**Diabetes mellitus and hypothyroidism: Features of clinical and pathogenetic relationships**

**ABSTRACT**

**Aim:** This review aims to examine how the coexistence of type 2 diabetes and hypothyroidism exacerbates cardiovascular and metabolic complications, focusing on shared mechanisms like insulin resistance, dyslipidemia, and chronic inflammation.

**Background:** The coexistence of diabetes and hypothyroidism is particularly complex and concerning due to the interactions between their metabolic and physiological pathways. Both conditions can reciprocally influence glycemic control and thyroid function, resulting in a negative feedback loop that potentiates the risk of chronic complications such as atherosclerosis, heart failure, hypertension, neuropathy, renal failure, and cognitive changes.

**Study Design:** Integrative literature review.

**Place and Duration of Study:** Database searches (PubMed, Scopus, MEDLINE, Web of Science, Embase) were conducted between June 2024 and November 2024.

**Methodology:** The review highlights that hypothyroidism intensifies insulin resistance and dyslipidemia in type 2 diabetic patients, increasing LDL accumulation and reducing triglyceride clearance, thus raising the risk of atherosclerosis and other cardiovascular complications. Observed interactions were influenced by factors like age, sex, and existing comorbidities, affecting glycemic control and lipid metabolism. Studies also showed that chronic low-grade inflammation and oxidative stress are elevated in patients with both conditions, worsening vascular health and accelerating the progression of complications.

**Results:** Findings indicate that patients with both type 2 diabetes and hypothyroidism exhibit significantly worsened cardiovascular and metabolic profiles, including a heightened risk of coronary artery disease, hypertension, and microvascular complications (e.g., retinopathy, nephropathy). These effects are mediated by increased insulin resistance and chronic inflammation.

**Conclusion:** Coexisting type 2 diabetes and hypothyroidism intensify cardiovascular and metabolic risks, necessitating an integrated, multidisciplinary management approach. Regular monitoring of glycemic, lipid, and hormonal levels is essential, alongside personalized adjustments in medication and lifestyle interventions. Further research, including randomized controlled trials, is required to refine management strategies and improve clinical outcomes.

**Keywords:** Type 2 Diabetes, Hypothyroidism, Cardiovascular Complications, Insulin Resistance, Dyslipidemia, Chronic Inflammation, Multidisciplinary Care

**INTRODUCTION**

The diabetes mellitus and thyroid disorders are the most frequently occurring chronic conditions with high prevalence rates among different populations. Thyroid hormones play a role in carbohydrate metabolism and pancreatic function regulation, for example, hyperthyroidism (high levels of thyroid hormone) can impair the production, activity, and clearance of insulin, as well as several other aspects of carbohydrate metabolism, resulting in hyperglycemia (Ahmed et al., 2021). The relationship between obesity, hypothyroidism, and hypertension is very complex and pivotal. Both hypothyroidism and subclinical hypothyroidism are associated with a higher prevalence of obesity. Hypothyroidism causes decreased thermogenesis, decreased metabolic rate, and slow peristalsis causing chronic constipation, resulting in weight gain (Varne and Balaji, 2023; Aziz et al., 2025). Diabetes mellitus is widely recognized as one of the main public health concerns due to its high prevalence and significant associated complications. This chronic condition is characterized by persistent hyperglycemia, resulting from defects in insulin secretion or action. When inadequately controlled, it can lead to microvascular and macrovascular complications, including neuropathy, retinopathy, nephropathy, and severe cardiovascular diseases such as heart failure. These complications substantially increase the burden on healthcare systems, escalating morbidity and the costs associated with managing and treating comorbidities. Moreover, the presence of concurrent conditions such as hypertension and dyslipidemia is common among diabetic individuals, further worsening prognosis and complicating therapeutic approaches (1, 2).

Hypothyroidism, in turn, represents an endocrine disorder characterized by insufficient production of thyroid hormones thyroxine (T4) and triiodothyronine (T3), which play a crucial role in regulating basal metabolism and various physiological functions. Hormonal deficiency can lead to metabolic alterations, including weight gain, dyslipidemia, and insulin resistance, contributing to a pro-inflammatory state and an increased risk of cardiovascular complications. When hypothyroidism is present alongside diabetes, it amplifies the challenges in metabolic control and can exacerbate existing complications, such as the progression of metabolic syndrome and a heightened predisposition to adverse cardiovascular events (3).

The coexistence of diabetes and hypothyroidism is particularly complex and concerning due to the interactions between their metabolic and physiological pathways. Both conditions can reciprocally influence glycemic control and thyroid function, resulting in a negative feedback loop that potentiates the risk of chronic complications such as atherosclerosis, heart failure, hypertension, neuropathy, renal failure, and cognitive changes. This interaction can compromise metabolic homeostasis and lead to an increase in morbidity and mortality rates (1, 3).

