Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i7.7043

TO STUDY THE EFFECT OF VITAMIN-C AS AN ADDITIONAL THERAPY WITH ANTIDIABETIC DRUGS IN TYPE-2 DIABETES MELLITUS PATIENTS

Dr. Stuti Singh[1], Dr. Palash Ratna[2], Dr. Luv Arya[3], Dr. Nashra Afaq[4], Dr. Nusrat Nabi[5], Dr. Firoza Bano[6], Dr.Saif Anees[7*]

[1]Assistant Professor, Department of Pharmacology, Uma Nath Singh Autonomous State Medical College, Jaunpur, India.
[2]Assistant Professor, Department of Pharmacology, Uma Nath Singh Autonomous State Medical College, Jaunpur, India.
[3]Senior Resident, Department of Pharmacology, Uma Nath Singh Autonomous State Medical College, Jaunpur, India.
[4]Research Associate, Department of Microbiology and Central Research Laboratory, Rama Medical College Hospital and Research Centre, Uttar Pradesh, India.
[5]Associate Professor, Department of Pharmacology, HIMSR & HAHC Hospital, Jamia Hamdard, New Delhi, India.
[6]Associate Professor, Department of Community Medicine, Al-Falah School of Medical Sciences and Research Centre, Faridabad, Haryana.
[7*]Assistant Professor, Department of Community Medicine, Dr Bhim Rao Ramji Ambedkar Government Medical College, Kannauj, India.

***Corresponding Author:** Dr. Saif Anees
*Email ID: saif.anees@gmail.com

ABSTRACT

INTRODUCTION: Diabetes mellitus is a metabolic condition characterised by hyperglycemia, which is commonly coupled with oxidative stress. Aside from hyperglycemia, oxidative stress plays a significant role in diabetes and its consequences, including diabetic neuropathy, nephropathy, and retinopathy. Reducing oxidative stress may improve the outcome of diabetes patients. The current study was designed to investigate the effect of oral hypoglycemic agents (OHA) and vitamin C on oxidative stress, lipid profile, and glycemic control.

AIM AND OBJECTIVE: To study the effect of vitamin-c as an additional therapy with antidiabetic drugs in type-2 diabetes mellitus patients

MATERIAL AND METHODS: This was a prospective study carried out in the Department of Pharmacology for a period of 12 months i.e, April 2023 to April 2024 at a tertiary care Centre. A total of 100 type-II diabetes mellitus patients were studied and divided into four groups, Group-A (Glimepiride), Group-B (Glimepiride + Vitamin-C), Group-C (Metformin + Voglibose) and Group-D (Metformin+ Voglibose+ Vitamin-C). Glycemic control, lipid profile and oxidative stress were compared before and after 3 months of treatment in all the 4 groups. The Data was analyzed By using SPSS Software.

RESULTS: In the present study after three months, all the four groups had significant glycemic control ($p<0.001$), but only Groups B and D experienced significant reductions in oxidative stress ($p<0.001$). Groups B, C, and D showed significantly improved lipid control.

CONCLUSION: Vitamin-C supplementation in conjunction with OHA therapy improves glycemic control and lipid levels, and as an antioxidant, it decreases oxidative stress in diabetes mellitus patients.

KEYWORDS: Vitamin C, Antidiabetic drug, Diabetes mellitus, Glimepiride, Voglibose

INTRODUCTION

Diabetes mellitus is a multifactorial condition that affects the metabolism of carbs, proteins, and lipids, resulting in hyperglycemia. High blood glucose levels can be caused by β-cell malfunction or insulin resistance. Diabetes mellitus is a complex, chronic common endocrine metabolic disorder necessitating incessant medical care with multifactorial risk-reduction approaches beyond glycemic control. It results from defects in insulin secretion, action, or both and associated with many microvascular and macrovascular complications, especially in the two main classes: Type I and Type 2 diabetes mellitus. Diabetes is a major public health problem and one of four priority non-communicable diseases (NCDs) targeted for intervention by world health campaign and foundations [1].

