

Vitamin C as a Therapeutic Support in Type 2 Diabetic Patients with Dermatological Complications: A Review

A Sridevi¹, Prof. Dr. Pallavi Singh²

¹ PhD Research Scholar, Department Public Health, Poornima University. Email: ysd174@gmail.com

² Associate Professor, Faculty of Public Health, Poornima University, Jaipur, Rajasthan.

Email: pallavi.singh@poornima.edu.in

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ABSTRACT

Vitamin C has long been recognized as an essential nutrient for maintaining overall health, and its potential benefits for individuals with type 2 diabetes (T2DM) have gained considerable attention. This review examines the role of vitamin C as a game-changer in managing patients with T2DM dealing with skin issues. The aim is to explore the existing evidence and shed light on the potential therapeutic effects of vitamin C supplementation. Numerous studies have revealed lower levels of vitamin C among individuals with T2DM, suggesting a possible association with skin complications. The correlation between vitamin C intake and T2DM has been extensively studied, with most research highlighting a strong relationship. While dietary vitamin C intake alone does not entirely account for the decreased levels observed in T2DM patients, the need for vitamin C supplementation in this population has been proposed. This review highlights the potential game-changing role of vitamin C in managing individuals with T2DM and related skin issues. Vitamin C supplementation shows promise in improving skin health, potentially through its involvement in collagen synthesis, antioxidant defense, and wound healing.

Keywords: Vitamin C Deficiency, Type 2 Diabetes, Vitamin C Supplements, Glycemic Control, Blood Pressure, Hb1Ac, T2DM.

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INTRODUCTION

Type II diabetes: Type 2 diabetes (T2DM) is a chronic metabolic disorder characterized by insulin resistance and high blood glucose levels. Alongside its systemic manifestations, T2DM is often associated with various skin issues that significantly impact the quality of life for affected individuals. These skin complications can range from dermatitis and skin infections to delayed wound

healing and impaired skin integrity (Zhen, 2021). Given the rising prevalence of T2DM worldwide, there is an increasing need to explore novel therapeutic approaches to address these skin issues and improve patient outcomes. The below pie chart (fig 1.1) shows that most of the cases of diabetes are actually T2DM, hence this study is even more important in its nature.

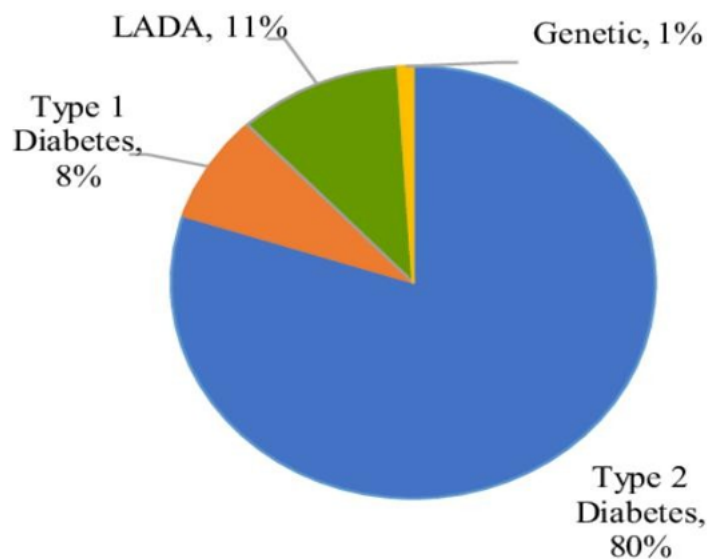


Fig 1.1: pie chart with diabetes case distribution

Source: Musafar, Karar & Huyop, Fahrul & Ewadh, Mufeed & Supriyanto, Eko & Rava, Mohammad. (2020). A Systematic Mapping Study on the Risk Factors Leading to Type II Diabetes Mellitus Mellitus. *Karbala International Journal of Modern Science*. 6. 10.33640/2405-609X.1677.

