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A REVIEW ARTICLE

Vitamin B6 and Glucose Control: A Forgotten Role in Prediabetes A Narrative Review

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Abstract

Prediabetes is a major global health concern that increases the risk of progression to diabetes and cardiovascular disease. Although current hyperglycemia management guidelines emphasize macronutrient intake and lifestyle modification, the role of micronutrients remains underrepresented. This narrative review examines the potential contribution of vitamin B6 to glucose regulation, particularly in prediabetes. Large epidemiological studies, including analyses from the National Health and Nutrition Examination Survey (NHANES), report significant inverse associations between vitamin B6 status and dysglycemia. At the biochemical level, pyridoxal 5-phosphate (PLP), the active form of vitamin B6, functions as a cofactor in more than 150 enzymatic reactions, acts as a carbonyl scavenger, and inhibits advanced glycation end-product formation, all of which are relevant to diabetes pathophysiology. Vitamin B6 also has antioxidant and anti-inflammatory properties, supports beta-cell function, and may influence intestinal glucose handling through alpha-glucosidase inhibition. Despite this mechanistic and observational evidence, vitamin B6 remains largely overlooked in prediabetes management, and a substantial gap persists between epidemiological findings and clinical application. This review therefore highlights vitamin B6 as a plausible modifiable determinant of dysglycemia in prediabetes and underscores the need for rigorous, targeted intervention trials to define its efficacy, optimal dose, and clinical relevance in prevention and management

1. Introduction

Prediabetes is characterized by impaired glucose regulation, with blood glucose concentrations above normal but below the diagnostic threshold for type 2 diabetes mellitus (T2DM) [1,2]. It is a major global public health problem affecting millions of people and conferring an increased risk of progression to diabetes and cardiovascular disease [2]. The scale of this problem warrants continued investigation of modifiable factors and novel nutrition-based approaches [3].

Current diabetes prevention and management guidelines primarily emphasize macronutrient composition (carbohydrate, fat, and protein) and dietary patterns such as the Mediterranean diet, whereas micronutrients often receive less attention [4]. Some micronutrients, including zinc, chromium, and magnesium, have received considerable attention because of their recognized roles in glucose metabolism and insulin signaling [5,6]. By contrast, despite substantial evidence supporting a role for vitamin B6 in short-term glucose regulation, its relevance remains underappreciated in prediabetes.

An important NHANES analysis (2021) reported an inverse association between vitamin B6 intake and HbA1c, with individuals in the highest B6 quintile having approximately 22% lower odds of elevated HbA1c (>=5.7%) than those in the lowest quintile [7]. Another NHANES-based study (2005-2008) involving 5,559 participants with diabetes found an inverse association between vitamin B6 intake and diabetic retinopathy (DR) [8]. Participants with better dietary B6 status had a 19% lower risk of DR (OR = 0.81, 95% CI 0.69-0.95; P = 0.012) and showed lower cardiovascular and all-cause mortality. These findings suggest that vitamin B6 may be relevant not only to glycemic markers but also to complications and prognosis. In a laboratory model, Mascolo et al. showed that Drosophila PI3K-induced T2DM-like phenotypes increased blood glucose, advanced glycation end products

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(AGEs), and reactive oxygen species (ROS), while reducing glycogen stores and body weight; supplementation with pyridoxal-5-phosphate (PLP) restored these markers toward normal [9]. Despite these findings, vitamin B6 remains largely absent from routine diabetes management discussions.

This inconsistency between strong, large-scale epidemiological evidence and limited clinical application raises an important question: Is vitamin B6 a forgotten modifiable determinant of hyperglycemia, particularly in prediabetes? In this narrative review, we analyze the epidemiological evidence, summarize plausible mechanisms through which vitamin B6 may influence glucose homeostasis, and identify major gaps in intervention trials. We aim to reposition vitamin B6 from an overlooked micronutrient to a focused topic in prediabetes research.

2. Chemistry and Metabolic Roles

Vitamin B6 is a water-soluble vitamin with an essential role in cellular metabolism [10]. It comprises six chemically related compounds: pyridoxine (PN), pyridoxal (PL), pyridoxamine (PM), and their corresponding 5-prime-phosphate derivatives (PNP, PLP, and PMP), all of which share a pyridine ring structure [11]. These vitamers differ in the substituent at the 4-prime position of the pyridine ring Figure 1. an aminomethyl group in pyridoxamine (PM), a hydroxymethyl group in pyridoxine (PN), or an aldehyde group in pyridoxal (PL) [10]. After phosphorylation, these derivatives function as cofactors in multiple metabolic pathways.

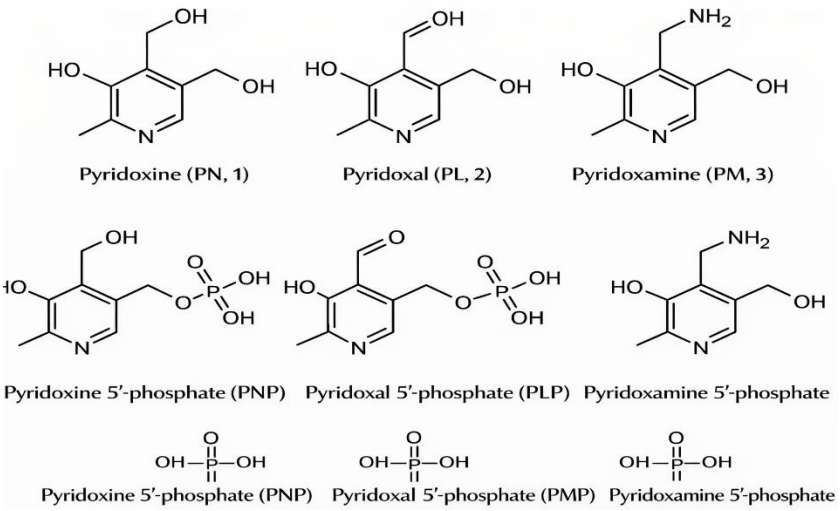

Figure 1. Vitamin B6 vitamers.

