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Effect of vitamin C supplementation on glycemic control in type 2 diabetic patients: a double-blind, prospective, randomized, controlled trial in Egypt

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A – Study Design, B – Data Collection, C – Statistical Analysis, D – Data Interpretation, E – Manuscript Preparation, F – Literature Search, G - Funds Collection

Summary Background. Diabetes mellitus (DM) is a metabolic disorder caused by many factors and related to serious complications. Diabetes mellitus includes oxidative stress and inflammation, in addition to hyperglycemia and resistance to insulin.

Objectives. This study aimed to evaluate the effect of supplementation with vitamin C on blood glucose control and body mass index in type 2 diabetic patients of the family medicine outpatient clinic in Suez Canal University, Ismailia, Egypt.

Material and methods. This was a double-blind, randomized, controlled clinical trial. Sixty patients (n = 60) were distributed randomly into two groups: the intervention group (on 1 g of vitamin C orally for 12 weeks), and the control group (on a placebo for the same period). Only 55 patients completed the study (28 in the intervention group and 27 in the control group). Glycated hemoglobin (HbA, %) and body mass index (BMI) were assessed at the beginning and after 12 weeks.

 $\textbf{Results.} \ \text{The HbA}_{1C} \ \text{percentage significantly decreased in the intervention group, supplemented with vitamin C, after 12 weeks as com$ pared to the placebo group. The body mass index did not change significantly after the intervention. The intervention group had 75% glycemic improvement, while only 33.3% of the subjects improved in the control group. Absolute risk reduction (ARR) was 42%, the number of patients in need of treatment (NNT) was 2.38, the relative risk (RR) was 0.37, and the relative risk reduction (RRR) was 62%. Conclusions. Patients with type 2 diabetes may benefit from adding vitamin C to their routine management to control blood glucose. Key words: ascorbic acid, Body Mass Index, clinical trial, diabetes mellitus type 2, glycated hemoglobin.

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Background

Diabetes mellitus is a chronic debilitating metabolic disorder caused by many factors, with hyperglycemia as the main symptom due to the inability of the body to metabolize foods [1]. Diabetes is a syndrome characterized by insulin resistance, decreased insulin production, and increased glucagon produc-

Diabetes may become an epidemic due to its progressive prevalence, according to the International Diabetes Federation (IDF) Diabetes Atlas, published in 2017, which analyzed data collected from 131 countries. It reported that diabetes affected 425 million people in 2017 and this number is predicted to increase to 629 million worldwide by 2045. The prevalence of diabetes in the Middle East and North Africa is also increasing, from 39 million people in 2017 to a projected 67 million by 2045. This rise is related to rapid lifestyle changes, fast economic development, and high urbanization. The prevalence of diabetes mellitus in Egypt is around 17.3% [3]. In addition, it is expected that the prevalence will double by 2045 [4].

Diabetes mellitus has serious complications if uncontrolled, including macrovascular and microvascular complications. Many studies have highlighted the increased direct and indirect costs of diabetes and its complications. Indirect costs are caused by morbidity, early mortality, and loss of work productivity. These

costs are higher in developing countries, which have a higher burden [5].

The important role of the family physician is to provide comprehensive, continuous, and integrated care for diabetic patients. Family physicians face a major challenge, especially in the screening and prevention of diabetes complications, as diabetes is a chronic and complex condition [6].

Diabetes mellitus includes oxidative stress and inflammation, in addition to hyperglycemia and resistance to insulin [7]. Numerous studies have highlighted the role of free radicals in diabetes mellitus [8]. Many mechanisms such as glucose autooxidation, protein glycosylation, the formation of advanced glycation products, and the polyol pathway contribute to oxidative stress, which causes diabetes mellitus [9].

Although there are many available treatments, diabetes complications are common. Thus, the evaluation of new strategies to improve the effectiveness of therapy will benefit the patients greatly. One of the new strategies being evaluated is the free-radical-scavenging antioxidant vitamin C [10].

