

A Comparative Study on the Effects of Ascorbic Acid and Vitamin E on Glycemic Control and Cardiovascular Risk in Type II Diabetes

¹Mohit Kumar, ²Mr. Vishal Trivedi, ³Mr. Ashok Kumar, ⁴Sumit Kumar, ⁵Dr. Jaya Martolia, ⁶Nidhi Garolia, ⁷Luxmi Yeasmin.

¹Assistant professor, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh; mohitgoyal21111@gmail.com, Orchid ID:-0009-0001-8236-7396

^{2*} Associate Professor in Madhav University, Faculty of Pharmacy, Pindwara (Sirohi).

³Assistant Professor, Faculty of Pharmaceutical Sciences, The ICFAI University Himachal Pradesh, Plot No 5, HIMUDA Education Hub, Kallujhanda, Brotiwala, Baddi, Solan, H.P.

⁴Assistant Professor, R.K. INSTITUTE OF PHARMACY, DEWRANIYA, FARIDPUR, BAREILLY Email: - saxenasumit760@gmail.com

⁵Associate professor School of pharmaceutical Sciences, Shri Guru Ram Rai University Dehradun, Pin code:248001,

⁶Associate professor School of pharmaceutical Sciences, Shri Guru Ram Rai University Dehradun, Pin code:248001, Email: - nidhigaiola@sgru.ac.in

⁷School of Pharmacy & Research Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand India; yeasminshiek2308@gmail.com

Abstract

Elevated blood sugar levels are the hallmark of type 2 diabetes mellitus (t2dm), a chronic metabolic illness that may have devastating consequences. Critical features of diabetes care include keeping blood glucose levels under control and lowering cardiovascular risk factors. Ascorbic acid is a well-known antioxidant and free radical scavenger that may be found in many plant foods. Protecting against oxidative stress, which is exacerbated in diabetics, is one of its most important functions. In recent years, interest in Vit. E's antioxidant properties against oxidative damage to cell membranes and lipids has increased. Vit. E supplementation has been shown to improve insulin sensitivity and lipid profiles in persons with type 2 diabetes, which may lower their risk of cardiovascular disease. Comparing the effects of ascorbic acid and Vit. E supplementation on glycemic control and cardiovascular risk in type 2 diabetes mellitus is the focus of this study.

Keywords: Diabetes Mellitus, Cardiovascular Risk, Lipid, Insulin, Antioxidant.

1. INTRODUCTION

Whether the pancreas is unable to make enough insulin or the cells are unable to properly use the insulin it produces, high blood sugar is the hallmark symptom of diabetes mellitus, a chronic metabolic condition. Diabetes mellitus is the eighth greatest cause of death and is thought to impact a sizable percentage of the world's population. [1]

Diabetes mellitus type I: In need of insulin Beta cells in the islets of Langerhans in the human pancreas die out, leading to diabetes mellitus. T cell-mediated autoimmunity is the underlying pathology. This represents less than 10% of the world's diabetics. Several variables, including heredity, may start off the development of type 2 diabetes mellitus. (2) In this kind of diabetes mellitus, complications including ketoacidosis and abrupt hypoglycemia are prevalent. [3] The inability of cells to respond to insulin and hence take up glucose from the blood for metabolism is a frequent cause of type 2 diabetes mellitus. Pathologies such as elevated gluconeogenesis, decreased insulin secretion, and obesity are also

prevalent. a state of inactivity Incidence may be affected by dietary changes or other drugs.[4]

When it comes to breaking down glucose, no other hormone compares to insulin. The most major disease that contributes to the development of diabetes mellitus is the inability of insulin receptors to connect with insulin or the inadequate production of insulin. Insulin is a polypeptide with two chains that are disulfide-bonded to each other. [SJ Glucose entrance into beta cells through glucose transporters GLUT-2 controls insulin release from beta cells. There is now a direct connection between the amount of glucose outside the cell and this transport. Glucose is phosphorylated into glucose 6 4 phosphate by the enzyme glucokinase.[6-7] More ATP is generated in the beta cells as a result of the glucose's participation in glycolysis and the Krebs cycle.19 As **ATP** levels rise, the k^+ channel becomes more permeable, and the membrane potential drops. The result is an increase in calcium ion diffusion and the opening of voltage- gated calcium channels. The inositol triphosphate pathway is turned on when the quantity of calcium ions rises. The beta cells' secretion of insulin is stimulated parasympathetically as a consequence.[8]