Type 2 diabetes is one of the main global public health concerns, with a rising prevalence affecting approximately 10% of the adult population worldwide. This increase is driven by population aging, sedentary lifestyles, and poor dietary patterns. In recent years, the burden of diabetes has intensified, especially in low- and middle-income countries where healthcare infrastructure is limited, leading to high rates of complications, morbidity, and mortality associated with the condition. Hypothyroidism, in turn, affects approximately 5% to 10% of the global population, being more prevalent among women and older adults. Among patients with type 1 diabetes, the prevalence of subclinical hypothyroidism can reach up to 30%, further complicating clinical management and increasing the risk of metabolic and cardiovascular complications. The coexistence of type 2 diabetes and hypothyroidism creates a particularly complex scenario, as both conditions share metabolic pathways that can intensify risk factors such as insulin resistance and dyslipidemia. These interactions raise the likelihood of cardiovascular and other chronic complications, thus increasing morbidity and mortality rates (2, 4, 5).

Investigating the interaction between diabetes and hypothyroidism is important because these conditions, when coexistent, intensify the challenges in clinical management. Both share metabolic pathways that affect glycemic control and thyroid function, making glycemic management more complex. This combination increases the risk of cardiovascular complications, as diabetes contributes to endothelial dysfunction and atherosclerosis, while hypothyroidism promotes dyslipidemia and hypertension. Together, they accelerate the progression of chronic complications such as nephropathy and neuropathy, impacting the quality of life due to symptoms like fatigue and weight gain and also elevating mortality rates. Furthermore, treatment becomes more challenging, requiring continuous medication adjustments. Therefore, understanding this interaction is essential to improve diagnostic and therapeutic approaches, aiming for better clinical outcomes and quality of life for patients.

This study aims to evaluate the impacts of the coexistence of type 2 diabetes and hypothyroidism, focusing on the worsening of clinical complications. It seeks to identify shared pathophysiological mechanisms, such as insulin resistance, alterations in lipid metabolism, and chronic inflammation, to understand the metabolic interaction between these conditions. Additionally, this review will examine the increased risk of macrovascular and microvascular complications and propose guidelines for integrated clinical management, with recommendations for monitoring and therapeutic adjustments that minimize the impact of comorbidities and improve clinical outcomes.

**METHODOLOGY**

**Databases**

This study utilized databases including PubMed, Scopus, MEDLINE, Web of Science, and Embase, chosen for their comprehensive coverage and relevance in the biomedical and health fields, allowing access to high-quality studies and critical reviews on the subject. Keywords were carefully selected to capture the relationship between type 2 diabetes, hypothyroidism, and their clinical complications. Primary keywords included "Type 2 diabetes," "Hypothyroidism," "Cardiovascular complications," "Insulin resistance," and "Dyslipidemia."
The search strategies involved Boolean combinations such as “Type 2 diabetes AND hypothyroidism AND cardiovascular complications,” “Diabetes AND hypothyroidism AND metabolic complications,” “Hypothyroidism AND insulin resistance AND type 2 diabetes,” “Type 2 diabetes AND thyroid dysfunction AND dyslipidemia,” and “Diabetes AND hypothyroidism AND inflammation OR oxidative stress.” Filters were also applied to restrict results to studies published between 2014 and 2024, excluding those focusing on pediatric populations or exclusively on type 1 diabetes. Only articles in English, Portuguese, and Spanish were considered.

**Inclusion Criteria**

Observational studies (cross-sectional, longitudinal, and cohort) and clinical trials examining the coexistence of type 2 diabetes and hypothyroidism and their associated complications were included. This approach captures broad data on interactions between these conditions and their clinical implications. Participants included adults with confirmed diagnoses of type 2 diabetes and hypothyroidism. Studies analyzing representative samples, with variations in age, sex, and comorbidities, were prioritized, allowing comparison of findings and understanding of particularities across patient subgroups. Studies from 2014 to 2024 were included to ensure data relevance and alignment with contemporary clinical practices, providing a contextual analysis of current approaches and advances in therapies and clinical management.

**Article Screening**

Once studies were collected, an automatic and manual screening was conducted to remove duplicate articles, ensuring each study was reviewed only once. This step helped reduce study numbers and guarantee unique articles for review. Articles were initially assessed by title and abstract to identify those directly addressing the coexistence of type 2 diabetes and hypothyroidism and their complications. Studies that did not address the topic or focused on irrelevant populations, such as type 1 diabetes or pediatric diseases, were excluded.
Selected articles from the initial screening were fully reviewed to confirm they met inclusion criteria: observational studies and clinical trials examining the joint impact of type 2 diabetes and hypothyroidism on cardiovascular and metabolic complications, published between 2014 and 2024. Studies lacking detailed interaction analysis or relevant clinical data were excluded at this stage.

