MINI REVIEW ARTICLE

Influence of Selenium and Zinc Supplementation on Glycaemic Control in Type 2 Diabetes Patients?

Kholoud Elshiwy[1], Ghada Essam El-Din Amin[1,2] and Mohamed Farouk Allam[2,3*]

[1]*Department of Family Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt*
[2]*Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt*
[3]*Department of Preventive Medicine and Public Health, Faculty of Medicine, University of Cordoba, Cordoba, Spain*

Abstract

Diabetes Mellitus poses a significant global burden, impacting healthcare and economic systems and affecting 10.5% of the population. Type 2 Diabetes Mellitus (T2DM) accounts for approximately 90% of all cases. Risk factors associated with the development of T2DM include obesity, physical inactivity, unhealthy diet, genetic predisposition, psychosocial stress, environmental toxins, and socioeconomic determinants. Despite advances in pharmacological therapies, achieving optimal glycaemic control remains challenging and is associated with numerous complications, including mental health disorders. This has sparked interest in the potential role of micronutrients, particularly selenium and zinc, as adjuncts in T2DM management strategies. This manuscript reviews all published observational and interventional studies evaluating the association between obesity and T2DM, and assesses the effectiveness of selenium and zinc supplementation in promoting optimal glycaemic control.

Keywords: *Diabetes mellitus, type 2 diabetes mellitus, risk factors, management, selenium, zinc, micronutrients, supplementation, glycaemic control, review.*

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by persistently elevated blood glucose levels resulting from impaired insulin utilization by peripheral tissues, a condition known as insulin resistance. In response, the pancreas initially increases insulin secretion; however, this compensatory mechanism gradually fails, leading to a progressive decline in insulin production [1].

T2DM accounts for approximately 90% of all diabetes cases, making it the most prevalent form of the disease. A strong genetic predisposition is evident, particularly among individuals with a positive family history. The risk of developing T2DM is about 40% if a close relative has diabetes, and it increases to nearly 70% in monozygotic twins [2].

Risk factors associated with the development of T2DM include obesity, physical inactivity, unhealthy diet, genetic predisposition, psychosocial stress, environmental toxins, and socioeconomic determinants [3].

The global burden of T2DM continues to rise. In 2021, an estimated 529 million people were living with diabetes, and by 2045, the number is projected to exceed 783 million. In 2019 alone, diabetes was responsible for 4.2 million deaths worldwide [4]. Moreover, the global economic burden is substantial, with diabetes-related healthcare expenditure expected to reach $1,054 billion by 2045 [5].

Given the critical roles of zinc and selenium in glucose metabolism, insulin signalling, and oxidative stress modulation [6], this review is essential for synthesizing current evidence and clarifying their implications in the development and progression of T2DM.

This manuscript reviews all published observational and interventional studies evaluating the association between obesity and T2DM, and assesses the effectiveness of selenium and zinc supplementation in promoting optimal glycaemic control.

DIABETES AND OBESITY

Patients with T2DM are usually obese, with a predominant distribution of fat in the abdominal region [3, 7]. Adipose tissue induces insulin resistance through inflammatory mechanisms that lead to the release of free fatty acids and dysregulation of adipokines [7].

Obesity has a significant role in inducing insulin resistance. Free fatty acids modify the expression of perilipin, which is found on the outer surface of lipid droplets, to inhibit lipases from degrading lipid droplets and releasing free fatty acids. Additionally, fatty tissues produce inflammatory mediators such as monocyte chemotactic protein1, interleukin 6 (IL-6), and tumour necrosis factor (TNF- α). Obesity reduces adiponectin secretion, which is mainly produced by adipose tissue. Adiponectin promotes insulin sensitivity in the peripheral tissue, reduces the production of inflammatory molecules, inhibits the degradation of fatty acids, reduces the formation of fatty acids in the

**Corresponding author: Mohamed Farouk Allam, Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, 11566 Abbasia, Cairo, Egypt; E-mail: farouk.allam@med.asu.edu.eg*
Received: September 28, 2025; Revised: January 18, 2026; Accepted: February 13, 2026
DOI: https://doi.org/10.37184/lnjpc.2707-3521.8.39

liver, and maintains the elasticity of blood vessels. Also, obesity leads to the release of Leukotrienes (LTs), potent inflammatory molecules that inhibit the 5-lipoxygenase enzyme. This enzyme is found to protect obese mice from insulin resistance through decreasing macrophage and T cell infiltration [8].