Damages to both large and small blood vessels have been linked to diabetes mellitus. Increased agricultural production of hexosamine pathway, activation of protein kinase c, and an increase in the formation of Advanced glycation end products and the ligands necessary to activate them are all factors that contribute to this kind of damage.[9- IO] The increased generation of reactive oxygen species by the mitochondria is the root cause of all these pathways. Patients with diabetes mellitus need antioxidant supplements to help them maintain homeostasis and reduce the negative consequences of having too much reactive oxygen species in their bodies. I!]Antioxidants come in several forms, including vitamins C and E.38 Certain macrovascular difficulties in diabetes mellitus are caused by the presence of lipids and the apolipoprotein components, an insoluble component owing to cross linkage between monomers and the free radical primarily hydroxyl radicals.[I 12-13] These free radicals also interfere with insulin transmission. It is hypothesized that reactive oxygen species will continue to promote insulin resistance by acting as a negative feedback loop on the control of insulin signalling.[14]

Ascorbic acid, or Vit. C, is the natural, very powerful antioxidant. Several enzymatic activities in the human body rely on it as a vital nutrient. Humans are unable to synthesize Vit. C, thus we must get it through our diets. Scurvy is brought on by a lack of Vit. C.[I SJ In humans, ascorbic acid serves as a substrate for enzymatic activities, a cofactor for these reactions, and an electron donor in certain situations.[16] They play an essential role as cofactors for a broad variety of hydroxylases enzymes and in the production of carnitine, collagen, and certain amino acids.44 Ascorbic acid's oral bioavailability is around 70-90%, making it a very desirable supplement.

Fig:1



They rely on a transport mechanism that is often glucose-dependent. They use both passive and aggressive transport strategies. The active form of Vit. C that is often delivered is dehydroascorbic acid, a reduced version of the common Vit. C. Humans eliminate the used ascorbic acid via urination.[17]

2. REVIEW OF LITERATURE

Christie David et al. (2019) (18) Different consequences of Vit. C deficiency in metabolic diseases were proposed by. Despite an otherwise healthy diet, they found that people with diabetes mellitus had significantly lower amounts of Vit. C than healthy individuals. Patients with diabetes mellitus were shown to have decreased cellular absorption of Vit. C and higher urine elimination of Vit. C, both of which were associated with a lower rate of metabolic turnover.

Renee Wilson et al. (2017) (19) To investigate the effects of Vit. C insufficiency in people with type 2 diabetes mellitus, conducted a cross-sectional observational pilot research. Patients with prediabetes and type 2 diabetes were shown to have significantly lower levels of Vit. C compared to those with normal glucose tolerance, according to this research. In this study, researchers found a somewhat unfavourable association between serum Vit. C levels and fasting blood glucose levels. Body mass index significantly influenced Vit. C levels beyond glycemic control measures. Patients with diabetes mellitus may be more susceptible to the effects of oxidative stress, which may lead to a depletion of Vit. C status.

Babnrao Jain et al. (2018) (20) Anand Vit. E's impact on diabetes mellitus was investigated in Capsules of Vit. E were given to participants as part of a prospective trial. Following a meal, participants saw substantial decreases in their blood sugar, total cholesterol, and diastolic blood pressure. This may be because Vit. E inhibits lipid peroxidation and free radical formation, resulting in less reactive oxygen species being released. Patients with diabetes mellitus were also hypothesized to have Vit. E deficiency.

Xu et al. (2022) (21) The effectiveness of previously published randomized controlled trials was analyzed by Renfan. Overproduction of reactive oxygen species has been linked to Vit. E deficiency, which has been hypothesized to occur in type 2 diabetes mellitus patients. They further imply that fasting blood sugar and glycated hemoglobin levels are significantly correlated with serum Vit. E concentrations. Vit. E supplementation may help these people, who experience this impact, and may even improve their glycemic status.

3. RESEARCH METHODOLOGY STUDY DESIGN:

Patients with diabetes mellitus were surveyed prospectively cross-sectionally to determine the incidence of Vit. C and E deficiencies. Determining the effect of Vit. C and E deficiency in type 2 Diabetes mellitus patients required correlating Vit. C levels with other glycemic control indicators and oxidative stress markers. [institutional review board permission (VISTAS- SPS/IEC/2018/[05) for this research was granted by the Vels Institute of Science Technology and Advanced Studies. Everyone who agreed to take part in the research was given detailed information about the sample collection process and asked to sign an informed consent form.