PLP, the biologically active form of vitamin B6, functions as a coenzyme in approximately 150 enzymatic reactions involved in amino acid metabolism, one-carbon metabolism, transsulfuration, heme and polyamine synthesis, and neurotransmitter metabolism [12]. Although the exact role of vitamin B6 in diabetes is not fully established, several mechanisms are supported by experimental evidence. (1) Role in glucose metabolism: PLP acts as a coenzyme for enzymes involved in glucose metabolism, including glycogen phosphorylase, which is important for glycogen utilization in the liver and skeletal muscle [13]. (2) Reduction of DNA glycation: Individuals with diabetes and nephropathy have shown increased DNA glycation in leukocytes [14], and 5-month supplementation with thiamine (B1) and pyridoxine (B6) reduced DNA glycation, suggesting a potential role in limiting diabetes-related complications [15].

(3) Regulation of Homocysteine: Vitamin B6 contributes to homocysteine metabolism, and homocysteine levels are often elevated in people with diabetes (Figure 2). Elevated homocysteine is associated with vascular complications, and reducing it may help lower cardiovascular risk in diabetic individuals [16].

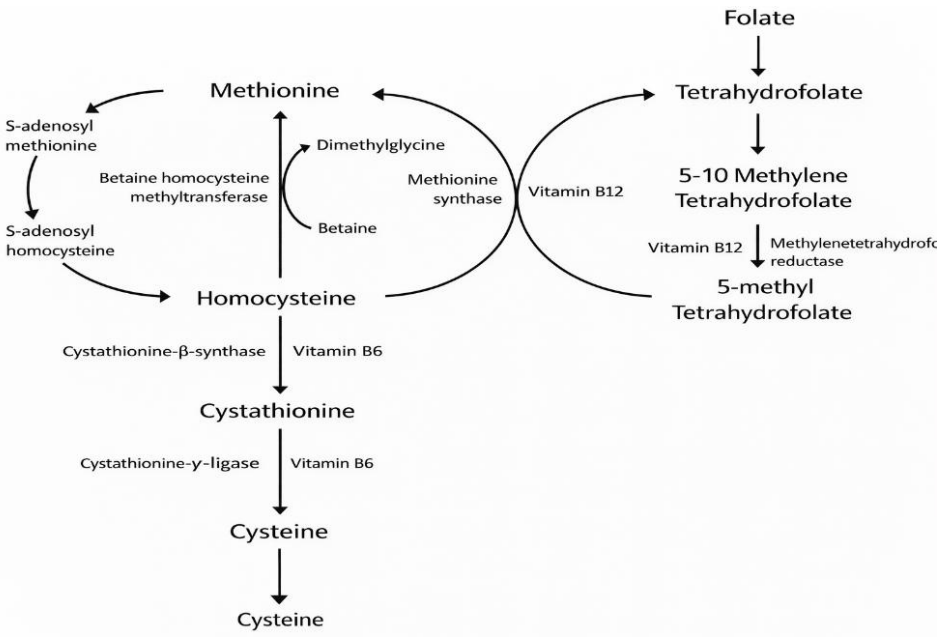

Figure 2. Role of vitamin B6 in homocysteine metabolism.

3. Epidemiological Evidence: Inverse Associations and Limitations

Large cross-sectional and prospective studies from different populations have examined the direct and indirect relationships between vitamin B6 status and glycemic control. Overall, the evidence shows a consistent inverse association between vitamin B6 status and dysglycemia, as well as inflammatory markers. The NHANES 1999-2018 analysis reported the strongest signal: each 1 mg increase in dietary vitamin B6 intake was associated with a 15.2% reduction in the odds of poor glycemic control (adjusted odds ratio [AOR] 0.848, 95% CI 0.738-0.973; P = 0.019), with an area under the curve (AUC) of 0.977 (95% CI 0.974-0.980). Receiver operating characteristic (ROC) analyses also suggested that vitamin B6 outperformed the other micronutrients evaluated. Importantly, the association showed an apparent linear dose-response pattern across intake quintiles (1.1-2.5 mg/day), without a clear threshold [7].

The 2012 Framingham Offspring Study [17] further reported that participants in the highest versus lowest tertile of a composite inflammatory score had a 24% lower geometric mean plasma PLP concentration (62 vs. 80 nmol/L; P < 0.0001). These findings support PLP as an inverse marker of inflammation and suggest that low plasma PLP in individuals with dysglycemia may contribute to oxidative stress and worsening insulin resistance.

A 2025 epidemiological study using two-sample Mendelian randomization examined associations between vitamins A, B6, C, and D and diabetes complications. Higher PLP was associated with an increased risk of hypoglycemia (OR 8.54, 95% CI 1.77-41.2; P < 0.0075) [18]. This finding may reflect enhanced insulin sensitivity or altered glucose handling, although the wide confidence interval indicates substantial uncertainty. Earlier, the Boston Puerto Rican Health Study (2010) reported an inverse relationship between plasma PLP quartiles (lowest: 5.5-28.3 nmol/L; highest: 65.3-737 nmol/L) and glycemic markers, including lower fasting blood glucose and HbA1c, higher HOMA-beta (beta-cell function), and lower HOMA-IR (insulin resistance); however, not all associations reached statistical significance [19].

Table 1. Summary of epidemiological studies (2010 onward) evaluating vitamin B6 status and glycemic or diabetes-related outcomes.