Vitamin C (ascorbic acid) is involved in many enzymatic reactions, such as collagen synthesis [11]. People cannot produce vitamin C due to a lack of the enzyme L-gluconolactone oxidase, which catalyzes the synthesis of ascorbic acid [12]. Many investigators have reported a decreased level of vitamin C in type 2 diabetic patients [13, 14]. Vitamin C is structurally similar to glucose and can replace it in many chemical reactions to prevent non-enzymatic protein glycosylation [14].

The importance of vitamin C in type 2 diabetes mellitus comes from a theory that hyperglycemia inhibits the cellular uptake of dehydro-ascorbic acid (DHA) (the oxidized form of vitamin C) [15]. Glucose strongly inhibits the uptake of DHA in red blood cells; therefore, hyperglycemia is thought to cause vitamin C deficiency within the cells in diabetic patients [16]. DHA uptake into the cells is facilitated through glucose transporter 1 (GLUT1) and glucose transporter 3 (GLUT3), which transport DHA in competition with glucose [17]; this effect may be overcome by a large intake of vitamin C [18].

Current studies on vitamin C supplementation are contradictory in terms of its effect on blood glucose and glycosylated hemoglobin (HbA_{1c}) levels [19]. Some scholars have reported that 1,000 mg/day of vitamin C might help in improving plasma glucose in addition to a normal diet and treatment schedule [14].

Objectives

In Egypt, there is insufficient data available about the effect of vitamin C supplementation on ${\rm HbA}_{\rm 1c}$ in type 2 diabetic patients. Egypt is a unique culture where people have different eating habits and different intake of vitamin C supplementation than in other countries and nations. In addition, in Egypt there is no regimen for the prescription of vitamin C to diabetic patients. This study aims to improve medical care provided to type 2 diabetics by evaluating the effect of vitamin C supplementation on ${\rm HbA}_{\rm 1c}$ and body mass index.

Material and methods

Setting and design

This is a double-blinded, randomized, controlled study. It was conducted among type 2 diabetic patients using non-insulin pharmacological agents who were treated in a family medicine outpatient clinic, in the Suez Canal University hospital in Ismailia, Egypt. The clinic receives diabetic patients daily for follow-up and prescription of the pharmacological drugs from the hospital pharmacy which are funded by the government. The diabetic patients have their medical records stored in the clinic's files. The study was conducted between October 2018 and December 2019.

Inclusion criteria

Patients with type 2 diabetes aged 30–60 years who visited the clinic for a routine follow-up, regularly took oral non-insulin pharmacological agents for more than six months, and had HbA_{lc} concentrations of > 7% were enrolled.

Exclusion criteria

Patients enrolled in another research study and receiving another modality, type 1 diabetic patients and type 2 diabetic patients on insulin, patients with severe or uncontrolled cardio-vascular disease, psychiatric disease, or cognitive impairment interfering with treatment compliance, pregnant or lactating women, and post-menopausal women were excluded from the study.

Sampling and randomization

The sample size was calculated with 80% power and a level of significance at 0.05 based on a previously published study [14], then a 10% drop-out was added to create the sample. The patients (n: 60) were allocated randomly into two groups. The **intervention group** (vitamin C group): the patients in this group (n: 30) were supplemented with 1 g of oral vitamin C in addition to the oral non-insulin pharmacological agents. The **control**

group (placebo group): the patients in this group (n: 30) were supplemented with an oral placebo in addition to the oral non-insulin pharmacological agents.

The sample was selected by a non-probability convenient sampling technique from type 2 diabetic patients of the family medicine outpatient clinic of the Suez Canal University hospital within one month. HbA $_{\rm 1C}$ testing was requested from all patients. Simple randomization was applied to the patients who fulfilled the inclusion and exclusion criteria. The allocation was carried out by concealing in an envelope labelled A or B by an independent colleague. Both participants and researchers were blinded. The drugs were similar in shape and packaging for both groups.

Intervention and data collection

A semi-structured interview contained information about age, gender, residence, education level, occupation, diabetes duration, drug usage, diabetic complications, and adherence to a healthy diet. The authors validated the questionnaire before starting the current study by a pilot study on 10 patients.

