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Vitamin D3 and Vitamin B12 in Type 2 Diabetes Mellitus: Implications for Glycemic Control and Diabetic Complications-A Narrative Review

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Abstract

Type 2 diabetes mellitus (T2DM) is a major global metabolic disorder associated with significant morbidity, mortality, and healthcare burden. Beyond hyperglycemia and insulin resistance, growing evidence indicates that micronutrient deficiencies, particularly vitamin D3 and vitamin B12 deficiencies, contribute substantially to the pathogenesis, progression, and complications of T2DM. This narrative review summarizes current evidence regarding the epidemiology, pathophysiological mechanisms, clinical implications, and therapeutic significance of vitamin D3 and vitamin B12 in patients with T2DM. Vitamin D3 plays an essential role in glucose homeostasis through modulation of pancreatic β-cell function, insulin secretion, insulin sensitivity, and inflammatory responses. Deficiency of vitamin D3 has been associated with poor glycemic control, increased insulin resistance, endothelial dysfunction, and higher risk of diabetic microvascular and macrovascular complications.

Vitamin B12 deficiency is also highly prevalent among patients with T2DM, especially in individuals receiving long-term metformin therapy. Chronic vitamin B12 deficiency may result in peripheral neuropathy, megaloblastic anaemia, cognitive impairment, and elevated cardiovascular risk due to hyperhomocysteinemia. Importantly, vitamin B12 deficiency-related neuropathy may overlap with diabetic neuropathy, potentially leading to underdiagnosis and delayed treatment.

Recent clinical studies suggest that combined deficiencies of vitamin D3 and vitamin B12 may adversely influence metabolic control and accelerate diabetic complications. Early identification and correction of these deficiencies may improve insulin sensitivity, glycemic status, neuropathic symptoms, and overall quality of life in diabetic patients.

This review discusses the epidemiological associations, underlying pathophysiological mechanisms, clinical implications, and therapeutic significance of vitamin D3 and vitamin B12 in type 2 diabetes mellitus. The review also highlights the importance of routine micronutrient assessment as part of comprehensive diabetes management strategies.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major public health challenge. According to the International Diabetes Federation (IDF) Diabetes Atlas, 10th Edition, approximately 537 million adults were living with diabetes globally in 2021, with projections suggesting a substantial increase over the coming decades. T2DM accounts for nearly 90–95% of all diabetes cases and is characterized by chronic hyperglycemia resulting from insulin resistance, impaired insulin secretion, and progressive pancreatic β-cell dysfunction. Persistent metabolic dysregulation contributes to the development of microvascular and macrovascular complications, including nephropathy, retinopathy, neuropathy, cardiovascular disease, and stroke.

While genetic susceptibility, obesity, sedentary lifestyle, and unhealthy dietary habits remain major contributors to T2DM, increasing attention has been directed toward the role of micronutrient deficiencies in disease progression and complication burden. Among these, vitamin D3 and vitamin B12 deficiencies have emerged as clinically significant because of their association with metabolic control, vascular health, and neurological function.

Vitamin D3 deficiency is highly prevalent among individuals with T2DM and has been associated with impaired glucose homeostasis, insulin resistance, and increased inflammatory activity. Similarly, vitamin B12 deficiency is frequently observed in diabetic patients, particularly among those receiving prolonged metformin therapy. Reduced vitamin B12 levels may contribute to peripheral neuropathy, hematological abnormalities, cognitive dysfunction, and elevated cardiovascular risk.

The coexistence of vitamin D3 and vitamin B12 deficiencies may further aggravate metabolic and vascular dysfunction in T2DM. Consequently, assessment of micronutrient status is increasingly being recognized as an important component of comprehensive diabetes care. This review summarizes current evidence regarding the epidemiology, pathophysiological associations, clinical implications, and therapeutic relevance of vitamin D3 and vitamin B12 in T2DM.

The objective of this narrative review is to critically examine the current evidence regarding the role of vitamin D3 and vitamin B12 in T2DM, with particular emphasis on their epidemiology, biological mechanisms, impact on glycemic control, association with diabetic complications, and therapeutic implications. The review also evaluates the strengths and limitations of existing clinical evidence and discusses current recommendations for screening and supplementation in diabetic populations.