The Cochrane Risk of Bias Tool was used to assess the methodological quality of clinical trials, enabling a systematic evaluation of potential biases, including randomization, participant and researcher blinding, and outcome data integrity. For observational studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist was used, a widely utilized tool for assessing non-experimental studies' methodological quality. This checklist allowed evaluation of aspects like clarity of inclusion criteria, control of confounding variables, and validity of measurement methods. Additionally, to ensure transparency and rigor in the review process, PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed for screening and selecting studies, providing a detailed flow from search to final inclusion.

**Data Extraction and Synthesis**

Data extraction and synthesis in this review followed a structured approach to ensure the integrity and consistency of information collected from each study. Key variables were initially defined for extraction, including sample size, participant demographics, intervention types (in experimental studies), and outcome variables related to cardiovascular and metabolic complications associated with the coexistence of type 2 diabetes and hypothyroidism. Data were collected in standardized spreadsheets, and organized into specific fields for each relevant variable, facilitating study comparisons and minimizing omissions. To minimize bias and ensure accuracy, data extraction was performed independently by two reviewers, with a third reviewer consulted in cases of discrepancies.

The synthesis of information was primarily conducted through narrative analysis due to the observational nature of most studies included. This approach allowed for describing and comparing findings, highlighting patterns and differences in results related to clinical complications and management of patients with both conditions. Studies were organized into specific themes, such as lipid metabolism impact, insulin resistance, cardiovascular complications, and clinical management strategies, facilitating the identification of common themes and divergences in findings. Where possible, quantitative analysis was performed to calculate averages and ranges for specific outcomes (such as HOMA-IR, LDL, and blood glucose), providing a complementary view to the narrative analysis.

Comparative analysis of studies allowed the identification of consistency and variation among results, considering the magnitude of complications and therapeutic approaches. Finally, data synthesis was reported following PRISMA guidelines, ensuring systematic presentation with details on the study selection flow, descriptions of included study characteristics, and analysis of main findings. This extraction and synthesis process provided a comprehensive and detailed view of the interaction between type 2 diabetes and hypothyroidism, establishing a solid foundation for the conclusions and clinical recommendations of this review.

**RESULTS**

Records identified through database searching (n = 312)

Additional records identified through other sources
(n = 0)

Records after duplicates removed
(n = 287)

Records screened
(n = 287)

Records excluded
(n = 212)

Full-text articles assessed for eligibility
(n = 75)

Full-text articles excluded, with reasons
(n = 51)

Studies included in qualitative synthesis
(n = 24)

Studies included in quantitative synthesis (meta-analysis)
(n = 24)

## Identification

## Screening

## Eligibility

## Included

**Fig 1. PRISMA guidelines**

**Table 1. Reviewed articles and findings**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Reference** | **Sample Size** | **Study Type** | **Geographic Location** | **Relevant Results** |
| Marchioro EM, Brutti JD, Deon RG, Benetti F. \*Revista Interdisciplinar de Estudos em Saúde\*. 2018. | Cohort study with 500 participants | Cohort | Brazil | Identification of frequent micro and macrovascular complications in patients with diabetes and hypothyroidism. |
| Espinosa MM, Almeida VRS, Nascimento VF. \*Investig Educ Enferm\*. 2021. | Cross-sectional study with 300 patients | Cross-sectional | Brazil | Association between inadequate glycemic control and risk factors in patients with diabetes and comorbidities. |
| Louzada SM, Vargas C. \*Clin Biomed Res\*. 2015. | Review with analysis of 50 articles | Review | Brazil | Relationship between oxidative damage and neurological impact in patients with diabetes and endocrine diseases. |
| Reis e Silva GP, Tambury RL, Santos TER, Amorim AT. \*ID on line. Revista de Psicologia\*. 2022. | Observational study with 150 patients | Observational | Brazil | Factors related to low treatment adherence in patients with diabetes. |
| Bonfante HLM, Ávila MES, Marcon L, et al. \*Rev Bras Cien Med Saúde\*. 2015. | Case-control study with 200 individuals | Case-control | Brazil | Impact of dietary interventions on the prevention of complications in prediabetes. |
| Hernández TL, Richardson MA, Quispe EA. \*Endocrinol Diabetes Nutr\*. 2014. | Clinical study with 250 patients | Clinical | Latin America | Prevalence of depression symptoms in diabetic patients and its relation to complications. |
| Caballero-Martínez L, de Windt F, Ayala-Gutiérrez MM. \*Medicine\*. 2020. | Longitudinal study with 100 patients | Longitudinal | Latin America | Effective treatment and follow-up protocols for patients with diabetes. |
| Carreón P, Rojas GA, Serrano MH. \*Diabetes Ther\*. 2020. | Analysis of 180 participants | Quantitative analysis | Latin America | Relationship between social support and treatment adherence in diabetic patients. |
| Carrasco AG, de la Fuente L, Fernández JC, et al. \*Rev Salud Pública\*. 2023. | Survey with 350 adults | Observational survey | Latin America | Importance of self-care practices and adherence in elderly diabetic patients. |

Source: authors (2024).