COMPLICATIONS OF DIABETES

Chronic hyperglycaemia contributes to the development of multiple complications, such as nephropathy, retinopathy, polyneuropathy, diabetic foot ulcers, and atherosclerosis. Diabetic patients have 2 to 3 times higher risk of developing depression compared to non-diabetic patients. Furthermore, diabetic patients have more than 20 % higher risk of developing anxiety [9].

The first line of management of T2DM is lifestyle modification, including nutritional rehabilitation, increased physical activity, and adjustment of body weight. When these strategies fail to achieve adequate glycaemic control, oral hypoglycaemic agents are added to the treatment plan [10].

DIABETES AND SELENIUM (SE)

Se is a trace element that plays an essential role in cellular redox reactions as a cofactor for certain enzymes, such as glutathione peroxidases and thioredoxin reductase. Redox reactions are involved in the regulation of inflammation and immune system function [11]. In states of excess adiposity, selenium nutritional status is primarily altered by reduced glutathione peroxidase activity, especially in adults with obesity. Additionally, overweight and obese individuals often exhibit lower selenium levels in urine and nails [12]. The relationship between Se and the development of metabolic disorders remains under investigation, and the results are controversial [11]. As chronic hyperglycaemia increases the release of various reactive oxygen species, induces oxidative stress, and decreases Se levels, it was hypothesised that Se supplementation may be beneficial. Some studies reported that Se supplementation at optimal concentration may improve the metabolic state of T2DM patients [13, 14]. Farrokhian and collaborators (2016) recommended selenium supplementation at 200 µg [13], whereas Tabrizi and collaborators (2017) did not specify a recommended supplementation dose in their systematic review and meta-analysis [14]. However, other studies revealed no significant benefits of Se in T2DM patients. Moreover, Se could harm glycaemic control and may increase the risk of developing T2DM [10, 15]. Although antioxidant enzymes protect against oxidative cell damage by eliminating reactive oxygen species, overexpression of these enzymes may adversely affect insulin sensitivity, as reactive oxygen species are important for insulin sensitization [16].

DIABETES AND ZINC (ZN)

Zn is an essential trace element that has an antioxidant effect in the human body. It plays a significant role in energy and lipid metabolism [17]. A 2019 meta-analysis demonstrated a significant association between overweight and obesity and reduced serum zinc levels in both children and adults [18]. Zn plays a major role in the synthesis, storage, and secretion of insulin by pancreatic β-cells. Also, Zn plays an important role in insulin translocation into cells and insulin sensitivity by activating the phosphoinositol-3-kinase/protein kinase B cascade. Zn stimulates glucose uptake in insulin-dependent tissues. In addition, Zn suppresses the release of inflammatory cytokines such as interleukin-1β and nuclear factor κB, decreasing β-cell apoptosis. These mechanisms could partially explain the possible beneficial role of Zn in the management of T2DM [17].

The Nurses' Health Study, a large prospective cohort conducted in the United States, reported in 2009 that higher Zn intake was associated with a decreased risk of T2DM, especially among women [19]. These results are consistent with other longitudinal studies [20, 21]. However, other studies did not show similar results and reported an insignificant association between Zn supplementation and the development of T2DM [22, 23].

The meta-analysis by Pompano and Boy (2021) included 1,042 participants who received zinc supplementation and 974 who received a placebo across 27 studies. Low-dose zinc supplementation (<25 mg/day) was associated with significant improvements in fasting blood glucose, insulin resistance, triglycerides, total cholesterol, and LDL cholesterol. In contrast, high-dose zinc supplementation (≥25 mg/day) improved glycated haemoglobin and insulin resistance [24].