Vitamin C and Type II Diabetes: Vitamin C intake can offer significant benefits for individuals with type 2 diabetes (T2DM). First and foremost, vitamin C acts as a potent antioxidant, protecting cells and tissues from oxidative stress (Kotbi, 2015), which is known to be heightened in T2DM. This antioxidant activity helps combat the damage caused by free radicals and may contribute to improved glycemic control (Cheng, 2006). Furthermore, vitamin C plays a crucial role in collagen

synthesis, supporting skin health and potentially aiding in the prevention and management of skin complications often associated with T2DM (Kotbi, 2015). Additionally, studies have suggested that vitamin C supplementation may help reduce blood pressure and improve arterial stiffness in individuals with T2DM, thereby mitigating the risk of cardiovascular complications. Overall, incorporating sufficient vitamin C intake, either through dietary sources or supplementation, may provide a valuable adjunctive approach to managing T2DM and its associated complications, promoting overall well-being and improved health outcomes for affected individuals. Studies have shown the distribution of Vit. C deficiency in various age groups, as shown in figure 1.2 below.

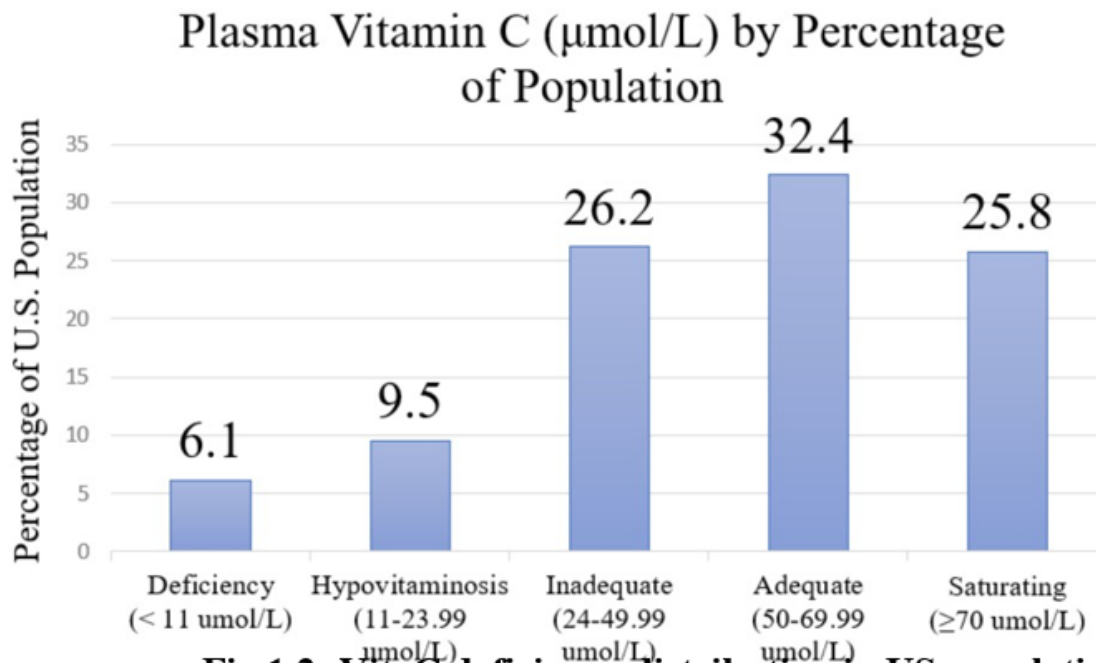


Fig 1.2: Vit. C deficiency distribution in US population.

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Source: Crook J, Horgas A, Yoon S-J, Grundmann O and Johnson-Mallard V 2021 Insufficient Vitamin C Levels among Adults in the United States: Results from the NHANES Surveys, 2003– 2006 *Nutrients* **13** 3910 Online: <http://dx.doi.org/10.3390/nu13113910>

Several studies have reported lower levels of vitamin C in individuals with T2DM, independent of dietary intake, suggesting an association between vitamin C deficiency and the development or exacerbation of skin issues. Consequently, researchers have been investigating the

therapeutic potential of vitamin C supplementation in managing these complications and improving skin health in T2DM patients. Understanding the effects of vitamin C on skin-related parameters such as elasticity, hydration, and wound healing is crucial for developing effective interventions that can positively impact the lives of individuals with T2DM (Darko, 2002). The below figure 1.3 summarizes the top level conceptual understanding gained from the existing data in a block diagram.

