

Effects of vitamin family members on insulin resistance and diabetes complications

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Abstract

The following letter to the editor highlights the article "Effects of vitamin D supplementation on glucose and lipid metabolism in patients with type 2 diabetes mellitus and risk factors for insulin resistance" in *World J Diabetes* 2023 Oct 15; 14 (10): 1514-1523. It is necessary to explore the role of vitamin family members in insulin resistance and diabetes complications.

Key Words: Vitamin; Insulin resistance; Diabetes complications; Letter

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Core Tip: Vitamins are a class of small molecular organic compounds that cannot be synthesized or are synthesized in extremely small amounts by the body. Many recent studies have shown that vitamin supplementation plays an important role in inhibiting inflammation, controlling blood sugar, and promoting insulin secretion in diabetic patients. However, the function of vitamin for diabetes remains to be studied. It is clinically significant to explore the effects of other vitamin family members on insulin resistance and diabetes complications.

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TO THE EDITOR

We read the article by Sun *et al*[1] entitled “Effects of vitamin D supplementation on glucose and lipid metabolism in patients with type 2 diabetes mellitus and risk factors for insulin resistance”. The authors found that 25 hydroxyvitamin D3 [25(OH)D3], a vitamin D deficiency marker, is an independent risk factor for insulin resistance (IR) and promotes glucose metabolism. Many recent studies have shown that vitamin D supplementation plays an important role in inhibiting inflammation, controlling blood sugar, and promoting insulin secretion in diabetic patients[2,3]. Therefore, it is clinically significant to explore the effects of other vitamin family members on IR and diabetes complications.

With societal and economic development, the prevalence of diabetes continues to increase. Approximately 1.6 million deaths per year are attributed directly to diabetes[4]. Currently, diabetes is classified primarily as type 1 diabetes (T1D) and T2D. It is estimated that by 2030, 578 million people worldwide will be diagnosed with diabetes[5]; T2D is the most common diagnosis, accounting for approximately 90%. An increasing number of studies show that most T2D patients have IR[6]. IR is a weakening of the body's response to insulin, resulting in increased blood sugar levels; physiologically, IR is defined as a state of reduced responsiveness of insulin-targeted tissues to high insulin levels[7]. When IR begins to occur, insulin levels increase to meet normal insulin requirements; however, over time, these increased levels lead to hyperglycemia-induced islet β cell failure, chronic hyperinsulinemia, and eventually T2D.

Vitamins are a class of small molecular organic compounds that cannot be synthesized or are synthesized in extremely small amounts by the body. Vitamins are necessary to maintain the normal physiological functions of the human body, and they must be obtained from food. Primarily, vitamins fall into two categories: fat-soluble vitamins and water-soluble vitamins. Many recent studies have shown that vitamins are involved in regulating T2D *via* IR. In fact, vitamin K4 supplementation can improve IR in patients with T2D[8]. Vitamin K deficiency under β cell stress may lead to β cell dysfunction by reducing endoplasmic reticulum Glc protein (ERGP) gamma carboxylation, thus increasing the risk of T2D, particularly in the case of overnutrition. Gamma carboxylated ERGP is needed to prevent uncontrolled insulin secretion by β cells and maintain normal insulin secretion[9]. A recent review reported that vitamin E, especially alpha tocopherol, has been shown to reduce lipid peroxidation, and the superoxide produced by vitamin E can damage the β cell structure as well as vital functional components for maintaining normal glucose concentrations[10]. Another study has shown that deficiencies in folic acid, vitamin B6, and vitamin B12 can lead to dyslipidemia, vascular endothelial dysfunction, abnormal glucose tolerance, and oxidative stress, leading to IR[11]. Pramono *et al*[12] have shown that obesity and IR are usually related to vitamin D deficiency. Vitamin D directly stimulates insulin secretion by reducing pancreatic β cells through vitamin D receptor (VDR) and improves peripheral IR. Moreover, VDR deficiency in cardiovascular tissue increases ventricular fibroblast mass dysregulation and accelerates the myocardial fibrosis process[13]. Studies have also shown that serum vitamin D deficiency aggravates inflammation due to circulating gamma-delta T cells in T2D patients. 1 α ,25(OH)2D3/fructose-1,6-bisphosphatase 1 (FBP1) signal transduction can inhibit glycolysis in $\gamma\delta$ T cells by promoting targeted FBP1 expression, thereby driving Akt/p38 MAPK dephosphorylation. This can also reduce inflammatory cytokine production (TNF- α and IFN- γ) in $\gamma\delta$ T cells to alleviate IR. The role of vitamin D in IR regulation to alleviate diabetes may be mediated by stimulating insulin receptor expression, improving insulin levels, and regulating cytokine expression and the calcium pool in various tissues[14]. Upon examining the mechanism through which vitamin D affects IR, supplementation with 1,25(OH)2D3 combined with insulin was shown to significantly improve the expression of glucose transporter 4, a key protein in regulating glucose metabolism and maintaining glucose homeostasis through glucose uptake[15].