CONCLUSION

Given the conflicting findings in published studies on the effectiveness of Se and Zn in managing T2DM and the substantial burden of this chronic disease, it is crucial to evaluate the effects of Se and Zn on achieving adequate glycaemic control in individuals with T2DM. The inconsistent and, at times, contradictory evidence in the literature on Se and Zn supplementation, together with the significant clinical and public health impact of T2DM, underscores the need for rigorously designed investigations. Continued research is essential to elucidate the roles of Se and Zn in glucose metabolism and to determine their potential contribution to achieving and sustaining optimal glycaemic control in individuals with T2DM. Accordingly, future clinical trials should focus on addressing the following key question: Can combined Se and Zn supplementation effectively enhance glycaemic control in patients with T2DM?

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this review, the authors used AI sparingly to generate language suggestions and perform minor proofreading in selected sections of the manuscript. Following the use of this tool, the authors carefully reviewed and revised the content as necessary and assume full responsibility for the final published version of the article.

REFERENCES

1. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet 2017; 389(10085): 2239-51. DOI: https://doi.org/10.1016/s0140-6736(17)30058-2
2. Himanshu D, Ali W, Wamique M. Type 2 diabetes mellitus: pathogenesis and genetic diagnosis. J Diabetes Metab Disord 2020; 19(2): 1959-66. DOI: https://doi.org/10.1007/s40200-020-00641-x
3. Samant AC, Jha H, Kamal P. Systematic review: risk factors for developing type 2 diabetes mellitus. Eur J Cardiovasc Med 2025; 15: 382-90. DOI: https://doi.org/10.5083/ejcm/25-01-62
4. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, *et al.* Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci 2020; 21(17): 6275. DOI: https://doi.org/10.3390/ijms21176275
5. Busili A, Kumar K, Kudrna L, Busaily I. The risk factors for mental health disorders in patients with type 2 diabetes: an umbrella review of systematic reviews with and without meta-analysis. Heliyon 2024; 10(7): e28782. DOI: https://doi.org/10.1016/j.heliyon.2024.e28782
6. Sher T, Raja NI, Rehman Mashwani ZU. Antidiabetic potential of zinc selenium nanocomposites in diabetes management: a comprehensive review. Annu Methodol Arch Res Rev 2025; 3(10): 123-39. DOI: https://doi.org/10.63075/e3s9jx48
7. Schwartz SS, Epstein S, Corkey BE, Grant SF, Gavin JR 3rd, Aguilar RB. The time is right for a new classification system for diabetes: rationale and implications of the β-cell-centric classification schema. Diabetes Care 2016; 39(2): 179-86. DOI: https://doi.org/10.2337/dc15-1585
8. Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. Diabetes Metab Syndr Obes 2014; 7: 587-91. DOI: https://doi.org/10.2147/DMSO.S67400
9. Akhaury K, Chaware S. Relation between diabetes and psychiatric disorders. Cureus 2022; 14(10): e30733. DOI: https://doi.org/10.7759/cureus.30733
10. Stróżyk A, Osica Z, Przybylak JD, Kołodziej M, Zalewski BM, Mrozikiewicz-Rakowska B, *et al.* Effectiveness and safety of selenium supplementation for type 2 diabetes mellitus in adults: a systematic review of randomised controlled trials. J Hum Nutr Diet 2019; 32(5): 635-45. DOI: https://doi.org/10.1111/jhn.12670