Diabetes mellitus can be caused by a variety of risk factors, including advancing age, obesity, stress, dietary changes, and a lack of physical activity. Genetic factors and sedentary lifestyle play a significant influence in the development of Type II diabetes mellitus and its consequences, such as nephropathy, neuropathy, and retinopathy, which affect the vascular system, kidney, retina, and peripheral nerve in chronic cases [2-4].

Diabetes affects 415 million people worldwide and is projected to reach over 642 million by 2040. According to Indian statistics, the prevalence of diabetes in India is 8.7, with 69.2 million diabetic cases documented among adults [5]. The presence of classical symptoms, fasting blood sugar (FBS) >126 mg/dl, postprandial blood glucose (PPBS) >200 mg/dl, or random blood glucose level >200 mg/dl, and HbA1C >6.5% are all diagnostic criteria for diabetes mellitus. [6].
Diabetic complications are primarily associated with oxidative stress and high total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL), and low high density lipoprotein (HDL-C), so a healthy lipid profile and low oxidative stress can help to limit complications and their progression. Currently, there are various antidiabetic medications accessible, but the outcome is poor because these treatments have no significant effect on oxidative stress in diabetic patients [7]. Hence, development of novel strategies to improve the outcome will be of great benefit.
Free radicals are proposed to change lipid/protein ratio of membranes by affecting polyunsaturated fatty acids and lipid peroxidation, thus enhancing functional irregularities of several cellular organelles and structures. It has been suggested that increased free radicals and decline of antioxidant defense mechanisms play a major role in the pathogenesis as well as accelerate the development of clinical complications of both types of diabetes mellitus [4].

Diabetic individuals will have higher levels of free radicals and lower levels of antioxidants, especially vitamin C. Vitamin C is a natural antioxidant that plays an important role in the prevention of diabetic complications by scavenging free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), preventing the initiation of chain reactions that lead to protein glycation [8], and protecting against lipid peroxidation [8-10]. Vitamin C supplementation has been reported to significantly improve glycemic control, lipid profile, and cutaneous capillary permeability in Type II diabetes [11].
Consequently, antioxidant supplements have been proposed as the perspective treatment of diabetes. In addition, antioxidant supplements have been found to prevent the progression of diabetes and the occurrence of its complications. Vitamin C or L-ascorbic acid is the most abundant and effective antioxidant in the human body. It is a potent water-soluble antioxidant that scavenges

reactive oxygen species (ROS) and reactive nitrogen species (RNS), thus prevents the increased production of free radicals induced by oxidative damage to lipids and lipoproteins in various cellular compartments [11].

Therefore, the current study was undertaken to assess the positive effects of antioxidant supplementation (vitamin C) combined with OHA in patients with type 2 diabetes mellitus.

MATERIAL AND METHODS

This was a Prospective, randomized, study carried out in the Department of Pharmacology and General Medicine for a period of 12 months i.e, April 2023 to April 2024 at a tertiary care Centre. A total of 100 type-II diabetes mellitus patients were studied and divided in to four groups, Group-A (Glimepiride), Group-B (Glimepiride + Vitamin-C), Group-C (Metformin + Voglibose) and Group-D (Metformin+ Voglibose+ Vitamin-C). Glycemic control, lipid profile and oxidative stress were compared before and after 3 months of treatment in all the 4 groups.

INCLUSION CRITERIA

• Newly diagnosed type II diabetic patients.
• Patients between 30-50 years old, all sexes, and willing to provide informed feedback.

EXCLUSION CRITERIA

• Women who smoke, use alcohol, or are pregnant or lactating.
• Patients with type I diabetes mellitus.
• Patients with psychiatric, liver, kidney, and cardiac issues, as well as chronic illnesses such as tuberculosis, leprosy, recent trauma, or surgery.
• Hypersensitivity to vitamin C or any study medication.
• Unwilling to provide informed consent or unable to take the medications.

