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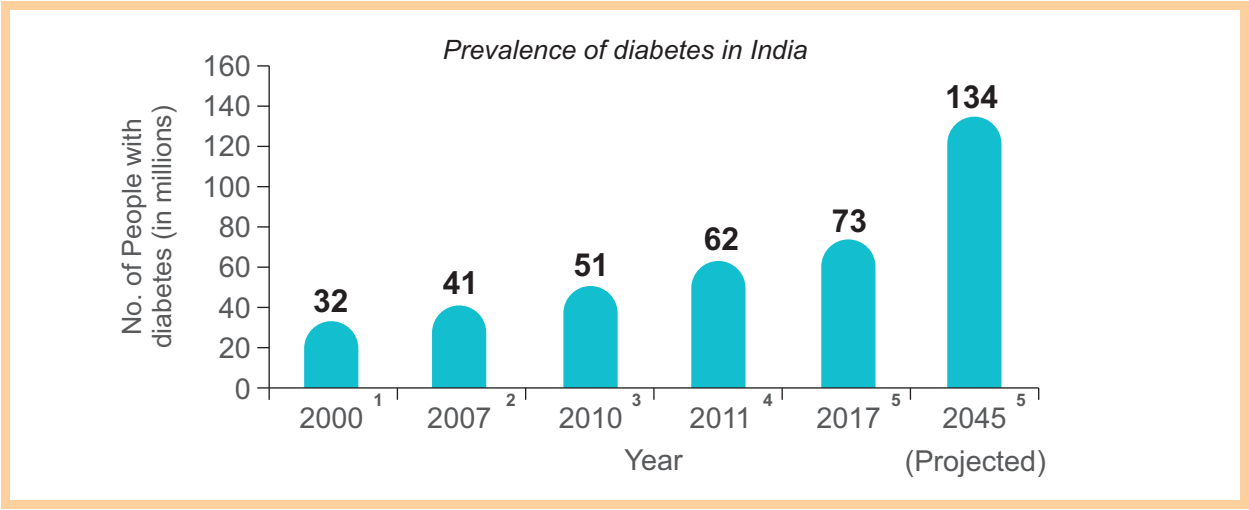
BLUE CROSS

# Medical Bulletin

## CURRENT PERSPECTIVES ON THE PLEIOTROPIC EFFECTS OF TENELIGLIPTIN

Diabetes mellitus is a chronic metabolic disorder characterized by inappropriately high glucose concentrations in the blood. The prevalence of diabetes is rising annually at a higher rate, and India is expected to be in the second position next to China, with nearly 134 million people expected to have diabetes mellitus by 2045. Persistently elevated blood glucose levels over time cause irreversible damage to blood vessels in the heart, kidney, retina, and nerves, which manifest as micro- and macrovascular complications.




Cardiovascular (CV) problems affect up to 80% of persons with type 2 diabetes, accounting for around 65% of deaths in this population. Furthermore, CV problems occur one to two decades sooner in diabetes compared to nondiabetic populations. In recent decades, “chronic low-grade systemic inflammation,” also known as “meta-inflammation,” has been recognized as an accelerating pathogenic mechanism behind the initiation and progression of diabetes-related complications. Antidiabetic agents with pleiotropic effects on this chronic inflammation could improve outcomes in these patients and be the better second-line agents of choice.

Teneligliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, exhibits pleiotropic effects beyond glycaemic control, including anti-inflammatory, cardioprotective, and renoprotective benefits in type 2 diabetes (T2D) patients. Recent studies highlight its role in reducing inflammation markers and mitigating diabetic complications, making it a promising add-on therapy.