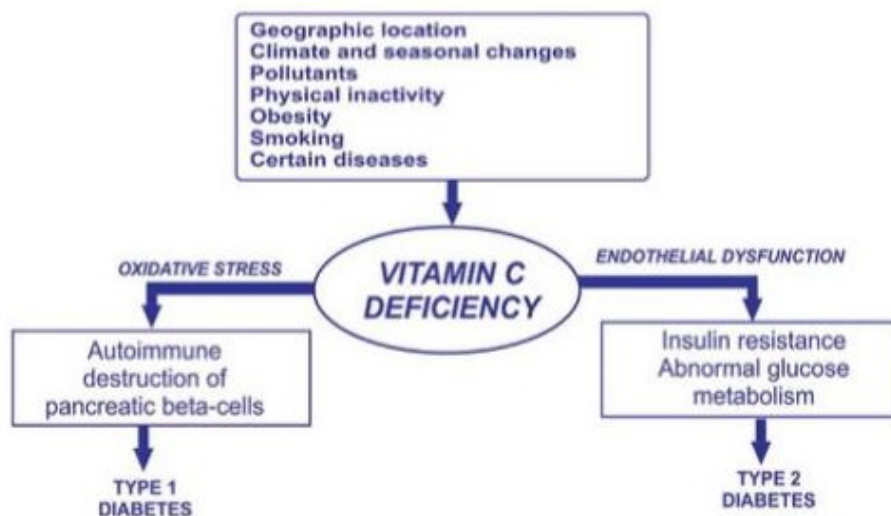


Fig 1.3: Linkage of Vit. C deficiency

Source: Yahaya TO et. al. (2021). Mechanistic links between vitamin deficiencies and diabetes mellitus: a review. <https://doi.org/10.1080/2314808X.2021.1945395>

Objective: This review aims to provide a comprehensive examination of the existing literature on the role of vitamin C as a game-changer in managing skin issues specifically in T2DM patients. By analyzing and synthesizing the available evidence, we seek to highlight the potential benefits of vitamin C supplementation and its impact on skin health. Additionally, we will explore the mechanisms through which vitamin C exerts its effects on the skin and discuss the implications of these findings for clinical practice.

Ultimately, this review aims to contribute to the growing body of knowledge surrounding the potential use of vitamin C as a therapeutic tool to improve skin complications in individuals with T2DM. By providing a deeper understanding of the underlying mechanisms and clinical implications, we can pave the way for further research and the development of evidence-based strategies to enhance the management of skin issues in this patient population.

METHODS

This review was carefully curated to contain only the most relevant and up-to-date literature in its field. The databases Scopus, PubMed, and Google Scholar were searched extensively using topics like "vitamin C," "type 2 insulin resistance," "skin issues," and others to find relevant articles. In order to find the most recent studies, the search was restricted to those written in English and

published between 2006 and 2023. To ensure that no relevant researches were overlooked, we also manually combed through the standard lists of publications that were fruitful in our first search.

A large number of articles were found in the original search; they were sorted through depending on how closely they related to the initial search terms. There were two phases to the screening procedure. First, we checked the titles and abstracts of the included studies to see whether they were relevant to our topic of interest: vitamin C's effect on skin problems in people with type 2 diabetes. The second phase was a comprehensive evaluation of full-text papers to make sure they contained sufficient information on the structures of action, clinical data, or practical issues associated with the consumption of vitamin C in this setting.

The review did not include any articles that did not fulfill the criteria for inclusion, such as those that only discussed other vitamins, a different patient demographic, or a skin problem unrelated to the study's topic. Studies that lacked proper research design or methodological rigor, such as instances or opinion articles, were also disregarded.

Using this methodical approach, we chose the best publications to present a thorough review of the issue, including observational studies, interventional studies, and mechanistic investigations. This review study provides a critical analysis of the selected publications, as well as a summary and synthesis of the important results and implications. Below fig 2.1 illustrates our selection process.