The patients in the two groups were asked to follow dietary restrictions and lifestyle modification as usual as they followed up in the clinic; they had leaflets with all necessary dietary and physical activity information to avoid contamination bias. Patients from both groups were instructed to take either a 1-g oral vitamin C or a placebo once daily for 12 weeks; both drugs were similar in structure, shape, size, texture, weight, and packing. The patients were allowed to ask questions about any possible side effects and the degree of compliance was monitored at week 4, 8, and 12 from the beginning of the study by patient interview and pill counts; those taking ≥ 90% of the drugs (e.g. ≥ 25 capsules of vitamin C in four weeks) were considered compliant. Adherence to the oral non-insulin pharmacological agents, healthy diet, and physical activity were assessed through self-perception. A 24-hour dietary recall was used at the beginning of the study and at every appointment as the subjects recall drug intake, diet, and physical activity the day before the appointment to assess their adherence to drugs, diet, and physical activity. Two patients (from the intervention group) were withdrawn after ten weeks of the study as their anti-diabetic therapy had changed to insulin. Three patients (from the placebo group) were withdrawn after eight weeks of the study without mentioning the reasons (Figure 1). Vitamin C and the placebo capsules were packaged in closed bottles similar in shape and size and coded A or B.

The placebo contained inulin powder, which is a soluble dietary fiber, a natural polysaccharide extracted from chicory, and does not affect blood glucose level.

Blood samples were collected from all patients (in both vitamin C and placebo groups) before the study (baseline sample) and then after 12 weeks of treatment to monitor the change in glycated hemoglobin (HbA_{1c}) as an indicator of glycemic control (study flowchart in Figure 1).

Hyperglycemia is defined as elevated blood glucose. Diabetes is diagnosed if the fasting plasma glucose (FPG) value equals or is more than 126 mg/dl or the 2-h plasma glucose after a 75-g oral glucose tolerance test (OGTT) equals or is more than 200 mg/dl, or HbA₁₀ equals or is more than 6.5% [2].

Outcome measures

The main outcome in both groups was as follows:

- HbA_{1c} measured in week 12 of the therapy and compared to the pre-intervention level,
- BMI measured in week 12 of the therapy and compared to the pre-intervention level.

The study led to two main outcomes: both HbA_{1c} and body mass index are long-term results as opposed to fasting blood glucose or post-prandial glucose, which are short-term and

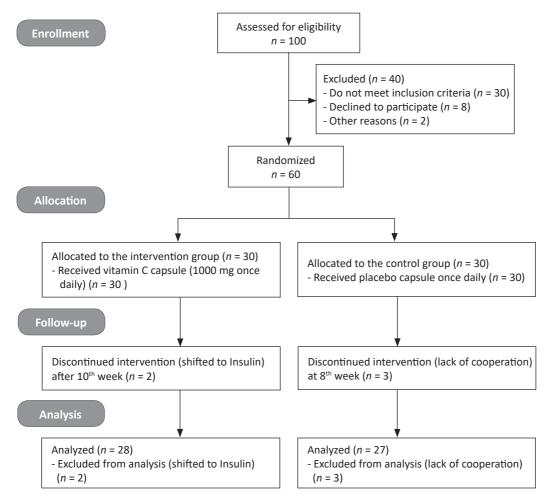


Figure 1. Study flowchart

could be affected with any change in diet, exercise, forgetting to take pills, or even psychological stress. The HbA_{1c} has many advantages over FPG and OGTT, such as more convenience (fasting is not required), more pre-analytical stability, and less day-to-day changes over life events [2].

 ${\rm HbA}_{\rm 1c}$ is assessed by using appropriate kits. The test was performed in the Suez Canal University Hospital Laboratory using COBAS 6000 FOR CLINICAL CHEMISTRY by the Tina-quant $^{\oplus}$ HbA $_{\rm 1c}$ assay, Roche. No fasting is required, but 2 ml of blood is needed. The laboratory devices are certified and calibrated on a routine basis.

