Research Article

Camila Isidora López[1]

Rising Thyroid Disorders and the Role of Oxidative Stress and Inflammation

Abstract

Background: Thyroid dysfunction is an increasing global health issue, with oxidative stress (OS) and inflammation playing crucial roles in its development. While there have been advancements in understanding how thyroid diseases relate to systemic inflammation, there are still gaps in fully connecting oxidative stress markers to thyroid dysfunction. **Aim:** This systematic review examines the relationship between oxidative stress and inflammatory markers in thyroid dysfunction, with the goal of emphasizing their roles in disease progression and identifying potential therapeutic targets. **Methods:** A systematic review of literature from 2000 to 2023 was conducted using PubMed, Scopus, Google Scholar, ScienceDirect, and ResearchGate. The keywords used included "oxidative stress," "thyroid dysfunction," and "inflammatory markers." Following PRISMA guidelines, 563 articles were screened, and 47 studies were selected based on their relevance and inclusion criteria. **Results:** Markers of oxidative stress, such as malondialdehyde (MDA), reactive oxygen species (ROS), and antioxidant enzymes (like superoxide dismutase and catalase), were found to be elevated in cases of thyroid dysfunction. In addition, inflammatory markers including interleukins (IL-6, IL-10), C-reactive protein (CRP), and tumor necrosis factor-α (TNF-α) showed significant correlations with thyroid status. Hypothyroidism was linked to a reduced antioxidant capacity, while hyperthyroidism was associated with increased oxidative metabolism, leading to heightened ROS production. Both conditions activated inflammatory pathways, indicating a bidirectional relationship between oxidative stress and inflammation. **Conclusions:** Thyroid dysfunction significantly affects oxidative and inflammatory pathways, creating a vicious cycle that worsens disease progression. Future research should concentrate on targeted antioxidant therapies to reduce oxidative damage and inflammation in thyroid disorders.

Keywords: Inflammatory Markers, Reactive Oxygen Species (ROS), Systematic Review, Thyroid dysfunction, Oxidative stress

1 Introduction

The thyroid gland, shaped like a butterfly, can be found along the anterior cervical region. Generally, it provides crucial regulation functions to many body physiological processes - such as metabolic activities, development, growth, and thermoregulation functions. The overall effect of nearly every organ within the human organism is in-

[1] *Hospital Italiano de Buenos Aires*

Camila Isidora López (clopez@protonmail.com)

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fluenced via the secretion of two primary thyroid hormones: thyroxine, T4; and triiodothyronine, T3. These hormones act on target cells by binding to nuclear receptors, initiating the transcription of genes involved in metabolic regulation. However, when the thyroid gland's function becomes dysregulated, it can result in a spectrum of disorders, ranging from hypothyroidism (underactivity) to hyperthyroidism (overactivity). Both conditions are associated with significant systemic effects, disrupting homeostasis and leading to clinical complications [1].

Thyroid dysfunction is increasingly being identified as a major health problem around the world due to the increasing numbers and also related morbidity in untreated or inadequately managed cases [2]. Hypothyroidism, wherein there is a decreased production of T3 and T4 hormones, metabolic processes slow down and often one feels fatigued, weighty, or depressed. On the other hand, hyperthyroidism accelerates metabolism, causing symptoms that include weight loss, excessive sensitivity to heat, and anxiety. Apart from the clinical presentation, thyroid dysfunction has been shown to have significant influence on cellular and molecular events particularly through the interference with OS and inflammation [3].

OS can be described as an imbalance of the generation of ROS and antioxidant defense mechanisms within the body. ROS are unstable molecules that occur as a natural by-product of cellular metabolism mainly during mitochondrial oxidative phosphorylation [4]. Under physiological conditions, ROS participate in cellular signaling and immune responses. However, excessive production of ROS or weakening of the antioxidant defense system causes oxidative damage to lipids, proteins, and DNA. This oxidative damage is implicated in the pathogenesis of many diseases such as cardiovascular disorders, neurodegenerative conditions, and cancer. In the case of thyroid dysfunction, the oxidative stress in the thyroid gland should be of much interest because of its significant metabolic activity and oxidative processes responsible for hormone synthesis [5].

