Print ISSN: 2321-6379
Online ISSN: 2321-595X

Review Article

The Overlooked Thyroid–Diabetes Connection: Unmasking the Role of Hypothyroidism in Type 2 Diabetes Mellitus

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Abstract

Type 2 diabetes mellitus (T2DM) and hypothyroidism are two of the most common endocrine disorders worldwide. The co-occurrence of these conditions is more frequent than previously recognized and carries significant implications for metabolic control, cardiovascular risk, and quality of life. Hypothyroidism, especially in its subclinical form, can aggravate insulin resistance, impair lipid metabolism, and worsen glycemic control. This review explores the pathophysiological links, clinical impact, screening recommendations, and management strategies for hypothyroidism in patients with T2DM, whereas highlighting emerging evidence and research gaps. Greater awareness and multidisciplinary care are essential for improving outcomes in this high-risk population.

Key words: Endocrinology, Hypothyroidism, Insulin resistance, Subclinical hypothyroidism, Thyroid screening, Type 2 diabetes mellitus

INTRODUCTION

The global burden of type 2 diabetes mellitus (T2DM) continues to rise, with India alone accounting for over 77 million cases as per the International Diabetes Federation 2021 report.[1] Hypothyroidism, both overt and subclinical, is also highly prevalent,[2] particularly among middle-aged and elderly women. The interaction between these two endocrine disorders has gained increasing attention in recent years, as accumulating evidence suggests that thyroid dysfunction in patients with T2DM is associated with poorer metabolic profiles, increased cardiovascular risk, and greater incidence of complications.

Epidemiological studies have reported thyroid dysfunction in 10–20% of patients with T2DM, with subclinical hypothyroidism being the most common form. Despite this significant overlap, thyroid screening is not universally implemented in diabetes care, leading to underdiagnosis and suboptimal management. This review aims to provide a comprehensive analysis of the mechanistic links, clinical manifestations, and management approaches for hypothyroidism in the context of T2DM.

Access this article online

www.ijss-sn.com

Month of Submission : 07-2025
Month of Peer Review : 08-2025
Month of Acceptance : 09-2025
Month of Publishing : 09-2025

PATHOPHYSIOLOGICAL LINK

Thyroid hormones, particularly triiodothyronine (T3), play a critical role in regulating carbohydrate and lipid metabolism. They influence hepatic gluconeogenesis, intestinal glucose absorption, peripheral glucose uptake via GLUT4 transporters, and insulin-mediated glucose disposal.[3] Hypothyroidism leads to reduced GLUT4 expression, impaired mitochondrial oxidative capacity, and altered adipokine profiles, all of which contribute to insulin resistance.

In addition, hypothyroidism is associated with elevated serum low-density lipoprotein (LDL) cholesterol, increased apolipoprotein B levels, and impaired clearance of triglyceride-rich lipoproteins, thereby worsening the atherogenic lipid profile commonly seen in T2DM.[4,5] Endothelial dysfunction, increased systemic vascular resistance, and diastolic hypertension are other hallmarks

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of hypothyroidism that may exacerbate cardiovascular morbidity in diabetic patients.[6]

Subclinical hypothyroidism, defined by elevated serum thyroid-stimulating hormone (TSH) with normal free thyroxine (T4), may appear clinically silent but can still contribute to dysglycemia and dyslipidemia.[7,8] The chronic low-grade inflammation seen in both T2DM and hypothyroidism further amplifies metabolic derangements.

CLINICAL CONSEQUENCES

The coexistence of hypothyroidism and T2DM has been associated with several adverse outcomes:

- Worsening fasting and postprandial hyperglycemia due to increased insulin resistance
- Aggravation of diabetic dyslipidemia, with increased LDL cholesterol and triglycerides, and reduced high-density lipoprotein cholesterol
- Exacerbation of weight gain and central obesity
- Fatigue, depression, and cognitive decline, which may mask symptoms of poor glycemic control[9]
- Greater propensity for cardiovascular disease, heart failure, and atherosclerotic events
- Increased risk of non-alcoholic fatty liver disease and chronic kidney disease progression
- Possible effects on bone metabolism and fracture risk in the long term.

The non-specific nature of hypothyroid symptoms means that many patients may remain undiagnosed unless active screening is undertaken.

SCREENING AND DIAGNOSIS

Given the high prevalence and clinical impact, routine screening for thyroid dysfunction in patients with T2DM is increasingly advocated. The American Thyroid Association, Indian Thyroid Society,[10,11] and other expert bodies recommend testing serum TSH at the time of T2DM diagnosis, particularly in women over the age of 50, and periodically thereafter.

Screening is especially warranted in patients with:

- Unexplained dyslipidemia
- Persistent fatigue or weight gain despite good glycemic control
- Goiter or positive family history of thyroid disease
- Autoimmune disorders (e.g., type 1 diabetes and celiac disease).

Primary screening involves serum TSH measurement, with reflex free T4 testing if TSH is abnormal. Anti-thyroid peroxidase (anti-TPO) antibodies should be tested in cases of suspected autoimmune thyroiditis. In resource-limited settings, targeted screening of high-risk subgroups may be a cost-effective approach.

MANAGEMENT IMPLICATIONS

Levothyroxine remains the mainstay of treatment for hypothyroidism. In patients with T2DM, thyroid hormone replacement may improve insulin sensitivity, lipid profiles, and overall metabolic control. However, certain precautions are warranted:

- Avoid rapid dose escalation to prevent precipitating angina or arrhythmias in patients with cardiovascular disease
- Monitor for hypoglycemia in insulin-treated patients after initiating therapy
- Consider metformin's TSH-lowering effect when interpreting thyroid function tests[12,13]
- Monitor glycemic and lipid parameters after thyroid function normalization.

Treatment thresholds for subclinical hypothyroidism remain debated, but intervention is generally recommended if TSH exceeds 10 mIU/L or if the patient is symptomatic, pregnant, or planning pregnancy.[14]

FUTURE DIRECTIONS AND RESEARCH GAPS

While observational data strongly suggest that hypothyroidism negatively impacts glycemic control in T2DM, robust randomized controlled trials are lacking.[15] Future research should address:

- The long-term impact of early levothyroxine initiation on cardiovascular outcomes in diabetics
- The cost-effectiveness of universal vs. targeted screening strategies
- The role of novel biomarkers in identifying subclinical thyroid dysfunction
- Potential benefits of combination therapy with other metabolic agents
- Genetic and environmental factors influencing susceptibility.

Integration of thyroid health into diabetes management pathways may ultimately improve patient outcomes.

CONCLUSION

Hypothyroidism remains a frequently overlooked comorbidity in T2DM, with the potential to worsen metabolic control, lipid abnormalities, and cardiovascular

risk. Early detection and tailored management can mitigate these effects and improve quality of life. Clinicians should maintain a high index of suspicion and integrate thyroid screening into routine diabetes care.

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How to cite this article: Agarwala S. The Overlooked Thyroid–Diabetes Connection: Unmasking the Role of Hypothyroidism in Type 2 Diabetes Mellitus. Int J Sci Stud 2025;13(6):4-6.

Source of Support: Nil, **Conflicts of Interest:** None declared.