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Original Article

Vitamin C Intervention in Type 2 Diabetes Mellitus: A Comprehensive Analysis of Lipid Profile and Glycemic Parameters

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ABSTRACT

Worldwide many people are affected by Type 2 Diabetes mellitus (DM). This study aimed to assess how lipid and glycemic parameters are affected by ascorbic acid in adult population suffering from type 2 DM. Two groups were formed one was control group with 103 patients and other was treatment group with 103 patients. The intervention group was administered 500 mg of vitamin C three times a day in conjunction with oral hypoglycemic medications for duration of three months. Fasting blood sugar, random blood sugar, glycosylated hemoglobin, total cholesterol, serum triglycerides, high density lipoproteins cholesterol, and low density lipoproteins cholesterol tests were conducted at start of study and again after three months. Means were compared between control and treatment groups. Correlation and regression analysis between vitamin C and laboratory parameters were also performed. Lipid profile, fasting blood sugar, and random blood sugar were affected significantly by ascorbic acid and there was significant correlation between them. However, regression analysis revealed that, except for high-density lipoprotein cholesterol, there was no statistical significance in the impact on the overall lipid profile. The current study's conclusion suggests that administering vitamin C as supplementary therapy alongside anti-diabetic medications, over an extended period and in divided doses, can influence glycemic parameters and lipids.

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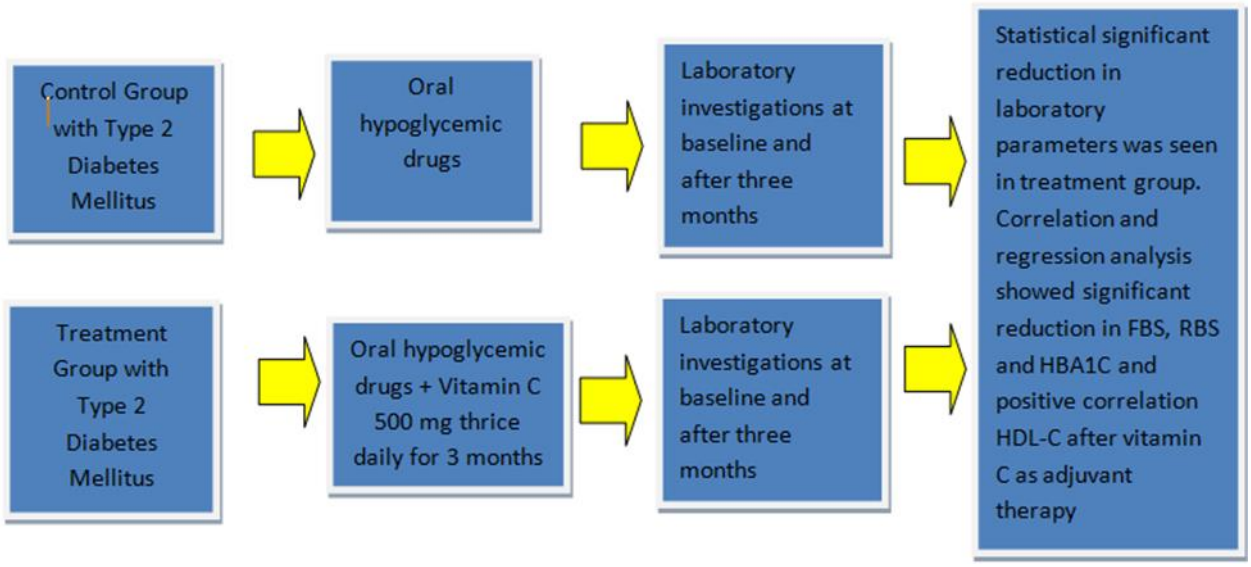
GRAPHICALABSTRACT