Vitamin D3 and Type 2 Diabetes Mellitus

Physiology of Vitamin D3

Vitamin D3 (cholecalciferol) is a fat-soluble vitamin synthesized

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in the skin following exposure to ultraviolet B radiation and obtained in smaller amounts through dietary intake. It undergoes hydroxylation in the liver to form 25-hydroxyvitamin D [25(OH)D], the major circulating form used to assess vitamin D status. Subsequently, 25(OH)D is converted in the kidneys by the enzyme 1α-hydroxylase (CYP27B1) into its biologically active form, 1,25-dihydroxyvitamin D [1,25(OH)2D]. The enzyme CYP24A1 regulates vitamin D catabolism and maintains physiological homeostasis by degrading active vitamin D metabolites.

The biological effects of vitamin D are mediated through vitamin D receptors (VDRs), which are expressed in pancreatic β-cells, skeletal muscle, adipose tissue, vascular endothelium, and immune cells. In patients with diabetic kidney disease, impaired renal function may reduce CYP27B1 activity and limit synthesis of active 1,25(OH)2D, thereby exacerbating vitamin D deficiency and its metabolic consequences. These observations support the potential relevance of vitamin D metabolism in the pathophysiology and complications of T2DM.

Association Between Vitamin D3 Deficiency and T2DM

Several epidemiological studies have demonstrated a high prevalence of vitamin D deficiency among patients with type 2 diabetes mellitus (T2DM). Low serum vitamin D levels have been associated with poor glycemic control, increased insulin resistance, obesity, metabolic syndrome, chronic inflammation, and higher risk of diabetic complications.

Vitamin D contributes to glucose homeostasis by supporting pancreatic β-cell function and improving peripheral insulin sensitivity. Deficiency may impair insulin secretion, reduce glucose uptake in skeletal muscle and adipose tissue, and promote metabolic dysregulation. In addition, hypovitaminosis D is associated with increased inflammatory cytokine activity and oxidative stress, both of which contribute to endothelial dysfunction and vascular injury in diabetes.

Vitamin D deficiency is particularly common in obese individuals because vitamin D becomes sequestered within adipose tissue, reducing circulating bioavailable levels. As a result, obesity and vitamin D deficiency frequently coexist in patients with T2DM and may synergistically worsen metabolic dysfunction.

Mechanisms Linking Vitamin D3 with T2DM

Impaired Insulin Secretion

Pancreatic β-cells contain vitamin D receptors and calcium-binding proteins essential for insulin exocytosis. Vitamin D helps maintain intracellular calcium homeostasis required for normal insulin release. Deficiency may therefore impair β-cell function and reduce insulin secretion.

Increased Insulin Resistance

Vitamin D enhances insulin receptor expression and improves insulin responsiveness in peripheral tissues. Reduced vitamin D levels may decrease glucose uptake in muscle and adipose tissue, thereby contributing to insulin resistance.

Chronic Inflammation

Vitamin D possesses anti-inflammatory and immunomodulatory properties. Deficiency may increase production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which are known to worsen insulin resistance and endothelial dysfunction.

Oxidative Stress and Endothelial Dysfunction

Vitamin D may help reduce oxidative stress through modulation of antioxidant pathways. Deficiency contributes to endothelial dysfunction, vascular inflammation, and oxidative injury, which play central roles in diabetic microvascular and macrovascular complications.

Vitamin D3 and Diabetic Complications

Diabetic Neuropathy

Diabetic peripheral neuropathy is a common complication of T2DM resulting from chronic hyperglycemia, oxidative stress, and microvascular injury. Low vitamin D levels have been associated with increased severity of neuropathic pain and sensory dysfunction. Vitamin D possesses neuroprotective properties and may support nerve growth factor synthesis and neuronal repair. Deficiency may therefore contribute to paresthesia, numbness, burning sensations, and impaired nerve conduction. Several studies have reported improvement in neuropathic symptoms following vitamin D supplementation in deficient patients.