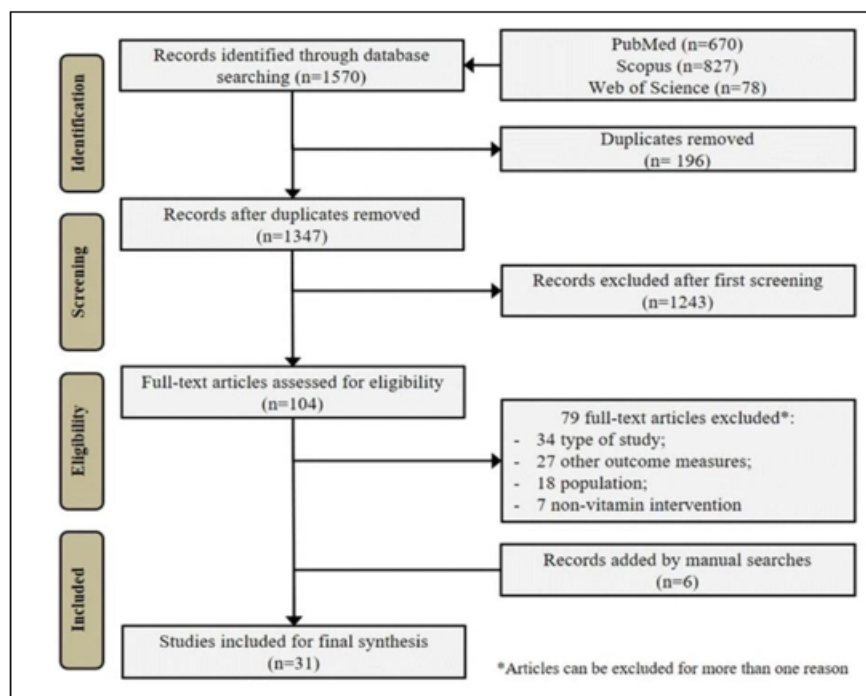


Fig 2.1: Methodology of Paper Selection

RESULTS

Many of the researchers (Darshika ,2014), (Praveen D, 2020) and others brought out the fact that Vitamin C levels are lower among people with T2DM and not completely explained by a difference in dietary vitamin C intake. A number of mechanisms underlying the decrease in vitamin C levels and increased requirements in T2DM were proposed by multiple authors. It was found that the dietary requirements or the need for supplementation of vitamin C may be greater in people with diabetes. But

interestingly, studies of vitamin C supplements alone or in combination have not demonstrated sufficient benefit to support a recommendation for routine supplementation, nor higher target serum vitamin C levels, in people with T2DM.

In one of the researches done involving the study of patient's Vit.C status in people with T2DM, it was seen in the frequency distribution plot (fig 4.1) that T2DM had a direct correlation with the Plasma Vit. C distribution in the body.

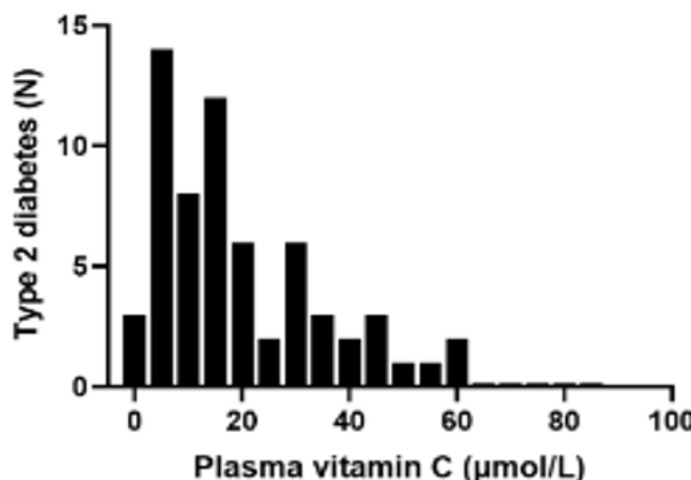


Fig 4.1: Correlation between Vit. C and T2DM patients' frequency.

Source: Carr, A.C., Spencer, E., Heenan, H., Lunt, H., Vollebregt, M., Prickett, T.C.R. (2022) 'Vitamin C Status in

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People with Types 1 and 2 Diabetes Mellitus and Varying Degrees of Renal Dysfunction: Relationship to Body Weight', Antioxidants, 11(2), 245, available: <http://dx.doi.org/10.3390/antiox11020245>.