Ethical considerations

The institutional Ethics Committee approved the study in July 2017 (Research 3172#). Informed written consent from all participants was included in the study. The clinical trial was registered in the Pan African Clinical Trials Registry retrospective (trial number: PACTR202006610508575).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 25.0). Numerical values were expressed as mean and standard deviation (SD). Continuous variables were compared using the independent samples t-Test for HbA $_{1C}$ and BMI. The Chi-squared and Fisher's exact tests were used to compare categorical variables between the groups. The paired t-Test was computed between primary outcome variables before (t_0) and after (t_2) the intervention. Multivariable linear regression analysis was used for predictors of HbA $_{1C}$ (the primary outcome). A p-value of < 0.05 was considered to be statistically significant.

Results

Out of 60 patients selected at the beginning of the research, 55 patients completed the study. Two patients in the vitamin-C group and three patients in the placebo group withdrew. A comparison of the baseline characteristics of both groups revealed no significant differences between the intervention and control groups: the age variable was comparable in both groups, with a mean age of 48.03 ± 7.91 years in the intervention group and 48.47 ± 6.66 years in the control group. Females accounted for the majority of the sample in both groups (63.3% of the intervention group and 70% of the control group). Urban residency was higher in both the intervention and the control group. The most prevalent educational levels among the patients were basic literacy and an intermediate education level (80% and 76.7% in the intervention and the control group, respectively). About 56.7% of the patients in the intervention group had diabetes for less than five years, while 40% of the patients in the control group had diabetes from five to ten years. Combined oral hypoglycemic drugs (Sulfonylurea and metformin) were taken by most (60%) of the participants in the intervention group and by 73.3% of the participants in the control group, while no other hypoglycemic drugs were taken. Eighty percent and 76.7% of the subjects in the intervention and the control group, respectively, were on vitamin B. Finally, comorbidities were present in 66.7% of the intervention group members versus 50% of the control group members (Table 1).

Adherence to a healthy diet, oral non-insulin pharmacological agents, and vitamin C or placebo did not statistically significantly differ between the intervention and the control groups. Acceptable or good adherence to a healthy diet ranged from 63.3% to 89.3%, and good adherence to drugs ranged from 66.7% to 96.4%, while excellent adherence to the placebo or vitamin C ranged from 76.7% to 96.4% (Table 2).

Variables	Intervention group	Control group	Test value	n .	
variables	(n = 30)	(n = 30)	lest value	p	
Age (years), mean ± SD	48.03 ± 7.91	48.47 ± 6.66	0.229	0.819 ^a	
Gender, <i>n</i> (%)					
male	11 (36.7%)	9 (30.0%)	0.300	0.584 ^b	
female	19 (63.3%)	21 (70.0%)			
Residency, n (%)					
urban	23 (76.7%)	24 (80.0%)	0.098	0.754 ^b	
rural	7 (23.3%)	6 (20.0%)			
Educational level, n (%)					
illiterate	4 (13.3%)	3 (10.0%)	0.930	0.870 ^c	
literate	18 (60.0%)	17 (56.7%)			
intermediate	6 (20.0%)	6 (20.0%)			
university	2 (6.7%)	4 (13.3%)			
Occupation, n (%)					
nonworking	12 (40.0%)	18 (60.0%)	2.593	0.274 ^b	
unskilled manual worker	9 (30.0%)	7 (23.3%)			
skilled or semiprofessional	9 (30.0%)	5 (16.7%)			
Duration of DM					
≤ 5 years	17 (56.7%)	10 (33.3%)	1.929	0.381 ^b	
5-10 years	6 (20.0%)	12 (40.0%)			
> 10 years	7 (23.3%)	8 (26.7%)			
Oral drug regimen					
Metformin	6 (20.0%)	3 (10.0%)	1.461	0.477 ^c	
Sulfonylurea	6 (20.0%)	5 (16.7%)			
combined therapy	18 (60.0%)	22 (73.3%)			
Supplementation usage					
vitamin B	24 (80.0%)	27 (90.0%)	1.176	0.472 ^b	
associated comorbidities	20 (66.7%)	15 (50.0%)	1.714	0.190 ^b	

^a p-values are based on an independent t-Test. Statistical significance at p < 0.05; ^b p-values are based on the Chi-squared test. Statistical significance at p < 0.05; ^c p-values are based on Fisher's exact test. Statistical significance at p < 0.05.