Introduction

Globally a metabolic disorder called type 2 Diabetes mellitus (DM) is a very common disease which is characterized by increased blood glucose levels and various factors play role in its development [1] . As per the 2021 International Diabetes Federation (IDF) Diabetes Atlas, around 537 million adults aged 20 to 79, constituting 10.5% of this population, are affected by diabetes, with nearly half of them unaware of their diabetic condition. It is anticipated that by 2045 about 783 million (46%) adults which amounts to 1 in 8 will have diabetes. Pakistan is among the IDF MENA region and 26.7% of adult population in Pakistan has diabetes [2]. Type 2 Diabetic patients have diabetic dyslipidemia in long standing disease and are more prone to cardiovascular (CVS) disease. Globally 32.2% diabetic patients are affected by CVS disease and 66% of deaths in individuals with DM are due to diabetic dyslipidemia [3, 4]. Free radicals induced oxidative stress and chronically presence of low grade inflammation are the key factors in causation of insulin resistance and type 2 DM along with its complications [5]. The oxidative stress in type 2 DM is increased by several mechanisms. These include the self-oxidation of glucose, the creation of advanced glycation end products, protein glycation, and the activation of the polyol pathway. These pathways lead to formation of free radicals which play significant role in lipid peroxidation resulting in tissue damage [6]. Humans do not have the essential enzyme for the production of crucial antioxidant vitamin C also called as ascorbic acid. Glucose transporters are involved in the transport of dehydroascorbic acid which is oxidized form of ascorbic acid. In presence of hyperglycemia, there is competition between glucose and vitamin C due to which it is not transported into the cells and is excreted from the body resulting in deficiency of vitamin C in DM and causing further tissue damage. It has been proposed that lipids are primarily modulated by vitamin C and conversion of cholesterol to bile acids is further carried by this important vitamin. In addition, vitamin C prevents low density lipoprotein cholesterol (LDL-C) from oxidizing and promotes its absorption through hepatocyte LDL receptors through its antioxidative properties [3, 7]. Despite the previous studies investigating the performance of vitamin C on glycemic and lipid parameters, comprehensive status of correlation and regression analysis of vitamin C on these parameters is lacking.

Hence, this study was conducted to see whether glycemic and lipid parameters are influenced by adjuvant intervention of vitamin C in type 2 DM along with their routine anti-diabetic medications.

Materials and Methods

A randomized clinical trial study was conducted in Pharmacology department of Shahida Islam Medical and Dental College, Lodhran, Pakistan spanning from May 2023 to July 2023. The ethical approval was taken from ethical review committee of institute and study was performed according to principles of Declaration of Helsinki. The Ethical Approval number was SIMC/H.R./7824-A23. The patients were recruited from outpatient department of Medicine of Shahida Islam Medical Complex, Lodhran, Pakistan. The consent was taken from each patient for enrollment in study.

The sample size was determined using online open Epi software based on the prevalence of type 2 DM in adult population in Pakistan as per statistics of IDF [2].

The research involved individuals between the ages of 40 and 65, with fasting blood sugar (FBS) levels not exceeding 200 mg/dl and glycosylated hemoglobin (HbA1C) levels below or equal to 8.5%, who willingly volunteered for participation. The research excluded individuals with diabetic complications (diabetic nephropathy, retinopathy, and neuropathy), those who had been using antioxidants or taking vitamin C within the three months preceding the commencement of the study, duration of diabetes less than 5 years, gestational diabetes, pregnant females, type 1 DM, and patients on insulin. All patients were examined for complications at enrollment.

Roche chemistry analyzer was used to estimate FBS, random blood sugar (RBS), HbA1C, and lipid parameters which included levels of serum total cholesterol (TC), serum triglycerides (TG), LDL-C, and high density lipoprotein cholesterol (HDL-C). Vitamin C analysis was done in Pharmacology laboratory using vitamin C ELISA kit provided by My BioSource.