Study	Sample size	Exposure	Outcome	Effect estimate	Adjusted covariates
NHANES 1999-2018 [7]	41,302	Dietary B6 (mg/day)	Poor glycemic control (HbA1c > 6.5%)	AOR 0.848 (95% CI 0.738-0.973) per 1 mg/day increase	Age, sex, BMI, race, diabetes, year, diet quality
Framingham offspring [17]	2,229	Plasma PLP (nmol/l)	Inflammatory score / plasma PLP	~24% lower PLP in highest vs lowest inflammatory tertile	Age, sex, creatinine, folate, and B12
A Mendelian Randomization Study [18]	>400,000	Plasma PLP (nmol/l)	Diabetic complication (hypoglycemia)	OR 8.54 (95% CI 1.77-41.2)	Age, sex, BMI, alcohol, and smoking
the Boston Puerto Rican Health Study [19]	1,205	Plasma PLP (nmol/l)	FBG, HbA1c, HOMA-beta, HOMA-IR	Inverse associations with FBG and HbA1c; improved HOMA-beta	Age, sex, BMI, smoking, medication, energy intake, homocysteine

Taken together, these findings suggest that vitamin B6 has a modest but potentially clinically meaningful association with glycemic health. In NHANES, higher vitamin B6 intake was associated with approximately 15% lower odds of dysglycemia, an effect size that may be important at the population level. In the Boston Puerto Rican Health Study, higher PLP status was associated with lower fasting glucose and HbA1c across quartiles, changes that could be relevant for risk stratification and early glycemic deterioration. The Framingham Offspring Study adds a complementary dimension by linking lower PLP to a higher inflammatory burden, which may be mechanistically relevant to insulin resistance and prediabetes [17].

Although these effect sizes are smaller than those typically observed with pharmacotherapy, they may be comparable to some lifestyle or adjunctive interventions, such as moderate physical activity, modest weight reduction, or anti-inflammatory strategies [22,23].

Table 2. Comparative Effects of Glucose-Lowering Interventions on HbA1c and Glycemic Outcomes.

Intervention strategy	Typical HbA1c reduction (%)	Clinical context / evidence base
Moderate weight reduction and physical activity [24]	0.5%-1.0%	Diabetes prevention program
Metformin therapy [25]	1.0%-1.5%	First line medication
Vitamin B6 / PLP (preliminary evidence)	Approximately 0.5% (estimated across limited studies)	Adjunct or nutritional strategy; evidence remains limited
Anti-inflammatory therapies [23]	0.25%-0.63%	Meta-analyzed adjunctive approaches in T2DM

Despite these consistent inverse associations, causality cannot be established because of three major limitations. First, residual confounding is likely [26]: vitamin B6 status is not an isolated exposure and often reflects overall diet quality, making it difficult to separate its effect from other dietary factors such as fiber, polyphenols, and whole grains. Second, reverse causation is plausible [26]. For example, the Framingham Offspring findings suggest that inflammation itself may reduce circulating PLP, implying that low B6 status may be a consequence, rather than a cause, of metabolic dysfunction [17]. This interpretation is supported by a German study in which participants with diabetic nephropathy had lower PLP, potentially due to microvascular damage and increased renal losses [27]. Third, generalizability is limited because most studies were conducted in U.S. or predominantly White populations. The relevance of these findings to Asian, African, and Hispanic populations, who may differ in genetic variants affecting B6 metabolism (e.g., ALPL rs1256335), remains uncertain [28].

4. Possible Role in Glycemic Control: B6 Beyond a Coenzyme

The inverse association between vitamin B6 status and glycemic outcomes observed in epidemiological studies is supported by several mechanistic pathways through which PLP may influence glucose homeostasis.

4.1. Carbonyl Scavenging and Antiglycation

Persistent hyperglycemia promotes the formation of advanced glycation end products (AGEs) through nonenzymatic glycation of proteins. AGEs are linked to beta-cell dysfunction, insulin resistance, and diabetic complications [29]. Methylglyoxal, a reactive dicarbonyl species, is a major precursor of AGEs [30]. PLP and the vitamer pyridoxamine (PM) can act as carbonyl scavengers that trap reactive intermediates and limit protein modification [31]. In vivo studies in streptozotocin-induced diabetic rats showed that pyridoxamine supplementation attenuated nephropathy progression by inhibiting AGE formation [32]. This antiglycation mechanism supports a potential role for vitamin B6 in reducing long-term hyperglycemia-related complications.

4.2. Effects on Oxidative Stress and Inflammation

Chronic inflammation and oxidative stress are central features of insulin resistance and type 2 diabetes [33]. Several studies report inverse associations between PLP and inflammatory markers such as C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF-alpha) [34]. A randomized trial of vitamin B6 supplementation in patients with ulcerative colitis also demonstrated a significant reduction in CRP [35]. Potential mechanisms include the role of PLP as a coenzyme in glutathione synthesis and its direct antioxidant activity through reactive oxygen species scavenging [36].

4.3. Pancreatic Function and Protection

PLP is a coenzyme for enzymes involved in glucose sensing and insulin secretion, supporting normal pancreatic function [37]. Vitamin B6 deficiency has also been linked to beta-cell dysfunction, a key feature of prediabetes and type 2 diabetes [38]. In both in vivo and in vitro streptozotocin models, PLP supplementation improved beta-cell survival and insulin secretion while reducing free radical production [39]. These findings support a cytoprotective role for vitamin B6 in pancreatic beta cells.

4.4. Glucose Absorption and alpha-Glucosidase

Vitamin B6 may also influence glycemic control by reducing intestinal carbohydrate digestion [40]. In a crossover study, administration of 50 mg pyridoxine significantly reduced postprandial glucose responses compared with control conditions, including a 13.8% reduction in peak glucose [41]. This effect has been attributed to inhibition of intestinal alpha-glucosidase, which slows carbohydrate digestion and absorption and therefore lowers postprandial glycemia [40]. Because postprandial hyperglycemia is a key feature of insulin resistance [42], this mechanism is particularly relevant to prediabetes.

4.5. PLP and HbA1c Assay Accuracy

In 2011, Behan et al. reported that chemical modifications to hemoglobin, such as carbamylation and acetylation, may introduce error in HbA1c measurement because these changes can alter the glucose-binding region or the epitope detected by some assay methods [43]. PLP can also form reversible Schiff-base adducts with lysine residues on proteins, including hemoglobin, and may therefore compete with glucose at amino-terminal binding sites [44]. This raises an important analytical question: could higher PLP falsely lower HbA1c values in some assay methods without a true improvement in glycemia? This possibility should be tested in future trials by using method-specific HbA1c assays and pairing HbA1c with glucose-based endpoints such as CGM metrics and fasting/postprandial glucose [45,46].