The same study also correlated the % of individuals with T2DM to their Vit C deficiency levels (fig 4.2). It was

seen that a high % of individuals suffering from T2DM were also suffering with Vit. C deficiency. This also established a direct and strong correlation between Vit. C levels and T2DM in the human body.

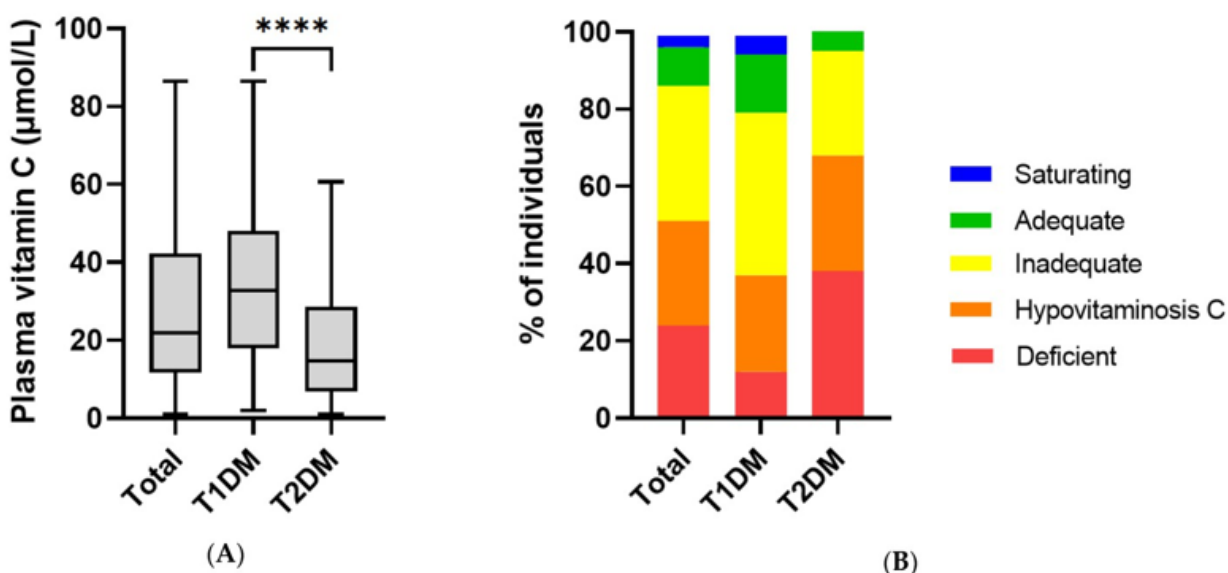


Fig 4.2: Correlation between Vit. C deficiency and T2DM occurrence

<http://dx.doi.org/10.3390/antiox11020245>.

Interestingly, many researches (Mullan et al., 2002) found the risk may be secondary to associated factors such as hyperglycemia, insulin resistance, dyslipidemia, and hypertension. They observed increased arterial stiffness in type 2 diabetes patients. They realized that stiffening of the arterial tree is an important additional and independent risk factor for cardiovascular disease. Their experimental evidence suggested that acute parenteral administration of high-dose ascorbic acid may have beneficial vascular effects in diabetes. They showed that chronic daily supplementation with 500 mg oral ascorbic acid can lower blood pressure and improve arterial stiffness in patients with type 2 diabetes.

The pressing question - Whether Vit. C supplements can improve glycemic control and BP for Type-II diabetic patients - was answered by different researches in different ways. The study on Vit. C supplementations (Mason, 2022) concluded from short-term studies that vitamin C supplementation may improve glycemic control and BP in people with type 2 diabetes, vitamin C supplementation cannot be surely recommended as a therapy until larger, long-term, and high-quality trials

confirm these findings. Many of the researchers found a significant decrease in FBS, TG, LDL, HbA1c and serum insulin ((Adrekani, 2006)) in the group supplemented with 1000 mg vitamin C. The dose of 500 mg vitamin C, however, did not produce any significant change in any of the parameters studied. This indicated that daily consumption of 1000 mg supplementary vitamin C may be beneficial in decreasing blood glucose and lipids in patients with type 2 diabetes and thus reducing the risk of complications.