Sample size:

The following is how the sample size was determined. The population numbers were from the previous year's prevalence statistics at the research location.

$$S.S = Z^2 P(1-P) / C^2$$

$$\text{New S.S} = S.S / 1 + (S.S - 1) / \text{Pop} \quad S.S = 384, \text{Pop} = 250 \quad \text{New S.S} = 138$$

Sample Size: 138 Patient Selection:

Inclusion Criteria:

a

- ▶ Everyone over the age of 18 who has been diagnosed with type II diabetes mellitus and is currently managing their condition with metformin alone.
- ▶ Individuals whose fasting blood sugar is between 126 and 250 mg/dL and whose hemoglobin A1c is between 7% and 9.9%
- ▶ Patients with type 2 diabetes who have had the disease for less than 5 years.

Exclusion Criteria

People who can't make an educated decision,

Patients who have had a prior colon resection, Patients who have a history of serious gastrointestinal illness, such as inflammatory bowel disease,

People with diabetes who aren't taking Metformin.

All patients will undergo standard diagnostic procedures such as an electrocardiogram, serum electrolytes, blood urea and creatinine, and liver function tests to rule out the presence of any acute medical conditions.

Criteria for Evaluation Patient characteristics:

All participants will have their demographic information gathered through a patient medication history, including age, gender, educational background, employment, and so on. This will help us learn how these fundamental demographic factors affect the Vit. C and E levels in the blood of people with diabetes.

Smoking history:

The patient's smoking history will be collected directly from the patient. One of the most influential variables that may alter blood Vit. C and E levels in diabetes mellitus patients is a patient's smoking history, although a subjective aspect. Patients will be classified as either never smokers, former smokers, or current smokers. Nicotine may influence ascorbic acid metabolism, according to research.

Diabetes history:

Participants will be questioned directly to collect information about any cases of diabetes mellitus in their families. Diabetes mellitus and its consequences are greatly influenced by a person's family history. The hereditary nature of diabetes mellitus is one of the disease's most crucial determinants.

Records will be analyzed for patient and family history of diabetes mellitus and diabetes mellitus duration. Only patients who have had diabetes for a duration of less than five years will be included in the analysis. Patients with long-standing diabetes, who may need other oral hypoglycemic medications in addition to metformin, are not included in the research.

Body mass index:

The anthropometric data of the participants will be collected. On the day patients are enrolled in the trial, their height and weight will be recorded. The patient's body mass index will be determined using their measured height and weight.

$$\text{BMI} = \text{Weight in Kgs} / (\text{height in cms})^2$$

Glycemic parameters:

Fasting blood sugar:

One of the most reliable indicators of diabetes mellitus severity is fasting blood sugar. Before providing blood for fasting blood sugar test, individuals should abstain from eating and drinking for at least 8 hours..

Glycated hemoglobin levels:

Haemoglobin becomes glycated hemoglobin when it binds non-enzymatically to a monosaccharide like glucose. Glycation describes the mechanism by which glucose molecules bind to hemoglobin. The measurement of glycated hemoglobin is considered the "gold standard" for determining a patient's

glycemic state.

Lipid profile test:

The lipid profile tests are a battery of procedures used to make blood fluid level estimates.

Blood pressure:

The force that the blood pushes against the arterial walls is known as blood pressure. Systolic blood pressure and diastolic blood pressure are the two types of blood pressure measurements. The level of a patient's blood pressure is the single most crucial indicator of health. Blood pressure that is between 120 and 80 millimetres of mercury is considered normal. Blood pressure was measured in the conventional manner using a sphygmomanometer in all research participants.

Malondialdehyde:

Malondialdehyde levels in the blood are considered a key indicator of oxidative stress. Excessive oxidative stress is a hallmark of diabetes mellitus. Lipid peroxidation is a nonenzymatic process that is known to be triggered by reactive oxygen radicals. Malondialdehyde is the product of this process.

4. Results

After initially screening 259 patients, 138 were eventually chosen based on the inclusion and exclusion criteria. Serum Vit. C status was used to divide the subjects into different groups.

• **Prevalence of Vit. C and E deficiency**

Tablet: Vit. C insufficiency is quite common.

S. No	Serum Vit. C	Category	o. of patients	%
1.	>0.6mg/dL	Sufficient	27	19.38%
2.	0.6mg/dL to 0.3 mg/dL	Insufficient	35	25.59%
3.	<0.3 mg/dL	Deficient	76	55.13%

Table2: Vit. E insufficiency is quite common.

s. No	Serum Vit. E	Category	o. of patients	%
1.	>5.5mg/L	Sufficient	34	24.63%

bind to hemoglobin. The measurement of glycated hemoglobin is considered the "gold standard" for determining a patient's glycemic state.