5. Intervention Trials

Rationale for Evaluating Vitamin B6 in Glycemic Management

Interventional evidence remains limited but suggests a possible metabolic benefit of vitamin B6. In a double-blind, placebo-controlled trial, pyridoxine hydrochloride (80 mg/day for 8 weeks) in overweight and obese women improved fasting insulin, HOMA-IR, adipokines, and anthropometric indices, with favorable changes in lipid profile and body composition [48]. In an older study of gestational diabetes, pyridoxine (100 mg/day for 2 weeks) improved glucose tolerance during intravenous glucose testing [47]; however, the pregnancy-specific setting and limited methodological rigor restrict generalizability to prediabetes or type 2 diabetes. Studies targeting diabetic complications have also provided

insufficient evidence for routine clinical use. Some early pyridoxamine studies suggested renal benefits, but larger confirmatory trials are lacking, and prolonged high-dose pyridoxine may be ineffective for nephropathy and may carry toxicity risk. Therefore, current evidence does not support routine high-dose vitamin B6 therapy for diabetes-related complications.

Table 3. Interventional trials of vitamin B6 and glycemic control.

Study (year)	Population / sample size	Intervention regimen	Assessment markers	Main findings
[44]	60 patients with T2DM	pyridoxine as an adjunct therapy with standard antidiabetic treatment.	FBS, HBA1c	Adjunct pyridoxine was associated with reductions in FBS and HbA1c.
[41]	20 healthy adults	Single oral dose pyridoxine	Postprandial glucose, insulin AUC	Reduced postprandial glucose excursion and insulin AUC after a single dose.
[47]	30 women with GDM	Pyridoxine 100 mg/day	FBS, oral glucose test	Improved glucose tolerance curve and lower fasting glucose in GDM cohort.
[48]	44 overweight/ obese women	Pyridoxine HCL 80mg / day for 8 weeks.	FBS, Insulin, HOMA-IR, Leptin, adiponectin, BMI	Improved insulin resistance markers and adipokines; favorable anthropometric changes.

6. Research Priorities:

Determining the Causal Role of Vitamin B6 in Glycemic Control**;** To move vitamin B6 from a neglected micronutrient to an evidence-based option in prediabetes care, hypothesis-driven research is needed. Despite strong epidemiological signals, causality cannot be established because the available evidence is vulnerable to reverse causation and observational bias [49, 50]. The following framework outlines research priorities for clarifying causal pathways.

6.1. Randomized Controlled Trials Using Continuous Glucose Monitoring Endpoints

A 12-week, double-blind, placebo-controlled randomized trial enrolling adults with confirmed prediabetes (HbA1c 5.7-6.4%) should be a priority [51,52]. A dose equivalent to 40 mg/day of pyridoxine (as PLP equivalent) would be pharmacologically active while remaining below the Institute of Medicine upper intake level of 100 mg/day [53]. Traditional endpoints such as HbA1c and fasting glucose may be relatively insensitive to short-term micronutrient effects [54]. Therefore, continuous glucose monitoring (CGM) should be used to capture dynamic glycemic responses.

1. Time in Range (TIR): The percentage of readings within the target range (70-180 mg/dl) is known as TIR, and it is a valid indicator that has been linked to diabetes complications [55].
2. Mean Amplitude of Glycemic Excursion (MAGE): measures the daily glycemic variability, an independent cardiovascular risk factor [56].
3. Area Under the Curve (AUC): This endpoint can test the alpha-glucosidase inhibition hypothesis by quantifying postprandial glucose exposure [57].

6.2. Secondary Mechanistic Studies

Three mechanistic domains should be prioritized in parallel with efficacy outcomes: carbonyl scavenging/antiglycation, inflammation, and redox homeostasis. These pathways should form the core of secondary mechanistic analyses.

1. Antiglycation pathway: Plasma methylglyoxal and AGEs should be quantified (e.g., by liquid chromatography) to test whether PLP supplementation produces a dose-dependent reduction in reactive carbonyl metabolites [58].
2. Inflammation markers: Proinflammatory cytokines (including interleukin-6 and tumor necrosis factor-alpha) and C-reactive protein should be measured, because B6 deficiency may activate nuclear factor kappa B signaling [59].

3. Antioxidant capacity: Erythrocyte glutathione peroxidase activity and total antioxidant capacity should be assessed to determine whether vitamin B6 supplementation reduces oxidative stress [60].
4. Insulin sensitivity: Peripheral insulin action should be assessed in a nested subgroup using the hyperinsulinemic-euglycemic clamp. In addition, the Matsuda index derived from the oral glucose tolerance test may provide a more informative estimate of insulin sensitivity than HOMA-IR [61, 62].

6.3. Individualized Nutrition and Food-Based Interventions

Responses to vitamin B6 may be modified by genetic variability affecting B6 metabolism. PLP bioavailability and distribution can be influenced by polymorphisms in pyridoxamine 5-phosphate oxidase and alkaline phosphatase genes [63]. Genomic stratification may therefore help distinguish responders from non-responders.

Translation to public health practice will also require food-based interventions rather than supplement-only trials. An isocaloric, vitamin B6-enriched dietary pattern should be tested in randomized designs, with careful control of co-varying dietary factors such as fiber and polyphenols [64].

7. Practical Implications

Clinicians and public health practitioners should interpret current evidence on vitamin B6 cautiously. The epidemiological associations are consistent and biologically plausible, but causality has not yet been established in adequately powered intervention trials.

The key practical messages are:

1. Assess dietary vitamin B6 intake in individuals with poor glycemic control, especially when intake of B6-rich foods (whole grains, legumes, poultry, and fish) appears low.
2. Encourage a food-first approach. Promoting B6-rich foods is safe and consistent with healthy dietary patterns. For most adults, the recommended dietary allowance (RDA) is approximately 1.3-1.7 mg/day, and observational data suggest that intakes near the upper end of this range are common among groups with better glycemic profiles [7].
3. Avoid routine high-dose supplementation or routine laboratory testing for vitamin B6 solely to improve glycemia until stronger trial evidence is available. Long-term intakes above supplemental needs may carry risk and should be medically supervised [18].