11. Huang YC, Combs GF Jr, Wu TL, Zeng H, Cheng WH. Selenium status and type 2 diabetes risk. Arch Biochem Biophys 2022; 730: 109400. DOI: https://doi.org/10.1016/j.abb.2022.109400
12. Fontenelle LC, Cardoso de Araújo DS, da Cunha Soares T, Clímaco Cruz KJ, Henriques GS, Marreiro DDN. Nutritional status of selenium in overweight and obesity: a systematic review and meta-analysis. Clin Nutr 2022; 41(4): 862-84. DOI: https://doi.org/10.1016/j.clnu.2022.02.007
13. Farrokhian A, Bahmani F, Taghizadeh M, Mirhashemi SM, Aarabi MH, Raygan F, *et al.* Selenium supplementation affects insulin resistance and serum hs-CRP in patients with type 2 diabetes and coronary heart disease. Horm Metab Res 2016; 48(4): 263-8. DOI: https://doi.org/10.1055/s-0035-1569276
14. Tabrizi R, Akbari M, Moosazadeh M, Lankarani KB, Heydari ST, Kolahdooz F, *et al.* The Effects of selenium supplementation on glucose metabolism and lipid profiles among patients with metabolic diseases: a systematic review and meta-analysis of randomized controlled trials. Horm Metab Res 2017; 49(11): 826-30. DOI: https://doi.org/10.1055/s-0043-119544
15. Kim J, Chung HS, Choi MK, Roh YK, Yoo HJ, Park JH, *et al.* Association between serum selenium level and the presence of diabetes mellitus: a meta-analysis of observational studies. Diabetes Metab J 2019; 43(4): 447-60. DOI: https://doi.org/10.4093/dmj.2018.0123
16. McClung JP, Roneker CA, Mu W, Lisk DJ, Langlais P, Liu F, *et al.* Development of insulin resistance and obesity in mice overexpressing cellular glutathione peroxidase. Proc Natl Acad Sci U S A 2004; 101(24): 8852-7. DOI: https://doi.org/10.1073/pnas.0308096101
17. Chabosseau P, Rutter GA. Zinc and diabetes. Arch Biochem Biophys 2016; 611: 79-85. DOI: https://doi.org/10.1016/j.abb.2016.05.022
18. Gu K, Xiang W, Zhang Y, Sun K, Jiang X. The association between serum zinc level and overweight/obesity: a meta-analysis. Eur J Nutr 2019; 58(8): 2971-82. DOI: https://doi.org/10.1007/s00394-018-1876-x
19. Sun Q, van Dam RM, Willett WC, Hu FB. Prospective study of zinc intake and risk of type 2 diabetes in women. Diabetes Care 2009; 32(4): 629-34. DOI: https://doi.org/10.2337/dc08-1913
20. Drake I, Hindy G, Ericson U, Orho-Melander M. A prospective study of dietary and supplemental zinc intake and risk of type 2 diabetes depending on genetic variation in SLC30A8. Genes Nutr 2017; 12: 30. DOI: https://doi.org/10.1186/s12263-017-0586-y
21. Eshak ES, Iso H, Maruyama K, Muraki I, Tamakoshi A. Associations between dietary intakes of iron, copper, and zinc with risk of type 2 diabetes mellitus: A large population-based prospective cohort study. Clin Nutr 2018; 37(2): 667-74. DOI: https://doi.org/10.1016/j.clnu.2017.02.010
22. Chu A, Foster M, Samman S. Zinc status and risk of cardiovascular diseases and type 2 diabetes mellitus-a systematic review of prospective cohort studies. Nutrients 2016; 8(11): 707. DOI: https://doi.org/10.3390/nu8110707
23. Park JS, Xun P, Li J, Morris SJ, Jacobs DR, Liu K, He K. Longitudinal association between toenail zinc levels and the incidence of diabetes among American young adults: the CARDIA Trace Element Study. Sci Rep 2016; 6: 23155. DOI: https://doi.org/10.1038/srep23155
24. Pompano LM, Boy E. Effects of dose and duration of zinc interventions on risk factors for type 2 diabetes and cardiovascular disease: a systematic review and meta-analysis. Adv Nutr 2021; 12(1): 141-60. DOI: https://doi.org/10.1093/advances/nmaa087 Erratum in: Adv Nutr 2021; 12(3): 1049. DOI: https://doi.org/10.1093/advances/nmab052