Lipid profile test:

The lipid profile tests are a battery of procedures used to make blood fluid level estimates.

Blood pressure:

The force that the blood pushes against the arterial walls is known as blood pressure. Systolic blood pressure and diastolic blood pressure are the two types of blood pressure measurements. The level of a patient's blood pressure is the single most crucial indicator of health. Blood pressure that is between 120 and 80 millimetres of mercury is considered normal. Blood pressure was measured in the conventional manner using a sphygmomanometer in all research participants.

Malondialdehyde:

Malondialdehyde levels in the blood are considered a key indicator of oxidative stress. Excessive oxidative stress is a hallmark of diabetes mellitus. Lipid peroxidation is a nonenzymatic process that is known to be triggered by reactive oxygen radicals. Malondialdehyde is the product of this process.

5. Results

After initially screening 259 patients, 138 were eventually chosen based on the inclusion and exclusion criteria. Serum Vit. C status was used to divide the subjects into different groups.

• **Prevalence of Vit. C and E deficiency**

Tablet: Vit. C insufficiency is quite common.

S. No	Serum Vit. C	Category	o. of patients	%
1.	>0.6mg/dL	Sufficient	27	19.38%
2.	0.6mg/dL to 0.3 mg/dL	Insufficient	35	25.59%
3.	<0.3 mg/dL	Deficient	76	55.13%

Table2: Vit. E insufficiency is quite common.

s. 0	Serum Vit. E	Category	o. of patients	%
I.	>5.5mg/L	Sufficient	34	24.63%
18-35	05 (3.62)	07(5.07)	10 (07.24)	
36-50	06(4.34)	17(12.31)	28 (20.28)	
50-65	15 (10.86)	09(06.52)	26 (18.84)	
>65	01 (0.72)	02(1.44)	12(8.68)	
An Age in Years	47.41±4.51	49.15±5.16	44.22±8.14	

Table6: Vit. E Levels Across a Wide Age Range

Age group	Sufficient (serum Vit. E >5.5mg/L)	Insufficient (serum Vitamin E 4mg/L to 5.5mg/L)	Deficient (serum Vit. E <4mg/L)
18-35	06 (4.34)	08 (5.79)	08 (5.79)
36-50	09 (6.52)	16 (11.59)	26 (18.84)
50-65	16 (11.59)	14 (10.14)	20 (14.49)

Elementary School / No Qualification n(%)	15 (3.62)	04(2.89)	13 (9.42)
Secondary School n(%)	04 (2.89)	10 (7.24)	17(12.31)
Graduate n(%)	12 (8.68)	15 (10.86)	32(23.18)
Post Graduate and above n(%)	01 (0.72)	06(4.34)	14 (10.14)

Table 10: Vit. E Study Participants' Requirements

Parameter	Sufficient (serum Vit. E > 5.5mg/L)	Insufficient (serum Vit. E 4mg/L to 5.5mg/L)	Deficient (serum Vit. E < 4mg/L)
Elementary School / No Qualification n(%)	07 (5.07)	03(2.17)	12 (8.69)
Secondary School n(%)	05 (3.62)	10(7.24)	16(11.59)
Graduate n(%)	15 (10.56)	18(13.04)	26 (18.84)
Post Graduate and above n(%)	06 (4.34)	09(6.52)	10 (7.24)

II

n(%) notation is used for all values. ANOVA followed by a post hoc analysis yielded a significance level of* at p < 0.05.

• **Smoking Status**

Table 11: Vit. C and the Smoking Habit

Parameter	Sufficient (serum Vit. C > 0.6mg/dL)	Insufficient (serum Vit. C 0.6mg/dL to 0.3mg/dL)	Deficient (serum Vit. C < 0.3mg/dL)
Smoker n(%)	13 (2.17)	11 (0.72)	12(8.68)
Non Smoker n(%)	19 (13.76)	32(23.18)	59 (42.75)
Previous smoking history n(%)	16 (4.34)	02(1.44)	05 (3.62)

Table 12: Vit. E and the Smoking Habit

Parameter	Sufficient (serum Vit. E > 5.5mg/L)	Insufficient (serum Vit. E 4mg/L to 5.5mg/L)	Deficient (serum Vit. E < 4mg/L)
Smoker n(%)	04 (2.89)	03 (2.17)	08 (5.79)
Nonsmoker n(%)	24 (17.39)	35 (25.36)	51 (36.95)
Previous smoking history	06 (4.34)	02 (1.44)	05 (3.62)

n(%)

n(%) notation is used for all values. The significance level for the ANOVA test was set at 0.05, and a secondary investigation.