Further studies have found that vitamin D is involved in the pathological process of multiple diabetes complications. In diabetic cardiomyopathy, the 1,25-dihydroxyvitamin D receptor inhibits autophagy by inhibiting nuclear FOXO1 translocation, thereby alleviating diabetic heart damage[16]. Vitamin D also improves blood glucose and insulin levels, reduces NF- κ B activity in heart tissue, and down-regulates advanced glycosylation end products and the hexosamine pathway to alleviate diabetic cardiomyopathy[17]. In diabetic kidney disease (DKD), vitamin D deficiency up-regulates zinc finger e-box binding homeobox and down-regulates miR-200b, which promotes the epithelial-mesenchymal transformation process and changes the renal structure and function of diabetic rats to accelerate DKD development[18]. Vitamin D supplementation can effectively reduce albuminuria and creatinine, markers of kidney disease in diabetic nephropathy patients[19]. 1,25(OH)2D3 also significantly inhibits the expression of sirtuin 1 (SIRT1) during oxidative stress[20], thereby attenuating renal oxidative damage. Increasing evidence has indicated that the vitamin D-VDR-RXR complex inhibits macrophage infiltration and immune effects in diabetic nephropathy[21]. Moreover, vitamin D deficiency is a potential risk factor for diabetic retinopathy (DR)[22]. Vitamin D is a strong antioxidant that can significantly reduce free radical formation, exert anti-inflammatory effects, and regulate autophagy and apoptosis; consequently, vitamin supplementation can help reduce the destructive effects of free radicals on DR[23]. Neuroprotective effects are exerted through the SIRT1/nrf-2/NF- κ B signaling pathway[24]. 25(OH)D3 may inhibit oxidative stress in human retinal microvascular endothelial cells induced by high glucose-mediated miR-93 down-regulation[25]. Supplementation with vitamin D also improves neuropathy[26], which might be related to its regulation of neurotrophic factor levels and neuronal calcium homeostasis. Additional studies have shown that vitamin D deficiency has a greater effect on

the long-term chronic complications of diabetes, especially in patients with painful diabetic neuropathy, where vitamin D supplementation can effectively improve pain symptoms and nerve function in patients[27].

In addition, IR-induced glucose abnormalities and lipotoxicity, resulting in unbalanced fatty acid intake, are key factors in diabetic cardiomyopathy[28]. Abnormal coronary microcirculation, mitochondrial dysfunction, subcellular component abnormalities, and myocardial insulin signaling and calcium homeostasis impairments were observed in IR states. These pathophysiological changes can lead to diastolic dysfunction, fibrosis[29], and hypertrophy, ultimately causing heart failure[30]. Impaired insulin signaling is an important pathophysiological abnormality in diabetic cardiomyopathy. However, supplementation with vitamin D can significantly improve glucose tolerance and insulin sensitivity[31]. Vitamin D plays a key role in insulin receptor expression and increases glucose transporter function in insulin reactivity [13].