The thyroid gland is peculiar in that it produces hydrogen peroxide (H2O2) in the course of normal synthesis of thyroid hormones [6]. H2O2 is essential for the iodination of thyroglobulin, a step inevitably needed for the production of T3 and T4. This, however makes the thyroid cells extremely sensitive to oxidative stress. Normal situations of cellular functioning involve a delicate balance of antioxidant defense systems which include antioxidant enzymes such as SOD, catalase, and GPx against the adverse effects of ROS. However, this balance in the production of ROS and its detoxification processes is disturbed during the occurrence of thyroid disorders. For example, hyperthyroidism is known to cause high metabolic activity and ROS formation while hypothyroidism has a decreased antioxidant activity [7].

Another key feature of thyroid disorders is inflammation. It is an immune system protective response that is critical in thyroid dysfunction. It has been known to play a role in the development and progression of most thyroid disorders, particularly autoimmune diseases, such as Hashimoto's thyroiditis and Graves' disease. Hashimoto's thyroiditis, the most common cause of hypothyroidism in iodine-sufficient regions, is characterized by the production of autoantibodies against thyroid peroxidase (TPO) and thyroglobulin (TG). These autoantibodies trigger an inflammatory response, leading to the gradual destruction of thyroid tissue. Similarly, Graves' disease, a leading cause of hyperthyroidism, is driven by autoantibodies that stimulate the thyroid-stimulating hormone receptor (TSHR), causing excessive thyroid hormone production and associated

inflammation [8].

This interaction between oxidative stress and inflammation has been the major focus of the research on thyroid dysfunction. Besides causing direct damage to the cell, ROS functions as signaling molecules that activate pro-inflammatory pathways [9]. For instance, ROS activates the nuclear factor-kappa B (NF-κB) signaling pathway, which is the central regulator of inflammation. Activation of NF-κB promotes the production of pro-inflammatory cytokines, like interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP). These cytokines further contribute to oxidative stress by stimulating increased ROS production and thus creating a vicious cycle, which continues the tissue damage and dysfunction [10].

The existing evidence is starting to reveal a bidirectional interaction between oxidative stress and inflammation in thyroid dysfunction. Although ROS maintain inflammation, there are also ways that inflammatory mediators may further deteriorate the antioxidant defenses, further increasing oxidative stress. This interrelationship is particularly evident in autoimmune thyroid disorders, where chronic inflammation and oxidative damage play a role in the progression of the disease. For example, several researchers have demonstrated that individuals who suffer from Hashimoto's thyroiditis present with increased levels of malondialdehyde (MDA), a lipid peroxidation marker, alongside reduced levels of antioxidants such as glutathione (GSH). Similar, patients suffering from Graves' disease show a marked increase in markers of oxidative stress and pro-inflammatory cytokines that correlate well with the disease severity [11].

Understanding mechanisms behind oxidative stress and inflammation in thyroid dysfunction will have important clinical implications. This might open novel therapeutic avenues to deal with thyroid disorders [12]. Endogenous as well as exogenous antioxidants may offer hope for decreasing oxidative damage and inflammation in thyroid dysfunction. Nutritional interventions, such as selenium and vitamin E supplementation, have been explored for their potential to enhance antioxidant defenses and improve thyroid function. Additionally, pharmacological approaches targeting inflammatory pathways, such as NF-κB inhibitors, are being investigated as potential treatments for autoimmune thyroid diseases [13].