A total of 100 diagnosed type-II diabetes mellitus patients satisfying inclusion/exclusion criteria were enrolled for the study. At the beginning of the study demographic data along with patient past medical history was taken and followed by basic investigations for glycemic control (HbA1c, FBS and PPBS) lipid profile (TC, TG, HDL, LDL and VLDL) and oxidative stress (using TAC and MDA as parameters) were recorded. Based on the treatment plan, patients were divided in to 4 groups and treated them for 3 months as follows

Group-A: (n=35) patients were given Glimepiride (4mg/day)
Group-B: (n=30) patients received glimepiride (4 mg/day) + vitamin-C (1000mg/day)
Group-C: (n=20) patients were given Metformin (1000 mg/day) + voglibose (0.4 mg/day)
Group-D: (n=15) patients treated with Metformin (1000 mg/day) + voglibose (0.4 mg/day) + vitamin-C (1000 mg/day).
In the present study it had 6 follow-up's which were scheduled after every 15 days. At every follow-up general medical condition was assessed and investigations for glycemic control (FBS and PPBS) were done. Similarly lipid profile and oxidative stress was assessed along with glycemic control after commencement of the study for each subject.

Determination of biochemical parameters

The Blood glucose was calculated using the glucose oxidase and peroxidase enzymatic methods [12], whereas HbA1c was estimated using the ion exchange resin method [13]. Malondialdehyde (MDA) was measured using thiobarbituric acid reactive substances (TBARS), total antioxidant capacity was assessed using ferric reducing ability of plasma (FRAP), TC by Modified Roeschlau's Method [14], TG by Tinder Method [15], HDL by Phosphotungstic Acid Method [16], and LDL by Friedewald formula [17].

Data was analyzed By using SPSS Software. Patients were enrolled in the study as per following inclusion and exclusion criteria. The Ethical clearance was duly obtained before the start of the study.

RESULTS

In the present study there were 100 cases studied out of which the ratio of Males were more 62% as compared to the females 38% with the maximum age group of 41-50 being affected the most followed by 31-40 years of age and least was observed in 5% cases.

Table 1: Genderwise distribution of the cases

Genderwise	Number of Isolates	Percentage
Male	62	62%
Female	38	38%
Total	100	

Table 2: Agewise distribution of the cases

Agewise Distribution	No. of Isolates	Percentage
20-30	5	5%
31-40	30	30%
41-50	**50**	**50%**
51-60	15	15%