In summary, Sun *et al*[1] investigated the protective effects of vitamin D supplementation on IR in diabetic patients, but they did not include a pathological exploration of diabetic complications. The mechanism through which vitamin D acts in the treatment of IR and multiple diabetes complications remains to be studied.

FOOTNOTES

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REFERENCES

- 1 Sun LJ, Lu JX, Li XY, Zheng TS, Zhan XR. Effects of vitamin D supplementation on glucose and lipid metabolism in patients with type 2 diabetes mellitus and risk factors for insulin resistance. *World J Diabetes* 2023; **14**: 1514-1523 [PMID: 37970127 DOI: 10.4239/wjcd.v14.i10.1514]
- 2 Mitri J, Pittas AG. Vitamin D and diabetes. *Endocrinol Metab Clin North Am* 2014; **43**: 205-232 [PMID: 24582099 DOI: 10.1016/j.ecl.2013.09.010]
- 3 MacGillivray R, Phoswa WN, Mokgalaboni K. Modulatory Properties of Vitamin D in Type 2 Diabetic Patients: A Focus on Inflammation and Dyslipidemia. *Nutrients* 2023; **15** [PMID: 37960227 DOI: 10.3390/nu15214575]
- 4 Ling W, Huang Y, Huang YM, Fan RR, Sui Y, Zhao HL. Global trend of diabetes mortality attributed to vascular complications, 2000-2016. *Cardiovasc Diabetol* 2020; **19**: 182 [PMID: 33081808 DOI: 10.1186/s12933-020-01159-5]
- 5 Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R; IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. *Diabetes Res Clin Pract* 2019; **157**: 107843 [PMID: 31518657 DOI: 10.1016/j.diabres.2019.107843]
- 6 Cao Y, Luo P, Tang H, Li P, Wang G, Li W, Song Z, Su Z, Sun X, Yi X, Fu Z, Cui B, Zhu S, Zhu L. Insulin resistance levels predicted metabolic improvement and weight loss after metabolic surgery in Chinese patients with type 2 diabetes. *Surg Obes Relat Dis* 2024; **20**: 80-90 [PMID: 37739868 DOI: 10.1016/j.soard.2023.08.004]
- 7 Lee SH, Park SY, Choi CS. Insulin Resistance: From Mechanisms to Therapeutic Strategies. *Diabetes Metab J* 2022; **46**: 15-37 [PMID: 34965646 DOI: 10.4093/dmj.2021.0280]
- 8 Nuszkiewicz J, Sutkowy P, Wróblewski M, Pawłowska M, Wesołowski R, Wróblewska J, Woźniak A. Links between Vitamin K, Ferroptosis and SARS-CoV-2 Infection. *Antioxidants (Basel)* 2023; **12** [PMID: 36978981 DOI: 10.3390/antiox12030733]
- 9 Lacombe J, Guo K, Bonneau J, Faubert D, Gioanni F, Vivoli A, Muir SM, Hezzaz S, Poitout V, Ferron M. Vitamin K-dependent carboxylation regulates Ca(2+) flux and adaptation to metabolic stress in β cells. *Cell Rep* 2023; **42**: 112500 [PMID: 37171959 DOI: 10.1016/j.celrep.2023.112500]
- 10 Brnoliakova Z, Knezl V, Sotnikova R, Gasparova Z. Metabolic Syndrome in Hypertriglyceridemic Rats: Effects of Antioxidants. *Physiol Res*