8. Conclusion

Consistent epidemiological evidence links better vitamin B6 status with more favorable glycemic control and lower inflammatory burden, and several mechanisms (including roles in glycogen metabolism, carbonyl scavenging and antiglycation, oxidative stress modulation, beta-cell protection, and possible effects on carbohydrate digestion) support biological plausibility. However, the evidence is not yet sufficient to infer causality because focused randomized trials in prediabetes are scarce. Future clinical trials should clarify efficacy, dose, safety, and mechanism, and should explicitly evaluate whether PLP interferes with HbA1c assay interpretation in a method-dependent manner. Well-designed trials using CGM and complementary biochemical endpoints are essential to unveil the potentially underrecognized role of vitamin B6 in prediabetes management.

In the global effort to address prediabetes, vitamin B6 may represent a safe, inexpensive adjunct to lifestyle-based strategies; however, its role should remain hypothesis-driven until confirmed by high-quality randomized trials.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Khan, R. M. M., Chua, Z. J. Y., Tan, J. C., Yang, Y., Liao, Z., & Zhao, Y. (2019). From Pre-Diabetes to Diabetes: Diagnosis, Treatments and Translational Research. Medicina, 55(9), 546. https://doi.org/10.3390/medicina55090546
2. Boltri, J. M., Tracer, H., Strogatz, D., Idzik, S., Schumacher, P., Fukagawa, N., Leake, E., Powell, C., Shell, D., Wu, S., & Herman, W. H. (2023). The National Clinical Care Commission Report to Congress: Leveraging Federal Policies and Programs to Prevent Diabetes in People With Prediabetes. Diabetes Care, 46(2), e39–e50. https://doi.org/10.2337/dc22-0620
3. Tegegne, B. A., Adugna, A., Yenet, A., Yihunie Belay, W., Yibeltal, Y., Dagne, A., Hibstu Teffera, Z., Amare, G. A., Abebaw, D., Tewabe, H., Abebe, R. B., & Zeleke, T. K. (2024). A critical review on diabetes mellitus type 1 and type 2 management approaches: from lifestyle modification to current and novel targets and therapeutic agents. Frontiers in Endocrinology, 15. https://doi.org/10.3389/fendo.2024.1440456
4. Iizuka, K., & Daisuke Yabe. (2023). Dietary and Nutritional Guidelines for People with Diabetes. Nutrients, 15(20), 4314–4314. https://doi.org/10.3390/nu15204314
5. Volpe, S. L. (2013). Magnesium in Disease Prevention and Overall Health. Advances in Nutrition, 4(3), 378S383S. https://doi.org/10.3945/an.112.003483
6. Lewicki, S., Zdanowski, R., Krzyżowska, M., Lewicka, A., Dębski, B., Niemcewicz, M., & Goniewicz, M. (2014). The role of Chromium III in the organism and its possible use in diabetes and obesity treatment. Annals of Agricultural and Environmental Medicine, 21(2), 331–335. https://doi.org/10.5604/1232-1966.1108599
7. Bai, Y., Zhang, H., Yang, J., & Peng, L. (2021). The Association between Daily Total Dietary Nutrient Intake and Recent Glycemic Control States of Non-Pregnant Adults 20+ Years Old from NHANES 1999–2018 (Except for 2003–2004). Nutrients, 13(11), 4168. https://doi.org/10.3390/nu13114168
8. Ruan, Y., Zhang, P., Jia, X., Hua, S., & Yao, D. (2024). Association of vitamin B6 intake with the risk and prognosis of diabetic retinopathy: a NHANES-based study. Clinical and Experimental Optometry, 107(8), 847–856. https://doi.org/10.1080/08164622.2023.2300298
9. Mascolo, E., Liguori, F., Merigliano, C., Schiano, L., Gnocchini, E., Pilesi, E., Volonté, C., Di Salvo, M. L., Contestabile, R., Tramonti, A., & Vernì, F. (2022). Vitamin B6 rescues insulin resistance and glucose-induced DNA damage caused by reduced activity of Drosophila PI3K. Journal of Cellular Physiology, 237(9), 3578–3586. https://doi.org/10.1002/jcp.30812
10. Hellmann, H., & Mooney, S. (2010). Vitamin B6: A Molecule for Human Health? Molecules, 15(1), 442–459. https://doi.org/10.3390/molecules15010442
11. Mooney, S., Leuendorf, J.-E., Hendrickson, C., & Hellmann, H. (2009). Vitamin B6: A Long Known Compound of Surprising Complexity. Molecules, 14(1), 329–351. https://doi.org/10.3390/molecules14010329
12. Rivero, M., Novo, N., & Medina, M. (2024). Pyridoxal 5′-Phosphate Biosynthesis by Pyridox-(am)-ine 5′-Phosphate Oxidase: Species-Specific Features. International Journal of Molecular Sciences, 25(6), 3174–3174. https://doi.org/10.3390/ijms25063174
13. Rogers, K. S., & Mohan, C. (1994). Vitamin B6 Metabolism and Diabetes. Biochemical Medicine and Metabolic Biology, 52(1), 10–17. https://doi.org/10.1006/bmmb.1994.1027
14. McFerran, D. J., & Wray, N. (2024). Autonomous Tinnitus Management (Self-Help for Tinnitus). Springer EBooks, 739–761. https://doi.org/10.1007/978-3-031-35647-6_58
15. Polizzi, F., Gülnur Andican, Cetin, E., Sabiha Civelek, Volkan Yumuk, & Gülden Burçak. (2012). Increased DNA-glycation in type 2 diabetic patients: the effect of thiamine and pyridoxine therapy. 120(6), 329–334. https://doi.org/10.1055/s-0031-1298016

16. Zhao, Y., Zhao, T., Liu, X., Li, R., & Xiao, H. (2025). Vitamin B6 Nutrition, Metabolism, and the Relationship of Diseases: Current Concepts and Future Research. Journal of Future Foods. https://doi.org/10.1016/j.jfutfo.2024.12.007

17. Sakakeeny, L., Roubenoff, R., Obin, M., Fontes, J. D., Benjamin, E. J., Bujanover, Y., Jacques, P. F., & Selhub, J. (2012). Plasma Pyridoxal-5-Phosphate Is Inversely Associated with Systemic Markers of Inflammation in a Population of U.S. Adults. The Journal of Nutrition, 142(7), 1280–1285. https://doi.org/10.3945/jn.111.153056