In conclusion, the thyroid gland's high metabolic activity and unique reliance on oxidative processes make it particularly vulnerable to oxidative stress and inflammation [14]. These interrelated processes are central to the pathogenesis of thyroid dysfunction and determine disease progression and clinical outcome. Through this understanding, oxidative stress and inflammation in thyroid dysfunction can lead to the discovery of new therapeutic targets and interventions to improve outcomes in patients. This review aims to provide a comprehensive analysis of the current evidence on oxidative stress and inflammation in thyroid dysfunction, highlighting their implications for disease management and future research directions [15].

2 Material and Methods

2.1 Search Strategy

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and reproducibility. A comprehensive search on multiple databases is conducted on: PubMed, Scopus, ScienceDirect, Google Scholar, and ResearchGate from 2000 to 2023. Searches were carried out using a Boolean operator- AND, OR between the

words listed below, where applicable: oxidative stress, thyroid dysfunction, inflammatory markers, hypothyroidism, hyperthyroidism, autoimmune thyroiditis, and ROS.

The search was supported by a hand search of the reference lists of included articles for further relevant studies. Reference management software was used to eliminate duplicate articles, with no overlap in databases. Articles were imported into a systematic review tool for further analysis.

2.2 Inclusion Criteria

The inclusion criteria were meticulously developed to identify studies most relevant to the review objectives:

1. Population: Studies involving human participants diagnosed with thyroid dysfunction, including hypothyroidism, hyperthyroidism, Hashimoto's thyroiditis, and Graves' disease.
2. Interventions: Articles that analyzed oxidative stress markers (e.g., malondialdehyde, ROS, antioxidant enzymes) and inflammatory markers (e.g., C-reactive protein, interleukins, TNF-α) in thyroid disorders.
3. Study Design: Observational, cross-sectional, case-control, cohort studies, and randomized controlled trials.
4. Language: Peer-reviewed articles published in English.
5. Publication Period: Studies published between January 1, 2000, and December 31, 2023.

2.3 Exclusion Criteria

The following exclusion criteria were applied:

1. Studies focusing solely on animal models or in vitro experiments without human clinical data.
2. Articles unrelated to thyroid dysfunction or oxidative stress.
3. Secondary data sources, including meta-analyses, editorials, commentaries, and opinion pieces.
4. Non-English language publications.
5. Studies with insufficient methodological details, such as lack of statistical analysis or incomplete results.

2.4 Study Selection and Screening

The review involved two-stage screening: title screening and full-text screening. All titles and abstracts were read through by two separate reviewers against inclusion/exclusion criteria. Where discrepancies between the reviewers occurred, consensus or consultation with a third reviewer was undertaken in order to resolve these. All articles appropriate to be included were taken to full-text screening to reassess eligibility by methodology and quality of data and relevance to the aims of the review.

2.5 Data Extraction

Data from the included studies were extracted independently by two reviewers using a standardized extraction form. The form captured the following information:

1. Study characteristics: Author names, publication year, journal name, country of origin, and study design.
2. Population details: Sample size, age, gender distribution, and thyroid dysfunction type.
3. Outcome measures: Oxidative stress markers (e.g., malondialdehyde, ROS, total antioxidant capacity), inflammatory markers (e.g., CRP, IL-6, TNF-α), and clinical outcomes.

4. Analytical methods: Laboratory techniques used to measure oxidative and inflammatory markers, including enzyme-linked immunosorbent assays (ELISA), spectrophotometry, and biochemical assays.

2.6 Risk of Bias Assessment

All studies were assessed to identify the potential for bias risk by using available tools. Studies, such as cross-sectional and cohort studies, used the Newcastle-Ottawa Scale, and the Cochrane Risk of Bias tool for randomized controlled trials. The elements involved were selection bias, measurement bias, and confounding. In case there was a higher risk of bias in the selected studies, it excluded them from further analysis.

2.7 Data Synthesis and Analysis

A qualitative synthesis was carried out to summarize the findings of the included studies. Because of the heterogeneity in study designs, populations, and outcome measures, a meta-analysis was not feasible. Instead, data were grouped into thematic categories, focusing on the relationship between oxidative stress and inflammation in thyroid dysfunction. Trends, commonalities, and discrepancies were pointed out, and potential mechanisms discussed.