### Anti-Inflammatory Actions

Teneligliptin significantly lowers high-sensitivity C-reactive protein (hs-CRP), a key inflammation marker, compared to glimepiride when added to metformin in Indian T2D patients. In a 2025 randomized controlled trial, 12 weeks of teneligliptin 20 mg daily significantly reduced hs-CRP levels. This effect stems from DPP-4 inhibition,

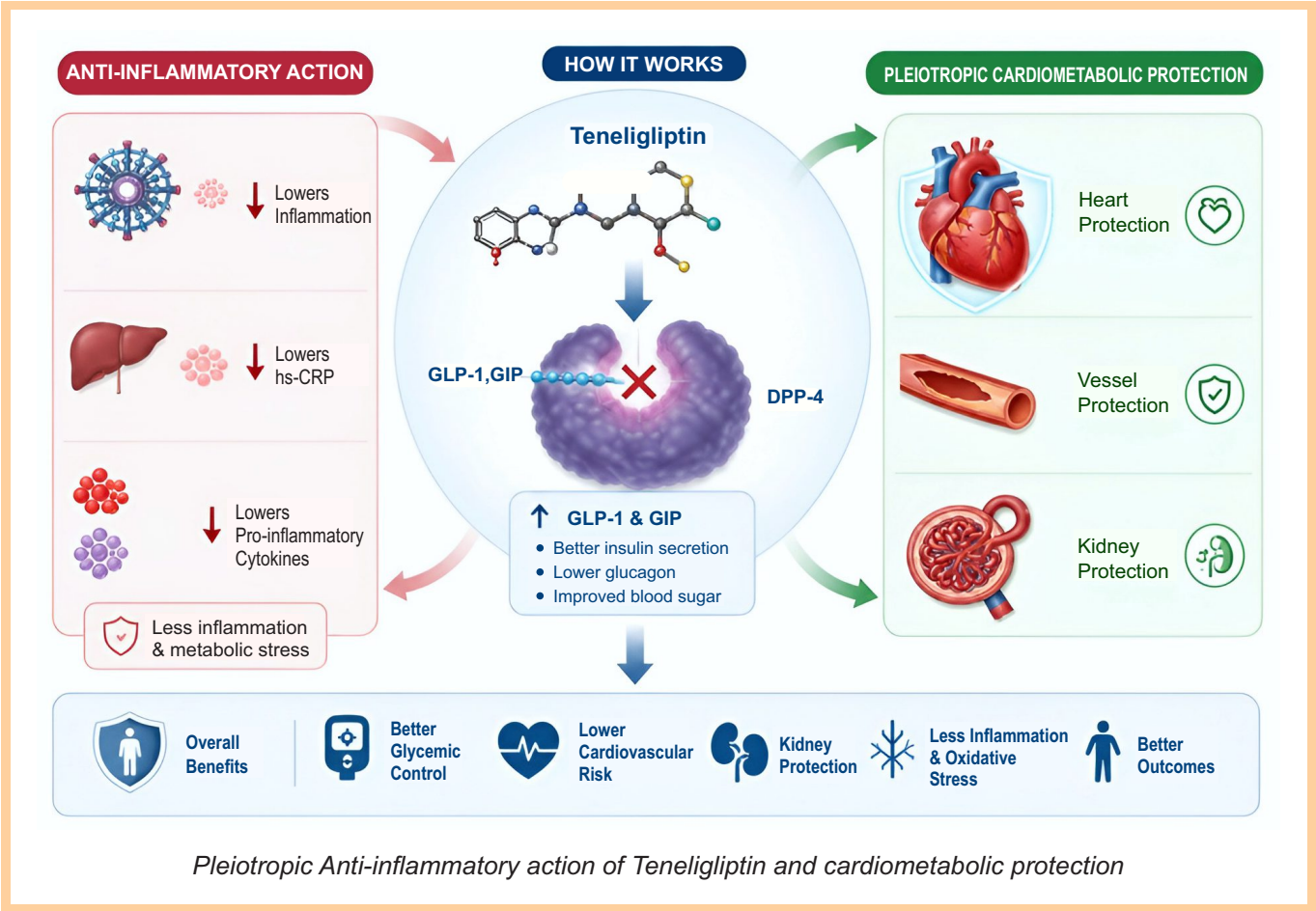
which boosts incretins like GLP-1, indirectly suppressing pro-inflammatory pathways. Earlier evidence also notes improvements in adiponectin and endothelial function, supporting its broad anti-inflammatory profile.