Table 2. Adherence in both groups before the intervention and at different follow-up time-points of the intervention ($n = 60$)					
Variables	Intervention group (n = 30)	Control group (n = 30)	Test value	p	
Adherence to diet					
at start	19 (63.3%)	20 (66.7%)	0.073	0.787 ^a	
week 4	18 (60.0%)	24 (80.0%)	2.857	0.158 ^a	
week 8	22 (73.3%)	21 (75.0%)	0.021	0.885 ^a	
week 12	25 (89.3%)	23 (85.2%)	0.208	0.705 ^b	
Adherence to drugs					
at start	25 (83.3%)	20 (66.7%)	2.222	0.233 ^a	
week 4	26 (86.7%)	27 (90.0%)	0.162	1.000 ^b	
week 8	28 (93.3%)	27 (96.4%)	0.526	0.100 ^b	
week 12	27 (96.4%)	25 (92.6%)	0.392	0.611 ^b	
Adherence to vitamin C/ placebo					
week 4	23 (76.7%)	28 (93.3%)	3.268	0.145 ^b	
week 8	27 (90.0%)	26 (92.9%)	0.150	1.000 ^b	
week 12	27 (96.4%)	25 (92.6%)	1.159	0.352 ^b	

^a p-values are based on the Chi-square test. Statistical significance at p < 0.05; ^b p-values are based on Fisher's exact test. Statistical significance at p < 0.05.

Table 3. Outcome measures of HbA _{1c} and BMI (after 12 weeks) (n = 60)					
Variables	Intervention group (n = 30) mean ± SD	Control group (n = 30) Test value mean ± SD		ie p	
Baseline measures HbA _{1c} (%) BMI	8.75 ± 0.64 32.03 ± 3.17	8.93 ± 0.65 31.81 ± 3.04	0.055 0.701	0.289 ^a 0.788 ^a	
Post-intervention HbA _{1c} (%) BMI	7.95 ± 1.12 31.19 ± 3.1	8.77 ± 0.78 31.36 ± 3.3	4.029 0.492	0.003 ^a * 0.847 ^a	

 $^{^{}a}$ p-values are based on an independent t-Test. *Statistical significance at p < 0.05; HbA $_{1C}$ – glycosylated hemoglobin; BMI – body mass index.

Table 4. Glycemic improvement (after 12 weeks) (n = 55)					
Intervention group (n = 28) n (%)	Control group (<i>n</i> = 27) <i>n</i> (%)	ARR	NNT	RR	RRR
21 (75.0%)	9 (33.3%)	42%	2.38	0.37	62%

ARR – absolute risk reduction, NNT – number needing treatment, RR – relative risk, RRR – relative risk reduction.

Table 5. Multivariable linear regression analysis of determinants of HbA _{1c} of the study participants						
Predictors	Unstandard	ized coefficients	Standardized coefficients	(95% CI)	p	
	в	Std. Error	β			
(Constant)	8.909	1.894			0.000	
Gender (ref: male) Education level	-0.859 0.158	0.341 0.168	-0.391 0.127	(-1.545 – -0.173) (-0.179 – 0.496)	0.015* 0.351	
Duration of diabetes Comorbidities BMI	0.270 -0.413 0.044	0.162 0.289 0.44	0.213 -0.199 0.134	(-0.056 - 0.596) (-0.994 - 0.168) (-0.046 - 0.133)	0.103 0.159 0.332	
Vitamin C vs placebo	-1.149	0.557	-0.253	(-2.268 – -0.030)	0.044*	

ANOVA < 0.001, R^2 = 35.1%, * Statistical significance at p < 0.05.