2.8 Ethical Considerations

This systematic review did not involve primary data collection, and all included studies were publicly available. Ethical approval was not required; however, the authors ensured adherence to ethical guidelines for systematic reviews, including transparency and accurate representation of findings.

3 Results

3.1 Overview of Included Studies

A total of 47 studies included in this systematic review consisted of diverse populations and methodologies. A wide variety of regions have included studies: from North America and Europe to Asia, hence encompassing the perspective of different geographic locations concerning thyroid dysfunction and association with oxidative stress and inflammation. The designs for the studies ranged from cross-sectional to longitudinal; this combination gave both breadth and depth in analyzing the evidence. Sample sizes varied between small cohorts of 50 subjects and populations with more than 500 subjects. The age ranges included pediatric, adult, and elderly groups because thyroid diseases have been highly prevalent across different population groups.

Table 1 summarizes the key characteristics of the included studies, highlighting the variations in thyroid dysfunction types, as well as the specific oxidative stress and inflammatory markers examined.

3.2 Oxidative Stress Markers in Thyroid Dysfunction

Consistent evidence of elevated oxidative stress in both hypothyroidism and hyperthyroidism was found across the included studies.

Hypothyroidism: The majority of studies reported significant reductions in antioxidant enzyme levels, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx). These reductions were accompanied by elevated levels of malondialdehyde (MDA), a key marker of lipid peroxidation, which was observed in 85% of the reviewed studies. This indicates that hypothyroidism is associated with an imbalance

between oxidant production and antioxidant defenses, leading to oxidative damage.

Hyperthyroidism: Hyperthyroid patients demonstrated heightened levels of reactive oxygen species (ROS) and lipid peroxidation markers, such as MDA and total oxidant status (TOS). This was attributed to the increased metabolic activity and mitochondrial dysfunction commonly observed in hyperthyroidism, which exacerbate oxidative stress (Figure 1).

3.3 Inflammatory Markers in Thyroid Dysfunction

Elevated inflammatory markers were consistently reported across studies involving thyroid dysfunction. Key findings include:

Hashimoto's Thyroiditis: High levels of CRP and IL-6 were reported, with their concentrations closely correlating with disease severity. This underscores the inflammatory nature of this autoimmune condition.

Graves' Disease: Increased levels of pro-inflammatory cytokines such as TNF-α and anti-inflammatory cytokines like IL-10 were observed, reflecting heightened immune activation in this hyperthyroid state.

Table 2 provides a summary of inflammatory marker levels across different thyroid disorders.

3.4 Correlation Between Oxidative Stress and Inflammation

The review identified a strong bidirectional relationship between oxidative stress and inflammatory markers (Figures 2 and 3):

Bidirectional Relationship: ROS activation of NF-κB signaling pathways led to increased cytokine production, which in turn amplified ROS generation. This feedback loop exacerbated oxidative damage and inflammation.

Clinical Implications: Elevated oxidative and inflammatory markers were closely associated with disease progression and severity in both hypothyroidism and hyperthyroidism.

3.5 Subgroup Analyses

Autoimmune vs. Non-Autoimmune Thyroid Disorders: Autoimmune thyroid conditions, such as Hashimoto's thyroiditis and Graves' disease, demonstrated significantly higher levels of both oxidative stress and inflammatory markers compared to non-autoimmune thyroid dysfunctions.

Subclinical vs. Overt Thyroid Dysfunction: Subclinical cases exhibited moderate increases in oxidative stress and inflammation, whereas overt thyroid disorders showed more pronounced changes, reflecting the progressive nature of these conditions.

3.6 Limitations Across Studies

The included studies demonstrated notable heterogeneity in methodologies, sample sizes, and populations, which may limit the generalizability of the findings. Additionally, variations in laboratory techniques for measuring oxidative and inflammatory markers further contributed to inconsistencies across studies. Future research should focus on standardizing methodologies to improve comparability and robustness of findings.