Table 1: Comparison of treatment and control group before and after supplementation of vitamin C

Parameters	Control group		Treatment group		*P*-value
	Day 0 (Mean±SD)	Day 90 (Mean±SD)	Day 0 (Mean±SD)	Day 90 (Mean±SD)	
FBS (mg/dl)	142±24.3	142±20	142±27	127±24	<0.001
RBS (mg/dl)	193±39.8	189±32.8	198±41.5	179±32	<0.001
HbA1C (%)	7.87±0.64	8.47±0.73	8.03±0.48	7.75±0.67	<0.001
TC (mg/dl)	158±27.5	163±24.6	158±27.5	142±21	<0.001
TG (mg/dl)	155±35.7	157±31.2	164±34.7	137±25	<0.001
HDL-C (mg/dl)	43.79±9.09	43.11±8.61	45.81±9.21	45.31±6.67	0.03
LDL-C (mg/dl)	92.21±21.9	91.79±20.9	93.84±24.8	85.88±17.5	0.03
Vitamin C (mg/dl)	0.41±0.13	0.41±0.12	0.24±0.25	1.57±0.85	<0.001

Table 2: Pearson's correlation coefficient between independent variable Vitamin C and Dependent variables in treatment group

Independent variable	Dependent variable	Correlation coefficient	P-value
Vitamin C	Fasting blood sugar	-0.405	<0.001
Vitamin C	Random blood sugar	-0.288	<0.001
Vitamin C	HbA1C	-0.483	<0.001
Vitamin C	Total cholesterol	-0.328	< 0.001
Vitamin C	Triglycerides	-0.293	< 0.001
Vitamin C	High density lipoproteins	0.226	0.001
Vitamin C	Low density lipoproteins	-0.142	0.04

The sample size calculated was 210 and 105 patients were enrolled in each control and treatment groups. Vitamin C in total dosage of 1500 mg in three equal divided doses (500 mg) per day was prescribed to patients in treatment group for duration of three months.

Oral hypoglycemic medications administered were combination agents specifically dipeptidyl transferase (DPP-4) inhibitors which were advised in dosage of 50 mg along with metformin in dosage of 500 mg or 850 mg twice daily depending on the glycemic indices of patients. The patients in control group received only oral hypoglycemic medications.

The data was processed through SPSS version 26. For demographic parameters like age, mean ± standard deviation was computed, and percentages were calculated for gender distribution. Means of Vitamin C, FBS, RBS, HbA1C, TC, TG, LDL-C, and HDL-C between control and treatment groups were compared by independent t test. The relationship between ascorbate and glycemic and lipid parameters was analyzed by Pearson's correlation. Regression analysis was further performed after performing correlation. The p-value less than 0.05 was considered statistically significant.

Results and Discussion

Two hundred and ten patients were included in study; four patients were lost to follow up 2 each in treatment and control groups. Analysis was done for remaining 206 patients, 103 in each treatment and control groups. There was no difference between mean age of control and treatment groups; 51.18±8.55 years in control group and 51.61±7.73 years in treatment group. The gender distribution in treatment group was 54.4% (n=56) for males and 45.6% (n=47) for females. In control group, 34% (n=35) were males while 66% (n=68) were females. Independent t test showed that there was statistical significance in mean differences of FBS, RBS, HbA1C, TC, TG, HDL-C, LDL-C, and vitamin C at day 0 and 90 between control and treatment groups, as indicated in Table 1. Statistically significant moderately negative Pearson's correlation with p-value < 0.001 was found between Vitamin C and FBS with a correlation coefficient (rs) of -0.405, as well as between vitamin C and HbA1C with an rs-value of -0.483. Vitamin C and RBS were found to have weak statistically significant correlation with p value<0.001 having correlation coefficient (rs) of -0.288; TC with rs = -0.328, p<0.001; TG with rs = -0.293, p<0.001; and LDL-C with rs = -0.142, p<0.04.