- 2023; **72**: S31-S35 [PMID: [37294116](#) DOI: [10.33549/physiolres.935021](#)]
- 11 **Zhu J**, Chen C, Lu L, Shikany JM, D'Alton ME, Kahe K. Folate, Vitamin B6, and Vitamin B12 Status in Association With Metabolic Syndrome Incidence. *JAMA Netw Open* 2023; **6**: e2250621 [PMID: [36630134](#) DOI: [10.1001/jamanetworkopen.2022.50621](#)]
 - 12 **Pramono A**, Jocken JWE, Blaak EE. Vitamin D deficiency in the aetiology of obesity-related insulin resistance. *Diabetes Metab Res Rev* 2019; **35**: e3146 [PMID: [30801902](#) DOI: [10.1002/dmrr.3146](#)]
 - 13 **Argano C**, Mirarchi L, Amodeo S, Orlando V, Torres A, Corrao S. The Role of Vitamin D and Its Molecular Bases in Insulin Resistance, Diabetes, Metabolic Syndrome, and Cardiovascular Disease: State of the Art. *Int J Mol Sci* 2023; **24** [PMID: [37895163](#) DOI: [10.3390/ijms242015485](#)]
 - 14 **Li P**, Li K, Yuan W, Xu Y, Li P, Wu R, Han J, Yin Z, Lu L, Gao Y. 1 α ,25(OH)(2)D(3) ameliorates insulin resistance by alleviating $\gamma\delta$ T cell inflammation *via* enhancing fructose-1,6-bisphosphatase 1 expression. *Theranostics* 2023; **13**: 5290-5304 [PMID: [37908738](#) DOI: [10.7150/thno.84645](#)]
 - 15 **Manna P**, Achari AE, Jain SK. Vitamin D supplementation inhibits oxidative stress and upregulate SIRT1/AMPK/GLUT4 cascade in high glucose-treated 3T3L1 adipocytes and in adipose tissue of high fat diet-fed diabetic mice. *Arch Biochem Biophys* 2017; **615**: 22-34 [PMID: [28063949](#) DOI: [10.1016/j.abb.2017.01.002](#)]
 - 16 **Guo X**, Lin H, Liu J, Wang D, Li D, Jiang C, Tang Y, Wang J, Zhang T, Li Y, Yao P. 1,25-Dihydroxyvitamin D attenuates diabetic cardiac autophagy and damage by vitamin D receptor-mediated suppression of FoxO1 translocation. *J Nutr Biochem* 2020; **80**: 108380 [PMID: [32299030](#) DOI: [10.1016/j.jnutbio.2020.108380](#)]
 - 17 **Derakhshanian H**, Djazayeri A, Javanbakht MH, Eshraghian MR, Mirshafiey A, Jahanabadi S, Ghadbeigi S, Zarei M, Alvandi E, Djalali M. Vitamin D downregulates key genes of diabetes complications in cardiomyocyte. *J Cell Physiol* 2019; **234**: 21352-21358 [PMID: [31173353](#) DOI: [10.1002/jcp.28743](#)]
 - 18 **Souza CS**, Deluque AL, Oliveira BM, Maciel ALD, Giovanini C, Boer PA, de Paula FJA, Costa RS, Franscecato HDC, de Almeida LF, Coimbra TM. Vitamin D deficiency contributes to the diabetic kidney disease progression *via* increase ZEB1/ZEB2 expressions. *Nutr Diabetes* 2023; **13**: 9 [PMID: [37391399](#) DOI: [10.1038/s41387-023-00238-2](#)]
 - 19 **de Oliveira E Silva Ullmann T**, Ramalho BJ, Laurindo LF, Tofano RJ, Rubira CJ, Guiguer EL, Barbalho SM, Flato UAP, Sloan KP, Araujo AC. Effects of Vitamin D Supplementation in Diabetic Kidney Disease: An Systematic Review. *J Ren Nutr* 2023; **33**: 618-628 [PMID: [37302723](#) DOI: [10.1053/j.jrn.2023.05.006](#)]
 - 20 **Wang D**, Li Y, Wang N, Luo G, Wang J, Luo C, Yu W, Hao L. 1 α ,25-Dihydroxyvitamin D(3) prevents renal oxidative damage *via* the PARP1/SIRT1/NOX4 pathway in Zucker diabetic fatty rats. *Am J Physiol Endocrinol Metab* 2020; **318**: E343-E356 [PMID: [31891537](#) DOI: [10.1152/ajpendo.00270.2019](#)]