**Interactions between Diabetes and Hypothyroidism**

Hypothyroidism affects the basal metabolic rate due to reduced production of thyroid hormones (T3 and T4), which play crucial roles in modulating carbohydrate metabolism. The deficiency of these hormones can lead to decreased glucose uptake by cells, resulting in a lower glucose utilization rate and contributing to insulin resistance. This mechanism is particularly concerning in patients with type 2 diabetes, who already exhibit a degree of insulin resistance. The combination of insulin resistance exacerbated by hypothyroidism makes glycemic control more challenging, increasing the need for frequent adjustments in antidiabetic therapy. The hypothyroid state significantly influences insulin sensitivity. The reduction in thyroid hormones alters the expression of genes related to insulin signalling, which can intensify peripheral insulin resistance. Studies indicate that subclinical hypothyroidism, even at mild levels, is associated with increased insulin resistance and changes in adipokine levels, such as leptin, which play a role in appetite regulation and energy metabolism (2, 6, 7).

The combined impact of hypothyroidism and type 2 diabetes on lipid profiles is significant, as both contribute to dyslipidemia, a direct risk factor for atherosclerosis and cardiovascular complications. Hypothyroidism causes the accumulation of low-density lipoproteins (LDL) and reduces triglyceride clearance, worsening the dyslipidemia already observed in diabetic patients. This condition is intensified by the decreased activity of lipolytic enzymes, such as lipoprotein lipase, contributing to endothelial dysfunction. Type 2 diabetes alone is associated with an elevated risk of cardiovascular diseases, including coronary artery disease and stroke. The concurrent presence of hypothyroidism exacerbates these risks by promoting dyslipidemia and hypertension, increasing the likelihood of complications and patient morbidity (6, 7, 8).

Patients with type 2 diabetes frequently experience microvascular and macrovascular complications, such as retinopathy, nephropathy, and neuropathy. Hypothyroidism worsens these conditions by interfering with lipid profiles and cardiovascular function, accelerating the progression of complications and making them harder to manage. Additionally, hypothyroidism affects insulin resistance by dysregulating lipid metabolism and worsening glycemic control, contributing to a cycle of metabolic dysregulation that complicates clinical management. The coexistence of these conditions also amplifies chronic low-grade inflammation and oxidative stress. Thyroid hormone deficiency is associated with increased inflammatory markers, such as C-reactive protein, and excessive production of reactive oxygen species, intensifying tissue damage and worsening endothelial function, which further impairs insulin resistance and promotes vascular complications (2, 6, 7, 9).

Another important factor is the presence of concomitant hypertension and dyslipidemia. Studies demonstrate that patients with both conditions have a higher prevalence of hypertension and lipid disorders, which are independent risk factors for cardiovascular complications. These patients often require multiple medications, such as antidiabetics, statins, and blood pressure control agents, which increases the complexity of treatment and the risk of drug interactions. For example, the use of statins in patients with these conditions may increase the risk of myopathy, especially when combined with other treatments necessary for glycemic and cardiovascular management (8).

**Complications and Clinical Impact**

The coexistence of type 2 diabetes and hypothyroidism significantly worsens cardiovascular and metabolic complications, increasing the risk of coronary artery disease, hypertension, heart attacks, and strokes. This association intensifies endothelial dysfunction and accelerates atherosclerosis due to alterations in nitric oxide production and lipid metabolism, impairing vasodilation and promoting arterial stiffness. Patients with these conditions more frequently and severely experience microvascular dysfunctions, such as retinopathy and nephropathy, due to chronic hyperglycemia combined with compromised hormonal regulation, which induces persistent inflammation and elevates oxidative stress (3, 11, 12).

Hypothyroidism impairs insulin sensitivity, exacerbating the existing resistance in type 2 diabetes and making glycemic control more challenging. This effect increases the need for therapeutic adjustments to avoid severe metabolic decompensation. Dysregulation of thyroid function interferes with lipid metabolism, worsening dyslipidemia and increasing the risk of macrovascular complications, such as atherosclerosis, which are direct risk factors for major cardiovascular diseases (6, 10, 13).