18. Cai, S., Man, W., Liu, W., Li, B., He, Z., & Duan, G. (2025). Causal Relationship Between Various Vitamins and Different Diabetic Complications: A Mendelian Randomization Study. Food Science & Nutrition, 13(7). https://doi.org/10.1002/fsn3.70536

19. Shen, J., Lai, C.-Q., Mattei, J., Ordovas, J. M., & Tucker, K. L. (2010). Association of vitamin B-6 status with inflammation, oxidative stress, and chronic inflammatory conditions: the Boston Puerto Rican Health Study. The American Journal of Clinical Nutrition, 91(2), 337–342. https://doi.org/10.3945/ajcn.2009.28571

20. Genuth, S., Eastman, R., Kahn, R., Klein, R., Lachin, J., Lebovitz, H., Nathan, D., Vinicor, F., & American Diabetes Association. (2003). Implications of the United kingdom prospective diabetes study. Diabetes Care, 26 Suppl 1, S28-32. https://doi.org/10.2337/diacare.26.2007.s28

21. Khalili, D., Marjan Khayamzadeh, Karim Kohansal, Noushin Sadat Ahanchi, Mitra Hasheminia, Farzad Hadaegh, Tohidi, M., Azizi, F., & Ali Siamak Habibi-Moeini. (2023). Are HOMA-IR and HOMA-B good predictors for diabetes and pre-diabetes subtypes? BMC Endocrine Disorders, 23(1). https://doi.org/10.1186/s12902-023-01291-9

22. Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., & Nathan, D. M. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. The New England Journal of Medicine, 346(6), 393–403. https://doi.org/10.1056/NEJMoa012512

23. Li, D., Zhong, J., Zhang, Q., & Zhang, J. (2023). Effects of anti-inflammatory therapies on glycemic control in type 2 diabetes mellitus. Frontiers in Immunology, 14, 1125116. https://doi.org/10.3389/fimmu.2023.1125116

24. Muhammad Muaaz Sikandar, Namra Tanvir, Qadir, A., Abdussalam, & Abbas, G. (2024). Impact of Diet and Exercise Interventions on Glycemic Control and Weight Management in Adults with Type 2 Diabetes: A Systematic Review of Randomized Controlled Trials and Observational Studies. 2(2), 1072–1082. https://doi.org/10.70749/ijbr.v2i02.333

25. Gu, S., Shi, J., Tang, Z., Sawhney, M., Hu, H., Shi, L., Fonseca, V., & Dong, H. (2015). Comparison of Glucose Lowering Effect of Metformin and Acarbose in Type 2 Diabetes Mellitus: A Meta-Analysis. PLOS ONE, 10(5), e0126704. https://doi.org/10.1371/journal.pone.0126704

26. Wang, X., & Cheng, Z. (2020). Cross-sectional studies: Strengths, weaknesses, and recommendations. Chest, 158(1), 65–71. https://doi.org/10.1016/j.chest.2020.03.012

27. Nix, W. A., Zirwes, R., Bangert, V., Kaiser, R. P., Schilling, M., Hostalek, U., & Obeid, R. (2015). Vitamin B status in patients with type 2 diabetes mellitus with and without incipient nephropathy. Diabetes Research and Clinical Practice, 107(1), 157–165. https://doi.org/10.1016/j.diabres.2014.09.058

28. Hazra, A., Kraft, P., Lazarus, R., Chen, C., Chanock, S. J., Jacques, P., Selhub, J., & Hunter, D. J. (2009). Genome-wide significant predictors of metabolites in the one-carbon metabolism pathway. Human Molecular Genetics, 18(23), 4677–4687. https://doi.org/10.1093/hmg/ddp428