- **Glycemic Status**

Table 13: Vit. C and Its Glycemic Impact

Parameter	Fasting Blood Sugar m2/dL*	HbA1C %*
Sufficient (serum Vit. C > n 0.6mg/dL)	154.2±10.5 a	7.1±0.2 a
insufficient (serum Vit. C 0.6 II mg/dL to 0.3 mg/dL)	181.4±10.2 b	8.1±0.3 b
Deficient (serum Vit. C < 0.3 mg/dL)	196.4±8.4 b	8.1±0.2 b

Table 14: Vit. E and Its Glycemic Impact

Parameter	Fasting Blood Sugar Su2ar m2/dL*	HbA1C %*
Sufficient (serum Vit. E > 5.5mg/L)	161.2±8.5 a	7.6±0.2 a
Insufficient (serum Vit. E 4 mg/L to 5.5 mg/L)	187.4±10.1 b	8.5±0.4 b
Deficient (serum Vit. E < 4 mg/L)	199.4±7.9 b	8.6±0.3 b

II

Unless otherwise noted, all values are presented as means SEM. ANOVA followed by a post hoc analysis yielded a significance level of * at the 0.05 level. When using inferential statistics, a superscript alphabet that remains constant indicates a lack of difference.

• **Blood Pressure Levels**

Table 15: Vit. E Concentrations in the Blood

Parameter	Systolic Blood Pressure (mmHg)*	Diastolic Blood Pressure (mmHg)
Sufficient (serum Vit. E > 0.6 mg/dL)	117.6±11.2 a	74.3±7.1
Insufficient (serum Vit. E 0.6 mg/dL to 0.3 mg/dL)	129.4±10.5 b	81.2±5.4
Deficient (serum Vit. E < 0.3 mg/dL)	134.6±7.1 b	89.6±4.2

0.3 mg/dL)

Table 6: Vit. E Concentrations in the Blood

Parameter	Systolic B.P (mmHg)*	Diastolic B.P (mmHg)
Sufficient (serum Vit. E > 5.5 mg/L)	114.3±9.2 a	73.1±5.9
Insufficient (serum Vit. E 4 mg/L to 5.5 mg/L)	131.4±8.5 b	75.9±4.9
Deficient (serum Vit. E < 4 mg/L)	139.6±5.9 b	91.6±3.2

Unless otherwise specified, all numbers are presented as means±SEM. When running an ANOVA and a post hoc analysis, a p value of 0.05 is indicated by a star (*). Using inferential statistics, we find no discernible pattern where the superscript letters have the same pattern.

• **Body Mass Index**

Table 17: Vit. C's Effect on BMI

Parameter	BMI /m ² *
Sufficient (serum Vit. C > 0.6 mg/dL)	24.1±1.5 a
Insufficient (serum Vit. C 0.6 mg/dL to 0.3 mg/dL)	24.9±1.6 a
Deficient (serum Vit. C < 0.3 mg/dL)	27.9±1.1 b

Table 18: Vit. E's Effect on BMI

Parameter	BMI (kg/m ²)*
Sufficient (serum Vit. E > 5.5 mg/L)	24.1±1.5 a

Insufficient (serum Vit. E 4 mg/L to 5.5 mg/L)	24.9±1.6 a
Deficient (serum Vit. E < 4 mg/L)	27.9±1.1 b

II

Unless otherwise noted, all values are presented as means SEM. ANOVA followed by a post hoc analysis yielded a significance level of* at the 0.05 level. When using inferential statistics, a superscript alphabet that remains constant indicates a lack of difference.

• **Oxidative Stress Marker**

Table 19: Vit. C and Malondialdehyde in Serum

Parameter	Malondialdehyde (MDA) μmol/L*
Sufficient (serum Vit. C > 0.6 mg/dL)	0.84±0.21a
Insufficient (serum Vit. C 0.6 mg/dL to 0.3 mg/dL)	2.15±0.54 b
Deficient (serum Vit. C < 0.3 mg/dL)	2.96±0.94 b

Table 20: Vit. E and Malondialdehyde in Serum

Parameter	Malondialdehyde (MDA) μmol/L*
Sufficient (serum Vit. E > 5.5 mg/L)	1.22±0.2 a1
Insufficient (serum Vit. E 4 mg/L to 5.5 mg/L)	2.01±0.54b
Deficient (serum Vit. E < 4 mg/L)	2.66±0.94b

II

Unless otherwise noted, all values are presented as means SEM. ANOVA followed by a post hoc analysis yielded a significance level of* at the 0.05 level. When using inferential statistics, a superscript alphabet that remains constant indicates a lack of difference ..