*Cardioprotective Mechanisms*

Teneligliptin alleviates diabetic cardiomyopathy (DCM) by inhibiting the NLRP3 inflammasome, reducing cardiac hypertrophy, myocardial injury, and inflammation. This positions teneligliptin as a targeted therapy for DCM, a major T2D complication, through direct modulation of inflammasome activation.

*Renoprotective Potential*

Teneligliptin's dual renal and hepatic excretion allows safe use in chronic kidney disease (CKD) without dose adjustment, even in patients with an eGFR of 15-60 mL/min/1.73m². The TOP RENAL study in Indian T2D-CKD patients found no significant changes in patients with an eGFR of serum creatinine, or BUN after 6 months of teneligliptin 20/40 mg, with excellent tolerability and no safety issues.




*Pleiotropic Anti-inflammatory action of Teneligliptin and cardiometabolic protection*

Recent updates (2024-2026) underscore teneligliptin's pleiotropic advantages, particularly in inflammation and organ protection, with low hypoglycaemia risk. Ongoing trials on dosing regimens and cost-effectiveness could expand its role in resource-limited settings like India.

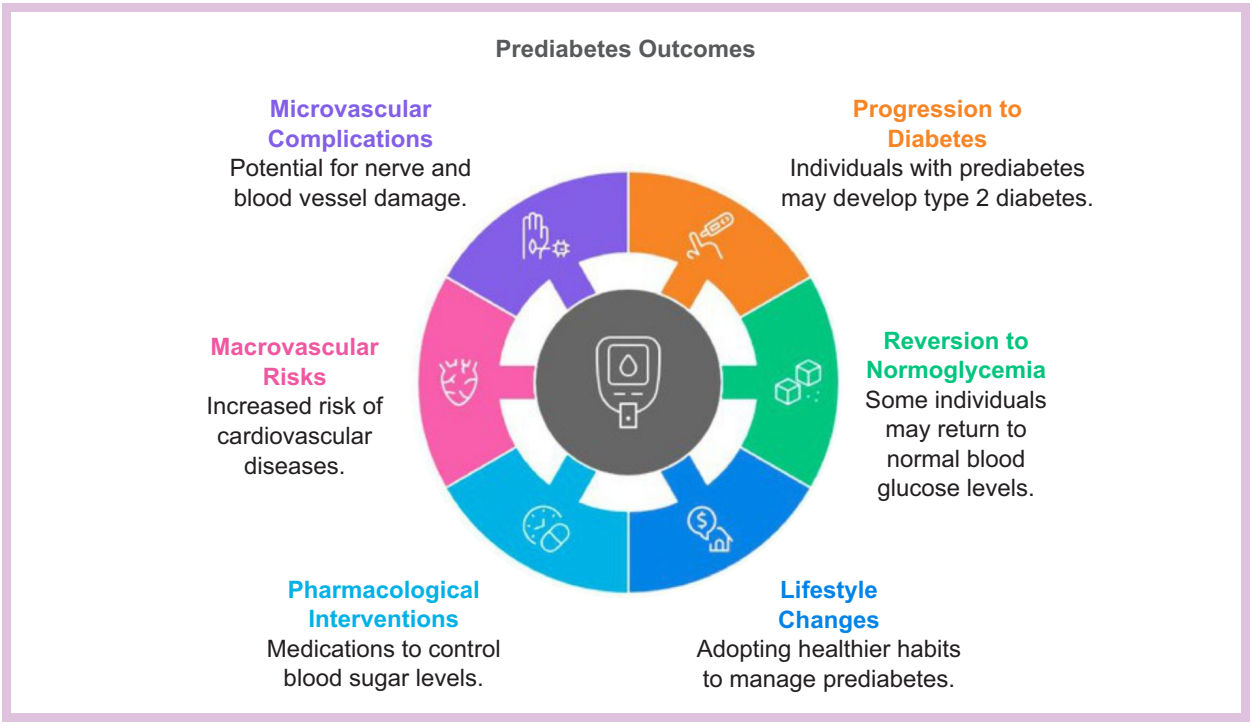
While promising, larger prospective studies are needed to confirm long-term outcomes in diverse populations. Teneligliptin offers a balanced profile for T2D management, prioritizing holistic benefits.