29. Vlassara, H. (2001). The AGE-receptor in the pathogenesis of diabetic complications. Diabetes/Metabolism Research and Reviews, 17(6), 436–443. https://doi.org/10.1002/dmrr.233
30. Davies, S. S., & Zhang, L. S. (2017). Reactive Carbonyl Species Scavengers—Novel Therapeutic Approaches for Chronic Diseases. Current Pharmacology Reports, 3(2), 51–67. https://doi.org/10.1007/s40495-017-0081-6
31. Stach, K., Stach, W., & Augoff, K. (2021). Vitamin B6 in health and disease. *Nutrients, 13*(9), 3229 https://doi.org/10.3390/nu13093229
32. Nakamura, S., Li, H., Adijiang, A., Pischetsrieder, M., & Niwa, T. (2007). Pyridoxal phosphate prevents progression of diabetic nephropathy. *Nephrology Dialysis Transplantation, 22*(8), 2165–2174. https://doi.org/10.1093/ndt/gfm166
33. Oguntibeju, O. O. (2019). Type 2 diabetes mellitus, oxidative stress and inflammation: Examining the links. *International Journal of Physiology, Pathophysiology and Pharmacology, 11*(3), 45–63.
34. Mascolo, E., & Vernì, F. (2020). Vitamin B6 and diabetes: Relationship and molecular mechanisms. *International Journal of Molecular Sciences, 21*(10), 3669. https://doi.org/10.3390/ijms21103669
35. Alavinejad, P., Mard, S. A., Panahandeh, F., Hesam, S., Hashemi, S. J., Morvaridi, M., & Taherpour, S. (2020). Efficacy of vitamin B6 supplementation on inflammatory markers, serum homocysteine level, fecal calprotectin and clinical outcomes among patients with ulcerative colitis: A randomized double-blind clinical trial. *Afro-Egyptian Journal of Infectious and Endemic Diseases, 10*(2), 114–119.
36. Cheng, C. H., Huang, S. C., Chiang, T. Y., Wong, Y., & Huang, Y. C. (2013). Higher plasma pyridoxal phosphate is associated with increased antioxidant enzyme activities in critically ill surgical patients. *BioMed Research International, 2013*, 572081. https://doi.org/10.1155/2013/572081
37. Rubí, B. (2012). Pyridoxal 5′-phosphate deficiency might contribute to the onset of type I diabetes. *Medical Hypotheses, 78*(1), 179–182. https://doi.org/10.1016/j.mehy.2011.10.014
38. Merigliano, C., Mascolo, E., Burla, R., Saggio, I., & Vernì, F. (2018). The relationship between vitamin B6, diabetes and cancer. *Frontiers in Genetics, 9*, 388. https://doi.org/10.3389/fgene.2018.00388
39. Kiran, S. G., Dorisetty, R. K., Umrani, M. R., Boindala, S., Bhonde, R. R., Chalsani, M., Singh, H., & Venkatesan, V. (2011). Pyridoxal 5′-phosphate protects islets against streptozotocin-induced beta-cell dysfunction—*in vitro* and *in vivo*. *Experimental Biology and Medicine, 236*(4), 456–465. https://doi.org/10.1258/ebm.2011.010283
40. Abdullah, K. M., Arefeen, A., Shamsi, A., Alhumaydhi, F. A., & Naseem, I. (2021). Insight into the *in vitro* antiglycation and *in vivo* antidiabetic effects of thiamine: Implications of vitamin B1 in controlling diabetes. *ACS Omega, 6*(19), 12605–12614. https://doi.org/10.1021/acsomega.1c01065
41. Kim, H. H., Kang, Y. R., Choi, H. Y., Lee, J. Y., Oh, J. B., Kim, J. S., Kim, Y. C., Lee, K. W., & Kwon, Y. I. (2019). Postprandial anti-hyperglycemic effect of vitamin B6 (pyridoxine) administration in healthy individuals. *Food Science and Biotechnology, 28*(3), 907–911. https://doi.org/10.1007/s10068-018-0505-7
42. Hiyoshi, T., Fujiwara, M., & Yao, Z. (2017). Postprandial hyperglycemia and postprandial hypertriglyceridemia in type 2 diabetes. *Journal of Biomedical Research, 33*(1), 1–10. https://doi.org/10.7555/JBR.31.20160075
43. Behan, K. J., & Merschen, J. (2011). HbA1c does not always estimate average glucose. *Clinical Laboratory Science, 24*(2), 71–77.
44. Dawood, M. H., Abdulridha, M. K., & Qasim, H. S. (2023). Assessing pyridoxine adjuvant therapy effects on blood glucose levels in type 2 diabetes: A randomized clinical trial. *Journal of Medicine and Life, 16*(10), 1474–1480. https://doi.org/10.25122/jml-2023-0204
45. Liddy, A. M., Grundy, S., Sreenan, S., & Tormey, W. (2023). Impact of haemoglobin variants on the use of haemoglobin A1c for the diagnosis and monitoring of diabetes: A contextualised

review. *Irish Journal of Medical Science, 192*(1), 169–176. https://doi.org/10.1007/s11845-022-02976-6

46. Lorenzo-Medina, M., De-La-Iglesia, S., Ropero, P., & Santana-Benitez, J. (2014). Effects of hemoglobin variants on hemoglobin A1c values measured using a high-performance liquid chromatography method. *Journal of Diabetes Science and Technology, 8*(6), 1168–1176. https://doi.org/10.1177/1932296814546502
47. Spellacy, W. N., Buhi, W. C., & Birk, S. A. (1977). Vitamin B6 treatment of gestational diabetes mellitus. *American Journal of Obstetrics and Gynecology, 127*(6), 599–602. https://doi.org/10.1016/0002-9378(77)90458-4
48. Haidari, F., Mohammadshahi, M., Zarei, M., Haghighizadeh, M. H., & Mirzaee, F. (2021). The effect of pyridoxine hydrochloride supplementation on leptin, adiponectin, glycemic indices, and anthropometric indices in obese and overweight women. *Clinical Nutrition Research, 10*(3), 230–240. https://doi.org/10.7762/cnr.2021.10.3.230
49. Yan, S., Li, M., Ma, X., Jiang, S., Sun, M., Wang, C., Pan, Y., Sun, C., Yao, Y., Jin, L., & Li, B. (2019). Association of multiple mineral and vitamin B group intake with blood glucose using quantile regression analysis: NHANES 2007–2014. *Food & Nutrition Research, 63*, 29219. https://doi.org/10.29219/fnr.v63.29219
50. American Diabetes Association. (2021). Classification and diagnosis of diabetes: Standards of medical care in diabetes—2021. *Diabetes Care, 44*(Suppl. 1), S15–S33. https://doi.org/10.2337/dc21-S002
51. Sabanayagam, C., Khoo, E. Y., Lye, W. K., Ikram, M. K., Lamoureux, E. L., Cheng, C. Y., Tan, M. L., Salim, A., Lee, J., Lim, S. C., & Tavintharan, S. (2015). Diagnosis of diabetes mellitus using HbA1c in Asians: Relationship between HbA1c and retinopathy in a multiethnic Asian population. *Journal of Clinical Endocrinology & Metabolism, 100*(2), 689–696. https://doi.org/10.1210/jc.2014-2498
52. Subcommittee on Upper Reference Levels of Nutrients, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Panel on Folate, Other B Vitamins, and Choline. (1998). *Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline.* National Academy Press.
53. Chkroun, C., Trouwborst, I., Cherta-Murillo, A., Owen, L., Darimont, C., & Rytz, A. (2023). Defining a continuous glucose baseline to assess the impact of nutritional interventions. *Frontiers in Nutrition, 10*, 1203899. https://doi.org/10.3389/fnut.2023.1203899
54. Battelino, T., Alexander, C. M., Amiel, S. A., Arreaza-Rubin, G., Beck, R. W., Bergenstal, R. M., Buckingham, B. A., Carroll, J., Ceriello, A., Chow, E., & Choudhary, P. (2023). Continuous glucose monitoring and metrics for clinical trials: An international consensus statement. *The Lancet Diabetes & Endocrinology, 11*(1), 42–57. https://doi.org/10.1016/S2213-8587(22)00319-9
55. Monnier, L., Mas, E., Ginet, C., Michel, F., Villon, L., Cristol, J. P., & Colette, C. (2006). Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. *JAMA, 295*(14), 1681–1687. https://doi.org/10.1001/jama.295.14.1681
56. Mohamed Sham Shihabudeen, H., Hansi Priscilla, D., & Thirumurugan, K. (2011). Cinnamon extract inhibits α-glucosidase activity and dampens postprandial glucose excursion in diabetic rats. *Nutrition & Metabolism, 8*, 46. https://doi.org/10.1186/1743-7075-8-46
57. Rabbani, N., & Thornalley, P. J. (2014). The critical role of methylglyoxal and glyoxalase 1 in diabetic nephropathy. *Diabetes, 63*(1), 50–52. https://doi.org/10.2337/db13-1609
58. Nasir, A., Rahman, M. U., Khan, M., Zahid, M., Shahab, M., Jiao, H., Zeb, A., Shah, S. A., & Khan, H. (2025). Vitamin B6 via p-JNK/Nrf-2/NF-κB signaling ameliorates cadmium chloride-induced oxidative stress-mediated memory deficits in mice hippocampus. *Current Neuropharmacology, 23*(1), 116–127. https://doi.org/10.2174/1570159X23666240214123052
59. Djordjević, V. V., Kostić, J., Krivokapić, Ž., Krtinić, D., Ranković, M., Petković, M., & Ćosić, V. (2022). Decreased activity of erythrocyte catalase and glutathione peroxidase in patients with