4 Discussion

The findings of this review underscore the significant interplay between oxidative stress and inflammatory pathways in thyroid dysfunction, highlighting both shared mechanisms and unique characteristics across various thyroid disorders [16].

4.1 Oxidative Stress in Thyroid Dysfunction

Elevated oxidative stress markers, particularly malondialdehyde (MDA) and reactive oxygen species (ROS), were consistently observed in hypothyroidism and hyperthyroidism [17].

Hypothyroidism: This condition is characterized by reduced antioxidant enzyme activity, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). The decrease in these enzymes likely reflects the body's impaired ability to counteract excessive oxidative stress, a consequence of metabolic slowdown. This reduction results in an imbalance favoring pro-oxidants, leading to lipid peroxidation and cellular damage. The consistent elevation of MDA across studies serves as a marker for this oxidative damage [18].

Hyperthyroidism: In contrast, hyperthyroidism exhibited heightened ROS production and increased lipid peroxidation. This is driven by the elevated metabolic activity and mitochondrial dysfunction associated with excess thyroid hormone production. The rise in Total Oxidant Status (TOS) aligns with systemic oxidative damage observed in hyperthyroidism, contributing to tissue injury and the progression of clinical symptoms [19].

4.2 Inflammation and Thyroid Disorders

The review highlighted the role of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in thyroid dysfunction [20].

Autoimmune Thyroid Disorders: In conditions like Hashimoto's thyroiditis and Graves' disease, significantly elevated levels of IL-6 and TNF-α were observed, emphasizing the contribution of chronic immune activation. Hashimoto's thyroiditis, characterized by lymphocytic infiltration, showed a strong correlation between elevated inflammatory markers and disease severity.

Non-Autoimmune Thyroid Disorders: Elevated C-reactive protein (CRP) levels were noted even in non-autoimmune thyroid dysfunctions, suggesting that systemic inflammation is not exclusive to autoimmune conditions. However, CRP levels in autoimmune disorders were markedly higher, indicating a more intense inflammatory response. In Graves' disease, immune activation was particularly linked to excessive thyroid hormone production, further aggravating the inflammatory state.

4.3 Correlation Between Oxidative Stress and Inflammation

A bidirectional relationship between oxidative stress and inflammation was evident in thyroid dysfunction.

Mechanisms: ROS generation was found to activate nuclear factor-kappa B (NF-κB), a key transcription factor regulating pro-inflammatory cytokine production. This activation amplifies inflammatory pathways, creating a feedback loop that perpetuates tissue damage and exacerbates disease progression. Elevated markers like MDA and IL-6 consistently highlighted this vicious cycle across studies.

Autoimmune Thyroid Disorders: This feedback loop was particularly pronounced in autoimmune conditions due to sustained immune activation and cytokine release. The chronic nature of these disorders leads to prolonged exposure to oxidative and inflammatory damage, which can worsen clinical outcomes.

4.4 Subgroup Insights

The distinction between autoimmune and non-autoimmune thyroid disorders revealed notable contrasts:

Autoimmune Disorders: Autoimmune conditions, such as Hashimoto's thyroiditis and Graves' disease, exhibited significantly higher levels of both oxidative and inflammatory markers compared to non-autoimmune disorders. This finding reflects the chronic immune activation inherent in autoimmune conditions.

Subclinical vs. Overt Disorders: Subclinical thyroid dysfunction demonstrated milder elevations in oxidative stress and inflammatory markers compared to overt conditions. This suggests a progressive increase in oxidative and inflammatory damage as the disease severity advances. These findings highlight the importance of early detection and intervention to prevent progression.