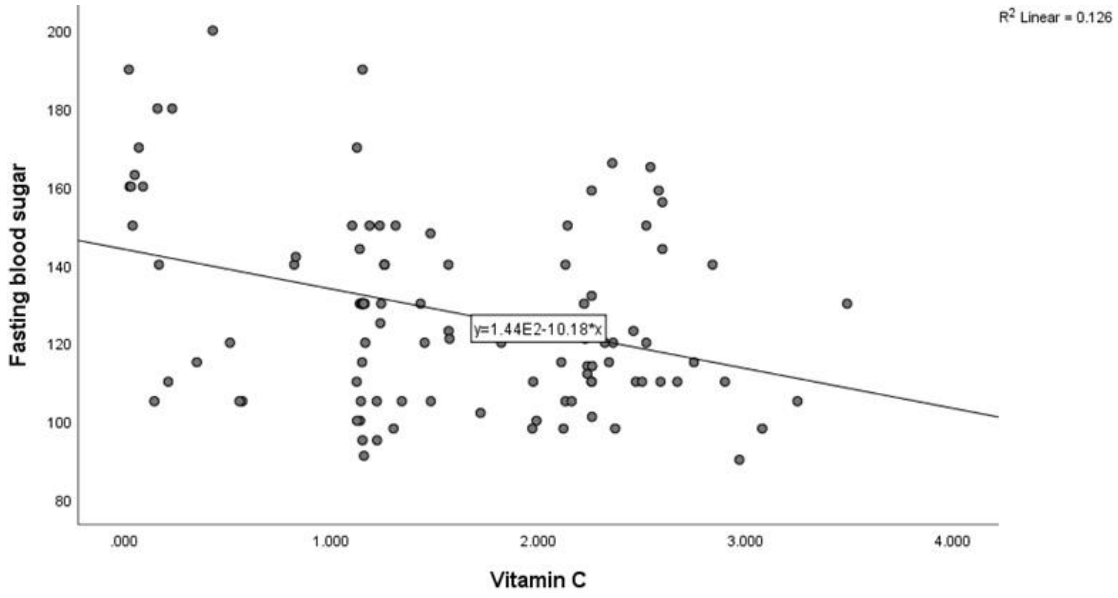


Figure 1: Scatter plot with line of best fit showing R2 Linear= 0.126 between vitamin C (mg/dl) and fasting blood sugar

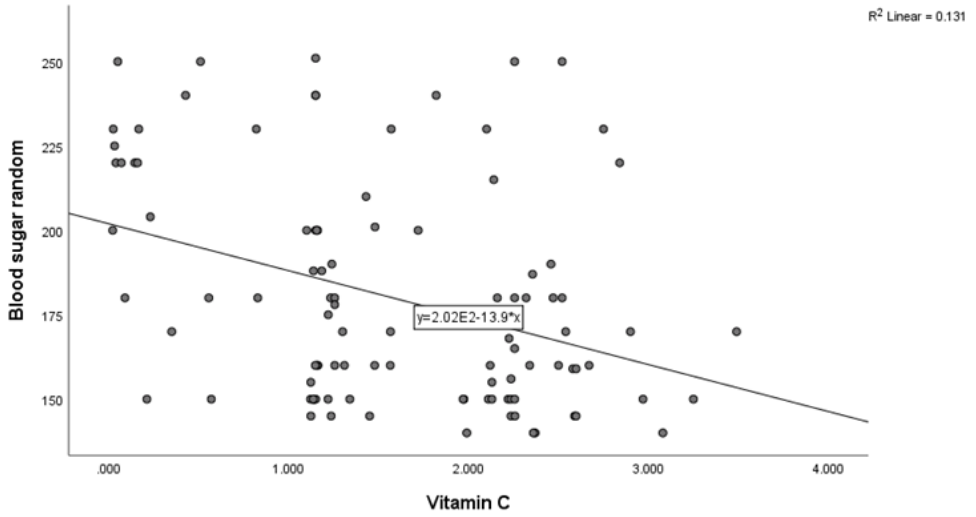


Figure 2: Scatter plot with line of best fit showing R2 Linear=0.131 between vitamin C (mg/dl) and random blood sugar(mg/dl)