Another set of studies followed an experimental approach (Kotbi, 2015) to examine the effect of oral vitamin C on fasting blood glucose (FBG), two hours postprandial blood glucose (PPBG) as well as glycosylated hemoglobin (HbA1c) in the treatment of type 2 diabetes mellitus (DM). Different experimentations on normal vs type II patients revealed that oral supplementation of 1000 mg vitamin C per day when given to type II diabetic patients with the oral anti diabetic drugs may exert an adding marvelous effect on decreasing the FBG; two hours PPBG, and HbA1c.

Many studies started with the goal to examine the effect of oral vitamin C with metformin on FBS, PMBG,

HbA1c (Lipeng, 2020), and plasma ascorbic acid level (PAA) with type 2 DM. All of them concluded that Vitamin C causes a significant decrease in FBG, PPBG, and HbA1c patients.

A lot of the researches focused in the direction of finding the correlation of Type II Diabetes (Kotbi, 2015) which strongly helps the Type II diabetic patients (Dakhale, 2021). Also, certain researches found a significant decrease in PPBS level in both the group supplemented with 1g and 2 g of vitamin C. However percentage of reduction in Postprandial blood sugar level was found to more in group receiving vitamin C 2g than the group receiving 1g. This resulted in a very important conclusion (Nayaka, 2013) that oral supplementation of vitamin C 2gm with glibenclamide reduces PPBS level. Hence, they concluded that supplementation of vitamin C along with oral hypoglycemic drug helps in maintaining good glycemic control in type 2 DM to fasting glucose, BMI, smoking history, and dietary vitamin C intake. They found that these are significant independent predictors of plasma vitamin C concentrations. An inverse association was established between fasting glucose and plasma vitamin C. Also, they even found plasma vitamin C

concentration to be inversely related to BMI, which proved to be instrumental in concluding that vitamin C is definitely a predictor for plasma vitamin C concentration.

The approach of randomized controlled trials was adopted by many researchers (Balbi et al, 2018) to assess the effect of vitamin supplementation on the antioxidant status and glycemic index of type 2 diabetes mellitus patients. But this could not conclude anything over the impact of vitamin C, rather it concluded on vitamin E related impacts, that it can be very useful for type II diabetes patients.

In summary, a mixed results were seen in the deep analysis done of the literature. Though some researches couldn't find a correlation, but their count was very low (just two of the 25). Most of the researches did conclude a strong correlation between type II diabetes and vit. C intake. Multiple approaches like randomized controlled trials, literature review, experimentation with agreed patients etc were utilized by many researchers. All in all, it was found that vit. C does help strongly in managing type-II diabetes. The below block diagram in fig 4.3 summarizes our findings in pictorial format.



Fig 4.3: Summary of the findings

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DISCUSSION

The correlation between vitamin C intake and type 2 diabetes (T2DM) has been a topic of interest among researchers. Several studies have reported lower levels of vitamin C among individuals with T2DM, which cannot be solely explained by differences in dietary intake. Various mechanisms have been proposed to explain the decrease in vitamin C levels and increased requirements in T2DM. It has been suggested that people with diabetes

may have greater dietary requirements or need for supplementation of vitamin C. However, studies examining the benefits of vitamin C supplementation alone or in combination have not shown sufficient evidence to support routine supplementation or higher target serum vitamin C levels for individuals with T2DM. The association between T2DM and vitamin C intake is not limited to vitamin C levels alone. Studies have found that T2DM is associated with factors such as

hyperglycemia, insulin resistance, dyslipidemia, and hypertension, which may contribute to increased arterial stiffness and cardiovascular disease risk. Experimental evidence has suggested that high-dose ascorbic acid administration may have beneficial vascular effects in diabetes, improving arterial stiffness and reducing blood pressure (Merkhan, 2020). Additionally, studies exploring the effect of vitamin C supplementation on glycemic control and blood pressure in individuals with T2DM have shown mixed results. Short-term studies have suggested potential improvements in glycemic control and blood pressure, but larger, long-term, and high-quality trials are needed to confirm these findings.

