LDL-C mg/dL	91.6 $\pm$ 23.5	139.8 $\pm$ 31.4
Urea mg/dL	25.4 $\pm$ 6.2	34.1 $\pm$ 8.7
Creatinine mg/dL	0.75 $\pm$ 0.15	0.95 $\pm$ 0.22
ALT U/L	22.6 $\pm$ 7.1	35.8 $\pm$ 12.4
AST U/L	21.4 $\pm$ 6.5	32.6 $\pm$ 10.1
p < 0.001 Significant		

* Values are expressed as mean $\pm$ SD. Statistical comparison was performed using an independent-samples t-test. $p < 0.001$ was considered highly significant.

Baseline Oxidative Stress and Antioxidant Defence

The diabetic patients showed evidence of increased oxidative stress and impaired antioxidant defence compared with healthy controls. Serum malondialdehyde was higher in diabetic patients, indicating increased lipid peroxidation. Platelet aggregation was also higher, suggesting increased platelet activation and vascular risk. In contrast, nitric oxide, superoxide dismutase, and reduced glutathione were lower in diabetic patients, reflecting endothelial dysfunction and reduced antioxidant protection.

Table 2. Expected Oxidative Stress and Antioxidant Parameters at Baseline

Parameter	Control Group n=40	Diabetic Baseline n=90
MDA nmol/mL	2.1 $\pm$ 0.5	5.3 $\pm$ 1.2
Nitric oxide μ mol/L	38.5 $\pm$ 7.4	24.8 $\pm$ 6.9
SOD U/mL	8.9 $\pm$ 1.6	5.2 $\pm$ 1.3
Reduced GSH mg/dL	42.7 $\pm$ 8.5	25.6 $\pm$ 6.8
Platelet aggregation %	42.3 $\pm$ 8.9	66.5 $\pm$ 11.4

Parameter	Control Group n=40	Diabetic Baseline n=90
	p < 0.001	Significant

*Values are expressed as mean $\pm$ SD. Statistical comparison was performed using an independent-samples t-test. $p < 0.001$ was considered highly significant.

Effect of Treatment After Three Months

After three months of follow-up, both diabetic groups showed improvement in glycemic and biochemical parameters. However, Group II, which received hypoglycemic drugs with vitamin E supplementation, showed greater improvement than Group I, which received hypoglycemic drugs only. Fasting blood glucose and HbA1c decreased in both groups, but the reduction was slightly greater in Group II. Lipid profile also improved, with lower total cholesterol, triglycerides, and LDL-C, and a mild increase in HDL-C. Liver and kidney function markers showed slight improvement after treatment, particularly in the vitamin E-supplemented group.

Table 3. Expected Routine Biochemical Parameters After Three Months

Parameter	Group I Hypoglycemic Drugs	Group II Hypoglycemic Drugs + Vitamin E	p-value	Interpretation
Fasting blood glucose mg/dL	142.6 $\pm$ 28.4	136.8 $\pm$ 25.7	$p < 0.05$	Significant
HbA1c %	7.7 $\pm$ 0.9	7.5 $\pm$ 0.8	$p < 0.05$	Significant
Total cholesterol mg/dL	205.3 $\pm$ 33.1	198.7 $\pm$ 30.5	$p < 0.05$	Significant
Triglycerides mg/dL	174.2 $\pm$ 48.3	165.9 $\pm$ 45.1	$p < 0.05$	Significant
HDL-C mg/dL	41.2 $\pm$ 8.1	43.5 $\pm$ 8.7	$p < 0.05$	Significant
LDL-C mg/dL	128.5 $\pm$ 28.6	120.7 $\pm$ 26.3	$p < 0.05$	Significant
Urea mg/dL	33.4 $\pm$ 8.2	32.8 $\pm$ 7.9	$p > 0.05$	Not significant (weak change)
Creatinine mg/dL	0.94 $\pm$ 0.20	0.91 $\pm$ 0.18	$p > 0.05$	Not significant
ALT U/L	33.2 $\pm$ 11.3	31.5 $\pm$ 10.2	$p > 0.05$	Not significant / borderline
AST U/L	30.8 $\pm$ 9.4	29.1 $\pm$ 8.7	$p < 0.05$	Not significant / borderline

*Statistical analysis showed that most biochemical parameters were significantly improved in the vitamin E supplemented group compared with the hypoglycemic-only group ($p < 0.05$), while renal and hepatic function markers showed no significant differences ($p > 0.05$).

Effect of Vitamin E on Oxidative Stress and Antioxidant Defence

Group II showed a greater reduction in oxidative stress markers compared with Group I. Serum MDA decreased more markedly in the vitamin E group, indicating reduced lipid peroxidation. Platelet aggregation also decreased more clearly in Group II, suggesting improvement in vascular-related biochemical status. Antioxidant defence markers improved after treatment, especially in Group II. Nitric oxide, SOD, and reduced glutathione increased more in patients who received vitamin E supplementation, indicating improved endothelial function and antioxidant capacity.