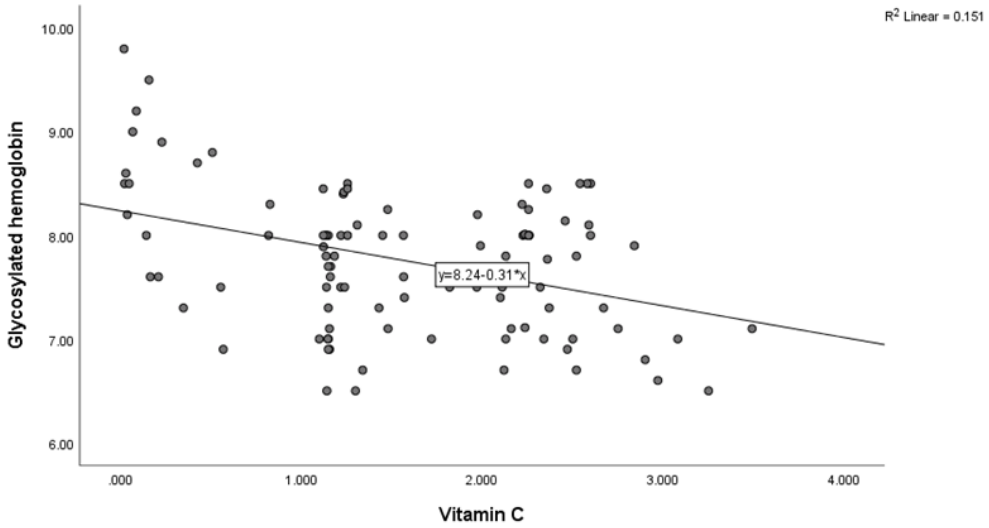


Figure 3: Scatter plot with line of best fit showing R2 Linear=0.151 between vitamin C (mg/dl) and HbA1c (%)

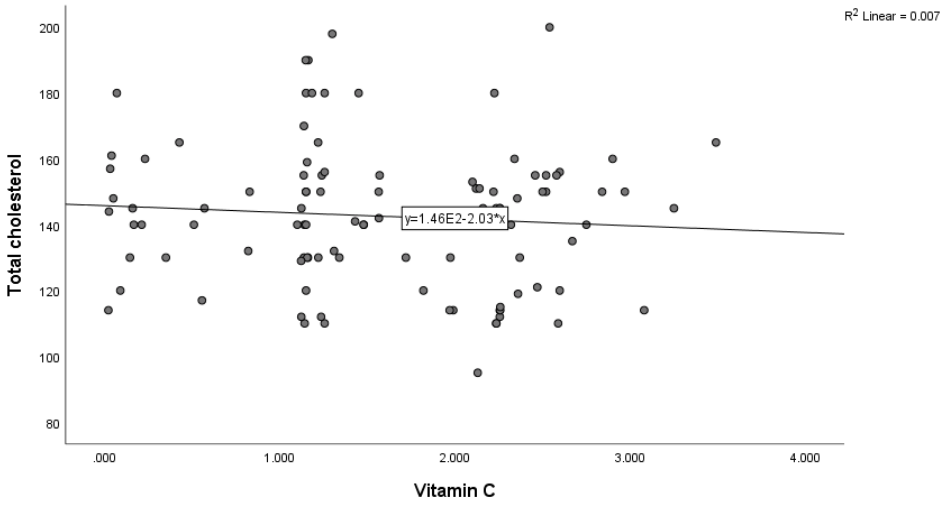


Figure 4: Scatter plot with line of best fit showing R2 Linear=0.007 between vitamin C (mg/dl) and total cholesterol (mg/dl)

A statistically significant weak positive correlation between vitamin C and HDL-C with a correlation coefficient (rs) of 0.226, p<0.001 was observed, as presented in Table 2.