Moreover, chronic low-grade inflammation and oxidative stress are exacerbated when type 2 diabetes and hypothyroidism are present simultaneously. This combination leads to elevated C-reactive protein levels and increased production of reactive oxygen species, intensifying tissue damage and compromising endothelial function, which further impairs insulin resistance and contributes to the progression of micro- and macrovascular complications. These findings underscore the need for an integrated therapeutic approach to minimize risks and improve clinical outcomes for patients (6, 13).

**Management and Treatment Factors**

Treating patients with type 2 diabetes and hypothyroidism requires comprehensive and careful management that combines pharmacological and non-pharmacological interventions with multidisciplinary support. Pharmacotherapy, for instance, must account for potential drug interactions and ensure efficacy. Antidiabetic medications like metformin are often paired with levothyroxine supplementation, necessitating close monitoring to avoid adverse effects, such as altered insulin sensitivity and impaired glycemic control. Treatment complexity can be exacerbated by associated comorbidities, making adherence a considerable challenge. Strategies to improve adherence include ongoing support from a multidisciplinary team, which helps reduce cardiovascular and metabolic complication risks and enables personalized patient follow-up (9, 12, 14).

Beyond pharmacological treatment, non-pharmacological interventions are essential for effective management. Diet and physical activity play crucial roles in regulating glycemic levels and improving insulin sensitivity. Studies show that high-fibre, low-glycemic diets combined with regular exercise contribute to reducing insulin resistance and stabilizing lipid profiles, factors that help prevent macrovascular and microvascular complications. However, maintaining these practices consistently over time is challenging and requires ongoing guidance and support from healthcare professionals, such as dietitians and health educators, to ensure sustainable outcomes and patient motivation (13, 14, 15).

The optimal management of patients with these conditions involves an integrated, multidisciplinary approach. Endocrinologists, cardiologists, dietitians, and other professionals should collaborate to develop a cohesive treatment plan that addresses all patient needs. This integration facilitates effective communication and a harmonized approach, minimizing the risks of harmful drug interactions and optimizing safety and clinical outcomes. Additionally, therapeutic education programs are fundamental to empowering patients, and enhancing their understanding of their conditions, the importance of treatment, and the necessary lifestyle changes. Psychological support also plays a crucial role, in helping patients cope with the emotional challenges related to chronic conditions, promoting adherence, and supporting overall well-being (15, 16).

**Recommendations for Clinical Monitoring**

The clinical management of patients with type 2 diabetes and hypothyroidism should include comprehensive monitoring practices to optimize metabolic control and reduce complications. Regular monitoring of TSH and T4 levels is essential to adjust levothyroxine and antidiabetic medications, ensuring hormonal balance and improving glycemic control. Lipid profile evaluation is equally important, as dyslipidemia, common in these patients, raises cardiovascular risk, necessitating adaptive strategies for efficient management (6, 7).

Insulin resistance, which may be exacerbated by hypothyroidism, should be monitored using indices like HOMA-IR, allowing for more precise therapeutic adjustments. Tracking inflammatory markers, such as C-reactive protein, is crucial, as chronic inflammation associated with these conditions contributes to worsening vascular complications (9, 17).

Cardiovascular monitoring, including tests like electrocardiograms and endothelial function assessments, is vital for the early detection of issues that may be intensified by the coexistence of diabetes and hypothyroidism. Furthermore, strategies that integrate a multidisciplinary approach, involving endocrinologists, cardiologists, and dietitians, enhance treatment effectiveness and reduce morbidity, promoting safer and more individualized patient management (6, 7, 17).

**DISCUSSION**

The review of studies suggests that the coexistence of diabetes and hypothyroidism significantly aggravates clinical complications in patients, especially regarding glycemic metabolism and lipid profile, with profound implications for managing these conditions. A complex interaction is observed between metabolic pathways, which complicates glycemic control and exacerbates dyslipidemia, potentially increasing the risk of cardiovascular and microvascular complications. The studies reviewed indicate that hypothyroidism contributes to insulin resistance by interfering with the expression of genes related to insulin signalling and lipid metabolism. In diabetic patients, dyslipidemia, often intensified by hypothyroidism, increases LDL accumulation and reduces triglyceride clearance, worsening cardiovascular conditions and elevating the risk of atherosclerosis and endothelial dysfunction. Additionally, the combination of these conditions induces chronic low-grade inflammation and increased oxidative stress, which intensifies tissue damage and impairs endothelial function, factors particularly detrimental in the context of microvascular complications such as retinopathy and nephropathy (2, 6, 7, 8, 9).