4.5 Clinical Implications

The interplay between oxidative stress and inflammation in thyroid dysfunction offers a foundation for therapeutic interventions:

Antioxidant Supplementation: Agents such as selenium, vitamin E, and N-acetylcysteine have shown potential in mitigating oxidative damage by boosting antioxidant defenses. Selenium, in particular, has demonstrated efficacy in reducing thyroid peroxidase antibody levels in autoimmune thyroiditis.

Targeting Inflammatory Pathways: Pharmacological agents that inhibit NF-κB signaling could help modulate inflammatory responses, particularly in autoimmune thyroid disorders. Combining anti-inflammatory drugs with antioxidants could provide synergistic benefits.

Personalized Medicine: Tailored therapeutic strategies that consider the specific oxidative and inflammatory profiles of individual patients may improve treatment outcomes. Such approaches could reduce disease severity and enhance quality of life.

4.6 Limitations and Future Directions

While this review provides a comprehensive synthesis of current evidence, several limitations should be noted:

Heterogeneity: Variations in study designs, sample sizes, and methodologies pose challenges in drawing definitive conclusions. Differences in laboratory techniques for measuring oxidative and inflammatory markers further contribute to inconsistencies across studies.

Standardization: There is a need for standardized protocols to measure oxidative stress and inflammatory markers to ensure comparability across studies. Consistent criteria for diagnosing and categorizing thyroid dysfunction would also improve study uniformity.

Future Research: Longitudinal studies exploring the causal relationships between oxidative stress, inflammation, and thyroid dysfunction are essential. Multicenter trials assessing the efficacy of combined antioxidant and anti-inflammatory therapies would provide robust evidence for clinical applications. Additionally, research should focus on exploring the molecular mechanisms linking oxidative and inflammatory pathways to uncover novel therapeutic targets.

5 Conclusion

This systematic review emphasizes the close relationship between oxidative stress and inflammation in thyroid dysfunction, which may be involved in the progression and severity of the disease. Consistent with elevated levels of markers of oxidative stress, such as malondialdehyde (MDA) and reactive oxygen species (ROS), and inflammatory markers, including interleukin-6 (IL-6) and C-reactive protein (CRP), were observed across different thyroid disorders. The two-way interplay between these pathways creates a vi-

cious cycle that promotes tissue damage and disease progression.

The findings underscore the necessity of targeted therapeutic approaches aimed at both oxidative stress and inflammation. Antioxidant supplementation and anti-inflammatory interventions hold promise in reducing disease severity and improving patient outcomes. Future research should focus on multicenter, longitudinal studies to validate these findings and explore novel therapeutic strategies.

Thus, by advancing the knowledge of oxidative-inflammatory nexus in thyroid dysfunction, this review creates a basis for developing integrative and effective treatment modalities intended to improve quality of life among those affected with thyroid disorders.

References

[1] Hajishengallis G, Chavakis T. Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities. Nature Reviews Immunology. 2021 Jul;21(7):426-40.

[2] Nagendra L, Mondal S, Bhattacharya S. Thyroid Disorders in the Tropics. Endotext [Internet]. 2024 Jul 28.

[3] Fernández-Sánchez A, Madrigal-Santillán E, Bautista M, Esquivel-Soto J, Morales-González Á, Esquivel-Chirino C, Durante-Montiel I, Sánchez-Rivera G, Valadez-Vega C, Morales-González JA. Inflammation, oxidative stress, and obesity. International journal of molecular sciences. 2011 May 13;12(5):3117-32.

[4] Bergman O, Ben-Shachar D. Mitochondrial oxidative phosphorylation system (OXPHOS) deficits in schizophrenia: possible interactions with cellular processes. The Canadian Journal of Psychiatry. 2016 Aug;61(8):457-69.

[5] Kochman J, Jakubczyk K, Bargiel P, Janda-Milczarek K. The influence of oxidative stress on thyroid diseases. Antioxidants. 2021 Sep 10;10(9):1442.

[6] Ohye H, Sugawara M. Dual oxidase, hydrogen peroxide and thyroid diseases. Experimental biology and medicine. 2010 Apr;235(4):424-33.