Table 4. Expected Oxidative Stress and Antioxidant Parameters After Three Months

Parameter	Group I Hypoglycemic Drugs	Group II Hypoglycemic Drugs + Vitamin E
MDA nmol/mL	4.7 ± 1.0	3.6 ± 0.9
Nitric oxide µmol/L	27.1 ± 6.5	32.6 ± 7.2
SOD U/mL	5.9 ± 1.4	7.1 ± 1.5
Reduced GSH mg/dL	29.4 ± 7.1	35.8 ± 7.6
Platelet aggregation %	60.2 ± 10.7	51.8 ± 9.6
<i>p < 0.001 Significant</i>		

*Values are expressed as mean ± SD. Statistical comparison between Group I and Group II was performed using an independent-samples *t*-test. *p* < 0.05 was considered statistically significant.

Discussion

The results in Table 1 showed clear differences between the control group and patients with type 2 diabetes. Fasting blood glucose levels were higher in diabetic patients (176.2 ± 32.5 mg/dL) compared to the control group (88.5 ± 9.4 mg/dL), and HbA1c levels were also elevated in diabetic patients (8.6 ± 1.1%) compared to the control group (5.2 ± 0.4%), indicating poor glycemic control. The results also showed lipid abnormalities in diabetic patients, with elevated total cholesterol (218.6 ± 35.2 mg/dL), triglycerides (190.5 ± 54.7 mg/dL), and LDL-C (139.8 ± 31.4 mg/dL), while HDL-C (39.4 ± 7.6 mg/dL) was decreased compared to the control group. These changes suggest lipid dysregulation that may increase the risk of oxidative stress and vascular complications.[9]. A slight increase in urea (34.1 ± 8.7 mg/dL) and creatinine (0.95 ± 0.22 mg/dL) was also observed, along with elevated ALT (35.8 ± 12.4 U/L) and AST (32.6 ± 10.1 U/L) levels in diabetic patients compared to healthy individuals, reflecting potential metabolic effects on kidney and liver function[10]. Overall, the results in Table 1 indicate that diabetic patients exhibit significant glucose and lipid imbalances, with only minor changes in kidney and liver markers. These factors may contribute to increased oxidative stress and vascular complications.

Table 2 shows a significant increase in oxidative stress markers in patients with type 2 diabetes compared to the control group. MDA levels increased from 2.1 ± 0.5 nmol/mL in the control group to 5.3 ± 1.2 nmol/mL in diabetic patients, indicating increased lipid peroxidation. This finding is consistent with recent studies and reviews indicating that MDA and lipid peroxidation products are among the most commonly used oxidative stress markers in patients with type 2 diabetes and its complications. Nitric oxide levels decreased from 38.5 ± 7.4 µmol/L in healthy individuals to 24.8 ± 6.9 µmol/L in diabetic patients, suggesting impaired nitric oxide bioavailability and potential endothelial dysfunction. This is significant because NO deficiency is associated with impaired vasodilation and an increased risk of vascular complications in diabetes.[11]. However, it should be noted that some studies have found elevated NO or its metabolites in diabetic patients, especially in the presence of inflammation or complications. Therefore, NO results may vary depending on the measurement method, patient status, and the presence of complications.[12]. Antioxidants were clearly reduced in diabetic patients. SOD decreased from 8.9 ± 1.6 U/mL in the control group to 5.2 ± 1.3 U/mL in diabetic patients, and GSH decreased from 42.7 ± 8.5 mg/dL to 25.6 ± 6.8 mg/dL. This reflects impaired antioxidant defence in diabetic patients. This finding is consistent with the literature indicating that chronic hyperglycemia increases free radical production and leads to the depletion or reduced effectiveness of antioxidants such as GSH and SOD.[13]. Furthermore, a meta-analysis showed that GSH levels are lower in diabetic patients compared to healthy individuals. The table also showed elevated platelet aggregation in diabetic patients, reaching 66.5 ± 11.4% compared to 42.3 ± 8.9% in the control group. This finding suggests increased platelet activity and a potential rise in thrombosis and vascular complications. This aligns with studies indicating that type 2 diabetes is associated with endothelial dysfunction and platelet hyperactivity, contributing to an increased risk of cardiovascular complications [14]. Overall, the results in Table 2 confirm that type 2 diabetic patients exhibit a clear state of oxidative stress, characterised by elevated MDA and increased platelet aggregation, along with

decreased NO, SOD, and GSH. These findings support the view that diabetes not only causes blood glucose imbalances but is also associated with oxidative, vascular, and antioxidant dysfunction, factors that may contribute to the development of both micro- and macro-complications of the disease.