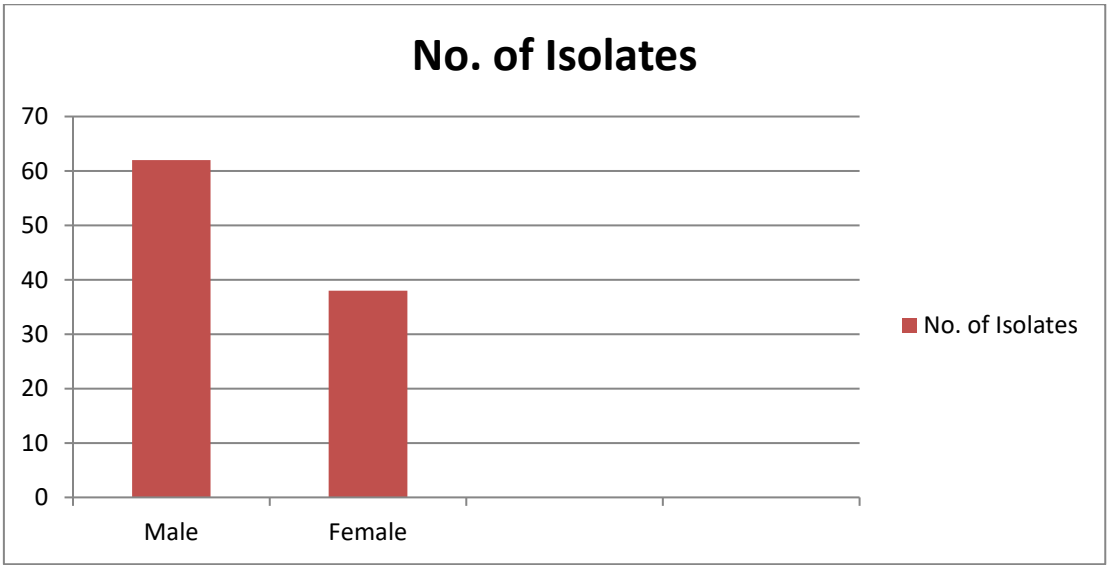


Table 3: Comparison of 3 months findings with baseline values in group-A

Variables	Baseline	3 months	Mean difference	p-Value
HbA1c (%)	6.7±0.1	6.3±0.30	42±0.42	0.001
FBS (Mg/dl)	146± 10.3	131.4± 7.41	15.58±5.7	0.001***
PPBS (Mg/dl)	231.6±16.7	210.5±14	21.08±9.4	0.001***
TAC (mmol/l)	0.85±0.1	0.78±0.14	0.06±0.28	0.06
MDA (mmol/l)	4.14±0.42	4.37±0.63	0.20±0.64	0.076
TC(Mg/dl)	173.9±23.76	167.9±33.77	4.97±46.68	0.527
TG(Mg/dl)	170.1±21.2	162.7±25.24	7.41±39.68	0.559
HDL(Mg/dl)	40.1±9.59	45.19±9.4	4.47±15.12	0.086
LDL(Mg/dl)	98.66±28.13	90.99±35.82	7.67 ± 50.92	0.373
VLDL(Mg/dl)	34.02±4.21	32.54±5.0	1.47±7.92	0.271

In the current study in group-A after 3 months of treatment, there was a significant reduction of FBS PPBS, HbA1c (p=0.000) and no significant reduction of TC (p= 0.527), TG (p=0.559), LDL (p=0.373), VLDL (p=0.271) and TAC (p=0.06) observed. Similarly elevation of HDL (p=0.086) and MDA (p=0.076) was observed but which is also not significant (Table 3).