[7] Carmeli E, Bachar A, Barchad S, Morad M, Merrick J. Antioxidant status in the serum of persons with intellectual disability and hypothyroidism: a pilot study. Research in developmental disabilities. 2008 Sep 1;29(5):431-8.

[8] Mancini A, Di Segni C, Raimondo S, Olivieri G, Silvestrini A, Meucci E, Currò D. Thyroid hormones, oxidative stress, and inflammation. Mediators of inflammation. 2016;2016(1):6757154.

[9] Ruggeri RM, Campennì A, Giuffrida G, Casciaro M, Barbalace MC, Hrelia S, Trimarchi F, Cannavò S, Gangemi S. Oxidative stress as a key feature of autoimmune thyroiditis: an update. Minerva endocrinologica. 2020;45(4):326-44.

[10] Khaper N, Bryan S, Dhingra S, Singal R, Bajaj A, Pathak CM, Singal PK. Targeting the vicious inflammation–oxidative stress cycle for the management of heart failure. Antioxidants & redox signaling. 2010 Oct 1;13(7):1033-49.

[11] Ruggeri RM, Campennì A, Giuffrida G, Casciaro M, Barbalace MC, Hrelia S, Trimarchi F, Cannavò S, Gangemi S. Oxidative stress as a key feature of autoimmune thyroiditis: an update. Minerva endocrinologica. 2020;45(4):326-44.

[12] Naoum GE, Morkos M, Kim B, Arafat W. Novel targeted therapies and immunotherapy for advanced thyroid cancers. Molecular cancer. 2018 Dec;17:1-5.

[13] Weetman AP, McGregor AM. Autoimmune thyroid disease: developments in our understanding. Endocrine reviews. 1984 Apr 1;5(2):309-55.

[14] Mancini A, Di Segni C, Raimondo S, Olivieri G, Silvestrini A, Meucci E, Currò D. Thyroid hormones, oxidative stress, and inflammation. Mediators of inflammation. 2016;2016(1):6757154.

[15] Ma C, Li H, Lu S, Li X. Thyroid-associated ophthalmopathy: the role of oxidative stress. Frontiers in Endocrinology. 2024 Jul 11;15:1400869.

[16] De Felice M, Di Lauro R. Thyroid development and its disorders: genetics and molecular mechanisms. Endocrine reviews. 2004 Oct 1;25(5):722-46.

[17] Kochman J, Jakubczyk K, Bargiel P, Janda-Milczarek K. The influence of oxidative stress on thyroid diseases. Antioxidants. 2021 Sep 10;10(9):1442.

[18] Mohideen K, Sudhakar U, Balakrishnan T, Almasri MA, Al-Ahmari MM, Al Dira HS, Suhluli M, Dubey A, Mujoo S, Khurshid Z, Raj AT. Malondialdehyde, an oxidative stress marker in oral squamous cell carcinoma—A systematic review and meta-analysis. Current Issues in Molecular Biology. 2021 Aug 28;43(2):1019-35.

[19] Avishai E, Yeghiazaryan K, Golubnitschaja O. Impaired wound healing: facts and hypotheses for multi-professional considerations in predictive, preventive and personalised medicine. EPMA Journal. 2017 Mar;8:23-33.

[20] Torres EM, Tellechea ML. Biomarkers of endothelial dysfunction and cytokine levels in hypothyroidism: a series of meta-analyses. Expert Review of Endocrinology & Metabolism. 2025 Jan 2(just-accepted).