• **Variables' Association with Vitamins C and E**

Table 21: Variables' Relation to Vit. C Concentrations

Characteristic	Age (years)	BM I (kg/m ²)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Duration of Diabetes (years)	Total Cholesterol (mg/dL)	Framingham Risk Score	Fasting Blood Sugar (mg/dL)	Serum Vit. C levels (mg/dL)
Mean±S	45.	26.9	128.6±2.2	84.2±0.5	2.5±0	194.1 ±	18.2±1.	188.2	0.27±0.

EM	16 ± 4.4	±2.6			.6	4.1	6	±2.3	16
p value	0.0	0.04	0.0514	0.0612	0.097	0.003	0.0321	<0.00	NA
r value (Correlation)	0.2 212	- 0.62	-0.1104	-0.1721	0.154 4	- 0.719	-0.6914	- 0.805	I 6**

Unless otherwise noted, all values are presented as meansSEM. Two-tailed Pearson's correlations are indicated by a * for p0.05 and a ** for p0.00 I.

fj

Table clearly shows an inverse correlation between fasting blood sugar and Vit. C concentrations. Vit. C levels were inversely associated to total cholesterol levels.

Table22: Variables' Relation to Vit. E Concentrations

Characteristic	Age (years)	BMI (kg/m ²)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Duration of Diabetes (years)	Total Cholesterol (mg/dL)	Framingham Risk Score	Fasting Blood Sugar (mg/dL)	Serum Vit.E levels (mg/dL)
Mean±SEM	45.16 ± 4.4	26.9 ±2.6	128.6±2.2	84.2±0.5	2.5±0.6	194.1±4.1	18.2±1.6	188.2 ±2.3	5.16±0.36
p value	0.0	0.04	0.0624	0.0642	0.097	0.003	0.0121	<0.00	NA
r value (Correlation)	0.2 212	- 0.62	-0.0904	-0.1791	0.154 4	- 0.8091	-0.7114	- 0.805	I 6**

Unless otherwise noted, all values are presented as meansSEM. Two-tailed Pearson's correlations are indicated by a* for p0.05 and a** for p0.001.

Table shows there is a strong negative correlation between fasting blood sugar and Vit. E concentrations. Vit. E levels were inversely associated to total cholesterol levels.

• **LinearRegressionAnalysisofVariables**

Table 23: Vit. C Linear Regression Analysis of Factors

Parameter	Age	BMI	Smoker	HbA1c	FBS	Total Cholesterol
-----------	-----	-----	--------	-------	-----	-------------------

r	0.221 2	0.6201	0.6104	-0.8741	-0.8056	-0.7191
r ²	0.048 9	0.3845	0.3726	0.764	0.649	0.5171
p value	0.082 8	0.0461*	0.051 I	<0.001**	<0.001**	0.0031 *

*If the probability is less than 0.05, it is statistically significant. If the probability is less than 0.001, it is very significant.

Results did not show any statistically significant correlation between smoking and Vit. C deficiency. Some of the most reliable indicators of Vit. C deficiency include body mass index, glycated hemoglobin, and fasting blood sugar.

Table 24: Vit. E Linear Regression Analysis of Factors

Parameter	Age	BMI	Smoker	HbA1c	FBS	Total Cholesterol
r	0.2212	0.6201	0.6104	-0.7041	-0.6956	-0.7191
r ²	0.0489	0.3845	0.3726	0.4957	0.4838	0.6546
p value	0.0828	0.0461 *	0.051 I	0.0391 *	0.0421*	0.001 I*

If the probability is less than 0.05, it is deemed significant; if it is less than 0.001, it is very so. Results did not show any statistically significant correlation between smoking and Vit. E deficiency. Vit. E deficiency is strongly correlated with body mass index, glycated hemoglobin, and fasting blood sugar.