Diabetic Nephropathy

Vitamin D deficiency has been implicated in the progression of diabetic nephropathy through activation of the renin–angiotensin–aldosterone system (RAAS), promotion of inflammation, and enhancement of renal fibrosis. Low vitamin D levels have been associated with albuminuria, declining estimated glomerular filtration rate (eGFR), and accelerated chronic kidney disease progression. Vitamin D receptor activation may additionally exert renoprotective effects by reducing inflammatory cytokine activity and mesangial cell proliferation.

Cardiovascular Disease

Cardiovascular disease remains the leading cause of morbidity and mortality in T2DM. Hypovitaminosis D has been linked with hypertension, endothelial dysfunction, arterial stiffness, dyslipidemia, and accelerated atherosclerosis. Vitamin D influences vascular smooth muscle activity, endothelial nitric oxide production, and inflammatory pathways involved in cardiovascular regulation. Observational studies have demonstrated associations between low vitamin D levels and increased risk of ischemic heart disease, stroke, heart failure, and cardiovascular mortality in diabetic individuals.

Diabetic Retinopathy

Diabetic retinopathy is a progressive microvascular complication characterized by retinal ischemia, capillary damage, and abnormal angiogenesis. Vitamin D deficiency may contribute to retinal vascular injury through inflammatory and oxidative mechanisms. Low

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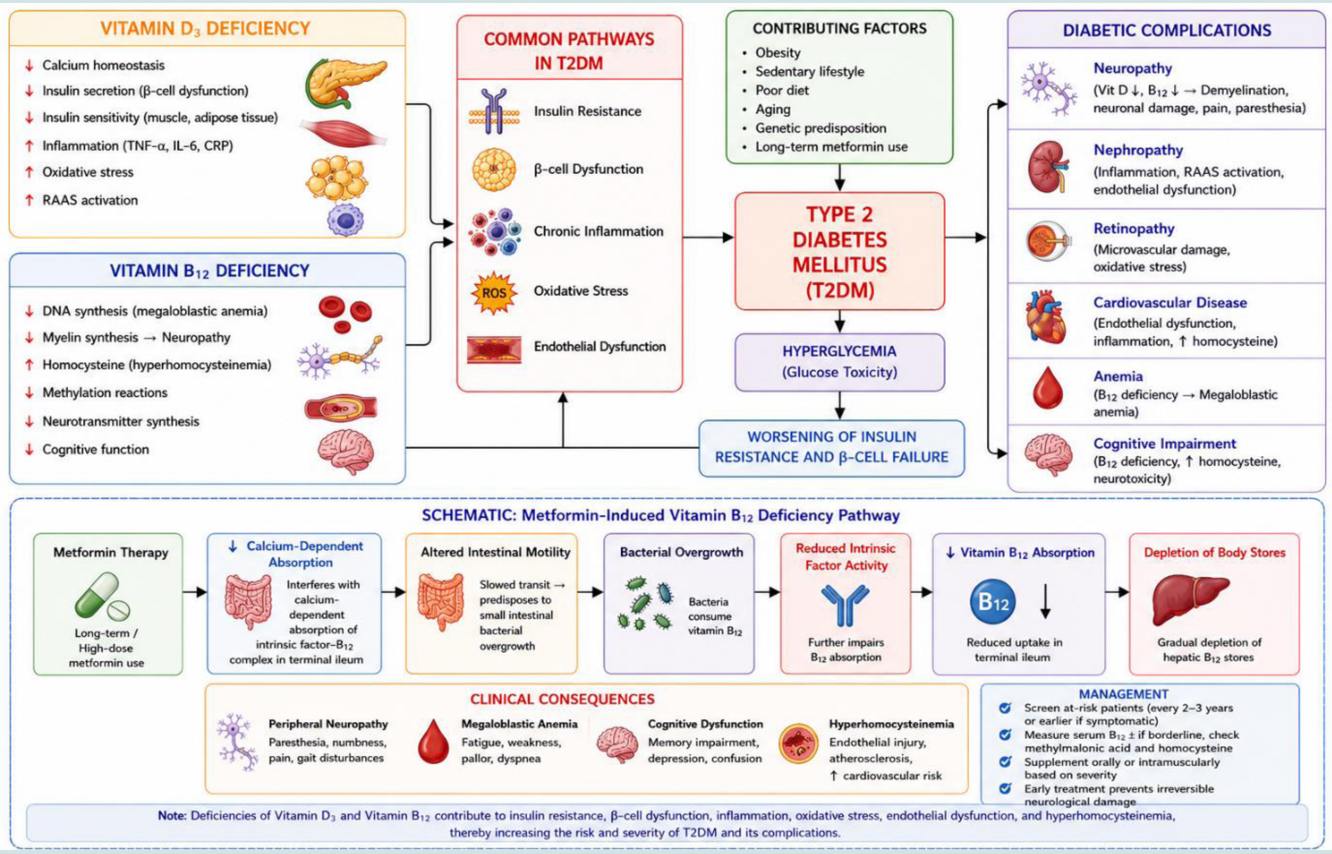