 - 21 **Hu X**, Liu W, Yan Y, Liu H, Huang Q, Xiao Y, Gong Z, Du J. Vitamin D protects against diabetic nephropathy: Evidence-based effectiveness and mechanism. *Eur J Pharmacol* 2019; **845**: 91-98 [PMID: [30287151](#) DOI: [10.1016/j.ejphar.2018.09.037](#)]
 - 22 **Navaei S**, Nazemi S, Emamian MH, Hashemi H, Fotouhi A. Vitamin D deficiency and diabetic retinopathy risk. *J Fr Ophtalmol* 2023; **46**: 737-741 [PMID: [37085359](#) DOI: [10.1016/j.jfo.2023.01.024](#)]
 - 23 **Fekri S**, Soheilian M, Roozdar S, Abtahi SH, Nouri H. The effect of vitamin D supplementation on the outcome of treatment with bevacizumab in diabetic macular edema: a randomized clinical trial. *Int Ophthalmol* 2022; **42**: 3345-3356 [PMID: [35543853](#) DOI: [10.1007/s10792-022-02333-2](#)]
 - 24 **Ali A**, Shah SA, Zaman N, Uddin MN, Khan W, Ali A, Riaz M, Kamil A. Vitamin D exerts neuroprotection *via* SIRT1/nrf-2/ NF-kB signaling pathways against D-galactose-induced memory impairment in adult mice. *Neurochem Int* 2021; **142**: 104893 [PMID: [33159979](#) DOI: [10.1016/j.neuint.2020.104893](#)]
 - 25 **Zhan D**, Zhao J, Shi Q, Lou J, Wang W. 25-hydroxyvitamin D3 inhibits oxidative stress and ferroptosis in retinal microvascular endothelial cells induced by high glucose through down-regulation of miR-93. *BMC Ophthalmol* 2023; **23**: 22 [PMID: [36639741](#) DOI: [10.1186/s12886-022-02762-8](#)]
 - 26 **Qu GB**, Wang LL, Tang X, Wu W, Sun YH. The association between vitamin D level and diabetic peripheral neuropathy in patients with type 2 diabetes mellitus: An update systematic review and meta-analysis. *J Clin Transl Endocrinol* 2017; **9**: 25-31 [PMID: [29067266](#) DOI: [10.1016/j.jcte.2017.04.001](#)]
 - 27 **Wei W**, Zhang Y, Chen R, Qiu X, Gao Y, Chen Q. The efficacy of vitamin D supplementation on painful diabetic neuropathy: Protocol for a systematic review and meta-analysis. *Medicine (Baltimore)* 2020; **99**: e20871 [PMID: [32756079](#) DOI: [10.1097/MD.00000000000020871](#)]
 - 28 **Nakamura K**, Miyoshi T, Yoshida M, Akagi S, Saito Y, Ejiri K, Matsuo N, Ichikawa K, Iwasaki K, Naito T, Namba Y, Sugiyama H, Ito H. Pathophysiology and Treatment of Diabetic Cardiomyopathy and Heart Failure in Patients with Diabetes Mellitus. *Int J Mol Sci* 2022; **23** [PMID: [35408946](#) DOI: [10.3390/ijms23073587](#)]
 - 29 **Jia G**, Hill MA, Sowers JR. Diabetic Cardiomyopathy: An Update of Mechanisms Contributing to This Clinical Entity. *Circ Res* 2018; **122**: 624-638 [PMID: [29449364](#) DOI: [10.1161/CIRCRESAHA.117.311586](#)]
 - 30 **Jia G**, Whaley-Connell A, Sowers JR. Diabetic cardiomyopathy: a hyperglycaemia- and insulin-resistance-induced heart disease. *Diabetologia* 2018; **61**: 21-28 [PMID: [28776083](#) DOI: [10.1007/s00125-017-4390-4](#)]
 - 31 **Liu J**, Zhang Y, Shi D, He C, Xia G. Vitamin D Alleviates Type 2 Diabetes Mellitus by Mitigating Oxidative Stress-Induced Pancreatic β -Cell Impairment. *Exp Clin Endocrinol Diabetes* 2023; **131**: 656-666 [PMID: [37935388](#) DOI: [10.1055/a-2191-9969](#)]



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