Linear regression showed that vitamin C given in doses of 500 mg thrice a day showed 12.6% variation in FBS with adjusted R^2=11.8%, as displayed in Figure 1; 13.1% variation in RBS with adjusted R^2=12.2%, as depicted in Figure 2; 15.1% variation in HbA1C with adjusted R^2=14.2%, as shown in Figure 3; 0.7% variation in TC with adjusted R^2=0.3%, as demonstrated in Figure 4; 2.1% variation in TG with adjusted R^2= 1.1%, as shown in Figure 5; 8.6% variation in HDL-C with adjusted R^2=7.7%, as shown in Figure 6; 0.6% variation in LDL-C with adjusted R^2= 0.4%, as illustrated in Figure 7.

The administration of Vitamin C over three months in divided doses resulted in a significant reduction in FBS levels with p value less than 0.001, with F(1, 103) = 14.6; RBS levels, with F(1, 103) = 15.2; and HbA1C levels, with F(1, 103) = 17.9. Regression analysis revealed that there was no statistical significance of vitamin C on TC levels F (1, 103) = 0.66, p<0.41; TG level F (1, 103) = 2.18, p<0.14; and LDL-C levels F (1, 103) = 0.60, p<0.43. However, there was statistical significance of vitamin C on HDL-C level F (1, 103) = 9.5, p<0.001.

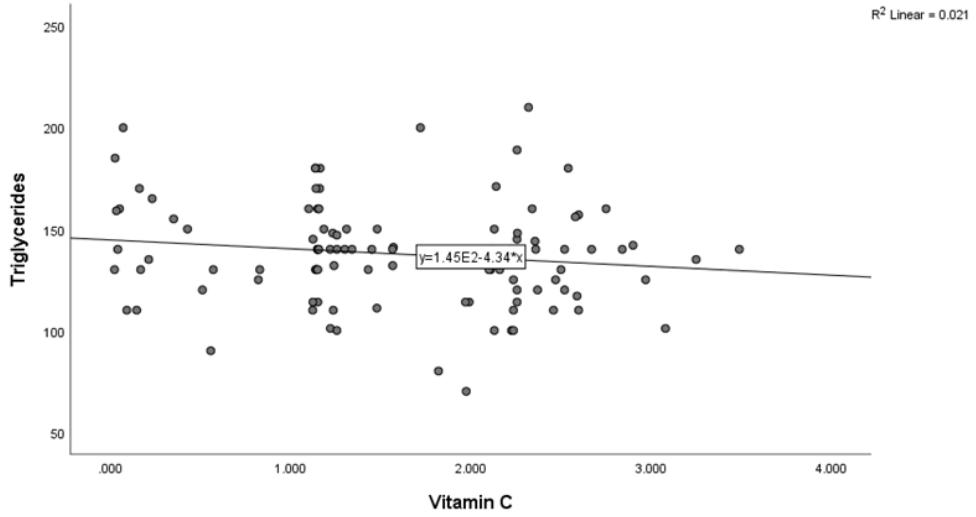


Figure 5: Scatter plot with line of best fit showing R2 Linear=0.021 between vitamin C (mg/dl) and triglycerides (mg/dl)