Figure 1: Pathophysiology Linking Vitamin D_3, Vitamin B_{12}, and Type 2 Diabetes Mellitus (T2DM)).

vitamin D levels have been associated with increased retinal vascular permeability and greater severity of diabetic retinopathy. Although causality remains under investigation, adequate vitamin D status may help preserve retinal vascular integrity and reduce progression of diabetic eye disease.

Vitamin D Supplementation in T2DM

Several interventional studies have evaluated the effects of vitamin D supplementation in patients with T2DM. Meta-analyses and randomized controlled trials have reported modest improvements in insulin sensitivity, fasting blood glucose, and HbA1c, particularly among individuals with documented vitamin D deficiency. However, the magnitude of benefit has generally been small and inconsistent across studies.

Large-scale randomized trials, including the VITAL study and findings from the D-HEALTH program, have not consistently demonstrated clinically meaningful improvements in glycemic outcomes among vitamin D–replete individuals. Variability in outcomes may be attributable to differences in baseline vitamin D status, supplementation dosage, treatment duration, ethnicity, obesity prevalence, and study design. Current evidence therefore suggests that vitamin D supplementation is most likely to benefit patients with confirmed deficiency, poor glycemic control, or increased risk of diabetic complications, rather than serving as a universal therapeutic strategy for all patients with T2DM.

Limitations of Current Evidence and Randomized Controlled Trials

Although numerous observational studies have demonstrated associations between low vitamin D levels and poor glycemic control, insulin resistance, and diabetic complications, causality remains uncertain. Individuals with obesity, sedentary lifestyles, chronic illness, and poor nutritional status are more likely to have both vitamin D deficiency and adverse metabolic outcomes, creating potential confounding.

Randomized controlled trials have produced less consistent findings than observational studies. Large studies such as the VITAL trial and other contemporary vitamin D supplementation trials have generally failed to demonstrate substantial improvements in glycemic control among participants without significant baseline vitamin D deficiency. Similarly, several meta-analyses have reported only modest reductions in fasting plasma glucose and HbA1c, with benefits being most apparent in patients who are vitamin D deficient at baseline.

These findings suggest that vitamin D deficiency may function both as a biomarker of poor metabolic health and as a potentially modifiable risk factor. Current evidence supports targeted supplementation in deficient individuals rather than universal supplementation for all patients with T2DM.

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Vitamin B12 and Type 2 Diabetes Mellitus

Physiology of Vitamin B12

Vitamin B12 (cobalamin) is a water-soluble vitamin essential for DNA synthesis, erythropoiesis, methylation reactions, and neurological function. It plays a critical role in myelin formation and neuron maintenance. Dietary vitamin B12 is absorbed in the terminal ileum after binding to intrinsic factors secreted by gastric parietal cells.

Vitamin B12 Deficiency in T2DM

Vitamin B12 deficiency is common among patients with T2DM, particularly in individuals receiving long-term metformin therapy. Reported prevalence ranges from 5% to 40% depending on study population, duration of therapy, and diagnostic criteria. Metformin interferes with calcium-dependent absorption of the intrinsic factor–vitamin B12 complex in the terminal ileum, leading to gradual depletion of hepatic vitamin B12 stores.

Table 1: Role of Vitamin D3 and Vitamin B12 in Type 2 Diabetes Mellitus (T2DM).