**Source:** *Kanimozhi M, et.al; Perspect Clin Res. 2025 Jan-Mar;16(1):14-22.*

# ACHIEVING NORMAL GLUCOSE REGULATION IN PREDIABETES: THE ROLE OF VITAMIN D THERAPY

Prediabetes, a condition characterized by elevated glycemia that falls below the threshold for diabetes, affects a substantial portion of the world population. It is defined as having glycaemic parameters fasting plasma glucose [FPG] 100-125 mg/dL, 2-hour glucose after a 75 gram oral glucose load [2hPG] 140-199 mg/dL, or hemoglobin A1c [HbA1c] 5.7-6.4%.

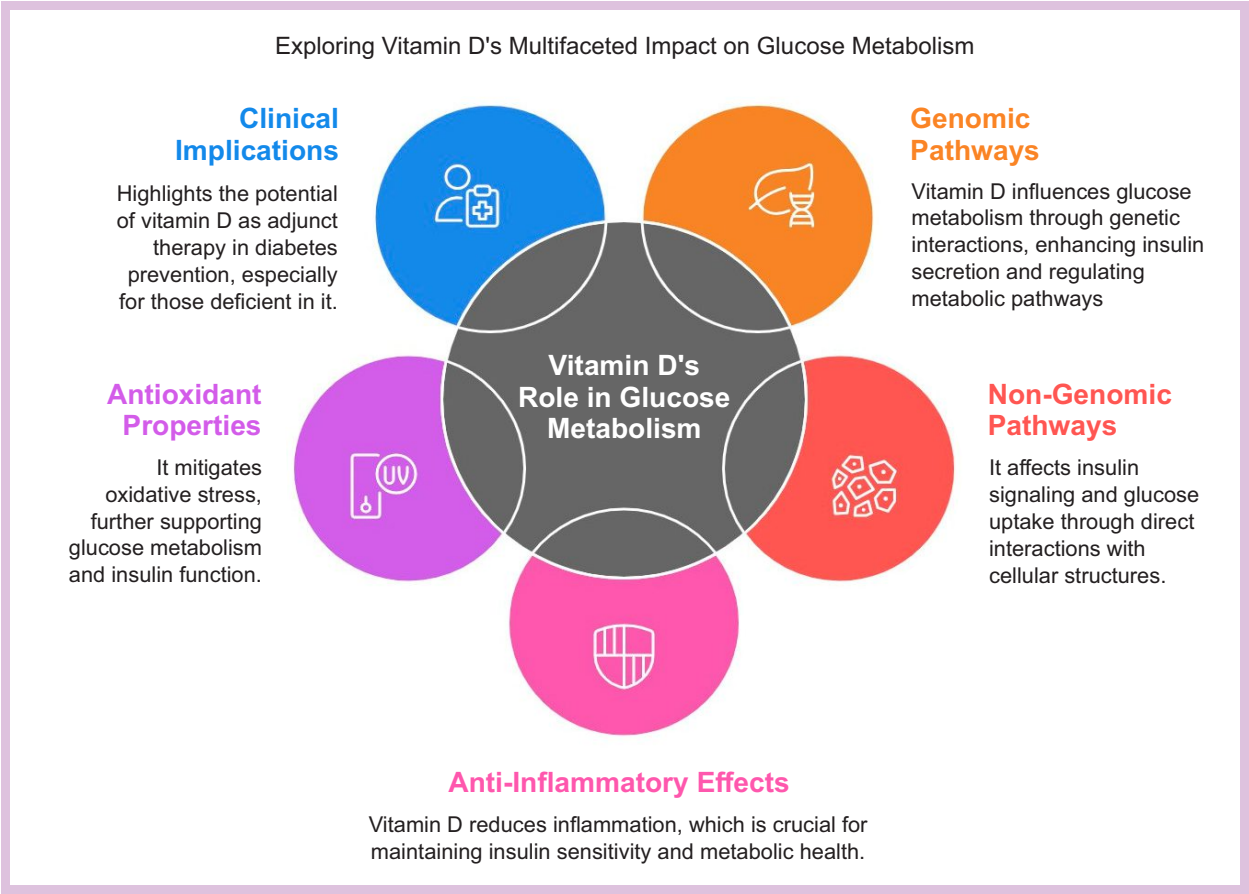
Worldwide, the prevalence of impaired glucose tolerance was 9.1% (464 million people) in 2021, with projections indicating an increase to 10% (638 million people) by 2045. In India, an estimated 136 million people have prediabetes. The prediabetes state not only increases the risk of progressing to diabetes but is also linked to an elevated risk of cardiovascular diseases and other complications.