Table 4: Comparison of 3 months findings with baseline values in group-B

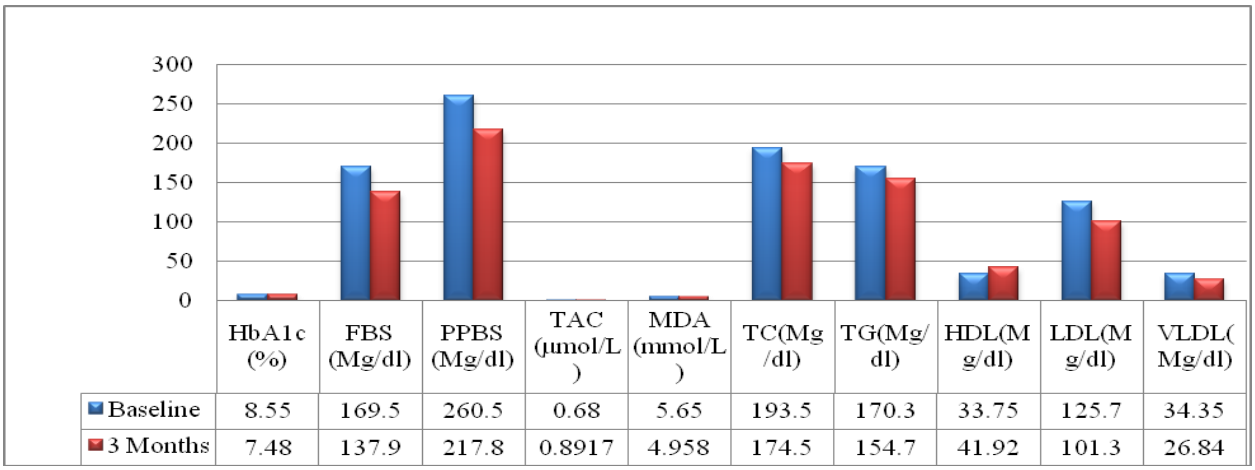
Variables	Baseline	3 months	Mean difference	p-Value
HbA1c (%)	7.5±5.1	6.3±0.30	0.7±0.42	0.001
FBS (Mg/dl)	147± 10.3	131.4± 7.41	20.8±5.7	0.001***
PPBS (Mg/dl)	231.6±16.8	210.5±14	28.09±9.4	0.001***
TAC (mmol/l)	0.84±0.1	0.78±0.14	0.1±0.24	0.060
MDA (mmol/l)	4.13±0.45	4.37±0.63	0.60±0.64	0.076
TC(Mg/dl)	172.9±23.77	167.9±33.77	10.2±46.68	0.527
TG(Mg/dl)	170.1±21.1	158.7±25.24	7.41±39.68	0.559
HDL(Mg/dl)	40.7±9.59	50.19±9.4	6.2±15.12	0.086
LDL(Mg/dl)	98.66±28.13	95.99±35.81	11.5 ± 50.92	0.372
VLDL(Mg/dl)	34.02±4.21	28.53±5.1	4.7±7.92	0.271

Table 5: Comparison of 3 months findings with baseline values in group-C

Variables	Baseline	3 months	Mean difference	p-Value
HbA1c (%)	8.14±0.28	7.25±0.27	0.89±0.13	0.001***
FBS (Mg/dl)	161.6±11.7	138.6±8.31	23±7.218	0.001***
PPBS (Mg/dl)	258.3±14.4	226.6±7.03	31.75±9.08	0.001***
TAC (mmol/l)	0.77±0.18	0.73±0.09	0.03±0.11	0.186
MDA (mmol/l)	0.77±0.18	5.66±0.97	0.39±0.92	0.074
TC(Mg/dl)	181.1±20.17	167±30.33	14.15±19.92	0.005**
TG(Mg/dl)	157.8±13.93	148.2±17.25	9.5±12.98	0.004**
HDL(Mg/dl)	39.45±4.67	45.2±7.53	5.75±7.77	0.005**
LDL(Mg/dl)	110.5±19.16	99.56± 28.8	10.96±18.39	0.017
VLDL(Mg/dl)	30±6.82	25.7±3.24	4.30±7.8	0.024**

Table 6: Comparison of 3 months findings with baseline values in group-D

Variables	Baseline	3 months	Mean difference	p-Value
HbA1c (%)	8.55±0.40	7.48±0.39	1.06±0.14	0.001***
FBS (Mg/dl)	169.5±8.59	137.9±4.81	31.58±7.48	0.001***
PPBS (Mg/dl)	260.5±12.57	217.8±11.54	42.75±15.97	0.001***
TAC (mmol/l)	0.68±0.12	0.89±0.26	0.20±0.28	0.029**
MDA (mmol/l)	5.65±0.78	4.95±0.87	0.7±0.93	0.025**
TC(Mg/dl)	193.5±16.62	174.5±15.33	19±14.56	0.001***
TG(Mg/dl)	170.3±13.38	154.7±16.52	15.67±4.90	0.001***
HDL(Mg/dl)	33.75±4.13	41.92±7.75	8.16±5.96	0.001***
LDL(Mg/dl)	125.7±17.36	101.3±15.43	24.35±19.92	0.001***
VLDL(Mg/dl)	34.35± 2.47	26.84 ± 5.81	7.50 ± 7.17	0.004***