Aspect	Vitamin D3	Vitamin B12
Physiological role	Regulates calcium homeostasis, insulin secretion, and immune modulation via vitamin D receptors	Essential for DNA synthesis, erythropoiesis, and neurological function (myelin formation)
Major source	Skin synthesis via UVB exposure; dietary intake	Animal-based foods; absorption in terminal ileum with intrinsic factor
Prevalence of deficiency in T2DM	Approximately 40–80% depending on population	Approximately 5–40%, especially in long-term metformin users
Key risk factors	Obesity, limited sun exposure, aging, chronic illness	Metformin therapy, elderly age, vegetarian diet, PPI use, malabsorption disorders
Mechanism in T2DM	Impairs insulin secretion, increases insulin resistance, enhances inflammation and oxidative stress	Impairs DNA synthesis and nerve function via reduced absorption and hepatic depletion
Metabolic effects	Worsening glycemic control, increased HbA1c, metabolic syndrome association	Indirect effect via neuropathy and hyperhomocysteinemia affecting vascular risk
Diabetic complications	Neuropathy, nephropathy, retinopathy, cardiovascular disease	Peripheral neuropathy, cognitive decline, megaloblastic anemia, cardiovascular risk
Diagnostic markers	Serum 25(OH)D levels	Serum B12, methylmalonic acid, homocysteine
Supplementation effects	Improved insulin sensitivity, modest HbA1c reduction, anti-inflammatory effects	Improved neuropathy, correction of anemia, prevention of neurological damage
Evidence strength	Moderate but inconsistent (heterogeneous RCTs)	Strong association with metformin use; consistent deficiency risk evidence
Clinical recommendation	Beneficial in deficiency states, especially severe deficiency	Routine screening recommended in long-term metformin users

Table 2: Key Clinical Trials and Studies on Vitamin D3 and Vitamin B12 in Type 2 Diabetes Mellitus (T2DM).

Study / Author	Study Type	Population	Intervention	Key Findings	Conclusion
Pittas et al., 2007	Randomized controlled trial (RCT)	Adults with impaired glucose tolerance / T2DM risk	Vitamin D + calcium supplementation	Improved insulin sensitivity in subgroups; modest effect on glucose metabolism	Vitamin D may improve insulin action, especially in deficient individuals
Holick MF, 2007	Review / Mechanistic analysis	General + diabetic populations	Vitamin D physiology analysis	Vitamin D receptors found in β-cells; role in insulin secretion and immune modulation	Supports biological plausibility of vitamin D in diabetes
de Jager et al., 2010	Randomized placebo-controlled trial	T2DM patients on metformin	Vitamin B12 monitoring / supplementation	Long-term metformin use associated with progressive B12 decline	Metformin is a major cause of B12 deficiency in T2DM
Reinstatler et al., 2012	Cross-sectional study	Diabetic patients on metformin	Serum B12 assessment	Significant association between metformin use and biochemical B12 deficiency	Routine screening recommended in long-term users
Dalgård et al., 2011	Prospective cohort study	General population incl. diabetics	Baseline vitamin D levels	Low vitamin D associated with higher risk of T2DM development	Vitamin D deficiency may contribute to diabetes risk
Palomer et al., 2008	Narrative review	T2DM pathophysiology	Vitamin D and metabolic regulation	Vitamin D influences insulin secretion, sensitivity, and inflammation	Supports role of vitamin D in glucose metabolism
Ooi & Loke, 2014	Systematic review	T2DM patients on metformin	Vitamin B12 deficiency analysis	High prevalence of B12 deficiency in metformin users; neurological risk identified	Regular monitoring recommended
Aroda et al., 2016 (Diabetes Prevention Program Outcomes Study)	Long-term follow-up study	Prediabetes / T2DM risk cohort	Metformin vs placebo	Metformin associated with reduced B12 levels over time	Confirms long-term metformin–B12 deficiency link

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Table 3: Biomarkers of Vitamin D and B12 deficiency.

Biomarker	Deficiency Cutoff	Clinical Significance
25(OH)D	<20 ng/mL	Vitamin D deficiency
Vitamin B12	<200 pg/mL	Deficiency
MMA	Elevated	Functional B12 deficiency
Homocysteine	Elevated	B12/Folate deficiency

Additional risk factors include advanced age, vegetarian diet, gastrointestinal disorders, and concomitant use of proton pump inhibitors. Because deficiency may remain clinically silent for years, routine monitoring is increasingly recommended in high-risk diabetic patients.