Although the most attention has been placed on preventing the progression from prediabetes to diabetes, there is a growing recognition of the benefit of achieving regression to normal glucose regulation (NGR). Regression to NGR is an important outcome because euglycemia is associated with a lower prevalence of microvascular disease compared to prediabetes, likely due to less long-term exposure to abnormal glucose levels, and because even transient regression to NGR confers a lower risk of developing diabetes. These benefits underscore the importance of identifying and implementing effective strategies for achieving this metabolic reversal.

Vitamin D, traditionally known for its role in promoting skeletal health, reduces the risk of progression to diabetes in people with prediabetes based on clinical evidence. Inflammation and oxidative stress are critical factors in prediabetes, disrupting insulin signalling and promoting metabolic dysfunction. Vitamin D's anti-inflammatory properties help mitigate these effects by reducing pro-inflammatory cytokines and supporting a more favourable inflammatory profile. Additionally, its antioxidant properties may counteract oxidative stress, which is often elevated in prediabetic individuals. Potential mechanisms by which vitamin D may affect glucose metabolism include stimulating insulin secretion through vitamin D receptors on pancreatic beta cells, decreasing systemic

inflammation, and improving insulin resistance in muscle and the liver. Moreover, insufficient vitamin D status could contribute to hypophosphatemia, which has been implicated in impaired glucose tolerance and decreased insulin sensitivity. At the cellular level, the proposed mechanism is Vitamin D enhances insulin secretion via calcium-dependent endopeptidases, modulates the Phosphoinositide 3-kinase / Protein Kinase B (PI3K/AKT) signalling pathway, interacts with vitamin D receptor (VDR) and vitamin D-binding protein (DBP) gene variations, and reduces inflammation and secondary hyperparathyroidism, which are the key contributors to type 2 diabetes progression. Future studies should aim for larger sample sizes, longer follow-up periods, and consistent baseline vitamin D levels to provide more definitive evidence on the role of vitamin D in managing prediabetes.




The potential of vitamin D in promoting regression to NGR offers a valuable addition to current diabetes prevention strategies. Vitamin D is cost-effective, low-burden, and has a favourable safety profile. With the projected rise in cases of impaired glucose tolerance and impaired fasting glucose globally, particularly in low-income countries, vitamin D could serve as an accessible intervention to mitigate the global diabetes burden.

The 2024 Endocrine Society Guideline on Vitamin D for the Prevention of Disease recommends empiric vitamin D in adults with high-risk prediabetes because of its potential to reduce progression to diabetes.

***Source:*** *J. Clin. Med. 2025, 14(4), 1239; Kretschmer P M, et.al; Journal of the Endocrine Society, 2025, Vol. 9, No. 5; Daniel S. Hsia,et.al;science direct,2023.*



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