	HbA1c (%)	FBS (Mg/dl)	PPBS (Mg/dl)	TAC (µmol/L)	MDA (mmol/L)	TC(Mg/dl)	TG(Mg/dl)	HDL(Mg/dl)	LDL(Mg/dl)	VLDL(Mg/dl)
Baseline	8.55	169.5	260.5	0.68	5.65	193.5	170.3	33.75	125.7	34.35
3 Months	7.48	137.9	217.8	0.8917	4.958	174.5	154.7	41.92	101.3	26.84

*Highly significant P<0.001***; Significant P<0.05***

It was observed that after 3 months of treatment with glimepiride+ vitamin C (Group-B), there was a significant reduction of FBS PPBS, HbA1c (p=0.000), MDA, TC, TG, LDL-C, VLDL(p<0.05) and significant elevation of TAC and HDL-C (p<0.05)observed (Table 4).

There was a significant reduction of FBS, PPBS, HbA1c (p=0.001), TC, TG, LDL, VLDL (p<0.05) and elevation of HDL (p<0.05) seen in group-C patients who were treated with Metformin + voglibose. Similarly reduction of TAC (p=0.186) and elevation of MDA (p=0.073) was seen but which is not statistically significant (Table 5).
In group-D after 3 month of treatment, there was a significant reduction of FBS, PPBS, HbA1c, TC, TG, LDL (p=0.001), MDA, VLDL (p<0.05) and significant elevation of HDL (p=0.001) and TAC (p<0.05) observed (Table-6).

DISCUSSION

Vitamin C, or L-ascorbic acid, is the most prevalent and potent antioxidant in the human body. It is a powerful water-soluble antioxidant that scavenges reactive oxygen species (ROS) and reactive nitrogen species (RNS), hence preventing the increased formation of free radicals caused by oxidative damage to lipids and lipoproteins in numerous cellular compartments [9]. Vitamin E, commonly known as α-tocopherol, is a lipid-soluble antioxidant that acts as a radical scavenger and inhibits lipoprotein lipid peroxidation [11]. This lipid-soluble chemical can easily pass cell membranes and exert effects both intracellularly and in membranes. It can also kill individual oxygen species and end free radical chain events. Several studies have found a reduction in vitamin C and/or vitamin
The present study aimed at studying the beneficial effect of vitamin-C after adding with oral hypoglycemic agents in type-II diabetes mellitus patients. Among 100 newly diagnosed type-II diabetes mellitus patients there are 62% males and 38% females. The maximum age group of 41-50 being affected the most followed by 31-40 years of age and least was observed in 5% cases.
There was another study by Bhatt et al. where the ratio of male was more as compared to the females 42/17 respectively [12]. The study by Gillani et al. also supported our study where the ratio of males was observed to more than females with 183/121 [13]. There was another study by Chen et al and Dakhale et al. which were in constrast to the current study where the rtaio of females were more with the ratio of 13/19 and28/38 respectively [14,15].

In the current study in group-A after 3 months of treatment, there was a significant reduction of FBS PPBS, HbA1c (p=0.000) and no significant reduction of TC (p= 0.527), TG (p=0.559), LDL (p=0.373), VLDL (p=0.271) and TAC (p=0.06) observed. Similarly elevation of HDL (p=0.086) and MDA (p=0.076) was observed but which is also not significant. It was observed that after 3 months of treatment with glimepiride+ vitamin C (Group-B), there was a significant reduction of

FBS PPBS, HbA1c (p=0.000), MDA, TC, TG, LDL-C, VLDL($p<0.05$) and significant elevation of TAC and HDL-C ($p<0.05$)observed.