Mechanisms of Metformin-Induced Vitamin B12 Deficiency

Metformin-associated vitamin B12 deficiency primarily results from impaired intestinal absorption of the intrinsic factor–vitamin B12 complex. Additional proposed mechanisms include altered intestinal motility, bacterial overgrowth, and reduced intrinsic factor activity. Prolonged and high-dose metformin therapy significantly increases the likelihood of biochemical and clinical deficiency.

Clinical Consequences of Vitamin B12 Deficiency

Peripheral Neuropathy

Vitamin B12 deficiency impairs myelin synthesis and neuronal repair, resulting in demyelination and progressive nerve damage. Patients may present with paresthesia, numbness, burning sensations, gait disturbances, and impaired proprioception. In diabetic individuals, vitamin B12 deficiency neuropathy may overlap with diabetic neuropathy, making diagnosis challenging. Early recognition and supplementation may improve symptoms and prevent irreversible neurological injury.

Megaloblastic Anemia

Vitamin B12 deficiency disrupts DNA synthesis and erythropoiesis, resulting in macrocytic anemia characterized by elevated mean corpuscular volume (MCV) and hyper segmented neutrophils. Clinical manifestations include fatigue, pallor, weakness, dyspnea, and reduced exercise tolerance.

Cognitive Dysfunction

Vitamin B12 is necessary for normal neurotransmitter synthesis and central nervous system function. Deficiency has been associated with memory impairment, depression, mood disturbances, poor concentration, and progressive neurocognitive decline. Elderly diabetic patients are particularly vulnerable because both aging and diabetes independently increase cognitive risk.

Hyperhomocysteinemia

Vitamin B12 functions as a cofactor in homocysteine metabolism. Deficiency leads to accumulation of homocysteine, which contributes to oxidative stress, endothelial dysfunction, thrombosis, and atherosclerosis. In patients with T2DM, hyperhomocysteinemia may further increase cardiovascular and cerebrovascular risk.

Combined Impact of Vitamin D3 and Vitamin B12 Deficiency in T2DM

Simultaneous deficiency of vitamin D3 and vitamin B12 may exert synergistic adverse effects in patients with T2DM. Vitamin D deficiency predominantly contributes to insulin resistance, chronic inflammation, and endothelial dysfunction, whereas vitamin B12 deficiency primarily affects neurological integrity and vascular health. Together, these deficiencies may accelerate progression of diabetic neuropathy, nephropathy, retinopathy, and cardiovascular disease.

Patients with obesity, sedentary lifestyle, poor nutritional intake, aging, chronic illness, and prolonged metformin therapy are particularly susceptible to dual micronutrient deficiency. These interacting abnormalities contribute to worsening metabolic control and increased complication burden.

Early identification and correction of vitamin D3 and vitamin B12 deficiencies may improve glycemic control, reduce inflammation, support neuronal function, and potentially slow progression of diabetic complications. illustrates the pathophysiological relationship linking vitamin D3 deficiency, vitamin B12 deficiency, and T2DM; and (Table 1) summarizes the roles of vitamin D3 and vitamin B12 in T2DM.

Clinical Implications

Assessment of vitamin D3 and vitamin B12 status in patients with type 2 diabetes mellitus may provide important clinical advantages in routine diabetic care. Early identification and timely correction of deficiencies may help improve metabolic control, reduce neuropathic symptoms, enhance overall quality of life, lower the risk of long-term diabetic complications, and reduce the overall healthcare burden. Therefore, individualized supplementation strategies should be incorporated into comprehensive and multidisciplinary diabetes management protocols. (Table 2) outlines key clinical trials and studies evaluating their clinical significance.

Clinical Guidelines and Screening Recommendations

Current clinical practice guidelines increasingly recognize the importance of micronutrient assessment in patients with type 2 diabetes mellitus (T2DM), particularly regarding vitamin D3 and vitamin B12 status. The American Diabetes Association (ADA) supports individualized evaluation of factors contributing to poor glycemic control and diabetic complications and acknowledges the association between long-term metformin therapy and vitamin B12 deficiency. Accordingly, periodic assessment of vitamin B12 levels is recommended in at-risk individuals, especially those presenting with anemia, neuropathy, or cognitive impairment.