Table 3 shows that by the end of week 12 of vitamin C or placebo supplementation, the reduction in the level of $\mathrm{HbA}_{1\mathrm{c}}$ in the vitamin C group compared to that in the placebo group was significant (p=0.003), with a mean (SD) $\mathrm{HbA}_{1\mathrm{c}}$ value of 7.95 (1.12) for the intervention group and 8.77 (0.78) for the control group. There was a reduction in body mass index after 12 weeks in both groups, but it was not significant.

Table 4 illustrates that 21 subjects (75% participants of the intervention group) had glycemic improvement (decreased post-intervention level of HbA_{1c} compared to the pre-intervention values) while only nine subjects (33.3%) improved in the control group. Absolute risk reduction (ARR) was 42%, the number of patients in need of treatment (NNT) was 2.38, the relative risk (RR) was 0.37, and the relative risk reduction (RRR) was 62%.

Table 5 shows that the female gender and administration of vitamin C were negative predictors for the ${\rm HbA}_{\rm 1c}$ level. There was a decrease of 0.859 points in ${\rm HbA}_{\rm 1c}$ in females compared to males. There was a decrease of 1.149 points in ${\rm HbA}_{\rm 1c}$ of diabetic patients who received vitamin C compared to those on placebo.

Discussion

This study indicated that supplementation with vitamin C in a dose of 1 g/day orally for 12 weeks significantly decreases HbA_{1c} in type 2 DM patients. These results were similar to those of Dakhale et al., 2011, India, who stated that HbA_{1c} decreased significantly (from 8.26% \pm 0.09% to 7.80% \pm 0.08% in the intervention group after intake of 1 g of oral vitamin C daily for 12 weeks [20].

The results of this study agree with the findings published in a study from Iran, which showed that HbA_{1c} reduced significantly from $8.82\% \pm 1.3\%$ to $7.66\% \pm 1.3\%$ in the intervention group after administration of 1 g of vitamin C twice daily but for six weeks only [14].

In addition, the present study results were similar to the data previously published in Saudi Arabia showing that 1 g of vitamin C per day administered to type 2 diabetes patients with oral antidiabetic drugs improved HbA $_{\rm 1C}$ by 12% after vitamin C intake compared to levels before the intervention [21].

In another study, it was concluded that supplementation of vitamin C lowers HbA_{1c} in diabetic patients in Cameroon, and this conclusion is consistent with the results of the present study [22]. All these congruent findings could be explained in another study which showed improvement in HbA_{1c} after 60 days on 1,000 mg vitamin C due to a decrease in lipid peroxidation, insulin levels, and insulin resistance and an increase in insulin sensitivity [23].

It was noted that the majority of the sample were on combined oral hypoglycemic drugs (about 60% of the participants). Vitamin C improved glycated hemoglobin in the intervention group, but not in the placebo group. This result is similar to another study which discovered that patients in the intervention group on metformin and ascorbic acid were twice more likely to reduce their ${\rm HbA}_{\rm 1C}$ than those control patients who took metformin alone for a year. When compared to acetylsalicylic acid, vitamin C was ten times more likely to reduce risk factors contributing to long-term diabetes complications [24]. This confirms the importance of ascorbic acid supplementation to the treatment of diabetics.

Another study confirmed the same idea of the effect of antioxidants such as vitamin C and/or vitamin E on HbA_{1c} and concluded their beneficial effect in type 2 diabetes in either improvement of clinical condition or diabetes pathogenesis and complications [25].

There are a few studies which investigated the role of vitamin C on the glycemic target level and showed a decrease in the glycemic level, though it was not significant. One of these studies was carried out in India and revealed a difference of 0.17 and 0.37 of ${\rm HbA}_{\rm 1c}$ levels in the control and the intervention group, respectively (p-value was more than 0.05) [26]. This discrepancy was attributed to a lower dose of vitamin C used as only 500 mg of oral vitamin C was taken for three months.