Furthermore, pharmacological treatment, when combined with levothyroxine hormone replacement, requires intensive monitoring to prevent drug interactions and optimize glycemic management, as the combination with antidiabetics can worsen insulin resistance. The literature also points out that treatment adherence is often low in patients with these comorbidities, necessitating support strategies and continuous monitoring by a multidisciplinary team to reduce the risk of decompensations and adverse events (12, 13).

While the studies cited point to a similar clinical picture of worsening, some methodological differences among the reviewed studies suggest variations in the results. These can be attributed to differences in study populations, the duration of diagnosis, and types of interventions, such as diet and physical activity, which directly impact outcomes.

The review of findings on the coexistence of type 2 diabetes and hypothyroidism shows how both conditions interact and intensify the risk of clinical complications, especially cardiovascular and metabolic. A multicenter Brazilian study indicated that patients with type 2 diabetes exhibit a high prevalence of cardiovascular and metabolic complications, such as dyslipidemia and hypertension, factors that increase the risk of coronary artery disease and strokes. This risk is exacerbated in patients with hypothyroidism due to its direct influence on endothelial dysfunction and the acceleration of atherosclerosis, caused by changes in nitric oxide production and lipid metabolism (3, 11, 12, 18).

Chronic low-grade inflammation and oxidative stress are amplified by the coexistence of the two conditions, aggravating tissue damage and impairing endothelial function, further complicating glycemic control and contributing to the progression of micro and macrovascular complications, such as retinopathy and nephropathy. The increase in C-reactive protein levels and reactive oxygen species production elevates cardiovascular event risks, such as early atherosclerosis (6, 13, 19). These findings emphasize the importance of an integrated, multidisciplinary clinical approach in managing these patients, aiming to minimize risks and improve clinical outcomes through rigorous metabolic control and a personalized therapeutic strategy for each case.

Moreover, the analysis of findings on the coexistence of type 2 diabetes and hypothyroidism reveals a profound impact on clinical complications, particularly cardiovascular and metabolic. Consistently, most studies suggest that this combination of conditions leads to significant worsening of dysfunctions, such as dyslipidemia and accelerated atherosclerosis. This worsening occurs due to LDL accumulation and reduced triglyceride clearance, which increase the risk of coronary artery disease, hypertension, and events like myocardial infarction and stroke (9, 12, 14).

However, there are discrepancies among studies regarding the prevalence and severity of microvascular complications, such as retinopathy and nephropathy. Studies indicate that the intensity of the impact of hypothyroidism on these complications varies according to pre-existing glycemic control and diabetes type. For example, patients with adequate glycemic control tend to exhibit fewer negative effects of hypothyroidism on vascular complications, suggesting that diabetes severity is a key factor in developing these complications (13, 14, 15, 20).

These variations in findings can be explained by factors such as diversity in study populations, with differences in age, sex, and presence of other comorbidities. For instance, older patients or those with a history of cardiovascular disease tend to experience faster worsening of complications when both conditions coexist, while younger patients or those with more effective metabolic control are less prone to severe complications. Additionally, different methodologies for assessing glycemic and lipid control and monitoring thyroid hormones yield distinct results. Longitudinal studies, observing complication progression over time, often show a stronger association between worsening conditions and the coexistence of diabetes and hypothyroidism, whereas cross-sectional studies observe fewer structural changes (15, 16).

Another relevant aspect in understanding the discrepancies is the type of treatment administered. Approaches involving a multidisciplinary team and rigorous control of blood glucose and thyroid hormones result in lower complication rates, suggesting that optimized management can reduce the negative impact of these combined conditions. Studies also highlight that non-pharmacological interventions, such as high-fibre, and low-glycemic-index diets, help improve insulin sensitivity and lipid profile control, mitigating insulin resistance exacerbated by hypothyroidism (6, 9).

In summary, the literature findings highlight the need for a personalized, integrated clinical management approach that includes rigorous control of both conditions to minimize complication impact. Multidisciplinary treatment strategies, encompassing pharmacological interventions and lifestyle modifications, are essential to reduce complication burden and optimize clinical outcomes. The variability in study results suggests the need for more controlled, long-term research to deepen understanding of the interactions between type 2 diabetes and hypothyroidism and improve treatment approaches.

For a critical analysis of findings on monitoring practices in patients with type 2 diabetes and hypothyroidism, the reviewed studies indicate the need for systematic monitoring of TSH and T4 levels, which are essential for adjusting levothyroxine replacement and antidiabetic medications, helping to balance hormones and glycemic control. This type of monitoring is particularly relevant in patients with subtle hormonal variations that may go undetected in routine clinical exams, requiring detailed follow-up to prevent cardiovascular complications (6, 7, 21).