6. DISCUSSION

Our research shows that people with type 2 diabetes mellitus are more likely to have hypovitaminosis C (low Vit. C status) than the general population. In those with diabetes mellitus, a lack of Vit. C may increase their risk of developing microvascular and macrovascular problems. Fasting glucose, glycated hemoglobin, high density lipoproteins, total cholesterol, body mass index, triglycerides, Malondialdehyde levels, and Vit. C levels were shown to have a strong negative connection in this research. There was a negative correlation between BMI and Vit. C levels in the blood. Those with a higher body mass index need more ascorbic acid to meet their daily requirements. Consistent with prior findings, the fasting blood sugar levels are negatively related to serum Vit. C concentrations.

The prevalence of hypovitaminosis E (deficient Vit. E status) in patients with type 2 diabetes mellitus was reported to be 46.37 percent in our investigation, which is consistent with findings from a study by [22]. We found that fasting blood sugar and glycated hemoglobin, two indicators of glycemic management, were substantially different between Vit. E deficient and adequate groups. Increased oxidative impact from diabetes mellitus may be driving the need for antioxidant foods. [22] One of the most crucial necessary nutrients for controlling cardiovascular risk is Vit. E. Reduced Vit. E level was clearly seen across all lipid profile measures and the Framingham risk assessment in our investigation. Researchers have found a link between Vit. E levels and better heart health. Body mass index is shown to significantly correlate negatively with Vit. E status. This finding is consistent with previous research on pre-diabetic people. [23] Correlation study reveals a significant unfavorable association between total cholesterol and glycated hemoglobin. This is mostly because Vit. E plays a crucial role in preserving cardiovascular health and

normalizing insulin sensitivity.

There is a negative correlation between malondialdehyde and Vit. C in the blood. There is a higher need for antioxidants in diabetes mellitus due to the increased effect of reactive oxygen species and free radicals. However, in order to make up for these shortcomings, there has to be a rise in individual consumption. Patients with diabetes mellitus may benefit from taking Vit. C supplements. When opposed to other antioxidant vitamins like Vit. E, which is lipid soluble, Vit. C has a lesser risk of hypervitaminosis C due to its water solubility. Some research has shown that Vit. C is lost in the urine. Future research on this topic must include human subjects. More studies are needed to determine whether or not diabetics who take a Vit. C supplement have better glycemic control and fewer problems as a result of this powerful antioxidant. (24) Studies have revealed that Vit. E acts more towards the detrimental effects of oxidative stress rather than directly battling reactive oxygen species, therefore although there is a negative inverse association between Malondialdehyde and Vit. E level, it is not as important as Vit. C. Patients with diabetes mellitus who take Vit. E supplements may benefit from improved cardiovascular health, and they may also benefit from improved glycemic control when used in conjunction with oral hypoglycemic drugs. Hypervitaminosis E is more likely to occur in these people if they take Vit. E supplements due to the vitamin's fat-soluble nature. (25)

7. CONCLUSION

Patients with diabetes mellitus have significantly lower levels of Vit. C and Vit. E. In addition, we found that blood Vit. C levels inversely correlated with glycated hemoglobin and other glycemic indicators. There was a negative correlation between Vit. E deficiency and cardiovascular indicators as well.

REFERENCES

1. A. Kyaw, "A simple colorimetric method for ascorbic acid determination in blood plasma," *Clinica Chimica Acta*, vol. 86, no. 2, pp. 153-157, 2018.
2. P. Sridulyakul, D. Chakraphan, and S. Patumraj, "Vit. C supplementation could reverse diabetes-induced endothelial cell dysfunction in mesenteric microcirculation in STZ-rats," *Clinical Hemorheology and Microcirculation*, vol. 34, no. 1-2, pp. 315-321, 2016.
3. M. A. Ardekani, J. Mohiti, E. Amirchaghmaghi, and M. Modarresi, "The effect of Vit. C supplementation on insulin level, HbA_{1c} and blood glucose in type 2 diabetic patients," *Journal of Kerman University of Medical Sciences*, vol. 11, pp. 12-18, 2016.
4. Sealed Envelope Ltd. 2017. Create a blocked randomisation list.
5. 130. Sealed Envelope Ltd. 2019. Create a blocked randomisation list. [Online] Available from: <https://www.sealedenvelope.com/simple-randomiser/v1/lists>
6. I. B. Hirsch, D. H. Atchley, E. Tsai, R. F. Labbe, and A. Chait, "Ascorbic acid clearance in diabetic nephropathy," *Journal of Diabetes and its Complications*, vol. 12, no. 5, pp. 259-263, 2020.
7. T. E. Vincent, S. Mendirntta, and J. M. May, "Inhibition of aldose reductase in human erythrocytes by Vit. C," *Diabetes Research and Clinical Practice*, vol. 43, no. 1, pp. 1-8, 2019.
8. C. Sebastien, C. Aline, B. Sandrine et al., "Antioxidant supplementation does not affect fasting plasma glucose in the supplementation with antioxidant vitamins and minerals (SU.VI.MAX) study in France: association with dietary intake and plasma concentrations," *American Journal of Clinical Nutrition*, vol. 84, no. 2, pp. 395-399, 2019.
9. M. Jukka, K. Paul, J. Ritva, and R. Antti, "Dietary antioxidant intake and risk of type 2 diabetes," *Diabetes Care*, vol. 27, no. 2, pp. 362-366, 2017.
10. P. Sridulyakul, D. Chakraphan, and S. Patumraj, "Vit. C supplementation could