In addition, the current study was inconsistent with the results of a study conducted in Iran in which 800 mg of vitamin C was prescribed for type 2 diabetic patients for eight weeks. The researchers found no significant change in the level of HbA $_{\rm 1C}$ [27]. This difference may be due to the consumption of a lower dose of vitamin C for a shorter duration than in our study.

A recent study evaluated Rutin and vitamin C as a combination effective on oxidative stress and glycemic control in Egypt. It included 53 type 2 diabetes patients randomized into three groups: one group was given a combination of 60 mg of Rutin with 160 mg of vitamin C three times daily besides usual treatment. The second group was given vitamin C 500 mg once daily, while the last group used their usual oral antidiabetic treatment only for eight weeks. There was a non-significant reduction in the levels of ${\rm HbA}_{\rm 1c}$ in both groups compared to the baseline. This could be ascribed to the lower duration or lower dose of vitamin C (< 1,000 mg) that leads to an inadequate increase in vitamin C levels in diabetes [28].

Another study investigated the effect of ascorbic acid on microvascular reactivity at the level of capillaries, and on inflammatory cytokines or ox-LDL and found no benefit. The study was only for two weeks not 12 weeks like in our study, so this could

be effect of duration of supplementation [29]. In addition, another study on a lower dose of ascorbic acid (500 mg daily for two months) suggested no benefit of vitamin C intake but was carried out on a group of fewer participants, with a lower dose, and shorter duration [30].

Regarding BMI (body mass index) in this study, the difference between the intervention and control group before and after the intervention was insignificant. The mean of BMI after 12 weeks was 31.19 ± 3.1 kg/m² and 31.36 ± 3.3 kg/m² for the intervention and the control group, respectively (p-value = 0.847). The results of our study correspond to the results of other studies [2, 31, 32]. There was a reduction in body mass index after 12 weeks in both groups but a not significant one, which may be due to the Hawthorne effect.

The decrease in glycated hemoglobin is mainly related to the effect of vitamin C on θ cells as an antioxidant, and on target tissues such as muscle and fat. Vitamin C caused reduction in glucose toxicity and prevented deficiency in θ cell mass and insulin. Another beneficial effect which helps in the reduction of blood glucose level is that vitamin C levels in the plasma regulate insulin action in diabetic patients. In addition, there is improvement in non-oxidative glucose metabolism [33]. Ascorbic acid competes with glucose for binding with amino groups on the hemoglobin beta chain [34]. Another pathway connected to the increase in the serum glutathione, and the decrease of glycosylated hemoglobin after long-term supplementation with ascorbic acid are interrelated [35].

Limitations of the study

The results of the current study may be limited as it was a single-center study on only 60 patients, which may reduce

its generalizability and external validity and applicability. In addition, the results dependent on glycated hemoglobin only; the study did not assess other variables such as fasting blood glucose, post-prandial glucose, and plasma ascorbic acid. Nevertheless, this point is strong as it measures control of blood glucose over a long period not dependent on the effect of food, which may be transient. Adherence to diet and physical therapy depends on recall and self-perception, which could affect results due to recall bias. However, this study has its strengths as it was double-blind, based on administration of a high dose of vitamin C (1 g), and control patients took a placebo similar in shape and form to the intervention capsules. In addition, it took 12 weeks to obtain accurate results for HbA_{1C} unlike in other studies with shorter duration.

Conclusions

The study concluded that supplementation with vitamin C for 12 weeks to type 2 diabetes patients may improve the quality of life and decrease diabetes complications due to its effect on glycated hemoglobin, as it improves ${\rm HbA}_{\rm 1c}$ in diabetic patients on oral hypoglycemic drugs. Absolute risk reduction was 42%, while relative risk reduction was 62%, and the number of patients who needed treatment was 2.38.

The study concluded that vitamin C benefit patients with type 2 diabetes, however further studies on vitamin C supplementation using different doses and durations in more than one center are needed to confirm our findings.

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Conflicts of interest: The authors declare no conflicts of interest.

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