schizophrenia. *Medicina, 58*(10), 1491. https://doi.org/10.3390/medicina58101491

60. DeFronzo, R. A., Tobin, J. D., & Andres, R. (1979). Glucose clamp technique: A method for quantifying insulin secretion and resistance. *American Journal of Physiology-Endocrinology and Metabolism, 237*(3), E214–E223. https://doi.org/10.1152/ajpendo.1979.237.3.E214
61. Matsuda, M., & DeFronzo, R. A. (1999). Insulin sensitivity indices obtained from oral glucose tolerance testing: Comparison with the euglycemic insulin clamp. *Diabetes Care, 22*(9), 1462–1470.https://doi.org/10.2337/diacare.22.9.1462
62. Carter, T. C., Pangilinan, F., Molloy, A. M., Fan, R., Wang, Y., Shane, B., Gibney, E. R., Midttun, Ø., Ueland, P. M., Cropp, C. D., & Kim, Y. (2015). Common variants at putative regulatory sites of the tissue nonspecific alkaline phosphatase gene influence circulating pyridoxal 5′-phosphate concentration in healthy adults. *The Journal of Nutrition, 145*(7), 1386–1393. https://doi.org/10.3945/jn.114.208769
63. Olde Loohuis, L. M., Albersen, M., De Jong, S., Wu, T., Luykx, J. J., Jans, J. J., Verhoeven-Duif, N. M., & Ophoff, R. A. (2019). The alkaline phosphatase (ALPL) locus is associated with B6 vitamer levels in CSF and plasma. Genes, 10(1), 8. https://doi.org/10.3390/genes10010008
64. Lichtenstein, A. H., Appel, L. J., Vadiveloo, M., Hu, F. B., Kris-Etherton, P. M., Rebholz, C. M., Sacks, F. M., Thorndike, A. N., Van Horn, L., & Wylie-Rosett, J., on behalf of the American Heart Association Council on Lifestyle and Cardiometabolic Health; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; and Stroke Council. (2021). 2021 dietary guidance to improve cardiovascular health: A scientific statement from the American Heart Association. Circulation, 144(23), e472–e487. https://doi.org/10.1161/CIR.0000000000001031

فيتامين ب 6 وتنظيم مستوى الغلوكوز: دور مُغفَل في مرحلة ما قبل السكري – مراجعة سردية.

ملخص:

تُعدّ مرحلة ما قبل السكري مشكلة صحية عالمية رئيسية تزيد من خطر تطور المرض إلى داء السكري وأمراض القلب والأوعية الدموية. ورغم أن الإرشادات الحالية لإدارة ارتفاع سكر الدم تُركّز على تناول المغذيات الكبرى وتعديل نمط الحياة، إلا أن دور المغذيات الصغرى لا يزال غير مُسلّط عليه الضوء بشكل كافٍ. تستعرض هذه الدراسة السردية المساهمة المحتملة لفيتامين ب 6 في تنظيم مستوى الجلوكوز، لا سيما في مرحلة ما قبل السكري. تُشير دراسات وبائية واسعة النطاق، بما في ذلك تحليلات من المسح الوطني لفحص الصحة والتغذية (NHANES)، إلى وجود ارتباطات عكسية هامة بين مستوى فيتامين ب 6 واضطرابات سكر الدم. على المستوى البيوكيميائي، يعمل بيريدوكسال 5-فوسفات (PLP)، وهو الشكل النشط لفيتامين ب 6، كعامل مساعد في أكثر من 150 تفاعلًا إنزيميًا، ويعمل ككاسح للكربونيل، ويُثبّط تكوين نواتج الغلكزة المتقدمة، وكلها عوامل ذات صلة بفيزيولوجيا مرض السكري. كما يتمتع فيتامين ب 6 بخصائص مضادة للأكسدة ومضادة للالتهابات، ويدعم وظيفة خلايا بيتا، وقد يؤثر على معالجة الجلوكوز في الأمعاء من خلال تثبيط إنزيم ألفا-غلوكوزيداز. على الرغم من هذه الأدلة القائمة على الملاحظة، لا يزال فيتامين ب 6 مهملاً إلى حد كبير في إدارة مرحلة ما قبل السكري، ولا تزال هناك فجوة كبيرة بين النتائج الوبائية والتطبيق السريري. ولذلك، تسلط هذه المراجعة الضوء على فيتامين ب 6 باعتباره عاملاً قابلاً للتعديل في تحديد اضطراب مستوى السكر في الدم خلال مرحلة ما قبل السكري، وتؤكد على الحاجة إلى تجارب تدخلية دقيقة وموجهة لتحديد فعاليته، والجرعة المثلى، وأهميته السريرية في الوقاية والتدابير العلاجية.

الكلمات المفتاحية : مقدمات السكري، فيتامين ب6، بيريدوكسين، التحكم في مستوى الجلوكوز، الهيموجلوبين السكري (HbA1c).