There was a significant reduction of FBS, PPBS, HbA1c (p=0.001), TC, TG, LDL, VLDL ($p<0.05$) and elevation of HDL ($p<0.05$) seen in group-C patients who were treated with Metformin + voglibose. Similarly reduction of TAC (p=0.186) and elevation of MDA (p=0.073) was seen but which is not statistically significant.
In group-D after 3 month of treatment, there was a significant reduction of FBS, PPBS, HbA1c, TC, TG, LDL (p=0.001), MDA, VLDL ($p<0.05$) and significant elevation of HDL (p=0.001) and TAC ($p<0.05$) observed.
In a study diabetic patients were treated with glimepiride and they had shown significant glycemic control [16]. The combination of Sulfonylureas with Vitamin-C showed significant reduction of FBS and PPBS [17]. Significant reduction of HbA1c, FBS and PPBS was seen in patients who were treated with metformin and voglibose [18].
Most of the antihyperglycemic agents also have lipid lowering effect along with their hypoglycemic effect, but this effect is variable. In present study significant control on lipid level was noticed in all groups except group-A ($P>0.05$), but the mean reduction of TC, TG, HDL, LDL, VLDL level was high in group-D (TC; 19±14.56, TG; 15.67±4.90 , HDL; 8.16±5.96 , LDL24.35±19.92 ; ,VLDL7.50 ± 7.17 ;) and group-B(TC 10.2±46.68; , TG7.41±39.68 ;, HDL6.2±15.12 , LDL ;,VLDL;) as compared to group-C (TC; , TG; , HDL , LDL 11.5 ± 50.92; , VLDL4.7±7.92 ;), but mean reduction of total cholesterol level was more in group-C (Metformin+ voglibose) than group-B (glimepiride+ vitamin-C). Another similar study had shown significant reduction of TC, TG, LDL, and VLDL and elevation of HDL in diabetic patients after treatment with glimepiride alone but such findings not supporting present study [19].

In study we found a significant control on lipid profile in patients treated with Sulfonylureas + vitamin C, similar results were mentioned in another study . Metformin+ voglibose (group-C) combination showed a significant reduction of TC, TG, LDL and VLDL and elevation of HDL level, these findings are in line with the previous studies [20]. Supplementation of Vitamin C reduces the insulin resistance by improving endothelial function and lowering oxidative stress [17]. Present study showed that there is a significant reduction of MDA and elevation of TAC level in group-B and group-D treated with OHA and vitamin C supplementation($P<0.05$), but Group-A and group-C had not shown significant difference in MDA and TAC level($p>0.05$).

In the current study it was noted that High mean reduction in MDA (0.7±0.93) and marked elevation of TAC (0.20±0.28) level was observed in Group-D as compared with group-B (MDA; 0.60±0.64 , TAC 0.1±0.24; . So supplementation of vitamin-C along with antidiabetic drugs has been proved to be more effective in control of blood glucose, oxidative stress and lipid level.
Consequently, antioxidant supplements have been proposed as the perspective treatment of diabetes. In addition, antioxidant supplements have been found to prevent the progression of diabetes and the occurrence of its complications [21,22].
It has been suggested that diabetics may have an increased need for vitamin C and an increased risk of deficiency due to increased cellular uptake and turnover of vitamin C [23].

CONCLUSION

The supplementing with vitamin-C in conjunction with OHA therapy improves glycemic control and lipid levels, and that Vitamin-C, as an antioxidant, reduces oxidative stress in diabetes mellitus patients. The treatment goal in Type II diabetes mellitus cases is not only to regulate blood glucose levels but also to prevent diabetic complications; however, this goal is not met by currently available antidiabetic medications. As a result, novel solutions are required to establish effective glucose control while also preventing diabetic complications and progression**.**

Declarations:
Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: We have consent to participate.
Consent for publication: We have consent for the publication of this paper.
Authors' contributions: All the authors equally contributed the work.