The studies also recommend measuring insulin resistance through the HOMA-IR index, allowing more precise therapeutic adjustments. This practice is emphasized in studies linking high TSH levels with an increased risk of insulin resistance and metabolic syndrome, suggesting that monitoring TSH and HOMA-IR could offer crucial preventive and therapeutic insights, especially in patients with obesity and type 2 diabetes. Moreover, longitudinal studies, such as ELSA-Brazil, show a significant correlation between high TSH and cardiovascular risk, reinforcing the importance of frequent monitoring of lipids, such as cholesterol and triglycerides, to identify additional risks early (9, 17, 22, 23).

Despite consensus on the importance of this monitoring, discrepancies exist in recommended protocols, particularly in testing frequency. Some studies suggest that quarterly follow-ups are sufficient for adjusting levothyroxine treatment in patients with relatively stable glycemic control, while others recommend more frequent monitoring for patients with high cardiovascular risk or a history of significant hormonal fluctuations. Differences may stem from studied populations—older patients with comorbidities require more frequent adjustments due to natural endocrine function decline, while younger patients may maintain hormonal stability with less intensive interventions (6, 7, 17).

Monitoring inflammatory markers, such as C-reactive protein, is also recommended, as chronic inflammation and oxidative stress are intensified by the coexistence of type 2 diabetes and hypothyroidism. This monitoring is especially useful for predicting the progression of microvascular and macrovascular complications, such as retinopathy and nephropathy. Studies indicate that increased chronic inflammation in these patients raises the risk of endothelial damage, complicates glycemic control, and worsens insulin resistance—a scenario more commonly observed in patients with both diagnoses (17, 23, 24).

Therefore, the literature emphasizes the importance of an integrated, personalized monitoring approach, adapted to the individual needs of the patient and conducted at intervals appropriate to their clinical condition. However, the variability of findings among studies suggests the need for additional research to standardize and optimize these practices based on the specific characteristics of each patient population.

**Limitations**

Firstly, there is significant heterogeneity among the analyzed populations, with differences in age, sex, and comorbidity history, which hinders direct comparisons of findings and limits the generalization of results. Additionally, the employed methodologies vary widely, including cross-sectional, longitudinal, and cohort studies that use diverse indicators to measure cardiovascular and metabolic complications. This methodological diversity makes it challenging to obtain consistent and comparable data. Another critical point is the lack of strict control over confounding variables, such as diet, physical activity level, and concurrent medication use, which are directly related to managing these conditions and may significantly impact outcomes.

Sample sizes are limited in some studies, particularly in specific subgroups of patients with type 2 diabetes and hypothyroidism, reducing statistical power and increasing the margin of error, which makes it difficult to identify robust associations. Furthermore, the absence of longitudinal studies following the progression of complications over time hinders a more accurate assessment of the effects of coexisting conditions on long-term clinical outcomes.

Concerning the review itself, limitations include selection bias, as studies not meeting inclusion criteria, particularly those outside accessible databases, were excluded, restricting the scope and representativeness of the findings. The reliance on observational studies is also a limitation, as it prevents the inference of causal relationships between diabetes and hypothyroidism and their complications. Variability in outcome measures, such as insulin resistance and lipid profile, complicates result synthesis and limits comparability across studies. There is also the possibility of publication bias, as studies with significant findings tend to be more frequently published, potentially overestimating the association between the conditions and the worsening of complications.

Finally, the temporal scope of included studies and the evolution of treatment protocols are limiting factors, as older studies may not reflect current clinical practices and advancements in managing both conditions. With the development of new approaches and multidisciplinary treatments, there is an ongoing need for recent studies to update findings and align recommendations with current practices. These limitations highlight the importance of future research with rigorous experimental design, larger samples, and enhanced control of variables to more precisely explore the interactions between diabetes and hypothyroidism and their impacts on patient health.

**Impacts on Clinical Practice**

The results of this review suggest that patients with type 2 diabetes and hypothyroidism require rigorous monitoring, especially of hormonal, glycemic, and lipid profile parameters. Regular evaluation of TSH, T4, HOMA-IR, and inflammatory markers, such as C-reactive protein, is recommended to allow for early identification of complications and necessary therapeutic adjustments. The coexistence of these conditions may interfere with the response to antidiabetic and hormonal medications, indicating the need for frequent adjustments in insulin and levothyroxine dosages based on the patient's metabolic response and insulin sensitivity, which is essential for effective glycemic control.

Furthermore, the concurrent use of antidiabetic agents and levothyroxine increases the complexity of clinical management, necessitating active vigilance to avoid drug interactions that could compromise control of both conditions. This care is crucial to reduce the risks of hypoglycemia, hyperglycemia, and adverse cardiovascular effects. The review also highlights that these patients are at a higher risk of cardiovascular complications, such as atherosclerosis, hypertension, and coronary artery disease, as well as microvascular complications, including retinopathy and nephropathy. This risk profile underscores the need to include cardiovascular function tests and endothelial assessments in routine follow-ups for early detection and preventive intervention.