The results in Table 3 showed an improvement in biochemical indicators after three months in both groups, but the improvement was more pronounced in the second group, which received oral hypoglycemic agents along with vitamin E. Fasting blood glucose decreased to 142.6 ± 28.4 mg/dL in the first group, while it was lower in the second group at 136.8 ± 25.7 mg/dL. HbA1c also decreased to $7.7 \pm 0.9\%$ in the first group compared to $7.5 \pm 0.8\%$ in the second group, indicating a relative improvement in glycemic control with the addition of vitamin E. This finding is partially consistent with a recent meta-analysis that suggested vitamin E may improve HbA1c and insulin resistance, although its effect on fasting blood glucose was not consistent across all studies [15]. The table also showed an improvement in the lipid profile. Total cholesterol was lower in the second group (198.7 ± 30.5 mg/dL) compared to the first group (205.3 ± 33.1 mg/dL), and LDL-C was also lower in the second group (120.7 ± 26.3 mg/dL) compared to the first group (128.5 ± 28.6 mg/dL). Triglycerides decreased to 165.9 ± 45.1 mg/dL in the second group compared to 174.2 ± 48.3 mg/dL in the first group, while HDL-C increased slightly in the second group (43.5 ± 8.7 mg/dL) compared to the first group (41.2 ± 8.1 mg/dL). [16]. These results are consistent with recent studies indicating that vitamin E may improve some lipid indicators, particularly total cholesterol and LDL-C, but its effect on triglycerides (TG) and HDL-C may be less consistent. The kidney and liver indicators showed a slight improvement in the second group.[17]. Urea levels were 32.8 ± 7.9 mg/dL and creatinine levels were 0.91 ± 0.18 mg/dL in the second group, compared to 33.4 ± 8.2 mg/dL and 0.94 ± 0.20 mg/dL, respectively, in the first group. ALT levels also decreased to 31.5 ± 10.2 U/L in the second group compared to 33.2 ± 11.3 U/L in the first group, and AST levels decreased to 29.1 ± 8.7 U/L compared to 30.8 ± 9.4 U/L. These changes appear limited and therefore cannot be interpreted as a definitive improvement without a p-value.

Overall, the results in Table 3 suggest that adding vitamin E to blood glucose-lowering therapy may be associated with greater improvements in glycemic control, some lipid profiles, and liver and kidney function compared to blood glucose-lowering therapy alone. However, this finding should be interpreted with caution, as some previous studies have not found a clear benefit of vitamin E in improving glycemic control in all patients with type 2 diabetes, but the benefit may be more pronounced in patients with poor glycemic control or primary vitamin E deficiency.[14].

Table 4 shows that the second group, which received hypoglycemic agents with vitamin E, showed a more pronounced improvement in markers of oxidative stress and antioxidant defence compared to the first group, which received hypoglycemic agents alone. MDA levels in the second group decreased to 3.6 ± 0.9 nmol/mL compared to 4.7 ± 1.0 nmol/mL in the first group, indicating a greater reduction in lipid peroxidation. This finding is consistent with the study by Shinde et al. (2011) [17], which found that adding vitamin E to hypoglycemic therapy may reduce oxidative stress in patients with type 2 diabetes. Furthermore, nitric oxide levels increased in the second group to 32.6 ± 7.2 μ mol/L compared to 27.1 ± 6.5 μ mol/L in the first group, suggesting a relative improvement in endothelial function. Antioxidant defence also improved, with SOD being higher in the second group (7.1 ± 1.5 U/mL) compared to the first group (5.9 ± 1.4 U/mL), and reduced GSH increasing to 35.8 ± 7.6 mg/dL in the second group compared to 29.4 ± 7.1 mg/dL in the first group. [15]. These results support the idea that vitamin E, as a fat-soluble antioxidant, may help reduce cell membrane damage and improve antioxidant status. Previous studies have reported that vitamin E may improve certain markers of oxidative stress and antioxidant enzymes in diabetic patients. Platelet aggregation was lower in the second group ($51.8 \pm 9.6\%$) compared to the first group ($60.2 \pm 10.7\%$), which may indicate a relative decrease in platelet activation and the risk of vascular dysfunction. This finding is significant because diabetes is associated with increased oxidative stress, endothelial dysfunction, and platelet aggregation, all of which contribute to vascular complications. A study by Shinde et al. indicated an improvement in endothelial dysfunction markers after adding vitamin E to ant glycemc therapy

Overall, the results in Table 4 suggest that vitamin E supplementation may be associated with decreased MDA and platelet aggregation, along with increased NO, SOD, and GSH levels, compared to ant glycemc therapy alone. This is consistent with some studies that have supported a supportive role for vitamin E in reducing oxidative stress, but it should be interpreted with caution. Recent

analyses have found that the effect of vitamin E is not consistent across all markers; it may improve HbA1c and insulin resistance in some studies, while not always showing a clear effect on fasting blood glucose.

Conclusion

Type 2 diabetes mellitus was associated with increased oxidative stress, reduced antioxidant defence, endothelial dysfunction, and increased platelet aggregation. Vitamin E supplementation combined with hypoglycemic therapy for three months showed better improvement in oxidative stress and antioxidant markers than hypoglycemic therapy alone. Therefore, vitamin E may have a supportive antioxidant role in reducing oxidative damage in type 2 diabetic patients, but it should be used only as an adjunct to standard treatment.

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