REFERENCES

1. El-Aal A.A., El-Ghffar E.A.A., Ghali A.A., Zughbur M.R., Sirdah M.M. The effect of vitamin C and/or E supplementations on type 2 diabetic adult males under metformin treatment: A single-blinded randomized controlled clinical trial. 2018; 12 (4) : pp. 483-489
2. Rahimi R, Nikfar S, Larijani B, Abdollahi M, et al. *Biomed Pharmacother.* 2005; 59(7):365-373.
3. Tiwari BK, Pandey KB, Abidi AB, Rizvi SI, et al. *JBiomark*, 2013; 378790.
4. Soumya D, Srilatha B. Late stage complications of diabetes and insulin resistance. J Diabetes Metab. 2011; 2: 167
5. Cho NH, Whiting D, Cavan D, et al. *Diabetes Atla.* 2015; 51-52.
6. American Diabetes Association. Standards of Medical Care in Diabetes. *Diabetes Care*. 2018; 41(1):13-27.
7. Bianchi C, Miccoli R, Daniele G, Penno G, Del Prato S,et al. *Diabetes care.* 2009; 2(2):342-348.
8. Bianchi C, Miccoli R, Daniele G, et al. Is there evidence that oral hypoglycemic agents reduce cardiovascular morbidity/mortality? Yes. Diabetes Care. 2009; 32(2): 342–348.
9. Ramachandaran A, Snehalatha C, Vijay V, et al. International Diabetes Moniter, 2003; 15(1):1-6.
10. Ramachandran A, Snehalatha C, Baskar, et al.Diabetologica, 2004; 47(1):860-863.
11. Wild S, Roglic G, Green A, Sicree R, King H, et al. Diabetes Care. 2004; 27(5):1047-1053.
12. BhattJK, ThomasS, NanjanM. Effect of oral supplementation of vitamin C on glycemic control and lipid profile in patients with type 2 diabetes mellitus. *Int J Pharm Nanjing Sci.* 2012;4:524–527.
13. GillaniSW, SulaimanSAS, AbdulMIM, BaigMR.Combined effect of metformin with ascorbic acid versus acetyl salicylic acid on diabetes-related cardiovascular complication; a 12-month single blind multicenter randomized control trial. *Cardiovasc Diabetol.* 2017;16:103.
14. ChenH, KarneRJ, Hall, et al. High-dose oral vitamin C partially replenishes vitamin C levels in patients with type 2 diabetes and low vitamin C levels but does not improve endothelial dysfunction or insulin resistance. *Am J Physiol Heart Circ Physiol.* 2006; 290:H137–H145.
15. DakhaleGN, ChaudhariHV, ShrivastavaM. Supplementation of vitamin C reduces blood glucose and improves glycosylated hemoglobin in type 2 diabetes mellitus: a randomized, double-blind study. Adv Pharmacol Sci. 2011; 195271.
16. Hadeel Delman Najim, Ibrahim Adham Majeed, Abbas Mahdi Rahmah, et al. International Journal of advances in Pharmacy, Biology and Chemistry, 2013; 2(2):323-327
17. Rekha Nayaka MR, et al. IJPR. 2015; 5(4):115-118
18. Dillu RD, Singh H, Bhardwaj BL, Singh KD, et al. 2016; 5(3):807-816.
19. Indirakumari N,.Vinutha S, Chandrakala Kambar et al. IOSR Journal of Dental and Medical Sciences. 2015; 14(1):13-22.
20. Faheem Mubeen MD, Deepak Bhosle, et al. Scholars Journal of Applied Medical Sciences. 2018; 6(9):3461- 3471
21. Kunsongkeit P, Okuma N, Rassameemasmaung S, Chaivanit P. Effect of vitamin C as an adjunct in nonsurgical periodontal therapy in uncontrolled type 2 diabetes mellitus patients. European journal of dentistry. 2019; 13(03):444-9.
22. Monitoring Editor: Alexander Muacevic and John R Adler. The Role of Vitamin C in Human Immunity and Its Treatment Potential Against COVID-19: A Review Article. Cureus. 2023; 15(1): e33740.
23. Kathleen M. Zelman, RD, LD, MPH. The Benefits of Vitamin C. 2024.