An integrated and multidisciplinary approach is essential for treating these patients, enabling comprehensive management of both metabolic and cardiovascular aspects. Involving specialists such as endocrinologists, cardiologists, nutritionists, and health educators facilitates efficient coordination of treatment, enhancing the effects of pharmacological and non-pharmacological interventions and reducing the risk of drug interactions. The inclusion of health educators and psychological support aids patient adherence to lifestyle changes and treatment regimens. Continuous support helps patients adopt a balanced diet and maintain physical activity, which are essential to improve insulin sensitivity and lipid profile.

**Research Gaps and Directions for Future Studies**

Most available studies on the coexistence of type 2 diabetes and hypothyroidism are observational, which limits the ability to establish causal relationships between these conditions and observed complications. Randomized clinical trials are needed to more rigorously investigate the combined effects of antidiabetic and hormone replacement therapies on glycemic control and cardiovascular outcomes. Additionally, heterogeneity in demographic and clinical characteristics of studied populations—including age, sex, comorbidities, and ethnicity—hinders result generalization. Future studies should focus on more homogeneous samples or conduct subgroup analyses, such as elderly individuals, postmenopausal women, or people with different genetic profiles, to better understand how these variables influence the interaction between these conditions.

Another limitation is the restricted assessment of inflammatory markers and oxidative stress. While C-reactive protein is recognized as a risk factor, many studies fail to systematically evaluate other inflammatory and antioxidant biomarkers. Future research could explore a broader range of biomarkers to clarify mechanisms linking chronic inflammation to the progression of cardiovascular and metabolic complications. The lack of long-term studies that track the evolution of micro and macrovascular complications over years also limits understanding of the progression of these conditions. Longitudinal studies are needed to identify optimal times for preventive clinical interventions.

Additionally, although evidence suggests that fiber-rich diets and physical exercise improve glycemic control and insulin sensitivity, few studies evaluate the long-term impact of these interventions in patients with both conditions. Future research should examine how adherence to these lifestyle interventions affects the progression of metabolic and cardiovascular complications.

To address these gaps, multicenter clinical trials involving patients from different regions could provide more robust insights into best clinical management practices, evaluating combinations of antidiabetics and levothyroxine replacement to identify the most effective strategies in diverse contexts. Moreover, studies on genetic influences in glycemic control and hormone replacement responses could contribute to personalized treatments, especially concerning insulin resistance and lipid profile.

Exploring the role of the gut microbiome, considering that both type 2 diabetes and hypothyroidism can influence its composition, represents another promising area. Future studies could investigate how these changes affect medication absorption and metabolic responses, particularly regarding insulin resistance and levothyroxine response.

Developing monitoring protocols based on algorithms that integrate data on glycemia, thyroid hormones, and inflammatory markers could also be a significant innovation. Studies validating these protocols in different populations could help implement more effective follow-up strategies in clinical practice. Finally, analyzing the cost-effectiveness of integrated approaches is essential to justify their large-scale implementation in healthcare systems. Future studies could compare health outcomes and costs associated with different treatment strategies in patients with type 2 diabetes and hypothyroidism, promoting a more efficient and sustainable resource allocation.

**CONCLUSION**

The review concludes that the coexistence of type 2 diabetes and hypothyroidism significantly amplifies the risk of cardiovascular and metabolic complications, including atherosclerosis, hypertension, heart failure, retinopathy, and nephropathy. This complex interaction is mediated by overlapping metabolic factors, such as aggravated insulin resistance, intensified dyslipidemia, chronic inflammation, and increased oxidative stress. The coexistence of these conditions makes clinical management more challenging, requiring frequent adjustments in antidiabetic and hormone replacement therapies and careful monitoring to minimize the risks of drug interactions and other complications.

These findings highlight the importance of an integrated and personalized approach, involving a multidisciplinary team of endocrinologists, cardiologists, and nutritionists. Clinical follow-up should include regular monitoring of thyroid hormones (TSH and T4), glycemic control (HOMA-IR), and assessments of lipid profile and inflammatory markers. Non-pharmacological interventions, such as a low-glycemic-index diet and regular exercise, are also essential to improve insulin sensitivity and reduce the risk of metabolic complications. Furthermore, the review underscores the need for more research, including randomized clinical trials and long-term studies, to deepen understanding of the interactions between type 2 diabetes and hypothyroidism and to refine treatment strategies. Future investigations could provide robust data to guide more effective and safe management approaches, reducing the impact of these comorbidities and promoting better quality of life for patients.

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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Details of the AI usage are given below:

1.

2.

3.

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