Further investigations have focused on the impact of vitamin C supplementation on various parameters in individuals with T2DM. Studies have found significant decreases in fasting blood glucose, triglycerides, low-density lipoprotein (LDL) cholesterol, glycosylated hemoglobin (HbA1c), and serum insulin levels with the supplementation of 1000 mg of vitamin C (Adrekani, 2006). However, lower doses of vitamin C did not produce significant changes in these parameters (Adrekani, 2006). Experimental approaches have also shown that oral supplementation of 1000 mg vitamin C per day, in combination with oral antidiabetic drugs, may significantly decrease fasting blood glucose, postprandial blood glucose, and HbA1c levels (Kotbi, 2015). Similarly, the supplementation of vitamin C along with oral hypoglycemic drugs has been found to help maintain good glycemic control in individuals with T2DM (Nayaka, 2013)

In conclusion, the relationship between vitamin C intake and T2DM is complex, involving factors such as vitamin C levels, glycemic control, blood pressure, lipid profiles, and arterial stiffness. While some studies have reported improvements in glycemic control (Duff, 2015) and other parameters with vitamin C supplementation (Shaun, 2021), further research is needed to establish the long-term effects and recommendations for routine supplementation in individuals with T2DM. Nonetheless, the overall body of evidence suggests that vitamin C plays a significant role in managing T2DM and its associated complications.

CONCLUSION

The correlation between vitamin C intake and type 2 diabetes (T2DM) has been extensively studied, with a majority of the research pointing towards a significant association. Although some studies did not find a direct correlation, they represented a small fraction of the

overall literature. The majority of the evidence suggests that vitamin C levels are lower among individuals with T2DM, and this cannot be solely explained by differences in dietary intake (Kotbi, 2015).

Various mechanisms have been proposed to explain the decreased vitamin C levels and increased requirements in T2DM. It has been suggested that individuals with T2DM may have greater dietary requirements (Wilson, 2017) or a need for supplementation of vitamin C (Kotbi, 2015). However, the efficacy of vitamin C supplementation alone or in combination for managing T2DM remains inconclusive. While short-term studies have shown potential benefits in terms of glycemic control and blood pressure, larger, long-term, and high-quality trials are needed to confirm these findings.

Interestingly, T2DM has been associated with factors such as hyperglycemia, insulin resistance, dyslipidemia, and hypertension, which contribute to increased cardiovascular disease risk. Experimental evidence suggests that high-dose ascorbic acid administration may have beneficial effects on arterial stiffness and blood pressure in individuals with T2DM. Additionally, studies have reported significant improvements in glycemic control, lipid profiles, and insulin levels with vitamin C supplementation, particularly at higher doses.

The predictors of plasma vitamin C concentrations in individuals with T2DM include fasting glucose, BMI, smoking history, and dietary vitamin C intake. Inverse associations have been observed between fasting glucose and plasma vitamin C levels, as well as between plasma vitamin C concentration and BMI. These findings suggest that vitamin C is a potential predictor for plasma vitamin C concentrations in individuals with T2DM.

In conclusion, the overall body of evidence suggests a strong correlation between vitamin C intake and the management of T2DM. While the precise mechanisms and optimal supplementation strategies require further investigation, maintaining adequate vitamin C levels appears to be beneficial for glycemic control, blood pressure, lipid profiles, and overall health in individuals with T2DM. Future research should focus on conducting larger, long-term trials to establish the efficacy and potential therapeutic recommendations for vitamin C supplementation in the management of T2DM.

WAY FOWARD

Further research is needed to consolidate the existing knowledge on the correlation between vitamin C intake and type II diabetes (T2DM). Large-scale, long-term, and high-quality clinical trials are necessary to establish

optimal dosages, treatment durations, and the specific mechanisms by which vitamin C exerts its beneficial effects in managing T2DM and its associated complications (Aluwong, 2016). Moreover, studies focusing on the potential synergistic effects of vitamin C with other therapeutic approaches commonly used in T2DM management, such as anti-diabetic medications and lifestyle interventions, should be conducted. Additionally, investigating the impact of vitamin C on specific skin issues related to T2DM and developing standardized outcome measures will further enhance our understanding and guide the development of evidence-based interventions (Aluwong, 2016). Ultimately, by advancing our knowledge in this area, we can pave the way for more personalized and effective approaches to support individuals with T2DM in achieving optimal glycemic control, improving overall health outcomes, and enhancing their quality of life.

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