The Endocrine Society recommends measurement of serum 25-hydroxyvitamin D [25(OH)D] levels in individuals at risk of deficiency, including patients with obesity, limited sun exposure, malabsorption syndromes, and chronic metabolic diseases such as diabetes mellitus. Vitamin D deficiency is generally defined as serum 25(OH)D levels below 20 ng/mL (50 nmol/L), insufficiency

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as 21–29 ng/mL, and sufficiency as levels ≥30 ng/mL (75 nmol/L). Supplementation is advised in deficient individuals, particularly those at risk for metabolic, skeletal, and cardiovascular complications.

For vitamin B12, serum levels below 200 pg/mL are typically considered deficient, while levels between 200–300 pg/mL are regarded as borderline. In such cases, additional biomarkers including methylmalonic acid and homocysteine may improve diagnostic accuracy, particularly in early or subclinical deficiency states (Table 3). Risk-based screening is especially important in elderly diabetic patients, individuals receiving prolonged metformin therapy, and patients with neuropathic manifestations or hematological abnormalities.

Vitamin B12 supplementation may be administered orally or intramuscularly depending on the severity of deficiency and neurological involvement. Early treatment has been shown to improve neuropathic symptoms, correct megaloblastic anaemia, and reduce the risk of irreversible neurological damage. Some studies further suggest that combined supplementation with folic acid and B-complex vitamins may enhance neurological recovery and improve overall nerve function.

Overall, current recommendations favour a targeted screening approach rather than universal testing. Early identification and correction of vitamin D3 and vitamin B12 deficiencies may improve metabolic outcomes, reduce diabetic complications, and support comprehensive long-term management of T2DM.

Future Perspectives

Further large-scale randomized controlled trials are required to establish optimal vitamin D dosing regimens, determine long-term clinical benefits of supplementation, and develop standardized screening guidelines for micronutrient assessment in diabetes care. Additionally, more evidence is needed to clarify the relationship between vitamin status and the progression of diabetic complications, as well as to evaluate the combined therapeutic effects of vitamin D3 and vitamin B12 supplementation. The integration of precision medicine approaches incorporating nutritional biomarkers may significantly improve future strategies for individualized diabetes management.

Conclusion

Vitamin D3 and vitamin B12 deficiencies are highly prevalent among patients with type 2 diabetes mellitus and play important roles in metabolic dysfunction and diabetic complications. Vitamin D3 deficiency contributes to impaired insulin secretion, insulin resistance, inflammation, and vascular dysfunction, whereas vitamin B12 deficiency—commonly associated with long-term metformin use—predisposes patients to neuropathy, anemia, and neurocognitive impairment. Early identification and appropriate supplementation of these deficiencies may improve glycemic control, reduce complications, and enhance overall patient outcomes. Incorporating routine assessment of vitamin D3 and vitamin B12 into diabetic care protocols may provide a cost-effective strategy for improving long-term management of T2DM.

References:

1. Pittas AG, Lau J, Hu FB, Dawson-Hughes B (2007) The role of vitamin D and calcium in type 2 diabetes. Journal of Clinical Endocrinology and Metabolism 92: 2017-2029.
2. Holick MF (2007) Vitamin D deficiency. New England Journal of Medicine 357: 266-281. Doi: 10.1056/NEJMra070553.
3. de Jager J, Kooy A, Lehert P, Wulffele MG, der Kolk JV, Bets D,et al. (2010) Long-term treatment with metformin in patients with type 2 diabetes and risk of vitamin B12 deficiency. BMJ. 20: 340: c2181.
4. Reinstatler L, Qi YP, Williamson RS, Garn JV, Oakley GP (2012) Association of biochemical B12 deficiency with metformin therapy and vitamin B12 supplements. Diabetes Care 35: 327-333.
5. Dalgard C, Petersen MS, Weihe P, Grandjean P (2011) Vitamin D status in relation to glucose metabolism and type 2 diabetes. Diabetes Care 34:1284-1288.
6. American Diabetes Association (2020) Standards of Medical Care in Diabetes—2020. Diabetes Care. 43(Suppl 1): S1-S2.
7. Thewjitcharoen Y, Peachaphol Chongvoranond P, Nakasatien S, Krittiyawong S, Himathongkam T (2024) Metformin-Associated Vitamin B12 Deficiency: An Underrecognized Complication JCEM Case Rep 2: luae029.
8. Palomer X, González-Clemente JM, Blanco-Vaca F, Mauricio D (2008) Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes, Obesity and Metabolism 10: 185-197.
9. American Diabetes Association (2025) Standards of Medical Care in Diabetes. Diabetes Care 48(Suppl 1): S1-S300.
10. Ooi CP, Loke SC (2009) Metformin-associated vitamin B12 deficiency. Curr Drug Saf 4: 209-211.
11. Aroda VR, Edelstein SL, Goldberg RB,Knowler WC, Marcovina SM, et al. (2016) Long-term metformin use and vitamin B12 deficiency in the Diabetes Prevention Program Outcomes Study. J Clin Endocrinol Metab 101: 1754-1761.
12. Pflipsen MC, Oh RC, Saguil A, Seehusen DA, Seaquist D, et al. (2009) The prevalence of vitamin B12 deficiency in patients with type 2 diabetes: A cross-sectional study. J Am Board Fam Med 22: 528-534.
13. Nervo M, Lubini A, Raimundo FV,Faulhaber GAM, Leite C, et al. (2011) Vitamin B12 in metformin-treated diabetic patients: A cross-sectional study in Brazil. Rev Assoc Med Bras 57: 46-49.
14. Ahmed MA, Muntingh G, Rheeder P (2016) Vitamin B12 deficiency in metformin-treated type 2 diabetes patients. BMC Pharmacol Toxicol 17: 44.
15. Bauman WA, Shaw S, Jayatilleke E, Spungen AM, Herbert V (2000) Increased intake of calcium reverses vitamin B12 malabsorption induced by metformin. Diabetes Care 23: 1227-1231.
16. Ting RZ, Szeto CC, Chan MH,Ma KK, Chow KM, et al. (2006) Risk factors of vitamin B12 deficiency in patients receiving metformin. Arch Intern Med 166: 1975-1979.
17. Baig F, Khan S, Rizwan A (2022) Frequency of Vitamin B12 Deficiency in Type 2 Diabetic Patients Taking Metformin. Cureus 14: e22924.
18. Nasser F, Islam T (2018) Association of Vitamin B12 and Metformin in Type II Diabetes Patients in Bahrain. J Diabetes Metab 9: 796.
19. Varghese N, Francis G, Muralidharan V, Idiculla J (2022) Clinical and Biochemical manifestations of Vit B12 deficiency in Type 2 Diabetes patients treated with Metformin-A comparative study., IJAR 10: 1099-1106.
20. Gacema SA, Shahwanb M, Najjarc O (2020) Assessment of vitamin B12 deficiency and associated risk factors among type 2 diabetic patients in Palestine Human Nutrition and Metabolism.
21. Al-Moghrabi TSM, Friawan Alsaleh MM, Almansi HAH, S. Abu Dalou MM, Hourani AMKO, et al. (2025) Vitamin B12 Deficiency In Type 2 Diabetes Patients Receiving Long-Term Metformin Therapy: Experience From Jordan, DIABETIC STUDIES 21.

ISSN: 2475-5591

22. International Diabetes Federation (2021) IDF Diabetes Atlas, 10th Edition. Brussels, Belgium: IDF.

23. Pittas AG, Dawson-Hughes B,Ware JH, Knowler WC, et al. (2019) Vitamin D supplementation and prevention of type 2 diabetes. New England Journal of Medicine 381: 520-530.

24. Manson JE, Cook NR, Lee IM, Christen W, Bassuk SS, et al. (2019) Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease (VITAL Trial). New England Journal of Medicine 380: 33-44.

25. Neale RE, Baxter C, Romero BD, McLeod DSA, English DR, et al. (2022) The D-HEALTH Trial: Vitamin D supplementation and major health outcomes. Lancet Diabetes and Endocrinology 10: 120-128.

26. Krul-Poel YHM, Ter Wee MM, Lips P, Simsek S (2017) Management of endocrine disease: The effect of vitamin D supplementation on glycaemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis. European Journal of Endocrinology 176: R1–R14.