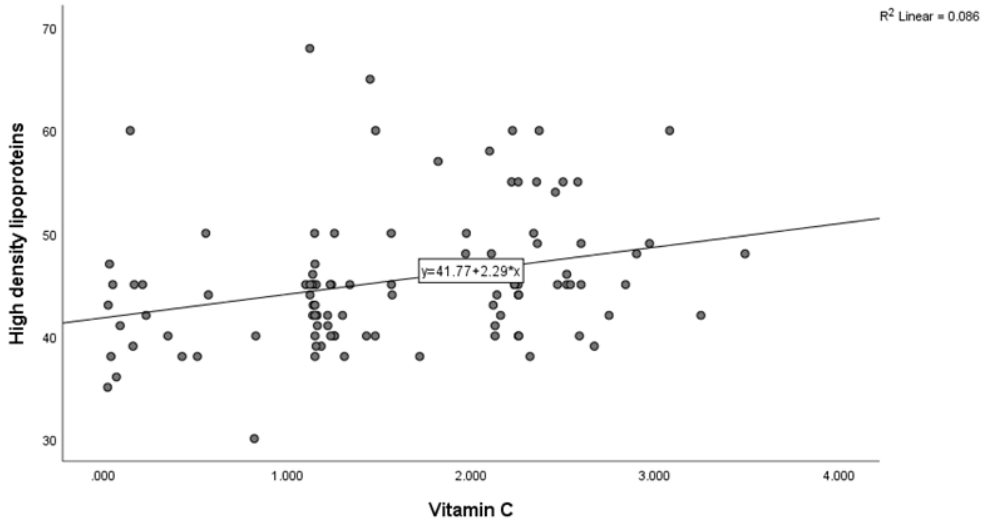


Figure 6: Scatter plot with line of best fit showing R2 Linear=0.086 between vitamin C (mg/dl) and high density lipoprotein cholesterol (mg/dl)

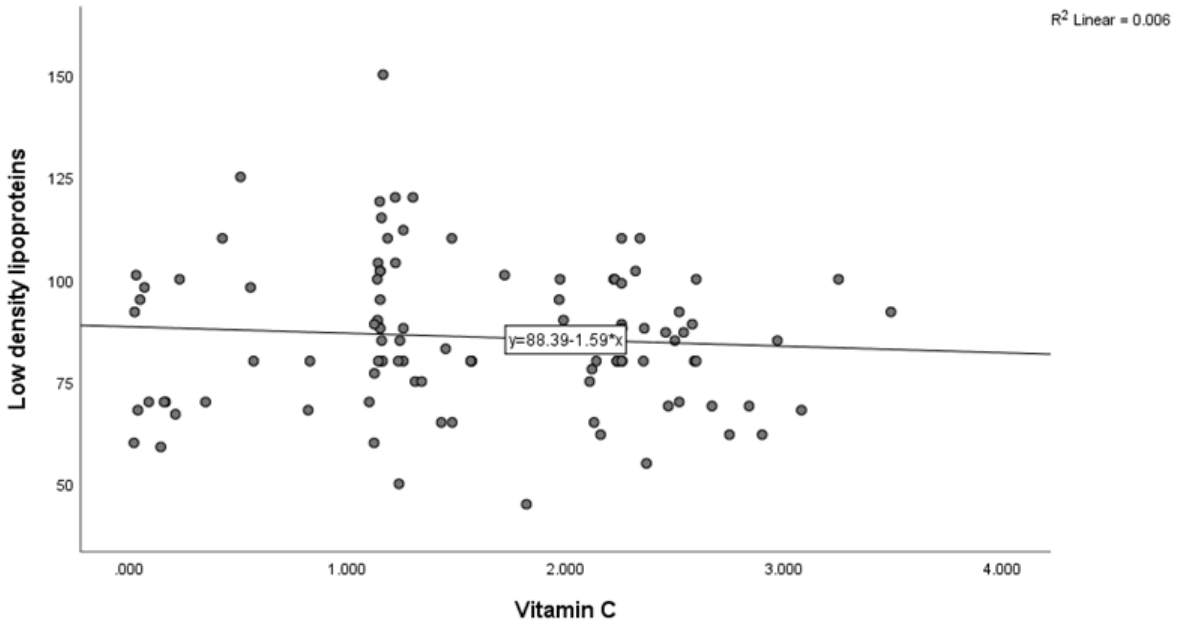


Figure 7: Scatter plot with line of best fit showing R2 Linear=0.006 between vitamin C (mg/dl) and low density lipoprotein cholesterol (mg/dl)