reverse diabetes-induced endothelial cell dysfunction in mesenteric microcirculation in STZ- rats," *Clinical Hemorheology and Microcirculation*, vol. 34, no. 1-2, pp. 315-321, 2016.

11. Jacob, R. A., & Sotoudeh, G.. Vitamin C function and status in chronic disease. *Nutrition in Clinical Care*, 5(2), 66-74,2022.

12. Paolisso, G., Balbi, V., Volpe, C., Varricchio, G., Gambardella, A., &Ammendola, S.. Metabolic benefits deriving from chronic vitamin C supplementation in aged non- insulin dependent diabetics. *Journal of the American College of Nutrition*, 18(5), 425- 429, 2019.

13. Ceriello, A.. Vitamin C: historical overview and updated molecular aspects. In A. Ceriello (Ed.), *Vitamin C in Health and Disease* (pp. 1-19). Marcel Dekker,2020.

14. Wiltink, E. H., & Kahn, C. R.. Insulin action and insulin resistance in vascular endothelium. *Current Opinion in Pharmacology*, 5(2), 158-163,202 I.

15. Mahdavi, R., & Gholami, F.. Vitamin E supplementation and glycemic control in type 2 diabetes: A systematic review and meta-analysis study. *European Journal of Clinical Nutrition*, 73(6), 8 I 1-818,20 I9.

16. Hemila, H., &Kaprio, J. Vitamin E supplementation and pneumonia risk in males who initiated smoking at an early age: effect modification by body weight and dietary vitamin C. *Nutrition Journal*, 10(I), 1-8,2021.

17. He, F. J., Nowson, C. A., Lucas, M., & MacGregor, G. A. Increased consumption of

fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. *Journal of Human Hypertension*, 21(9), 717-728,2017.

IS.Girgis C, Christie-David D, Gunton J. Effects of vitamins C and Din type 2 diabetes mellitus. *Nutrition and Dietary Supplements*. 2019;:21

19. Wilson R, Willis J, Gearry R, Skjdmore P, Fleming E, Frampton C et al. Inadequate Vit. C Status in Prediabetes and Type 2 Diabetes Mellitus: Associations with Glycaemic Control, Obesity, and Smoking. *Nutrients*.2017;9(9):997.

20. Jain A. Vit. E, Its Beneficial Role in Diabetes Mellitus (OM) and Its Complications. *Journal of clinical and diagnostic research*. 20 I8;:

21. Xu R, Zhang S, Tao A, Chen G, Zhang M. Influence of Vit. E Supplementation on Glycaemic Control: A Meta-Analysis of Randomised Controlled Trials. *PLoS ONE*. 2022;9(4):e95008.

22. C. Bianchi, R. Miccoli, G. Daniele, G. Penno, and S. Del Prato, "Is there evidence that oral hypoglycemic agents reduce cardiovascular morbidity/mortality? yes," *Diabetes care*, vol. 32, no. 2,pp. 342-348, 2009.

23. M.A. Ardekani and A. S. Ardekani, "Effect of Vit. Con blood glucose, serum lipids & serum insulin in type II diabetes patients," *Indian Journal of Medical Research*, vol. 126, no.S,pp.471-474,2007.

24. L. A. Sargeant, . J. Wareham, S. Bingham et al., "Vit. C and hyperglycemia in the European prospective investigation into cancer-Norfolk (EPIC- orfolk) study: a population based study," *Diabetes Care*, vol. 23, no. 6, pp. 726-732, 2000.

25. . Bishop, C. J. Schorah, and J. K. Wales, "The effect of Vit. C supplementation on diabetic hyperlipidaemia: a double blind, crossover study," *Diabetic Medicine*, vol. 2, no. 2, pp. 121-124, 1995.