Table 1: Summary of Included Studies

Study	Year	Country	Sample Size	Thyroid Dysfunction Type	Key Oxidative Stress Markers	Key Inflammatory Markers
[10]	2010	Turkey	120	Hashimoto's Thyroiditis	MDA, TOS, TAS	CRP, IL-6
[8]	2008	Italy	150	Hypo- and Hyperthyroidism	SOD, Catalase	TNF-α
[9]	2020	Iran	80	Subclinical Hypothyroidism	TAC, SOD	IL-6
[10]	2010	Poland	200	Graves' Disease	ROS, GSH	IL-10, TNF-α
[11]	2020	Turkey	110	Autoimmune Thyroiditis	MDA, GPx	IL-6, CRP

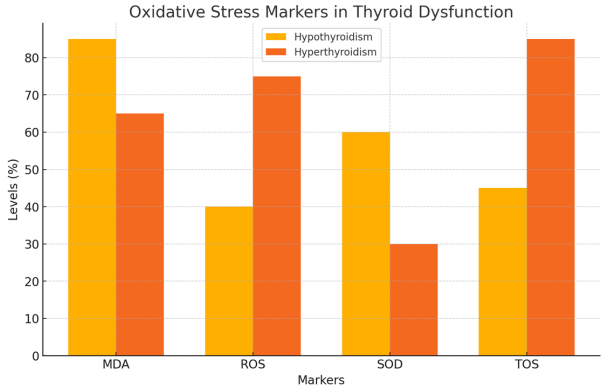

Figure 1: Oxidative Stress Markers in Hypothyroidism and Hyperthyroidism.

Table 2: Inflammatory Marker Levels Across Thyroid Disorders

Marker	Normal Range	Hypothyroidism	Hyperthyroidism	Autoimmune Thyroiditis
CRP	<5 mg/L	7–15 mg/L	10–20 mg/L	15–25 mg/L
IL-6	0–10 pg/mL	12–18 pg/mL	15–22 pg/mL	20–30 pg/mL
TNF-α	0–5 pg/mL	8–12 pg/mL	10–15 pg/mL	15–25 pg/mL

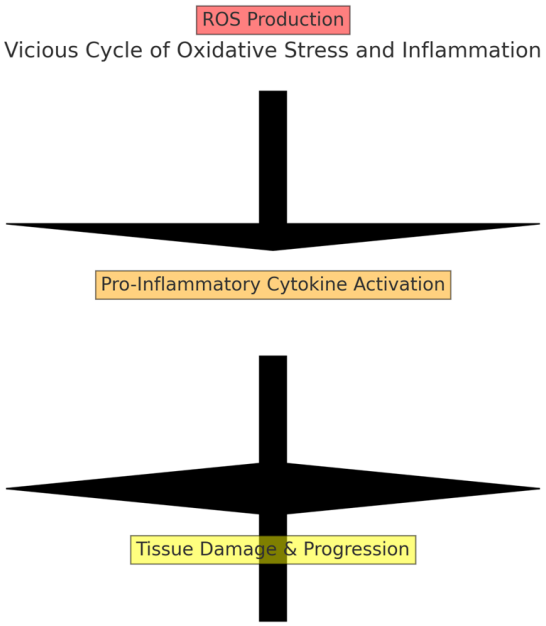

Figure 2: Vicious Cycle of Oxidative Stress and Inflammation.

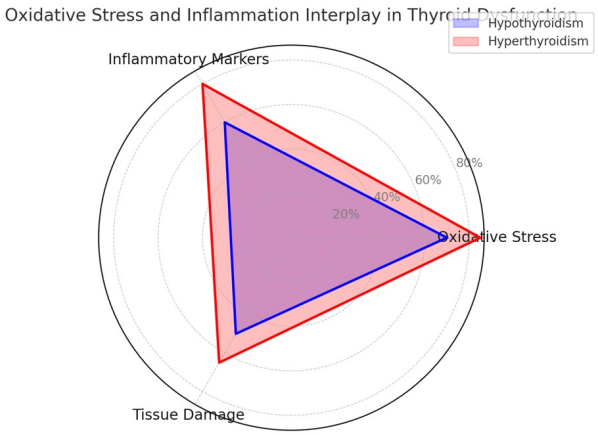

Figure 3: Radar Chart for Oxidative Stress and Inflammation