Consuming vitamin C in one's diet serves as a preventive measure against oxidative damage induced by free radicals generated as a result of prolonged type 2 DM and hyperglycemia. Free radicals results in complicating type 2 DM causing lipid peroxidation. In this study serum TC, TG, and LDL were reduced in treatment group which is similar to research conducted in Italy by Paolisso *et al.* who prescribed Vitamin C for four months with total dosage of 1000 mg per day in two equal divided doses showed decrease in TC, LDL, and TG, but this study showed contradictory results in fasting blood glucose which were unaffected as compared to this study which showed decreased results [8]. In another study conducted in United States by Mayer-Davis *et al.*, HDL-C, TG, and LDL-C were not affected significantly which is in contradiction to this study [9]. In study conducted by Upritchard *et al.* in New Zealand vitamin C was prescribed at dose of 500 mg for 4 weeks showed no significant reduction in fasting blood glucose and serum LDL levels in contrast to this study. However, there was similar finding for reduction in TG levels and TC levels while HDL level were increased [10]. Chen *et al.* did not find ant statistical significant reduction in FBS when vitamin C was prescribed at 800mg/day for 4 weeks which is in contrast to this study [11]. FBS, HbA1C, TG, and LDL-C were significantly reduced in research conducted by Afkhami-Ardekani *et al.* when vitamin C was prescribed at dose of 1000 mg daily for 6 weeks which is similar finding to this study [12]. Mazloom *et al.* found significant reduction in FBS similar to this study, but contradictory result were noted in case of lipids where no significant reduction was noted when vitamin C was prescribed at dose of 1000 mg per day for six week [13]. The study conducted by Gutierrez *et al.* showed no significant on lipid parameters when vitamin C was at dose of 250, 500, or 1000 mg for 2 weeks [14].

Ellulu *et al.* conducted study in Palestine where vitamin C was prescribed at dose of 500 mg twice per day for 8 weeks showed significant reduction in FBS, and TG levels similar to this study, but contradictory results were seen in serum T [15]. Mason *et al.* conducted study in Australia where vitamin C intake decreased FPG at dosage of 500 mg twice daily for 4 months [16]. Sanguanwong *et al.* found significant reduction in FBS, HbA1C, serum cholesterol, TG and increased HDL levels which is similar to this study [17]. El-aal *et al.* research showed results in harmony with this study. Vitamin C given in total dosage of 1000 mg in two equal divided dose per day for three months showed decrease in FBS, HbA1C, TC, TG, LDL, and increased HDL levels [18].

Conclusion

To sum up, this study provides compelling evidence supporting the beneficial role of vitamin C as an adjuvant therapy alongside oral hypoglycemic agents in the management of type 2 diabetes mellitus. The statistically significant negative correlations observed between vitamin C supplementation and key markers such as HbA1c, fasting blood sugar, random blood sugar, low density lipoproteins, total cholesterol, and triglycerides underscore the potential of this antioxidant in improving glycemic control and lipid profile in diabetic individuals.

Notably, the observed increase in high-density lipoprotein cholesterol further suggests a positive impact on cardiovascular health. However, our regression analysis revealed no statistically significant effect of vitamin C on low-density lipoprotein cholesterol, triglycerides, and total cholesterol. While these findings indicate a nuanced relationship, the overall favorable impact on several crucial parameters underscores the potential of vitamin C as a complementary therapeutic approach in the multifaceted management of type 2 diabetes mellitus. Further research and larger-scale clinical trials are warranted to elucidate the underlying mechanisms and optimize the dosage and duration of vitamin C supplementation in diabetic patients. Nevertheless, our study contributes valuable insights into the potential of vitamin C as an adjunctive therapy, emphasizing its role in improving metabolic outcomes and potentially reducing the risk of cardiovascular complications in individuals with type 2 diabetes mellitus.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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Authors' Contribution

All authors contributed to data analysis, drafting, and revising of the article and agreed to be responsible for all the aspects of this work.

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